Solvation of Ions. IX.[1] The Effect of Anion Solvation on Acid Dissociation Constants in Methanol, Water, Dimethylformamide, and Dimethyl Sulfoxide

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Abstract: Acid dissociation constants of a variety of acids in methanol, dimethylformamide, and dimethyl sulfoxide have been measured by the indicator method. The acid-base equilibrium $HA + B^- \rightleftharpoons HB + A^-$ is strongly influenced by transfer from dimethylformamide to methanol if A^- and B^- have different hydrogen bond acceptor properties. Rates of S_N2 reactions in methanol and in dimethylformamide have been used to estimate hydrogen-bonding activity coefficients which predict closely the effects of anion solvation on acid–base equilibria.

The acid–base equilibrium (eq 1) is not independent of solvent. To take an extreme example from the

$$HA + B^- \rightleftharpoons HB + A^- \qquad (1)$$

literature cited in Table II of this paper, picric acid is 3.5 pK units more acidic than benzoic acid in water, 5.3 units more acidic in methanol, and 11.9 pK units more acidic than benzoic acid in dimethyl sulfoxide. The greatest scatter occurs when acidities in a protic solvent (*e.g.*, water) are compared with acidities in a dipolar aprotic solvent (*e.g.*, dimethyl sulfoxide[3]). In particular, the acidities of phenols *vs.* carboxylic acids change significantly on transfer from protic to dipolar aprotic solvent.[3–5]

Grunwald and Price[6] have considered in some detail the changes in the equilibrium constant of eq 1 on transfer from water to methanol. They make the valuable suggestion that the chemical potential of those anions which are delocalized oscillators (*e.g.*, picrate, 2,4-dinitrophenoxide) is lowered, relative to localized oscillators (*e.g.*, acetate, benzoate), on transfer from water to methanol. Thus the equilibrium constant for eq 1, A^- = picrate, B^- = acetate or benzoate, is greater in methanol than in water, because dispersion forces are stronger in methanol and because picrate ion has stronger dispersion interactions than has acetate ion.

Although their sophisticated treatment may supply part of the answer, anion solvation does not account entirely for the increase in the equilibrium constant for eq 1, A^- = picrate, B^- = benzoate, on transfer from water to methanol. Kolthoff, Lingane, and Larson[7,8] derived distribution coefficients, from solubilities of HA and HB and of the silver salts AgA and AgB, which account satisfactorily for the changes in the position of equilibrium, on transfer from water to methanol. One of the reasons why equilibrium 1, A^- = picrate, B^- = benzoate, shifts to the right on transfer from water to methanol is that benzoic acid is less soluble, *i.e.*, is very much less solvated, in water than in methanol, whereas the difference in the solvation energy of undissociated picric acid in water and methanol is considerably smaller.[9]

Solvation of all the various species involved in eq 1, not only anions, must be considered in evaluating solvent effects on acid–base equilibria. Although solvation energies of ions are much greater than those of dipoles, *differences* in solvation of dipoles, on transfer from one solvent to another, may be as large as the differences for ions. Considering acid strengths rather than equilibria (eq 1), we see that a number of phenols and carboxylic acids are from 200 to 300 times more soluble in methanol than in water[9] (picric acid is only 30–40 times more soluble) whereas their conjugate bases are more solvated by water.[10] Thus, apart from considerations of the basicity toward a proton of methanol *vs.* water, acids tend to be weaker in methanol than in water because of solvation of HA and A^-.[11]

In this paper we consider changes in the equilibrium constant of eq 1 on transfer from methanol to dimethylformamide at 18–22°. We have not used water as a typical protic solvent, because it is becoming increasingly obvious that solvent water exerts a profound and rather unique influence on the chemical potential of anions and of dipolar "organic" molecules. Methanol and dimethylformamide are a better choice than water and dimethylformamide for comparison of protic *vs.* dipolar aprotic effects. They have very similar bulk dielectric constants, so that a variety of nonspecific interactions, of the type considered by Born,[12] may be comparable in both solvents. Effects due to dispersion forces will be less significant between methanol and dimethylformamide than between water and dimethylformamide,[6] but dispersion forces should be greatest in dimethylformamide. Acids AH and BH are generally slightly soluble in water, soluble in methanol, and very soluble in dimethylformamide.

One solute–solvent interaction which is not comparable in methanol and dimethylformamide is hy-

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[1] Part VIII: D. Cook, I. P. Evans, E. C. F. Ko, and A. J. Parker, *J. Chem. Soc.*, in press.

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[8] I. M. Kolthoff and S. Bruckenstein, "Treatise on Analytical Chemistry," Part I, Vol. 1, I. M. Kolthoff and P. J. Elving, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, Chapter 13.

[9] A. Seidell, "Solubilities of Inorganic and Organic Compounds," Vol. 1-3, D. Van Nostrand Co., Inc., New York, N. Y., 1940.

[10] H. M. Koepp, H. Wendt, and H. Strehlow, *Z. Elektrochem.*, 64, 483 (1960).

