The Hydrogen Bond Studied by Nitrogen-14 Nuclear Magnetic Resonance. III.[1] A Study of Electron Redistribution Associated with Hydrogen Bonding and Metal-Complex Formation of Formamide and *N*-Methylacetamide

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Abstract: Hydrogen bonding and metal-complex formation of formamide and *N*-methylacetamide are studied by ^{14}N and proton magnetic resonance. Downfield movement of both ^{14}N and proton shifts and a linear correlation between them are observed. As an explanation of the downfield movement of the ^{14}N shift, we propose an electron redistribution model of $2p_z$ electrons at the nitrogen atom after hydrogen bonding and metal-complex formation. The cause of the downfield shift of the proton signal differs for interaction with a proton donor (metal ion) and a proton acceptor. For the former case, the shift is caused by a variation of the diamagnetic shielding effect due to polarization of the N–H bond. For the latter case the shift arises in part from the electric-field effect of the proton acceptor and in part from the diamagnetic shielding effect. The diamagnetic shielding effect of the proton hydrogen-bond shift is estimated as about 20%, in comparison with the gradients of the linear correlation between ^{14}N and proton shifts.

A number of studies of the hydrogen bond have been carried out by proton nmr spectroscopy. The downfield shift of the proton signal is usually employed as a probe of the hydrogen bond. The variation of proton shift is explained by several causes such as an electrostatic interaction, a charge-transfer effect,[2] and many kinds of contributions.[3] It is difficult to discriminate one effect from the other by the usual proton spectra. In the case of heteronuclear resonance, on the other hand, the sensitivity of the chemical shifts due to electron distribution is enhanced by the paramagnetic contribution, and the effect of electron redistribution caused by molecular interaction becomes dominant in the variation of chemical shifts. For this reason some workers[1,4–9] have been concerned with heteronuclear magnetic resonance studies on molecular interaction. The ^{13}C studies of carbonyl compounds,[4] isocyanide,[5] and chloroform,[6] ^{14}N studies of pyridine[7] and acetonitrile,[5] ^{17}O studies of water,[8] and a ^{15}N study of ammonia[9] have been published.

In the previous paper,[1] we observed the downfield ^{14}N shifts in pyrroles and indole by means of the heteronuclear double resonance method[10] in N–H···base hydrogen bonding. We proposed that the downfield shift was due to electron redistribution from the nitrogen atom toward another part of the molecule after transfer from a proton acceptor. It is the object of this paper to confirm the above proposal in the study of hydrogen bonding and complex formation between metal ions and amides, the isoelectronic compounds of pyrroles. The results obtained are consistent with the case of pyrroles. A correlation of ^{14}N and proton shifts with the variation in the diamagnetic shielding and the electric-field effect of the hydrogen bonding is discussed.

Experimental Section

Measurements of ^{14}N chemical shifts were performed by the heteronuclear magnetic double resonance method.[1] A Varian HA-100 spectrometer was used with a probe doubly tuned to accept the 7.22-MHz ^{14}N irradiation frequency as well as the 100-MHz proton frequency used for the observation of proton peaks for a monitor. An NMR Specialties HD-60 B heteronuclear spin decoupler equipped with a Hewlett-Packard 200ABR audiofrequency oscillator was used to drive 7.22-MHz modulated frequency. The irradiation frequency was monitored by a Takeda-Riken TR-3977 Rf frequency counter. DSS (internal standard) and TMS (internal and external standard) were used to lock the spectrometer. ^{14}N and proton chemical shifts are expressed in parts per million downfield from those of ammonium ion and tetramethylsilane, respectively. Commercial zinc chloride was used without any purification. Other chemicals were distilled after drying over the pertinent drying agent.

Results and Discussion

Self-Association of *N*-Methylacetamide (NMA) and Formamide (FA). Before a detailed study of molecular association of amides with solvent and metal ion, the self-association of NMA and FA was investigated. A plot of ^{14}N chemical shift *vs.* the concentration of NMA in dioxane solution is shown in Figure 1. Dilution with dioxane[11] breaks up the species of self-associations (Figure 2) and makes the ^{14}N signal shift upfield (6 ppm). A similar trend is obtained in a plot of N–H proton shifts. A good linear correlation, the gradient of which is given in Table I, is observed between ^{14}N

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(1) For part II, see H. Saitô and K. Nukada, *J. Amer. Chem. Soc.*, **93**, 1072 (1971).

