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Kinetics of Ionization of 1,3-Indandione in Me_2SO–Water Mixtures. Solvent Effect on Intrinsic Rates and Brønsted Coefficients

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Abstract: Rate constants (k_1^B, k_{-1}^{BH}) of the reversible deprotonation of 1,3-indandione (ID) are reported in carboxylate, amine, and aryloxide buffers in 10%, 50%, 70%, and 90% aqueous Me_2SO at 20 °C. An increase in the Me_2SO content of the solvent produces the following effects. (1) The intrinsic rate constants ($k_0 = k_1^B/q = k_{-1}^{BH}/p$ at $\Delta pK + \log p/q = 0$) increase irrespective of buffer type, but the increase is larger for anionic ($RCOO^-$, ArO^-) than for neutral (RNH_2, R_2NH) bases. (2) The Brønsted β values increase. (3) With the carboxylate ions, there is downward curvature in the Brønsted plots in the Me_2SO-rich solvents. (4) The negative deviation of the hydroxide ion point from the Brønsted plot defined by carboxylate ions increases while the negative deviation of the water point from the amine Brønsted plots decreases. All these effects can be understood as a manifestation of the Principle of Imperfect Synchronization. In the present context this principle states that a reactant destabilizing factor (e.g., reduced solvation of $RCOO^-$) whose loss is ahead of proton transfer in the transition state, or a product destabilizing factor (e.g., decreased solvation of the carbanion) whose development lags behind proton transfer in the transition state, increases the intrinsic rate constant (k_0). On the other hand, a product stabilizing factor (e.g., increased solvation of RNH_3^+), which develops late, decreases k_0.

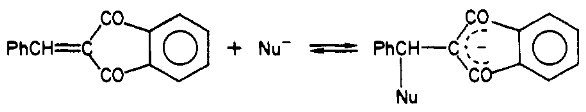
We recently reported a study of the ionization of acetylacetone (AA) in various Me_2SO–water mixtures.[1] One of the most remarkable results of that study was that the Brønsted plots defined by six carboxylate ions showed distinct downward curvature in the Me_2SO-containing solvents (50%, 90%, and 95% Me_2SO by volume) but not in water. To the best of our knowledge, this was the first reported example of a curved Brønsted plot *within the family of carboxylate ions*.

Even though the curvature was in the direction predicted by the Hammond–Leffler[2] principle or the Marcus equation,[3] the fact that the Brønsted plots, defined by a series of primary amines covering a similar pK_a range as the carboxylate ions, were linear was taken as evidence against a Hammond–Leffler effect. Instead, the curvature was attributed to increased solvation of the anionic bases with increasing basicity. As had been shown previously, mainly by Hupe and Jencks,[4,5] the partial desolvation of the base which is required for the reaction to occur can lead to such downward curvature, if this desolvation is adhead of proton transfer (as measured by the Brønsted β value) in the transition state.[5]

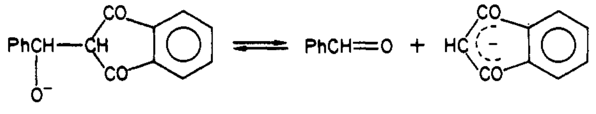
It would appear that if desolvation of the base is mainly responsible for the mentioned curvature, this behavior should be relatively independent of the carbon acid being ionized and hence should manifest itself in other cases as well. We therefore set out to investigate the ionization of 1,3-indandione (ID) under similar conditions as that of acetylacetone. The results indeed show a very similar pattern in the Brønsted plots as with acetylacetone.

A second motivation for this study was our continued interest[1,7] in how the change from protic to dipolar aprotic solvents affects the intrinsic rate constants (or intrinsic barriers) of proton transfers.

Furthermore the intrinsic rate constant for the deprotonation of ID was needed for correlation with the intrinsic rate constants of reactions 1 and 2 which have recently been reported.[8]



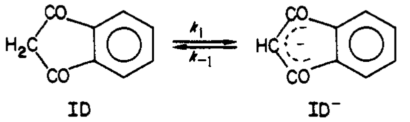
(1)



(2)

Results

Rates of Proton Transfer. We have measured proton-transfer rates and pK_a values in 10%, 50%, 70%, and 90% aqueous Me_2SO (v/v) at 20 °C. The rates were measured in buffer solutions, under pseudo-first-order conditions with the substrate as the minor component. Under most conditions, the reaction can be represented by eq 3–5 where B and BH refer to buffer species. The pseudo-first-order rate constant for equilibration of reaction 3 is given by eq 6. k_{obsd} was determined in buffers whose buffer ratio was usually close to unity. At any given pH, runs were conducted at four to five buffer concentrations. All plots of k_{obsd} vs. buffer concentration gave excellent straight lines.



(3)

$$k_1 = k_1^{H_2O} + k_1^{OH}a_{OH^-} + k_1^{B}[B] \tag{4}$$

$$k_{-1} = k_{-1}^{H}a_{H^+} + k_{-1}^{H_2O} + k_{-1}^{BH}[BH] \tag{5}$$

$$k_{obsd} = k_1 + k_{-1} \tag{6}$$

At pH ≫ pK_a^{ID}, eq 6 reduces to eq 7. Determination of k_1^B from the slopes of the buffer plots was straightforward. k_1^{OH} was obtained from intercepts ($k_1^{OH}a_{OH^-} \gg k_1^{H_2O}$) in 10% and 50% Me_2SO. In 70% and 90% Me_2SO, the intercepts were too small to give reliable information on k_1^{OH} while the rates in KOH solution were too fast for the stopped-flow method. Hence k_1^{OH}

$$k_{obsd} = k_1^{H_2O} + k_1^{OH}a_{OH^-} + k_1^{B}[B] \tag{7}$$

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[1] Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* in press.

[2] (a) Leffler, J. E. *Science (Washington, D.C.)* **1953**, *117*, 340. (b) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[3] Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.

[4] (a) Hupe, D. J.; Wu, D. *J. Am. Chem. Soc.* **1977**, *99*, 7653. (b) Hupe, D. J.; Wu, D.; Shepperd, P. *Ibid.* **1977**, *99*, 7659.