[11] R. G. Bates, "Determination of pH," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapter 7.

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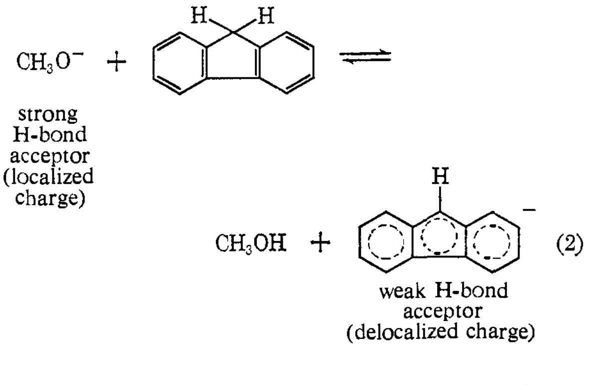
drogen-bond donation by the solvent.[13] In this series of papers, we have been concerned with the extent to which hydrogen-bonding solvation of anions, by protic solvents, accounts for the large changes in the chemistry of anions, on transfer from dipolar aprotic to protic solvents. In this paper we investigate quantitatively an observation which we had already made qualitatively,[13] that acid–base equilibria (eq 1), are very susceptible to transfer from dipolar aprotic to protic solvent, presumably because of hydrogen-bonding interactions between anions and protic solvents.

There is a tendency to correlate properties such as half-neutralization potentials,[5] substituent effects, nucleophilicity, catalytic activity, and basicity toward other atoms with the enormous amount of precise data on acid–base equilibria in water. Leffler and Grunwald cite many examples.[14] It needs to be stated once more that acid-base equilibria in water may behave very differently on transfer to other solvents, so that chemistry in nonaqueous solvents cannot logically be correlated with pK_a in water. Attempts have been made to set up acidity scales for acids ranging in pK_a from 1 to 50.[11,15] Water is commonly used for acids of pK_a up to 14, and dimethyl sulfoxide is popular for acids in the range pK_a 12–30. In view of the following discussion, linking of a scale in water or alcohols to one in dimethyl sulfoxide or related dipolar aprotics is likely to involve serious errors, if one of the anions involved in the linkage is small, with localized charge (*e.g.*, methoxide, cyanide, *t*-butoxide), and the other is large, with delocalized charge (*e.g.*, Ph_3C^-, indene⁻, fluorene⁻). For example, equilibrium 2 lies to the left in methanol, to the right in dimethyl sulfoxide.[15] An explanation can be found in terms of hydrogen-bonding solvation of anions by methanol, but not by dimethyl sulfoxide. If the indicator is an anilinium ion, its conjugate base is an extremely weak H-bond acceptor, so that equilibria lie much further in a direction favoring production of ions, in protic relative to dipolar aprotic solvents. Such a situation was considered by Stewart, *et al.*,[16] who observed an increase in H^- of sodium methoxide from 12.2 in methanol to 19.4 in 95% dimethyl sulfoxide–methanol. Zaugg and Schaefer[17] use reasoning similar to ours to explain the reversal of the acidity sequence 4-nitrophenol > 3-phenyl-2-benzofuranone on transfer from water to dimethylformamide.



(2)

Given only the pK_a of 7.07 for 2,6-dimethyl-4-nitrophenol in water and 7.15 for 4-nitrophenol in water (Table II), the average organic chemist might conclude that the *o*-methyl groups were exerting a small acid-strengthening steric effect, balanced by a small acid-weakening electron-donating effect, relative to the *ortho* hydrogens of 4-nitrophenol. "Explanations" of this type ignore the solvent. We wonder what explanation would have evolved, had dimethyl sulfoxide occupied the position held by water as the solvent of choice for nearly all physical measurements. Table II shows that in dimethyl sulfoxide, the pK_a of 4-nitrophenol is 9.9, that of 2,6-dimethyl-4-nitrophenol is 9.0. We are certain that even larger discrepancies in the allegedly solvent independent "electronic and steric behavior of substituents" will be encountered on transfer from water to dipolar aprotic solvents.

Experimental Section

Solvents. DMSO and DMF were dried over molecular sieves and twice distilled under nitrogen at a pressure of a few millimeters through a 20-in. column packed with glass helices. The second distillation of DMSO was from sodium hydride. The solvents were stored over molecular sieves in the dark. Methanol was fractionally distilled from sulfuric acid, then from magnesium methylate.

Using a spectrophotometric method to detect the 4-nitrophenoxide ion, our DMF was shown to have up to 1×10^{-5} *M* basic impurities capable of removing a proton from 4-nitrophenol.[17] DMSO did not contain strongly basic impurities at $>1 \times 10^{-6}$ *M* nor did it protonate the 4-nitrophenoxide ion at 1×10^{-4} *M*.