(2) C. A. Coulson and U. Danielsson, *Ark. Fys.*, **8**, 235, 245 (1954).

(3) A. D. Buckingham, T. S. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, **32**, 1227 (1960).

(4) (a) G. E. Maciel and G. C. Ruben, *J. Amer. Chem. Soc.*, **85**, 3903 (1963); (b) G. E. Maciel and G. B. Savitsky, *J. Phys. Chem.*, **68**, 437 (1964); (c) G. E. Maciel, *J. Chem. Phys.*, **42**, 2746 (1965); (d) G. E. Maciel and J. H. Natterstad, *ibid.*, **42**, 2752 (1965); (e) G. E. Maciel and D. Trificante, *J. Amer. Chem. Soc.*, **88**, 220 (1966).

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(7) H. Saitô, K. Nukada, H. Kato, T. Yonezawa, and K. Fukui, *Tetrahedron Lett.*, 111 (1965).

(8) (a) A. E. Florin and M. Alei, Jr., *J. Chem. Phys.*, **47**, 4268 (1967); (b) M. Alei, Jr., and A. E. Florin, *J. Phys. Chem.*, **73**, 863 (1969); (c) J. Reuben, *J. Amer. Chem. Soc.*, **91**, 5725 (1969).

(9) W. M. Litchman, M. Alei, Jr., and A. E. Florin, *ibid.*, **91**, 6574 (1969).

(10) P. Hampson and A. Mathias, *Mol. Phys.*, **11**, 541 (1966).

(11) For an investigation of self-association, use of a nonpolar solvent is desirable. However, FA is insoluble in carbon tetrachloride or chloroform. Dioxane is employed since this is a relatively weak proton acceptor compared with the carbonyl group of amides, and this dissolves zinc chloride without strong complex formation.

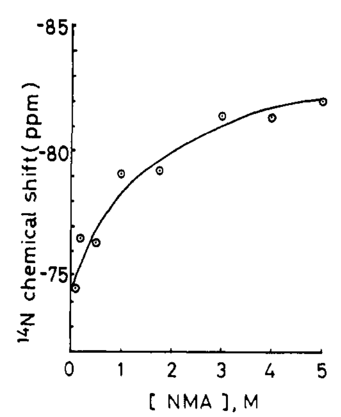

Figure 1. A plot of ^{14}N chemical shifts against the concentration of *N*-methylacetamide in dioxane solution.

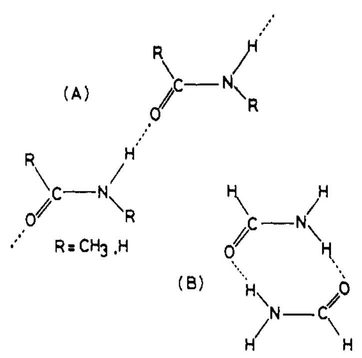

Figure 2. Self-associations of *N*-methylacetamide and formamide: (A) linear dimer (polymer), (B) closed dimer.

and proton shifts as shown in Figure 3. In the proton spectra of FA we can discriminate between two kinds of N-H protons, H_2 (cis) and H_3 (trans). The assignment of two peaks is staightforward with the inspection of spin coupling constants,[12] J_{12} = 13 Hz and J_{13} = 2.1 Hz.

Table I. The Gradients of the Linear Correlations between ^{14}N and Proton Shifts

	$\frac{\partial\delta^{14}N}{\partial\delta^{1}H}$	Ref
Self-association		
N-Methylacetamide	5.2	*a*
Formamide	5.6	*a*
Amide–metal-ion complex		
Formamide–$ZnCl_2$	11.6 (10.7)[b]	*a*
N-Methylacetamide–$ZnCl_2$	17.1	*a*
Pyrroles		
Pyrroles–proton acceptors	3.9	*c*

[a] This paper. [b] 0.2 *M* dioxane solution. [c] Reference 1.