[5] Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, A.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045.

[6] Kebarle, P. *Ann. Rev. Phys. Chem.* **1977**, *28*, 445.

[7] Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.

[8] Bernasconi, C. F.; Laibelman, A., Zitomer, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 6563.

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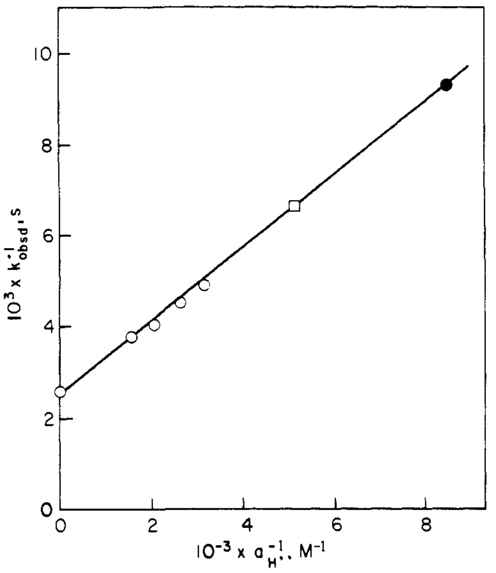

Figure 1. Plot according to eq 11 in 50% Me_2SO. (○) HCl; (□) intercept of buffer plot in $ClCH_2COOH$; (●) intercept of buffer plot in $MeOCH_2COOH$.

could not be determined in these solvents. $k_1^{H_2O}$ was determined from $k_{-1}^{H_2O}$ measured in acidic solution, coupled with pK_a^{ID}.

At pH ≈ pK_a^{ID}, eq 6 cannot be simplified by neglecting some terms. After appropriate substitutions, eq 6 leads to eq 8 for the slope of a plot of k_{obsd} vs. buffer *acid* concentration, from which k_1^B and k_{-1}^{BH} are easily obtained in combination with pK_a^{BH}

$$\text{slope} = k_1^B \frac{K_a^{BH}}{a_{H^+}} + k_{-1}^{BH} \tag{8}$$

At pH ≪ pK_a^{ID}, simplification of eq 6 is again possible because the reaction is virtually irreversible. However here formation of the enol form of ID as a transient species affected the kinetics in some cases, even though at ***equilibrium*** the enol content is always negligible (e.g., ~0.03% in 10% Me_2SO, 0.15% in 50% Me_2SO, 0.36% in 70% Me_2SO, 0.51% in 90% Me_2SO). This is because oxygen protonation of ID^- is much faster than carbon protonation, and nonnegligible amounts of the enol form are being generated when the pH of the reaction solution approaches the pK_a of the enol form or is below it. In those cases the reaction scheme needs to be expanded to eq 9 and k_{obsd} (with k_1 being negligible) becomes eq 10.

$$ID \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ID^- \underset{K_a^{enol}}{\overset{H^+}{\rightleftharpoons}} ID_{enol} \tag{9}$$

$$k_{obsd} = k_{-1} \frac{K_a^{enol}}{K_a^{enol} + a_{H^+}} \tag{10}$$

From such experiments K_a^{enol} could be determined, along with the rate constants of carbon protonation of ID^-. One approach was to use intercepts of buffer plots, combined with data in HCl solution, so that $k_{-1} \approx k_{-1}^H a_{H^+}$ and eq 10, after inversion, becomes eq 11.

$$\frac{1}{k_{obsd}} = \frac{1}{k_{-1}^H a_{H^+}} + \frac{1}{K_a^{enol} k_{-1}^H} \tag{11}$$

Figure 1 shows a representative plot according to eq 11. A second approach was based on the slopes of buffer plots which, after inversion, are given by eq 12. A representative plot according to eq 12 is shown in Figure 2.

$$\frac{1}{\text{slope}} = \frac{1}{k_{-1}^{BH}} + \frac{a_{H^+}}{K_a^{enol} k_{-1}^{BH}} \tag{12}$$

In those cases where both approaches were used (10% and 50% Me_2SO), excellent agreement between the two pK_a^{enol} values was found. In solvents of higher Me_2SO content, reactions performed in HCl solutions only afforded $k_{-1}K_a^{enol}$ because $K_a^{enol} \ll a_{H^+}$ (eq 10). Furthermore, in these solvents, the intercepts of the buffer plots were quite small and hence afflicted with a large experimental uncertainty. Therefore, pK_a^{enol} was only determined via eq 12 in these solvents.

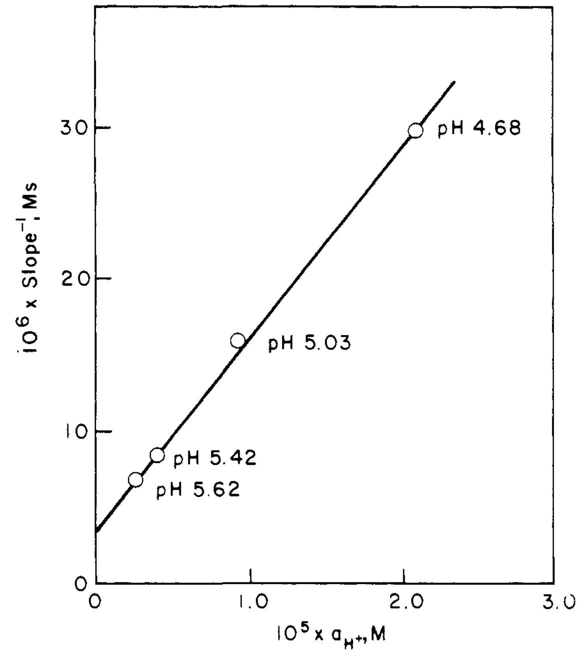

Figure 2. Plot according to eq 12 in 90% Me_2SO for $Cl_2CHCOOH$.

