BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 2877 (1971)

# Basicities of Formamide, Acetamide, and Their Alkyl Derivatives in Aqueous Solution

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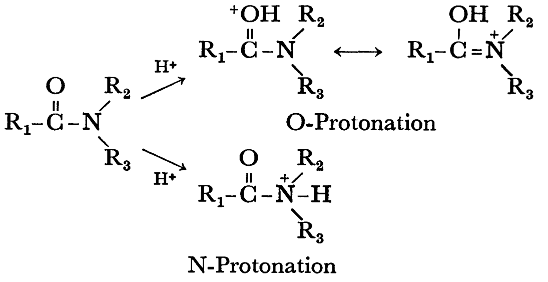
(Received May 10, 1971)

The basicity constants p$K_a$ of formamide, acetamide and their alkyl derivatives, generally represented by $R_1CONR_2R_3$ where $R_1$, $R_2$, and $R_3$ stand for H, $CH_3$, $C_2H_5$, $CH_2Cl$, or $CHCl_2$ respectively, were measured in aqueous solution spectrophotometrically,[1] using *o*-nitroaniline as indicator. Measurements were carried out at 25°C for wavelengths of 380, 410, and 440 nm, and ionic strength of $\mu$=0.55M. The acid dissociation constant of *o*-nitroaniline, $K_{In}=[H^+][In]/[HIn^+]$, was taken to be 1.27M.[1]

The results of the determination of p$K_a$ related to various amides are listed in Table 1, together with the values of their donor numbers $DN(SbCl_5)$[2] and dielectric constants $D$. The thermodynamical constants p$K_a{}^0$ can be approximately estimated by the following equation.

$$pK_a{}^0 = pK_a - 0.5\sqrt{\mu}$$

According to recent NMR studies,[3] the protonation of most amides was found to occur predominantly at O-atom and not at N-atom, as revealed by the fact that the double bond character between C and N atoms and the barrier to rotation around the C–N bond increase with the protonation of amides.[4] The nature of amides is thus acidic and far less basic than ammonia and alkylamines.



Alkylamines usually exhibit p$K_a$ values 9—11, in remarkable contrast to $-0.1\pm0.2$ as the mean value of p$K_a{}^0$ of the nine amides in Table 1. The values of p$K_a{}^0$ of some amides given in Table 1 were separately measured by potentiometric titration with perchloric acid in acetic scid with chloranil electrode and coincide well with our results within the mean discrepancy $\pm0.4$[5]

Although the p$K_a$ does not seriously vary with the substitution of H by alkyl radicals in both formamide and acetamide, there is a slight tendency for p$K_a$ to grow higher as $R_2$ or $R_3$ changes in the direction H→$CH_3$→$C_2H_5$. The effect of chlorine atom in $R_1$ in acetamide upon p$K_a$ is distinct, making the compound less basic. No close relationship of p$K_a$ with the donor numbers and the dielectric constants is noticed, as far as our data are concerned.

TABLE 1. BASICITY CONSTANTS, DONOR NUMBERS AND DIELECTRIC CONSTANTS OF VARIOUS AMIDES

| Compound | $R_1$ | $R_2$ | $R_3$ | p$K_a$ | p$K_a{}^0$ | $DN$ ($SbCl_5$) | $D$ |
|---|---|---|---|---|---|---|---|
| Formamide | H | H | H | 0.12 | −0.25 | | 109 |
| *N*-Methylformamide | H | H | $CH_3$ | 0.52 | 0.15 | | 177 |
| *N*,*N*-Dimethylformamide | H | $CH_3$ | $CH_3$ | 0.18 | −0.19 | 26.6 | 36.1 |
| *N*,*N*-Diethylformamide | H | $C_2H_5$ | $C_2H_5$ | 0.36 | −0.01 | 30.9 | |
| Acetamide | $CH_3$ | H | H | −0.025 | −0.40 | | |
| *N*-Methylacetamide | $CH_3$ | H | $CH_3$ | 0.26 | −0.11 | | 179 |
| *N*,*N*-Dimethylacetamide | $CH_3$ | $CH_3$ | $CH_3$ | 0.62 | 0.25 | 27.8 | 38.9 |
| Chloroacetamide | $CH_2Cl$ | H | H | −0.26 | −0.63 | | |
| Dichloroacetamide | $CHCl_2$ | H | H | −0.26 | −0.63 | | |

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[3] A. Berger, A. Loewenstein, and S. Meiboom, *J. Amer. Chem. Soc.*, **81**, 62 (1959); G. Fraenkel and C. Franconi, *ibid.*, **82**, 4478 (1960); R. J. Gillespie and T. Birchall, *Can. J. Chem.*, **41**, 148 (1963); W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970); B. G. Cox, *J. Chem. Soc.*, B, **1970**, 1780.

[4] In the cases of urea and its alkyl derivatives, the protonation probably occurs at both O and N atoms. G. A. Olah and M. Calin, *J. Amer. Chem. Soc.*, **90**, 401 (1968).

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