Downfield shifts of both H_2 and H_3 peaks are shown with decreasing concentration of FA in dioxane (Figure 4). These are caused by two types of self-associations, *i.e.*, a closed dimer and an open dimer (polymer) as shown in Figure 2. H_2 and H_3 preferably participate in the closed and the open dimer (polymer), respectively. The ^{14}N shift of FA is similarly moved downfield (9 ppm) and a correlation of ^{14}N and proton shifts is given in Figure 5. The gradient of the line computed by the least-squares method is close to the value for NMA (Table I).

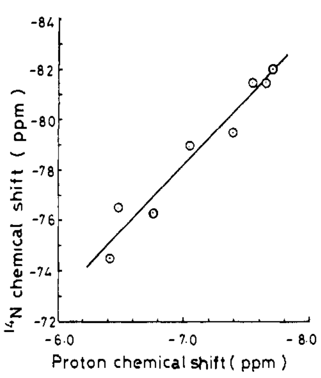

Figure 3. A correlation between ^{14}N and proton chemical shifts in the N-H group of *N*-methylacetamide (dioxane solution).

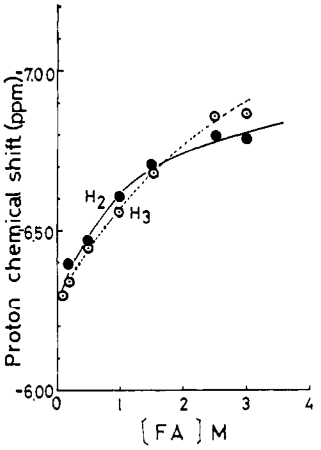

Figure 4. Variation of H_2 (cis) and H_3 (trans) proton shifts with the concentration of formamide in dioxane: H_2, ●; H_3, ⊙.

Sheraga and his coworkers[13] and Rao and his coworkers[14] computed the electronic structure of the above two kinds of dimers by the CNDO/2 method. According to their results the positive charge on H_3 and the negative charge on the nitrogen atom in the proton donor of the open dimer rise as the two molecules approach one another. On the other hand, there is little change on the nitrogen of the proton acceptor. In the case of the closed dimer, the H_2 proton becomes more positive and the nitrogen atom more negative as the distance between the N—H and C=O groups decreases toward the minimum-energy position. The increase of electron population on the nitrogen atom, which is in accord with our calculation of pyrrole proton acceptors,[1] leads to the upfield shift by employing the Karplus–Pople theory.[15] Thus the Karplus–Pople theory is insufficient to predict the ^{14}N hydrogen-bond shift of the proton donor. Downfield shifts of H_2 and H_3 in the open and closed dimer, respectively, are partially explained by the deshielding effect due to the decrease of electron population in addition to the well-recognized electric-field effect of the proton acceptors.

^{14}N and Proton Shifts of NMA and FA in Proton-Donating and -Accepting Solvents. ^{14}N and proton

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(12) L. H. Piette, J. D. Ray, and R. A. Ogg, *J. Mol. Spectrosc.*, **2**, 66 (1958).

(13) F. A. Momany, R. F. McGuire, J. F. Yan, and H. A. Scheraga, *J. Phys. Chem.*, **74**, 2424 (1970).

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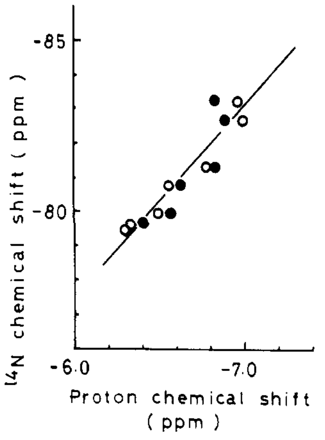

Figure 5. A correlation of ^{14}N and proton shifts in formamide (dioxane solution): H_2, ●; H_3, O.