Table I. pK_a Values and Enolization Constants of ID at 20 °C

	10% Me_2SO	50% Me_2SO	70% Me_2SO	90% Me_2SO
pK_a^{ID}	7.00 ± 0.02	6.35 ± 0.02	6.56 ± 0.02	7.82 ± 0.02
pK_a^{enol}	3.5 ± 0.3[a]	3.52 ± 0.05	4.12 ± 0.05	5.53 ± 0.05
K_E[b]	≈3 × 10^{-4}	1.48 × 10^{-3}	3.63 × 10^{-3}	5.13 × 10^{-3}
% enol	≈0.03	0.15	0.36	0.51

[a] Large uncertainty because of small intercept in plot according to eq 11. [b] ±12% except in 10% Me_2SO where the error is ±100%.

pK_a^{BH}, pK_a^{ID}, and Enolization Constants. The pK_a of the keto form, pK_a^{ID}, was determined by classical spectrophotometric procedures. In conjunction with pK_a^{enol}, the enolization constants, K_E, was then also obtained as eq 13.

$$K_E = \frac{[ID_{enol}]}{[ID_{keto}]} = \frac{K_a^{ID}}{K_a^{enol}} \tag{13}$$

The pK_a^{BH} values of the buffers in the various solvents were determined potentiometrically, unless already known from previous work in our laboratory.

Discussion

Solvent Effect on pK_a^{ID}. pK_a values of the keto form (pK_a^{ID}) of ID are summarized in Table I. Our pK_a^{ID} value in 10% Me_2SO–90% water (7.00) agrees fairly well with the value of 7.41 determined by Gren and Vanag[9] in 1% methanol–99% water at 25 °C. Most, and perhaps all, of the small discrepancy between the two values is likely due to the different solvents and temperature (our pK_a^{ID} is at 20 °C). That pK_a^{ID} should be lower in 10% Me_2SO than in water is manifested in the results shown in Table I.

The decrease in pK_a^{ID} at small Me_2SO conncentration and increase at high concentrations is not unusual and has been observed with other carbon acids. For example, the pK_a of malononitrile at 20 °C is 11.39 in water,[10] 10.21 in 50% Me_2SO,[10] 9.92 in 70% Me_2SO,[11] and 11.10 in pure Me_2SO (25 °C).[12] The pK_a

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(9) Gren, E. Y.; Vanag, G. Y. *Zh. Org. Khim.* **1965**, *1*, 3.

(10) Bernasconi, C. F.; Zitomer, J. L.; Fox, J. P.; Howard, K. A. *J. Org. Chem.* **1984**, *49*, 482.

Table II. Solvent Activity Coefficients for the Transfer from Water to Me_2SO–Water Mixtures and from 10% Me_2SO to Other Me_2SO–Water Mixtures

compd	% Me_2SO	log $^{W}\gamma^{D}$	log $^{10}\gamma^{D}$	remarks
ID	50		−0.42	*a*
	70		−0.91	*a*
	90		−1.60	*a*
ID^-	50		0.38	*a*
	70		0.76	*a*
	90		1.79	*a*
AA	50	0.14		*b*
	90	∼−0.50		*c*
AA^-	50	2.07		*d*
	90	4.5		*c, d*
H^+	10	−0.48		*e*
	50	−1.93	−1.45	*e*
	70	∼−2.83	−2.11	*f*
	90	−3.05	∼−2.57	*f*
	100	−3.31		*g*
OH^-	10	0.56		*e*
	50	3.40	2.84	*e*
AcOH	10	∼0.43		*h*
	50	∼−0.06	∼−0.49	*h*
	70	∼−0.52	∼−0.95	*h*
	90	∼−1.50	−1.93	*h*
	100	−2.15		*g*
AcO^-	10	1.12		*e*
	50	3.08	1.96	*e*
	70	∼4.40	∼3.28	*c, e*
	90	∼6.50	∼5.38	*c, e*
	100	8.16		*g*
$CH_3CH_2CH_2NH_2$	10	−0.06		*i*
	50	−0.35	−0.29	*i*
	70	∼−0.20	∼−0.14	*i*
	90	∼0.09	∼−0.15	*i*
$CH_3CH_2CH_2NH_3^+$	10	−0.40		*e*
	50	−1.81	−1.41	*e*
	70	∼−2.4	∼−2.0	*c, e*
	90	∼−2.8	∼−2.4	*c, e*

[a] Bernasconi, C. F.; Bunnell, R. D., unpublished results. [b] Watarai, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3019. [c] Estimated. [d] From equation analogous to eq 14 based on log $^{W}\gamma_{AA}{}^{D}$, $^{W}\Delta^{D}pK$, and log $^{W}\gamma_{H^+}{}^{D}$. [e] Wells, C. F. In *Thermodynamic Behavior of Electrolytes in Mixed Solvents-II*; Furter, W. F., Ed.; Advances in Chemistry 177; American Chemical Society: Washington, DC, 1979. [f] Extrapolated from data in *e*. [g] Cox, B. G.; Hedwig, G. R.; Parker, A. J.; Watts, D. W. *Aust. J. Chem.* **1974**, *77*, 497. [h] From equation analogous to eq 14 based on log $^{W}\gamma_{AcO}{}^{D}$, $^{W}\Delta^{D}pK$, and log $^{W}\gamma_{H^+}{}^{D}$. [i] From equation analogous to eq 14 based on log $^{W}\gamma_{NH^+}{}^{D}$, $^{W}\Delta^{D}pK$, and log $^{W}\gamma_{H^+}{}^{D}$.

values of 4-nitrophenylacetonitrile are 14.45, 12.75, 11.65, and 12.3 in 9%, 50%, 72%, and 100% Me_2SO, respectively.[13]

These solvent effects come about because the stabilities of the carbon acid, the carbanion, and the hydronium ion change in a different way with the solvent. If one expresses the solvent effect on $pK_a{}^{ID}$ in terms of solvent activity coefficients,[14] one can write eq 14 for the change of $pK_a{}^{ID}$ from the more aqueous solvent (W) to the one containing more Me_2SO (D). Table II summarizes various solvent activity coefficients relevant to the present work.

$$^{W}\Delta^{D}pK_a{}^{ID} = \log {}^{W}\gamma_{ID^-}{}^{D} + \log {}^{W}\gamma_{H^+}{}^{D} - \log {}^{W}\gamma_{ID}{}^{D} \quad (14)$$