Acid and Base Solutions. Sodium or lithium salts of the acids were prepared from the acid and sodium or lithium hydroxide and were purified by recrystallization, then dried, as described in an earlier paper.[1] Brom cresol green and brom thymol blue were commercial products and were used as obtained. The organic acids were purified by distillation or recrystallization. Hydrogen chloride and hydrogen sulfide gas were dried and bubbled into the solvent. Solutions were analyzed for acid and for chloride or sulfide content.[18] Hydrazoic acid was made *in situ* by mixing a solution of sodium azide, standardized *vs.* silver nitrate, with a standard solution of perchloric acid in dimethylformamide or methanol. The perchloric acid solutions were made with a few drops of 60% perchloric acid in 100 ml of solvent. The small quantity of water thus introduced does not influence significantly the chemical potential of species dissolved in DMF.[19]

Solutions of hydrogen sulfide, thiophenol, 4-nitrothiophenol, and their sodium salts were made up under nitrogen, in solvents flushed with nitrogen to prevent oxidation. All measurements were made without delay. Stock solutions were diluted by weight and no solutions were kept for more than 4 hr.

Spectrophotometric Measurements. These were made on a Hitachi-Perkin-Elmer ultraviolet spectrophotometer. All measurements were at ambient temperature in stoppered 1-mm or 1-cm cells, under nitrogen in the case of sulfur compounds. Spectra were determined for the acid and base forms of colored indicators wherever practicable.[20]

Results

Equilibrium constants, *K*, for (1), expressed as concentration quotients, are given in Table I. Ionic strength corrections have not been made.[3] Dilute solutions, 2×10^{-4} to 1×10^{-2} *M* in methanol and 2×10^{-4} to 5×10^{-3} *M* in dimethylformamide or dimethyl sulfoxide, were used in an effort to avoid ion-pairing

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(13) A. J. Parker, *Quart. Rev.* (London), 163 (1962).

(14) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963.

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Table I. Equilibrium Constants ($K = ([A^-][BH]/[AH][B^-])$ as Concentration Quotients for Reaction 1 at 20–22° [a]

AH	Buffer (BH·NaB)	K (MeOH)	K (DMF)	K (DMSO)
2,4-Dinitrophenol	...	...	7.1×10^{-7} [b]	5.7×10^{-6} [b]
2,4-Dinitrophenol	Dichloroacetic	0.032	20	...
2,4-Dinitrophenol	Chloroacetic	0.72	...	...
2,4-Dinitrophenol	Hydrochloric	...	0.0042	...
4-Nitrophenol	Thiophenol	0.4	1.3	...
4-Nitrophenol	Benzoic	0.011	0.20	1.13
4-Nitrophenol	Acetic	0.015	1.5[c]	...
4-Nitrophenol	Hydrazoic	0.0063	...	...
4-Nitrophenol	Chloroacetic	...	0.013	...
Brom cresol green	2,4-Dinitrophenol	0.017	0.0037	...
Brom cresol green	Thiophenol	0.07	...	...
Brom cresol green	Acetic	0.40	...	...
Brom cresol green	Dichloroacetic	...	0.12	...
Brom cresol green	Chloroacetic	...	4.7	...
Brom cresol green	Hydrazoic	...	1.6	...
Brom thymol blue	4-Nitrophenol	...	...	0.50
Brom thymol blue	Benzoic	...	...	0.88
4-Nitrothiophenol	...	...	...	4.0×10^{-6} [b]
4-Nitrothiophenol	2,4-Dinitrophenol	...	0.60	0.47
4-Nitrothiophenol	Benzoic	0.22	...	...
Hydrazoic acid–NaN_3	4-Nitrophenol	200	240	...
Hydrogen sulfide	4-Nitrophenol	0.20	2.5	...
Thiophenol	Acetic	...	5.4[c]	...
2,6-Dimethyl-4-nitrophenol	Benzoic	...	...	10

[a] Buffers at 2×10^{-4} to 1×10^{-2} M in methanol and 2×10^{-4} to 5×10^{-3} M in dimethylformamide and dimethyl sulfoxide. Colored indicators at 2×10^{-5} to 1×10^{-3} M. [b] Value is the dissociation constant measured in pure solvent and in solvent containing small amounts of sulfuric acid. [c] Lithium salt.

effects, homoconjugation (AHA^-), and heteroconjugation (AHB^-). These effects were encountered by Kolthoff, Bruckenstein, and Chantooni for acid–base systems in acetonitrile.[21,22] DMSO and DMF are much more basic and are stronger H-bond acceptors than acetonitrile,[3,13,19] so that the undissociated acids HA and HB are more solvated[23,24] and have less tendency to hydrogen bond with anions. Following Kolthoff and Reddy,[3] who made measurements in DMSO, we had no difficulty in obtaining equilibrium constants, reproducible to within 0.2 log unit, over our range of buffers and indicators. At least eight buffer ratios, with duplicate sets of measurements from different stock solutions, were used to estimate K by the conventional indicator method [20] using spectrophotometric measurements in the visible or near-ultraviolet region at ambient temperature.