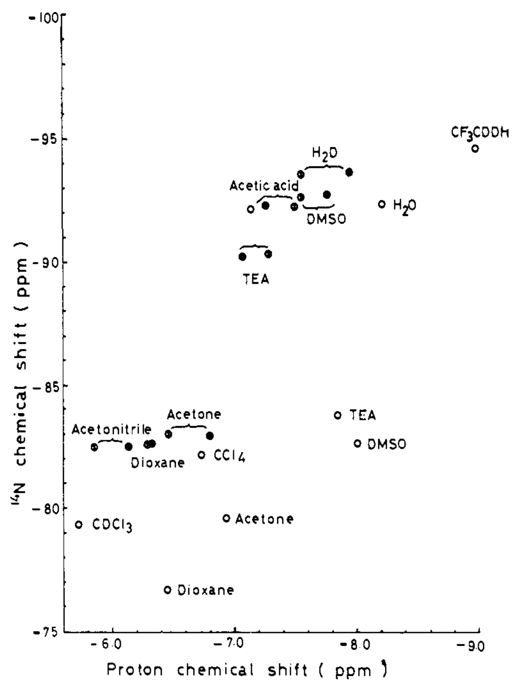

Figure 6. A plot of ^{14}N *vs.* proton shifts of formamide and *N*-methylacetamide in proton donors and acceptors: FA, H_2, ⦶; H_3, ●; NMA, O.

shifts are observed in 0.01 mol fraction solutions of proton-accepting (dioxane, acetone, acetonitrile, triethylamine (TEA), DMSO) and proton-donating solvents (trifluoroacetic acid, acetic acid, water), as illustrated in Figure 6. The correlation between ^{14}N and proton shifts is not so simple as shown in Figures 3 and 5. A proton-donating solvent forms hydrogen bonds exclusively with the carbonyl group of amides,[16] whereas a proton-accepting solvent associates with the N-H proton. Then variations of ^{14}N shift against proton shift may be quite different between two kinds of solvents. We will discuss this point in detail in a later section.

The amounts of downfield shifts of both ^{14}N and proton shifts are larger in proton donors than in proton acceptors. Hydrogen bonding or protonation by proton-donating solvents toward the carbonyl group increases the contribution of resonance structure II. This

I II

R = CH$_3$, H

is confirmed by the increased potential barrier of the internal rotation around the C-N bond axis.[16] The downfield ^{14}N shift is explained by the decreased $2p_z$ electron population at the nitrogen atom according to the increased contribution of resonance structure II.[17] The $2p_z$ electron migration into the carbonyl group polarizes the σ electrons in the N-H bond and induces the downfield shift of N-H proton signal. It should be noted that such a downfield shift in this case is not due to the electric-field effect, which is predominant in proton-accepting solvents.

The ^{14}N shifts in weak proton-accepting solvents are not free from self-association among the solute molecules.[18] In strong proton-accepting solvents such as DMSO or TEA, however, both ^{14}N and proton shifts lie at lowest field among proton-accepting solvents employed (Figure 6). These observations are consistent with the variations of ^{14}N and N-H proton shifts of pyrroles which are caused by hydrogen bonding with proton acceptors.[1] As a cause of proton hydrogen-bond shift of proton donors, the variation of the diamagnetic shielding effect, caused by polarization of the N-H bond owing to charge transfer, should be considered in addition to the electric-field effect generally recognized. The former contribution is evaluated by CNDO/2 calculation in the case of pyrrole-proton acceptor.[1] An alternative evaluation will be proposed at the end of this paper. The ^{14}N downfield shift of amides in proton acceptors is explained by electron redistribution. The electrons transfer from the proton acceptor to the N-H bond and push the $2p_z$ electrons at the nitrogen atom toward the carbonyl group. This process is equivalent to the increase of resonance structure II in the proton-donating solvent.

$ZnCl_2$-Amide Complexes. The same type of electron redistribution as described above is found in complex formation between metal ions and amides. The ^{14}N shift of FA is plotted against the concentration of zinc chloride (Figure 7). The correlation of ^{14}N and proton shifts is illustrated in Figure 8. In both 0.1 and 0.2 *M* solutions in dioxane, a single N-H peak is observed as the consequence of the overlap of H_2 and H_3 signals. No further splitting of H_2 and H_3 peaks is observed with an addition of zinc chloride. Figures 7 and 8 show that the addition of zinc chloride displaces both ^{14}N and proton shifts downfield. The curves in Figure 7 are analyzed by the procedure proposed by Wang and Li.[19] When complex formation between zinc chloride (M)

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(16) (a) G. Fraenkel and G. Francoi, *J. Amer. Chem. Soc.*, **82**, 4478 (1960); (b) G. Fraenkel and C. Nieman, *Proc. Nat. Acad. Sci., U. S.*, **44**, 688 (1958).