Enolization. Our kinetic measurements have allowed us to measure $pK_a{}^{enol}$ and hence to obtain the enolization constants, $K_E = K_a{}^{ID}/K_a{}^{enol}$. These constants and the percentage of enol in the various solvents are summarized in Table I. We note that K_E and hence the enol content are very small in all solvents. This is in agreement with reports in the literature according to which no enol of ID could be detected within the precision of NMR measurements.[15,16]

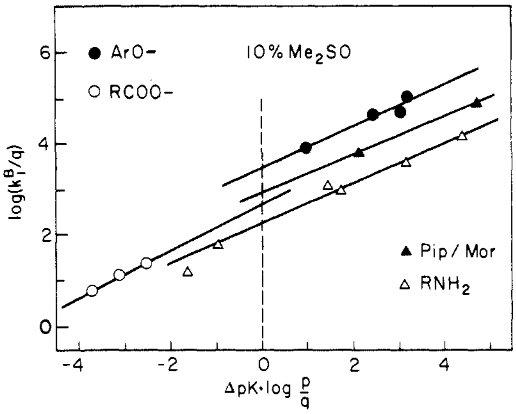

Figure 3. Brønsted plots in 10% Me_2SO. Data from Table III.

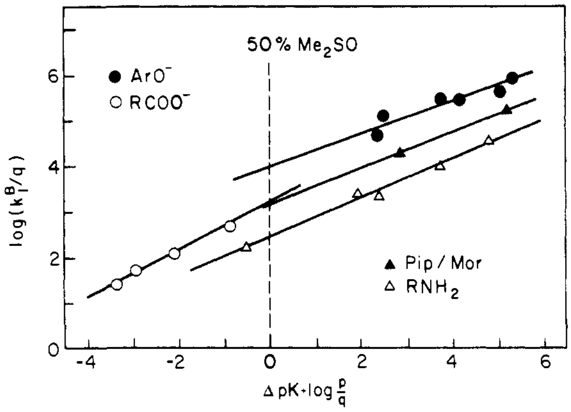

Figure 4. Brønsted plots in 50% Me_2SO. Data from Table IV.

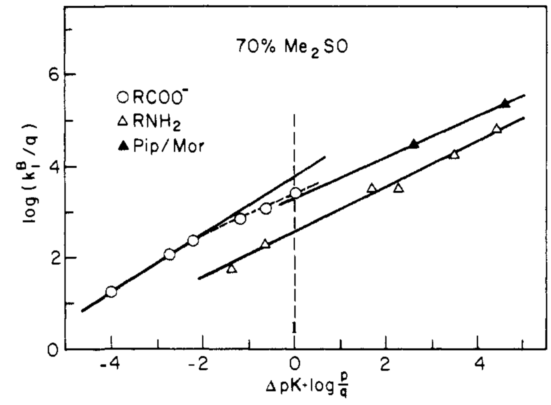

Figure 5. Brønsted plots in 70% Me_2SO. Data from Table V.

There is a marked increase in K_E with increasing Me_2SO content of the solvent. For example, the increase in K_E from 10% to 90% Me_2SO amounts to a factor of 17. A similar, though less dramatic, increase has recently been observed with acetylacetone where $K_E = 0.183$ in water and $K_E = 1.14$ in 90% Me_2SO.[1] These increases are consistent with numerous observations which show that the enol form of β-diketones becomes more strongly favored in less polar solvents.[17-19]

It is worth noting that the introduction of a phenyl group at the 2-position of ID increases the enol content to 2.4% in water.[18] This is consistent with the general tendency of electron-withdrawing substituents to make the enol form more favorable.[19]

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(11) Bernasconi, C. F.; Kanavarioti, A.; Killion, R. B. *J. Am. Chem. Soc.* **1985**, *107*, 3612.

(12) Ritchie, C. D.; Uschold, R. E. *J. Am. Chem. Soc.* **1967**, *89*, 2752.

(13) Walters, E. A. *J. Phys. Chem.* **1977**, *81*, 1995 and personal communication by Bordwell, F. G. cited therein.

(14) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1.

(15) Burdett, J. L.; Rogers, M. T. *J. Am. Chem. Soc.* **1964**, *86*, 2105.

(16) Burdett, J. L.; Rogers, M. T. *Can. J. Chem.* **1965**, *43*, 1516.

(17) Reichardt, C. *Solvent Effects in Organic Chemistry*; Verlag Chemie: Weinheim, 1979; p 61.

(18) Stella, V. J.; Gish, R. *J. Pharm. Sci.* **1979**, *68*, 1042, 1047.

(19) Forsen, S.; Nilsson, M. In *The Chemistry of the Carbonyl Group*; Zabicky, J., Ed.; Wiley-Interscience: New York, 1970; Vol. 2, p 157.

Table III. Rate Constants in 10% Me_2SO–90% Water (v/v) at 20 °C, μ = 0.5 M

no.	base	pK_a^{BH}	k_1^B, M^{-1} s^{-1}	k_{-1}^{BH}, M^{-1} s^{-1}	$\Delta pK + \log (p/q)^a$
1	H_2O	-1.70	3.01×10^{-3}	1.51×10^6	-8.52
5	$MeOCH_2COO^-$	3.60	1.17×10^1	2.94×10^4	-3.70
6	$ClCH_2CH_2COO^-$	4.12	2.58×10^1	1.95×10^4	-3.12
7	AcO^-	4.78	4.57×10^1	7.58×10^3	-2.52
8	$MeONH_2$	4.88	1.44×10^1	1.90×10^3	-1.64
9	$NCCH_2NH_2$	5.58	6.52×10^1	1.71×10^3	-0.94
10	$EtOOCCH_2NH_2$	7.97	1.17×10^3	1.26×10^2	1.45
11	$H_2NCOCH_2NH_2$	8.29	9.66×10^2	4.95×10^1	1.77
12	$MeOCH_2CH_2NH_2$	9.73	4.00×10^3	7.45	3.21
13	n-$BuNH_2$	10.98	1.46×10^4	1.53	4.46
14	morpholine	8.84	6.97×10^3	1.01×10^2	2.14
15	piperidine	11.43	7.74×10^4	2.88	4.73
16	$4\text{-}CNC_6H_4O^-$	7.99	7.85×10^3	8.03×10^2	0.99
19	$4\text{-}ClC_6H_4O^-$	9.49	4.22×10^4	1.37×10^2	2.49
20	$C_6H_5O^-$	10.03	5.26×10^4	4.91×10^1	3.03
21	$3,5\text{-}Me_2C_6H_3O^-$	10.21	9.93×10^4	5.34×10^1	3.21
22	OH^-	15.93	1.24×10^5	1.46×10^{-4}	9.23

[a] $\Delta pK = pK_a^{BH} - pK_a^{ID}$ with pK_a^{ID} = 7.00.