Acid dissociation constants for water, methanol, dimethylformamide, and dimethyl sulfoxide are given as pK_a in Table II. Somewhat incorrectly, but in line with convention,[11] the concentration of each solvent [S] in the expression $K_a = ([A^-][SH^+]/[S][HA])$ is taken as unity. This error does not influence our treatment of the results. Values of pK_a were calculated from the equilibrium constants in Table I, using 2,4-dinitrophenol as the primary standard, whose pK_a was measured directly in dilute solutions of sulfuric acid. The pK_a of 2,4-dinitrophenol was 6.0 in DMF, 5.2 in DMSO, and 7.9 in methanol. Literature values of 9.8 for brom cresol green in methanol,[8] 3.4 for hydrochloric acid in DMF,[25] and 10.0 for benzoic acid in DMSO[3] provided checks on the series.

Table II. pK_a of Acids at 20–25° [a]

No.	Acid	pK_a (H_2O)	pK_a (MeOH)	pK_a (DMF)	pK_a (DMSO)
1	Picric	0.71[b]	3.8[c]	1.2[o]	−1.9[d]
2	2,4-Dinitrophenol	4.10[c]	7.9[c]	6.0[g]	5.2[g]
3	4-Nitrophenol	7.15[b]	11.2[g]	10.9[g]	9.9[g]
4	Phenol	9.98[b]	14.2[h]	>15[p]	...
5	4-Nitrothiophenol	...	8.4[g]	6.3[g]	5.6[g]
6	Thiophenol	6.5[b]	10.9[g,i]	10.7[g]	...
7	Dichloroacetic	1.29[b]	6.4[g]	7.2[g]	...
8	Chloroacetic	2.86[b]	7.7[g]	9.0[g]	...
9	Acetic	4.76[b]	9.6[g,j]	11.1[g]	11.4[d]
10	Benzoic	4.20[b]	9.1[g,k]	10.2[g]	10.0[d,g]
11	Brom cresol green	4.9[d]	9.8[g,l]	8.3[g]	7.4[d,g]
12	Brom thymol blue	7.3[d]	12.4[l]	...	10.2[d,g]
13	Hydrazoic	4.74[e]	8.9[g]	8.5[g]	...
14	Hydrogen sulfide	7.0[b]	11.9[g]	10.5[g]	...
15	Hydrochloric	−6.3[b]	1.23[m]	3.4[g,m]	...
16	Hydrobromic	−9[b]	1[n]	1.8[m]	...
17	Bisulfate	1.92[d]	...	...	9.1[d]
18	2,6-Dimethyl-4-nitrophenol	7.07[f]	...	...	9.0[g]

[a] Solvents [S] are assumed to be at unit concentration in the expression for pK_a, which is derived from the concentration quotient $K_a = ([A^-][SH^+]/[S][HA])$. [b] See ref 20. [c] See ref 6. [d] See ref 3. [e] F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1962. [f] G. J. Leary, Ph.D. Thesis, University of Canterbury, New Zealand, 1964. [g] This work. [h] B. D. England and D. A. House, *J. Chem. Soc.*, 4421 (1962). [i] R. F. Hudson and G. Klopman, *ibid.*, 1062 (1962), report 8.65. [j] Ref 6 reports 9.7. [k] In agreement with L. D. Goodhue and R. M. Hixon, *J. Am. Chem. Soc.*, **56**, 1329 (1934), but ref 7 reports 9.3. [l] See ref 8. [m] See ref 25. [n] Ref 25 states that pK_a of halogen acids in methanol differs by no more than 100%. Hence this estimate. [o] P. G. Sears, R. K. Wolford, and L. R. Dawson, *J. Electrochem. Soc.*, **103**, 633 (1956). [p] Estimated value from the observation that $10^{-2}M$ LiOAc in DMF generated $<10^{-5}$ M phenoxide ion from 10^{-3} M phenol. *Cf.* also ref 5.

Our pK_a values, like those of Kolthoff and Reddy,[3] are suitable for our general survey of a variety of acids in methanol, dimethylformamide, and dimethyl sulfoxide.

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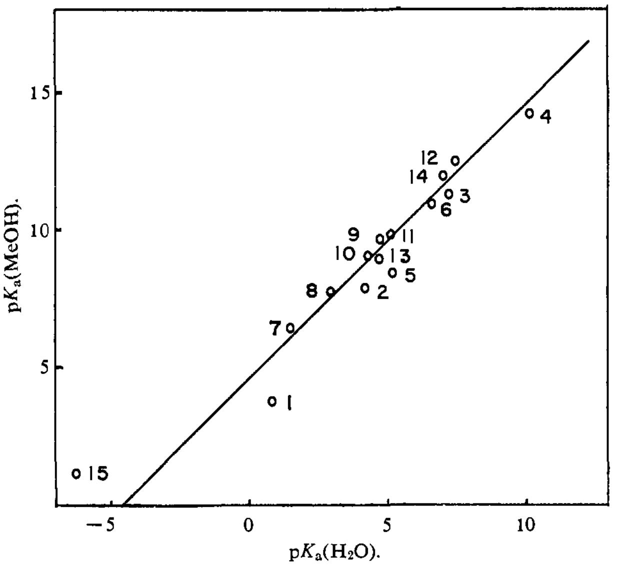

Figure 1. Plot of pK_a (MeOH) *vs.* pK_a (H_2O) at 20–25°. Numbers refer to the acids in Table II.