(17) H. Kamei, *Bull. Chem. Soc. Jap.*, **41**, 1030 (1968). The CNDO/2 calculation by Rao, *et al.*,[14] shows that the negative charge on the nitrogen atom decreases markedly (~50%) in protonated NMA.

(18) A ^{15}N double-resonance study of NMA-^{15}N appeared after we completed this manuscript: L. Paolillo and E. D. Becker, *J. Magn. Resonance*, **2**, 168 (1970). The difference between the ^{15}N shifts in CCl_4 and DMSO solutions are in good agreement with our ^{14}N results. These results show that the self-association of the NMA is dominant in CCl_4 solution.

(19) S. M. Wang and N. C. Li, *J. Amer. Chem. Soc.*, **88**, 4592 (1966).

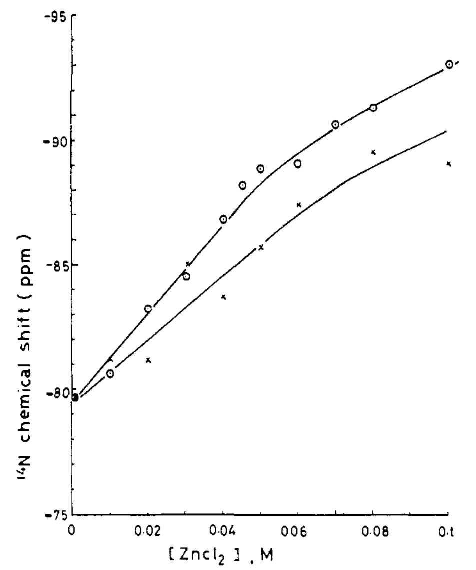

Figure 7. $ZnCl_2$ concentration dependence of ^{14}N chemical shifts of formamide in 0.1 *M* (⊙) and 0.2 *M* (×) dioxane solutions.

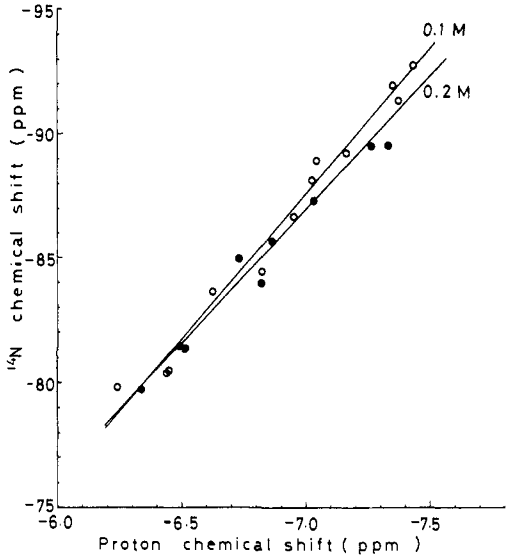

Figure 8. A correlation of ^{14}N and proton chemical shifts in the $ZnCl_2$-formamide complex in 0.1 *M* (O) and 0.2 *M* (Δ) dioxane solutions.

and the amide (B) is expressed as

$$M + nB \longrightarrow MB_n \tag{1}$$

the equilibrium constant *K* is shown as follows

$$K = \frac{MB_n}{(M_0 - MB_n)(B_0 - n(MB_n))^n} \tag{2}$$

where M_0, B_0, MB_n, and n denote the original concentrations of the metal ion, the amides, and the complex and the coordination number, respectively. ^{14}N and proton chemical shifts are expressed by

$$\delta = \delta_f + \frac{n(MB_n)}{B_0}(\delta_c - \delta_f) \tag{3}$$

where δ_c and δ_f are chemical shifts of the complex and free molecule, respectively. If experiments are performed under conditions such that $B_0 \gg M_0$, then $B_0 \gg MB_n$. Equation 2 is approximated as