Table IV. Rate Constants in 50% Me_2SO–50% Water (v/v) at 20 °C, μ = 0.5 M

no.	base	pK_a^{BH}	k_1^B, M^{-1} s^{-1}	k_{-1}^{BH}, M^{-1} s^{-1}	$\Delta pK + \log (p/q)^a$
1	H_2O	-1.44	2.11×10^{-2}	1.30×10^6	-7.62
3	$NCCH_2COO^-$	3.29	5.15×10^1	5.91×10^4	-3.36
4	$ClCH_2COO^-$	3.71	1.01×10^2	4.41×10^4	-2.94
5	$MeOCH_2COO^-$	4.56	2.38×10^2	1.47×10^4	-2.09
7	AcO^-	5.78	9.58×10^2	3.56×10^3	-0.87
9	$NCCH_2NH_2$	5.39	1.69×10^2	1.54×10^3	-0.48
10	$EtOOCCH_2NH_2$	7.83	2.61×10^3	8.66×10^1	1.96
11	$H_2NCOCH_2NH_2$	8.28	2.10×10^3	2.47×10^1	2.41
12	$MeOCH_2CH_2NH_2$	9.63	9.88×10^3	5.19	3.76
13	n-$BuNH_2$	10.68	3.40×10^4	1.59	4.81
14	morpholine	8.70	1.81×10^4	8.10×10^1	2.83
15	piperidine	11.05	1.59×10^5	3.17	5.18
16	$4\text{-}CNC_6H_4O^-$	8.69	5.12×10^4	2.34×10^2	2.34
17	$3,5\text{-}Cl_2C_6H_3O^-$	8.87	1.18×10^5	3.56×10^2	2.52
18	$3\text{-}ClC_6H_4O^-$	10.12	2.45×10^5	4.16×10^2	3.77
19	$4\text{-}ClC_6H_4O^-$	10.51	2.74×10^5	1.89×10^1	4.16
20	$C_6H_5O^-$	11.40	4.28×10^5	3.81	5.05
21	$3,5\text{-}Me_2C_6H_3O^-$	11.66	7.32×10^5	3.59	5.31
22	OH^-	17.34	6.80×10^5	5.94×10^{-6}	11.29

[a] $\Delta pK = pK_a^{BH} - pK_a^{ID}$ with pK_a^{ID} = 6.35.

Table V. Rate Constants in 70% Me_2SO–30% Water (v/v) at 20 °C, μ = 0.25 M

no.	base	pK_a^{BH}	k_1^B, M^{-1} s^{-1}	k_{-1}^{BH}, M^{-1} s^{-1}	$\Delta pK + \log (p/q)^a$
1	H_2O	-1.22	2.82×10^{-2}	1.70×10^6	-7.95
2	Cl_2CHCOO^-	2.87	3.43×10^1	1.68×10^5	-3.99
3	$NCCH_2COO^-$	4.13	2.29×10^2	6.16×10^4	-2.73
4	$ClCH_2COO^-$	4.65	4.55×10^2	3.70×10^4	-2.21
5	$MeOCH_2COO^-$	5.67	1.42×10^3	1.10×10^4	-1.19
6	$ClCH_2CH_2COO$–	6.23	2.50×10^3	5.34×10^3	-0.63
7	AcO^-	6.90	5.67×10^3	2.59×10^3	0.04
8	$MeONH_2$	4.70	5.86×10^1	4.23×10^3	-1.38
9	$NCCH_2NH_2$	5.42	1.93×10^2	2.67×10^3	-0.66
10	$EtOOCCH_2NH_2$	7.75	3.41×10^3	2.20×10^2	1.67
11	$H_2NCOCH_2NH_2$	8.34	3.32×10^3	5.51×10^1	2.26
12	$MeOCH_2CH_2NH_2$	9.57	1.89×10^4	1.85×10^1	3.49
13	n-$BuNH_2$	10.49	7.10×10^4	8.30	4.41
14	morpholine	8.66	3.04×10^4	2.42×10^2	2.58
15	piperidine	10.66	2.34×10^5	1.86×10^1	4.58

[a] $\Delta pK = pK_a^{BH} - pK_a^{ID}$ with pK_a^{ID} = 6.56.

Brønsted Plots. Rate constants for proton transfer according to eq 3–5 in 10%, 50%, 70%, and 90% Me_2SO are summarized in Tables III–VI, respectively. The tables also include pK_a^{BH}'s of the buffers in the respective solvents, $\Delta pK + \log (p/q)$ with $\Delta pK = pK_a^{BH} - pK_a^{ID}$, with p and q being the usual statistical factors used for Brønsted plots. The estimated uncertainty in our rate constants is ±4% except for the aryloxide buffers where it is ±15 to 20% (see below); the error limits in the pK_a^{BH} values is ±0.02.