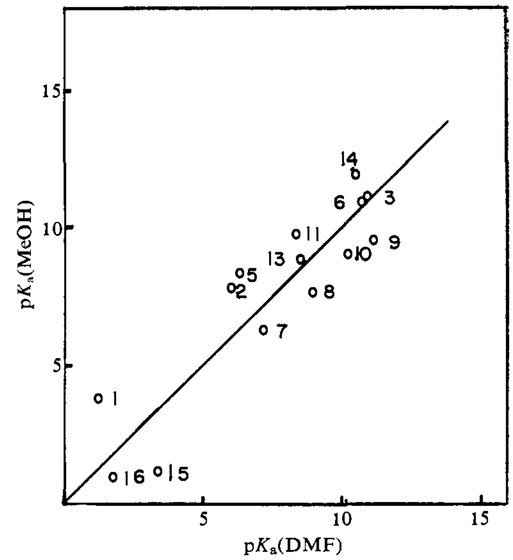

Figure 2. Plot of pK_a (MeOH) *vs.* pK_a (DMF) at 20–25°. Numbers refer to acids in Table II.

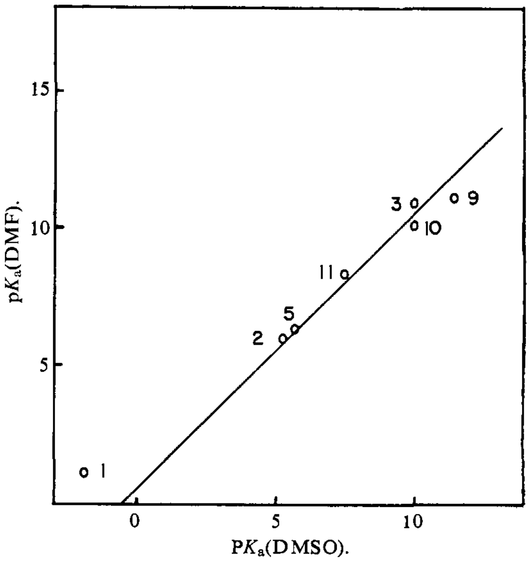

Figure 3. Plot of pK_a (DMF) *vs.* pK_a (DMSO) at 20–22°. Numbers refer to acids in Table II.

We do not claim a high order of precision, but feel that most of the values are correct to within ±0.15 pK_a unit.

Plots of pK_a (MeOH) *vs.* pK_a (H_2O), of pK_a (MeOH) *vs.* pK_a (DMF), and of pK_a (DMF) *vs.* pK_a (DMSO) are in Figures 1, 2, and 3, respectively. The following points should be noted. (1) Comparison of a protic with a dipolar aprotic solvent (Figure 2) produces a scatter diagram. The carboxylic and mineral acids roughly form one line, phenols, indicators, and sulfur compounds form another. (2) With the exception of picric acid, acidities in DMF correlate roughly with acidities in another dipolar aprotic solvent, DMSO (Figure 3). However more data would be desirable before a firm conclusion can be made. (3) With the exception of hydrochloric acid, acidities in water and methanol (Figure 1) show some correlation. Picric and acetic acids deviate in opposite directions from the mean. The deviation of hydrochloric acid, relative to picric acid, possibly is an extreme example of the effect of dispersion forces.[6]

Discussion

The changes in the chemical potential of a species, i, on transfer from dimethylformamide (unimolar ideal solution) to methanol is conveniently expressed in terms of medium activity coefficients, ${}_m\gamma_i$.[11,26] These should not be confused with the more familiar Debye–Hückel concentration activity coefficient, ${}_s\gamma_i$.[11] Values of ${}_m\gamma_i$, on transfer from dimethylformamide to methanol, are 10^{-2}–10^{-7} for anions,[26] so that for dilute solutions ($<10^{-2}$ *M*), in solvents of dielectric constant >33, ${}_s\gamma_i$ is effectively unity for anions and uncharged species.[13] The change in standard chemical potential $\Delta\mu_i°$ of a solute, i (hypothetically ideal, in respect to Henry's law unimolar solution), on transfer from DMF to methanol is represented by eq 3.[26]

$$\Delta\mu_i° = RT \ln {}_m\gamma_i \qquad (3)$$

It has proved convenient to split ${}_m\gamma_i$ into γ_i^H and γ_i^*.[26] The changes in the standard chemical potential of i due to hydrogen bonding by methanol on transfer from dimethylformamide are accommodated by γ_i^H; all changes due to other interactions are included in γ_i^*. For the S_N2 reaction (eq 4), the second-order rate constants, k^M in methanol and k^D in dimethylformamide, are related through eq 5.[26] In part VI,[26] we