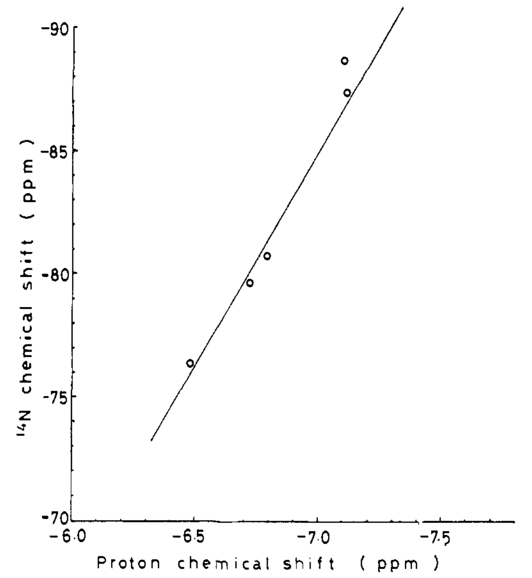

Figure 9. A correlation of ^{14}N and proton chemical shifts in $ZnCl_2$-*N*-methylacetamide complex in 0.2 *M* dioxane solution.

$$K = \frac{MB_n}{(M_0 - MB_n)B_0^{\,n}} \tag{4}$$

and eq 3 is reduced to

$$\delta = \delta_f + \frac{nB_0^{\,n-1}K(\delta_c - \delta_f)M_0}{1 + B_0^{\,n}K} \tag{5}$$

Equation 5 shows that a plot of δ *vs.* M_0 is linear. By a trial-and-error method, $\delta_c - \delta_f = -13.2$ ppm and $K = 4 \times 10^7\ l.^4\ mol^{-4}$ in the case of $n = 4$[20] are calculated to fit the initial straight line shown in Figure 7.[21]

A similar study of the complex between NMA and zinc chloride was carried out. The study was limited to a 0.2 *M* dioxane solution because of the obstacle in the S/N ratio for the double irradiation. The value $|\delta_c - \delta_f|$ is estimated as larger than 14 ppm. A linear correlation between ^{14}N and proton shifts is shown in Figure 9.

The variations in ^{14}N and proton shifts of metal-complex formation are quite similar to those of protonation or hydrogen bonding toward the carbonyl group of amides. The cause of the downfield movement of ^{14}N and proton shifts in complex formation seems to be polarization of the N-H bond by the migration of $2p_z$ electrons of the nitrogen atom into the carbonyl group.

Gradients between ^{14}N and Proton Shifts. An Evaluation of the Diamagnetic Term in Proton Hydrogen-Bond Shifts. The variations of ^{14}N shifts due to an interaction with proton donor, metal ion, and proton acceptor are accounted for by electron redistribution from

[20] The maximum coordination number of Zn(II) ion toward amides is found to be six: (a) A. McKay and J. Poziomek, *Inorg. Chem.*, 7, 1454 (1968); (b) R. S. Drago, D. W. Meek, M. D. Joesten, and L. LaRoche, *ibid.*, 2, 124 (1963). The complex in solution should contain fewer moles of amides than the maximum coordination number of the metal, depending on the concentration, solvents, and anions. In Figure 7, the linearity of the plot holds below 0.04 *M* zinc chloride. In analogy with the results of Wang and Li[19] we performed the analysis with coordination number four.

[21] This equilibrium constant is larger than that for the imidazole-$ZnCl_2$ complex[19] ($K = 1.4 \times 10^6$) in DMSO solution. We also studied the FA-$ZnCl_2$ complex in DMSO solution, but no variation of ^{14}N and proton shifts is observed, indicating that the equilibrium between $ZnCl_2$ and the solvent is exclusively attained.

the nitrogen to the carbonyl group (Figure 10c). Such an electron redistribution is induced by charge transfer at the carbonyl group (Figure 10a) or at the N-H group (Figure 10b). The arrows in Figure 10 indicate the direction of the migration of electrons. The amount of the ^{14}N downfield shift seems mainly to depend on the extent of 2p$_z$ electron migration toward the carbonyl group by hydrogen bonding with the proton donor (Figure 10a) or proton acceptor (Figure 10b). The variation of proton shift, however, differs in two types of interactions (Figure 10a and b). For the interaction in Figure 10a, the variation of proton shift $\Delta\delta^{1}$H is expressed by a change of the diamagnetic shielding on the proton[22] as follows

$$\Delta\delta^{1}\mathrm{H} = \Delta\sigma_{\mathrm{dia}} = 17.8Z\Delta q_{\mathrm{H}} \qquad (6)$$