Figures 3–6 show the Brønsted plots (in the direction of deprotonation of ID) in the four solvents. There are some "missing points" on most of these plots because the rates for certain buffers were too fast for the stopped-flow technique. For example, in 10% Me_2SO, the most acidic buffer amenable to study was methoxyacetic acid, and in 50% Me_2SO it was cyanoacetic acid; for more acidic buffers $k_{-1}^{BH}[BH]$ and $k_{-1}^{H}a_{H^+}$ are too high for accurate measurements. Or, in 70% and 90% Me_2SO, phenol buffers could not be studied because $k_1^B[B]$ is too large. The

Table VI. Rate Constants in 90% Me$_2$SO-10% Water (v/v) at 20 °C, μ = 0.06 M

no.	base	pK_a^{BH}	k_1^B, $M^{-1}\,s^{-1}$	k_{-1}^{BH}, $M^{-1}\,s^{-1}$	$\Delta pK + \log (p/q)$[a]
1	H_2O	-0.74	1.94×10^{-2}	7.11×10^6	-8.39
2	Cl_2CHCOO^-	4.68	1.96×10^2	2.70×10^5	-3.44
3	$NCCH_2COO-$	6.25	2.87×10^3	1.07×10^5	-1.87
4	$ClCH_2COO-$	6.84	7.62×10^3	7.28×10^4	-1.28
5	$MeOCH_2COO^-$	8.17	3.68×10^4	1.65×10^4	0.05
7	AcO^-	9.53	1.38×10^5	2.69×10^3	1.41
8	$MeONH_2$	5.15	5.83×10^1	2.73×10^4	-2.19
9	$NCCH_2NH_2$	5.95	1.81×10^2	1.34×10^4	-1.39
10	$EtOOCCH_2NH_2$	8.22	3.76×10^3	1.50×10^3	0.88
11	$H_2NCOCH_2NH_2$	9.19	5.84×10^3	2.49×10^3	1.85
12	$MeOCH_2CH_2NH_2$	10.20	3.09×10^4	1.28×10^2	2.86
13	n-$BuNH_2$	10.98	9.62×10^4	6.66×10^1	3.64
14	morpholine	8.90	3.82×10^4	3.18×10^3	1.56
15	piperidine	10.72	2.82×10^5	2.82×10^3	3.38

[a] $\Delta pK = pK_a^{BH} - pK_a^{ID}$ with pK_a^{ID} = 7.82.

Table VII. Intrinsic Rate Constants, log k_0[a]

% Me$_2$SO	pK_a^{CH}[b]	$RCOO^-$[c]	RNH_2	pip/mor	ArO^-
1,3-Indandione (ID)					
10	7.00	2.64 ± 0.26	2.27 ± 0.13[e]	2.97 ± 0.01	3.44 ± 0.26
50	6.35	3.18 ± 0.10	2.44 ± 0.17	3.13 ± 0.10	4.0 ± 0.2
70	6.56	3.77 ± 0.10	2.59 ± 0.18	3.33 ± 0.10	
90	7.82	4.53 ± 0.05	2.97 ± 0.05	3.85 ± 0.10	
Acetylacetone (AA)[d]					
0	9.11	3.14[f,g]	1.90	2.60	
50	9.12	3.80[f]	2.06	2.75	
90	11.10	5.27[f]	2.91	3.64	

[a] $\log k_0 = \log (k_1^B/q)$ at $\Delta pK + \log (p/q) = 0$; error limits are standard deviations except for the pip/mor pair. [b] $pK_a^{CH} = pK_a^{ID}$ or pK_a^{AA}. [c] Based on linear portion of Brønsted plots. [d] From ref 1. [e] $MeONH_2$ excluded from the correlation. [f] Values are only approximate because of long extrapolation. [g] This value is slightly different from $\log k_0$ = 2.89 given in ref 1 and is based on the five least basic carboxylate ions only. See footnote *e* in Table VIII.

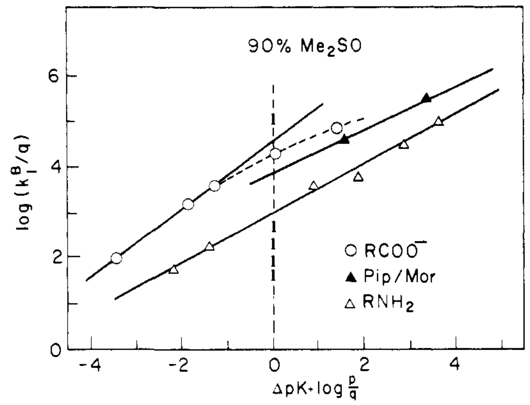

Figure 6. Brønsted plots in 90% Me$_2$SO. Data from Table VI.

impossibility to measure k_1^{OH} in these two high Me$_2$SO solvents was already commented upon in the Results section.

Figures 3–6 show that each family of buffers defines its own Brønsted plot. For a given $\Delta pK + \log (p/q)$ value, the relative reactivity is aryloxide ions > secondary amines ~ carboxylate ions > primary amines, except for 90% Me$_2$SO where the carboxylate ions become somewhat more reactive than the secondary amines.

Similar reactivity patterns have been recently reported for the ionization of acetylacetone[1] and of nitroaromatic hydrocarbons[20] (except for a low reactivity of carboxylate ions[20]), and the greater reactivity of secondary compared to primary amines is a well-known phenomenon.[21,22]

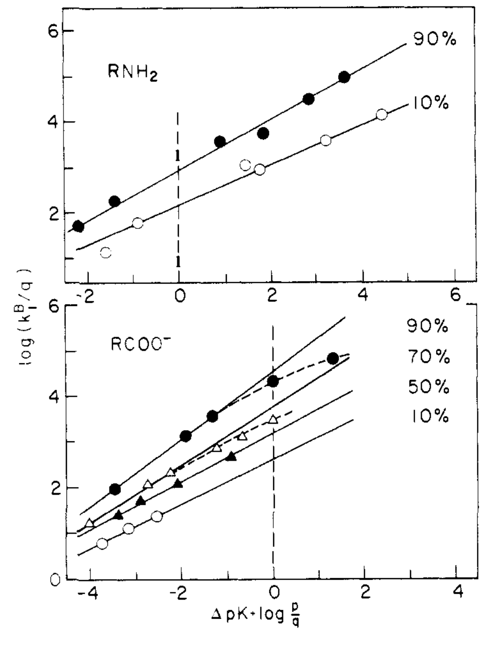

Figure 7. Brønsted plots for the primary amines in 10% and 90% Me$_2$SO and for the carboxylate ions in 10%, 50%, 70%, and 90% Me$_2$SO.