$$A^- + CH_3I \rightleftharpoons [ACH_3I]^- \longrightarrow ACH_3 + I^- \qquad (4)$$

$$k^M = k^D \frac{\gamma_{A^-}{}^* \gamma_{CH_3I}{}^*}{\gamma_{TS}{}^*} \frac{\gamma_{A^-}{}^H \gamma_{CH_3I}{}^H}{\gamma_{TS}{}^H} \qquad (5)$$

gave some justification for the assumption that, for two solvents of almost the same dielectric constant, such as methanol and dimethylformamide, and for poor hydrogen-bond acceptors, such as methyl iodide and the transition state of (4), $k^M/k^D = \gamma_{A^-}{}^H$.

Values of k^M, k^D, and log k^D/k^M for reactions 4 of a variety of anions at 0° are in Table III. It will be noted that $\gamma_{A^-}{}^H$, which we assume equals k^M/k^D,[26] decreases strongly from large polarizable anions (*e.g.*,

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[26] A. J. Parker, *J. Chem. Soc.*, in press.

Table III. Hydrogen-Bonding Activity Coefficients ($\gamma_{A^-}{}^{H}$) for Anions on Transfer from Dimethylformamide to Methanol at 0°. Second-Order Rate Constants, k, for the SN2 Reaction of A^- with Methyl Iodide at 0°

A^-	10^4k^M	10^4k^D	Log k^D/k^M
Cl^- [a]	0.0010	2400	6.38
Br^- [a]	0.0183	1170	4.81
I^- [a,e]	6.7×10^{-7}	2.6×10^{-4}	2.59
SCN^- [a]	0.30	69	2.36
N_3^- [a]	0.030	3100	5.01
N_3^- [a,b]	1.6×10^{-5}	0.79	4.70
$C_6H_5O^-$ [c]	0.020	38×10^3	6.3
$4\text{-}NO_2C_6H_4O^-$ [c]	9.6×10^{-4}	14.0	4.17
$2,4\text{-}(NO_2)_2C_6H_3O^-$ [c]	1.9×10^{-5}	0.10	3.72
$C_6H_5S^-$ [b,d]	0.077	2500	4.51
$4\text{-}NO_2C_6H_4S^-$ [c]	57	13600	2.38
$C_6H_5CO_2^-$ [c]	7.76×10^{-4}	220	5.45
$CH_3CO_2^-$ [c]	4.47×10^{-4}	740	6.22
$ClCH_2CO_2^-$ [c]	1.2×10^{-4}	250	6.3

[a] See ref 26. [b] For reaction with $4\text{-}NO_2C_6H_4F$. [c] See ref 1. [d] B. O. Coniglio, W. R. McDonald, D. E. Giles, and A. J. Parker, *J. Chem. Soc.*, in press. [e] For reaction with $2,4\text{-}(NO_2)_2C_6H_3Br$.

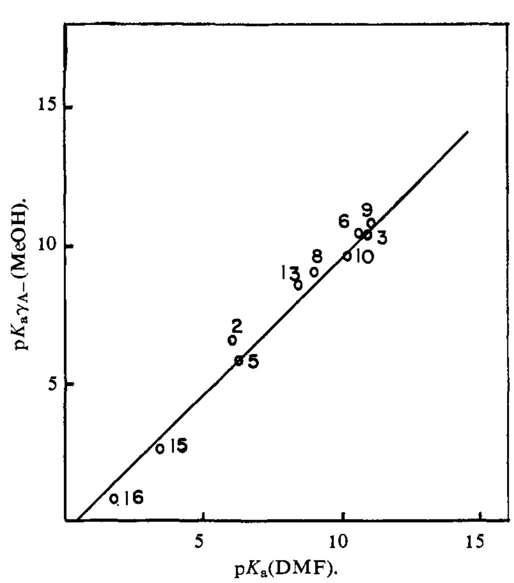

Figure 4. Plot of $pK_a\gamma_{A^-}$ (MeOH) *vs.* pK_a [DMF) for acids HA at 20–22°. Numbers refer to acids in Table II.

SCN⁻, 4-nitrothiophenoxide) to small anions with localized charges (*e.g.*, Cl⁻, $CH_3CO_2^-$), *i.e.*, decreases from weak to strong hydrogen-bond acceptors.