In eq 6, Δq_{H} (<0) is the variation of electron density at the N-H proton after the charge transfer (Figure 10a), and Z is usually taken as 1.2. In the interaction shown in Figure 10b, the electric-field effect,[23] σ_{E}, caused by access of the proton acceptor, becomes important in addition to the diamagnetic shielding effect. The hydrogen-bond shift is expressed as follows

$$\Delta\delta^{1}\mathrm{H} = \Delta\sigma_{\mathrm{dia}} + \sigma_{\mathrm{E}} \qquad (7)$$

$$\sigma_{\mathrm{E}} = -2 \times 10^{-12}E_z - 10^{-18}E^2 \qquad (8)$$

The linear correlation between ^{14}N and proton shifts is established for FA and NMA as well as pyrroles.[1] The gradients $\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H}$ are summarized in Table I. If we assume that electron redistribution occurs through σ–π interaction at the nitrogen atom, we obtain the following relation

$$\Delta\delta^{14}\mathrm{N} = f\Delta\sigma_{\mathrm{dia}} \qquad (9)$$

where f is a proportionality constant. For the interaction of Figure 10a

$$(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{a}} = \Delta\delta^{14}\mathrm{N}/\Delta\delta^{1}\mathrm{H} = f \qquad (10)$$

For the interaction of Figure 10b

$$\left(\frac{\partial\delta^{14}\mathrm{N}}{\partial\delta^{1}\mathrm{H}}\right)_{\mathrm{b}} = \frac{\Delta\delta^{14}\mathrm{N}}{\Delta\delta^{1}\mathrm{H}} = f\frac{\Delta\sigma_{\mathrm{dia}}}{\Delta\sigma_{\mathrm{dia}} + \sigma_{\mathrm{E}}} \qquad (11)$$

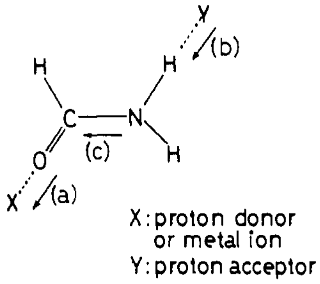

Figure 10. A schematic representation of the charge-transfer process (a and b) and the electron redistribution (c) according to these interactions. The arrows indicate the migration of electrons associated with these processes.

It is well recognized through a comparison of eq 5, 10, and 11 that the gradient of the metal complex is larger than those of the self-association of amides, in good agreement with Table I.

The contribution of the diamagnetic shielding effect in the hydrogen-bond shift is obtained as follows

$$\frac{(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{b}}}{(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{a}}} = \frac{\Delta\sigma_{\mathrm{dia}}}{\Delta\sigma_{\mathrm{dia}} + \sigma_{\mathrm{E}}} \qquad (12)$$

In the case of the self-association of amides, eq 12 is inadequate, since there is a contribution of the interaction of Figure 10a in the hydrogen bond at the carbonyl group in addition to the interaction of Figure 10b. If we assume that two types of interactions are superposed in this case, the following equations are obtained

$$(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{s}} = f\frac{2\Delta\sigma_{\mathrm{dia}}}{2\Delta\sigma_{\mathrm{dia}} + \sigma_{\mathrm{E}}} \qquad (13)$$

$$\frac{(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{s}}}{(\partial\delta^{14}\mathrm{N}/\partial\delta^{1}\mathrm{H})_{\mathrm{a}}} = \frac{2\Delta\sigma_{\mathrm{dia}}}{2\Delta\sigma_{\mathrm{dia}} + \sigma_{\mathrm{E}}} \qquad (14)$$

Employing the f value of the amide–metal complex system (17.1 for NMA and 11.6 for FA; Table I) the diamagnetic contributions, $\Delta\sigma_{\mathrm{dia}}$, in the hydrogen-bond systems (self-association) are found to be 17 and 24% for NMA and FA, respectively. These values are in good agreement with a direct calculation by eq 6 for the hydrogen bonds of pyrrole–proton acceptor systems (16%). A similar estimation of the diamagnetic term by eq 12 is applied for chloroform, in which the self-association effect is disregarded, by employing the relation between ^{13}C and proton hydrogen-bond shifts. The detailed results will be published elsewhere.

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(22) J. A. Pople, *Proc. Roy. Soc., Ser. A*, **239**, 549, 557 (1954).
(23) A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).