There are some deviant points in most Brønsted plots. Possible reasons for the deviations will be discussed below for the carboxylate ions and the primary amines. The unusually large scatter in the aryloxide plots can probably be attributed to large experimental error because the rates were very high and virtually near the time resolution of the stopped-flow technique. We shall therefore put relatively little weight on the aryloxide data in the discussion to follow.

Solvent Effects. The effect of changing the solvent on intrinsic reactivity and Brønsted behavior is most easily appreciated from Figure 7, where the carboxylate and the primary amine data in

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(20) Terrier, F.; Lelièvre, J.; Chatrousse, A.-P.; Farrell, P. G. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1479.

(21) (a) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University: Ithaca, NY, 1973; Chapter 10. (b) Spencer, T. A.; Kendall, M. C. R.; Reingold, I. D. *J. Am. Chem. Soc.* **1972**, *94*, 1250 and references cited therein. (c) Bernasconi, C. F.; Hibdon, S. A. *Ibid.* **1983**, *105*, 4343.

(22) (a) Hine, J.; Mulders, J. *J. Org. Chem.* **1967**, *32*, 2200. (b) Hine, J.; Mulders, J.; Houston, J. G.; Idoux, J. P. *Ibid.* **1967**, *32*, 2205.

Table VIII. Brønsted β Values[a]

% Me_2SO	$RCOO^-$[b]	RNH_2	pip/mor	ArO^-
		1,3-Indandione (ID)		
10	0.50 ± 0.05	0.43 ± 0.03[d]	0.41 ± 0.03	0.46 ± 0.09
50	0.53 ± 0.03	0.42 ± 0.03	0.40 ± 0.03	0.36 ± 0.06
70	0.63 ± 0.02	0.49 ± 0.04	0.45 ± 0.03	
90	0.74 ± 0.01	0.53 ± 0.02	0.47 ± 0.03	
		Acetylacetone (AA)[c]		
0	0.61 ± 0.03[e]	0.40 ± 0.02	0.37 ± 0.03	
50	0.69 ± 0.04	0.45 ± 0.01	0.42 ± 0.03	
90	0.83 ± 0.01	0.53 ± 0.02	0.51 ± 0.03	

[a] Error limits are standard deviations except for pip/mor pair. [b] Refers to linear portion of Brønsted plots. [c] From ref 1. [d] $MeONH_2$ excluded from the correlation. [e] Omitting AcO^- which deviates negatively; in ref 1 AcO^- was included which resulted in $\beta = 0.51$.

Table IX. Negative Deviations of the Hydroxide Ion and the Water Reactions from the Brønsted Lines[a]

% Me_2SO	k_1^{OH}[b]	$k_1^{H_2O}$[c]
	1,3-Indandione (ID)	
10	−2.24 ± 0.45	−1.43 ± 0.26
50	−3.33 ± 0.22	−1.22 ± 0.23
70		−0.55 ± 0.32
90		−0.53 ± 0.17
	Acetylacetone (AA)	
0	−3.30 ± 0.35	−1.63 ± 0.23
50	−4.87 ± 0.40	−1.07 ± 0.17

[a] Numbers given are in log units. [b] Deviation from $RCOO^-$ lines defined by the weakly basic $RCOO^-$. [c] Deviation from RNH_2 lines.

the various solvents are grouped together (for clarity only 10% and 90% Me_2SO is shown for the amines). We note the following features: (1) The Brønsted plots based on the carboxylate ions show downward curvature at high pK_a in the Me_2SO-rich solvents. This finding confirms the major conclusion from our recent study of the ionization of acetylacetone,[1] namely that this curvature is basically independent of the carbon acid and a solvation effect of the carboxylate ions.

(2) The rate constants for a given $\Delta pK + \log (p/q)$ value are seen to increase with increasing Me_2SO content of the solvent, indicating that the ***intrinsic rate constant*** increases (or the intrinsic barrier decreases). We shall define the intrinsic rate constants as $k_0 = k_1^B/q = k_{-1}^{BH}/p$ where $\Delta pK + \log (p/q) = 0$ (dashed vertical line in Figures 3–7). The log k_0 values in the various solvents are summarized in Table VII, along with similar data for the ionization of acetylacetone (AA). It should be noted that log k_0 for the carboxylate ions in 70% and 90% Me_2SO is based on the *linear* portion of the Brønsted plots.

(3) The increase in log k_0 is significantly larger for the reactions with carboxylate ions than for the amine reactions. For example, for the change from 10% to 90% Me_2SO, log k_0 increases by 1.89 units for $RCOO^-$, by 0.72 for RNH_2, and by 0.88 units for pip/mor (Table VII). The solvent effect on log k_0 for the aryloxide reactions is probably in the same order of magnitude as for the carboxylate ion reactions, but the small solvent range accessible to study and the large experimental error preclude a firm conclusion.

(4) The Brønsted β values which are summarized in Table VIII are seen to increase with increasing Me_2SO content of the solvent, at least above 50% Me_2SO. This increase is more pronounced with the carboxylate ions than with the amines. For example, for the change from 10% to 90% Me_2SO, β increases by 0.24 for $RCOO^-$, by 0.10 for RNH_2, and by 0.08 for pip/mor.

(5) The point for the OH^- reaction displays the usual[23] negative deviation from Brønsted plots defined by the carboxylate ions (not shown in the figures), but this deviation is substantially larger in 50% Me_2SO than in 10% Me_2SO (Table IX). In a similar way, the water reaction deviates negatively from the Brønsted plots defined by the amines[23] (not shown in the figures), but this deviation becomes *smaller* with increasing Me_2SO content of the solvent (Table IX).

All these observations are qualitatively similar to those observed in the deprotonation of acetylacetone (AA).[1] In both the ID and the AA system, they may be understood as manifestations of the Principle of Imperfect Synchronization.[24] This principle states that the intrinsic rate constant, k_0, of a reaction decreases if a product stabilizing factor (e.g., resonance or solvation) develops late but increases k_0 if it develops early along the reaction coordinate. By the same token a *reactant* stabilizing factor decreases k_0 if it is *lost* early but increases k_0 if it is lost late. For product and reactant *de*stabilizing factors, the opposite relations hold.