The hydrogen-bonding activity coefficients, $\gamma_{A^-}{}^{H}$, derived from rates of SN2 reactions, can be used to interpret the changes in equilibrium 1 on transfer from dimethylformamide to methanol. The equilibrium constants for eq 1, *expressed as concentration quotients*, in methanol, K^M, and dimethylformamide, K^D, are related as in eq 6.[26]

$$K^D = K^M \frac{\gamma_{HB}{}^{*}\gamma_{A^-}{}^{*}}{\gamma_{HA}{}^{*}\gamma_{B^-}{}^{H}} \frac{\gamma_{HB}{}^{*}\gamma_{A^-}{}^{H}}{\gamma_{HA}{}^{H}\gamma_{B^-}{}^{H}} \qquad (6)$$

i.e.

$$\log K^D = \log K^M + \log \frac{\gamma_{A^-}{}^{H}}{\gamma_{B^-}{}^{H}} + \log \frac{\gamma_{HB}{}^{*}\gamma_{A^-}{}^{*}}{\gamma_{HA}{}^{*}\gamma_{B^-}{}^{*}} + \log \frac{\gamma_{HB}{}^{H}}{\gamma_{HA}{}^{H}} \qquad (7)$$

If the differences in $\log K^D - \log K^M$ for a series of anions A⁻ are due entirely to differences in hydrogen-bonding solvation of A⁻ relative to B⁻,[13] *then* the final two terms in eq 7 must be constant. This requirement is tested as follows. Consider a variety of acids HA and some standard acid, HB, in equilibrium 1. Since log K for eq 1 is given by the difference in the acid dissociation constants, log K_a, for HA and HB, and since HB is constant throughout a series of the acids HA, eq 7 can be written as eq 8, remembering that the assumption that the last two terms in eq 7 are constant is being tested.

$$\log K_a{}^{D}[HA] = \log (K_a{}^{M}[HA]\gamma_{A^-}{}^{H}) + \text{constant} \qquad (8)$$

The plot of $p(K_a{}^{M}\gamma_{A^-}{}^{H})$ *vs.* $pK_a{}^{D}$ for a variety of acids, HA, is shown in Figure 4. It is linear and of unit slope. This suggests to us that hydrogen-bonding solvation of anions by methanol accounts almost entirely for the changes in the position of the acid–base equilibrium (eq 1) on transfer from dimethylformamide to methanol.[27] *If A⁻ and B⁻ differ markedly in their hydrogen-bond acceptor properties, large changes in K occur on transfer from dimethylformamide to methanol. If A⁻ and B⁻ are equivalent acceptors, the change, if any, will be small.*

Some observations which support this conclusion, but are not shown in Figure 4, follow. (a) $\gamma_{A^-}{}^{H}$ for picrate ion cannot be measured *via* reaction 4. To fit $p(K_a\gamma_{A^-}{}^{H})$ (MeOH) to the line in Figure 4, a value of 1.7×10^{-2} for $\gamma_{pic^-}{}^{H}$ is required. This is not unreasonable, considering the trend in the phenoxides, as charge becomes more delocalized.[13] (b) The pK_a for phenol in dimethylformamide is above 15. Figure 4 requires a pK_a of 15.8. (c) Values of $p\gamma_{A^-}{}^{H}$ which would fit Figure 4 are 5.3 for dichloroacetate ion, 3.0 for the conjugate base of brom cresol green, and 3.2 for hydrosulfide ion. All these logarithmic values are of the magnitude expected from their likely strengths as H-bond acceptors and from the $p\gamma_{A^-}{}^{H}$ values of related species.[1,13]

Although we have chosen to interpret the line of unit slope, shown in Figure 4, in terms of hydrogen-bonding activity coefficients, this excellent plot merely demonstrates that a solvent–anion interaction, which decreases strongly as the charge on the anion becomes more delocalized, almost certainly is responsible for the change in the equilibrium constant of reaction 1, and for the change in k_2 for reaction 4, on transfer from dimethylformamide to methanol. Logarithmic plots can be linear and of unit slope for a variety of reasons.

The following procedure, which involves no assumptions except that concentration activity coefficients, ${}_{s}\gamma_i$, are unity, puts the conclusions to be drawn from Figure 4 in perspective. In terms of medium activity coefficients, ${}_{m}\gamma_i$, for transfer from DMF to methanol,[11] eq 5 becomes eq 9 and eq 7 becomes eq 10.

$$\frac{k^M}{k^D} = \frac{{}_{m}\gamma_{A^-}\,{}_{m}\gamma_{CH_3I}}{{}_{m}\gamma_{TS}} \qquad (9)$$

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[27] It should be noted that we have used $\gamma_{A^-}{}^{H}$ values from rate data at 0° and log K_a values from equilibrium constants measured at 18–22°. Many SN2 reactions (4) are very fast in dimethylformamide at 0° and we do not have rate constants for many reactions (4) at 18–22° in dimethylformamide. Although it is obviously desirable to use $\gamma_{A^-}{}^{H}$ at the same temperature as K_a in eq 8, we feel that the conclusion we have derived from Figure 4 would not be seriously altered if we had been able to use $\gamma_{A^-}{}^{H}$ values at 20°. We are investigating solubilities of silver salts in methanol and in DMF in an attempt to estimate $\gamma_{A^-}{}^{H}$ values, not accessible through reaction 4.

$$\log K^{D} = \log K^{M} + \log \frac{{}_{m}\gamma_{A^-}}{{}_{m}\gamma_{B^-}} + \log \frac{{}_{m}\gamma_{HB}}{{}_{m}\gamma_{HA}} \quad (10)$$

For a series of anions A^- relative to a standard anion B^-, eq 10 becomes eq 11. Substitution for $\log {}_{m}\gamma_{A^-}$ from eq 9 gives eq 12.

$$\log K_a^{D}[HA] = \log K_a^{M}[HA] + \log {}_{m}\gamma_{A^-} - \log {}_{m}\gamma_{HA} + \text{constant} \quad (11)$$

$$\log K_a^{D}[HA] = \log K_a^{M}[HA] + \log \frac{k^{M}}{k^{D}} + \log {}_{m}\gamma_{CH_3I} - \log {}_{m}\gamma_{TS} - \log {}_{m}\gamma_{HA} + \text{constant} \quad (12)$$

Methyl iodide is the standard for rate determinations, so ${}_{m}\gamma_{CH_3I}$ is constant. The medium activity coefficients, ${}_{m}\gamma_{TS}$, are for a series of transition states, involving different A, of the type $(ACH_3I)^-$. Since the plot (Figure 4), $\log K_a^{D}[HA]$ *vs.* $\log K_a^{M}[HA] + \log k^{M}/k^{D}$, is linear and of unit slope for a quite representative range of anions A^-, the expression $\log {}_{m}\gamma_{TS}{}_{m}\gamma_{HA}$ must be a constant for transfer from dimethylformamide to methanol. The large solvent effect on the acid–base equilibrium (eq 1) is therefore most likely due to differences in anion solvation of the type described. The result that can be accepted with confidence from this work is that medium effects on K_a can be correlated with medium effects on k, as in eq 13. The speculation regarding $\delta_{A^-}{}^{H}$ requires further investigation and this is in progress.[27]

$$\log K_a^{D}/K_a^{M} = \log k^{M}/k^{D} + 4.5 \quad (13)$$

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Oxygen-18 Exchange Reactions of Aldehydes and Ketones

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Abstract: Using infrared spectroscopy, the equilibrium exchange times have been determined for a series of ketones, aromatic aldehydes, and β-keto esters reacting with oxygen-18 enriched water. In acidic tetrahydrofuran, the exchange times for the aromatic aldehydes increase in the order acetaldehyde < benzaldehyde < 2-naphthaldehyde < 1-naphthaldehyde < 9-anthraldehyde < 9-phenanthraldehyde ≪ indolealdehyde, chlorophyll b, and pheophytin b. A series of cyclic ketones in piperidine have exchange times in the order of acetone, ninhydrin < cyclohexanone, cyclobutanone < cyclopentenone ≪ cyclopentanone, fluorenone ≪ indanone. A different sequence was found for the acid-catalyzed exchange reactions of ketones in tetrahydrofuran since cyclohexanone, acetone < cyclopentanone < cyclobutanone ≪ ninhydrin < cyclopentenone < indanone ≪ fluorenone. The β-keto esters had slower exchange times than their respective simple ketones. These exchange times have been evaluated in terms of steric and electronic considerations, and applied to a discussion of the exchange times of chlorophyll a and chlorophyll derivatives.

This investigation of the exchange reactions of aldehydes and ketones with O^{18} enriched water has been undertaken in order to be able to examine the participation of chlorophyll carbonyl groups as chemical intermediates in the oxidation of water during photosynthesis. Photosynthetic mechanisms have been proposed by Calvin[1] and Franck[2] in which the separation of oxidant and reductant, required for oxygen evolution and carbon dioxide fixation, is a photocatalytical chlorophyll reaction. Essential to these mechanisms is the ability of a chlorophyll carbonyl group to undergo hydration. The present work evaluates the exchange ability of chlorophyll in comparison with simple ketones, aldehydes, and β-keto esters.

The literature on the O^{18} exchange reactions of carbonyl functions indicates that aldehydes exchange very rapidly in comparison to ketones. Acetaldehyde exchanges completely at room temperature in neutral solution within 24 hr,[3] while acetone exchange is incomplete after 24 hr at 100°.[4] A comprehensive survey of the literature by Samuel and Silver[5] gives exchange rates in various solvents, acidic and basic, for acetone, acetaldehyde, acetoacetate, *para*-substituted benzophenones, methylcyclohexanones, and substituted benzaldehydes.

Compounds were chosen for this study because of their similarities to chlorophylls a and b (see Figure 1). Ring V of chlorophyll a is a β-keto ester of cyclopentanone which is fused to an aromatic nucleus, and chlorophyll b has a pyrrole aldehyde subunit as a part of a larger aromatic system. Thus, cyclopentanones, other cyclic ketones, simple β-keto esters, and aromatic and heterocyclic aldehydes have been studied.

An infrared technique is used to analyze the rate of O^{18} incorporation in the carbonyl group. Halmann and Pinchas[6] showed in 1958 that the $C{=}O^{18}$ band of

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