For example, in the deprotonation of a carbon acid by carboxylate ions, the solvation of the base is a reactant stabilizing factor, the solvation of the carbanion a product stabilizing factor. The effect of these two factors on k_0 can be expressed by an equation of the form of eq 15. $\delta \log k_0$ is the change in log k_0

$$\delta \log k_0 = (\alpha_{des}^{COO^-} - \beta)\delta \log K_1^{des}(COO^-) + (\alpha_{sol}^{C^-} - \beta)\delta \log K_1^{sol}(C^-) \tag{15}$$

with reference to a (hypothetical) state in which the two ions are not stabilized by solvation; $\delta \log K_1^{des}(COO)^- < 0$ is the decrease in the equilibrium constant K_1 brought about by solvation of $RCOO^-$; $\delta \log K_1^{sol}(C^-) > 0$ is the increase in K_1 caused by the solvation of the carbanion; $\alpha_{des}^{COO^-}$ measures the progress of desolvation of $RCOO^-$ at the transition state, $\alpha_{sol}^{C^-}$ the progress in the solvation of C^-, while β is the Brønsted β value.

If solvation of C^- develops late ($\alpha_{sol}^{C^-} - \beta < 0$), this leads to a negative contribution to $\delta \log k_0$; the same is true if desolvation of the base is early ($\alpha_{des}^{COO^-} - \beta > 0$).

Carboxylate Ions and OH^-. When considering the effect of a solvent *change* on k_0, it is convenient to choose one of the *actual* solvents as the reference state. The change in the solvational stabilization of the ions induced by the solvent change is then expressed by means of solvent activity coefficients[14] for the transfer from the reference solvent into another medium. Thus, for the transfer of the reaction of ID with carboxylate ions from 10% Me_2SO (our reference solvent) to the other solvents, we can write eq 16–18. γ_{COO^-} and γ_{C^-} are the solvent activity coefficients for

$$\delta \log k_0(RCOO^-/CH) \approx \delta \log k_0(COO^-) + \delta \log k_0(C^-) \tag{16}$$

$$\delta \log k_0(COO^-) = (\alpha_{des}^{COO^-} - \beta) \log \gamma_{COO^-} \tag{17}$$

$$\delta \log k_0(C^-) = (\alpha_{sol}^{C^-} - \beta)[-(\log \gamma_{C^-})] \tag{18}$$

the carboxylate and carbanion, respectively (we will from here on omit the superscripts "W" and "D" for economy; see eq 14 or Table II), while $\alpha_{des}^{COO^-}$ and $\alpha_{sol}^{C^-}$ have similar meanings as in eq 15, although *numerically* they may be somewhat different from $\alpha_{des}^{COO^-}$ and $\alpha_{sol}^{C^-}$ in eq 15.[24] Note that there is a minus sign in front of log γ_{C^-} in eq 18 but not in front of log γ_{COO^-} in eq 17 because C^- is a product but COO^- is a reactant.

Equation 16 is only approximate because it does not take into account the (typically smaller) changes in the solvation of neutrals

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(23) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475.

(24) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219.

Table X. Solvent Effects on pK_a^{COOH} of RCOOH

		% Me$_2$SO			
	water[a]	10	50	70	90
$Cl_2CHCOOH$	1.23	*b*	2.15 (0.92)	2.87 (1.64)	4.68 (3.45)
$NCCH_2COOH$	2.35	*b*	3.29 (0.94)	4.13 (1.78)	6.25 (3.90)
$ClCH_2COOH$	2.72	*b*	3.71 (0.99)	4.65 (1.93)	6.84 (4.12)
$MeOCH_2COOH$	3.40	3.60	4.56 (1.16)	5.67 (2.27)	8.17 (4.77)
$ClCH_2CH_2COOH$	3.90	4.12	5.20 (1.30)	6.23 (2.33)	8.39 (4.49)
AcOH	4.57	4.78	5.78 (1.21)	6.90 (2.33)	9.53 (4.96)

[a] From ref 1. [b] Not determined. [c] Number in parentheses are $\Delta pK_{COOH} = pK_a^{COOH}(X\%\ Me_2SO) - pK_a^{COOH}(water)$.

BH and CH, a point to which we shall, however, return below.

Qualitatively we can easily see from eq 16 that k_0 must increase ($\delta \log k_0(RCOO^-/CH) > 0$) upon addition of Me$_2$SO. This is because COO$^-$ and C$^-$ are less solvated by Me$_2$SO which translates into $\log \gamma_{COO^-}$ and $\log \gamma_{C^-}$ values which are positive (Table II) and because solvation of anions always seems to lag behind (or desolvation is always ahead of) proton transfer, which means $\alpha_{des}^{COO^-} - \beta > 0$ and $\alpha_{sol}^{C^-} - \beta < 0$. Hence both terms on the right side of eq 16 are positive. Note also that the somewhat larger solvent effect on k_0 for the acetylacetone deprotonation is consistent with larger $\log \gamma_{C^-}$ values (Table II).

How can we understand the increased Brønsted β values and the downward curvature in the Me$_2$SO-rich solvents?

The traditional view[21a,25] is to consider β to be a fairly accurate measure of the degree of proton (or charge) transfer at the transition state and hence to interpret the changes in β simply as a reflection of changes in the degree of proton transfer. With respect to the downward curvature, we have shown previously[1] that it is probably *not* caused by a reduced degree of proton transfer in the transition state but by a solvation effect of the carboxylate ions.

We would like to suggest that the increased β values in the Me$_2$SO-rich solvents may also, at least in part, be the consequence of a solvation effect of the carboxylate ions rather than a reflection of change in the transition-state structure.

Both the downward curvature and the increased β values may be understood in the context of eq 19 which is the same as eq 16 except that it is applied to k_1^B (B = RCOO$^-$) for any given $\Delta pK + \log p/q$ rather than just to k_0 (at $\Delta pK + \log p/q = 0$).

$$\delta \log k_1^B \approx (\alpha_{des}^{COO^-} - \beta) \log \gamma_{COO^-} + (\alpha_{sol}^{C^-} - \beta)[-(\log \gamma_{C^-})] \tag{19}$$

If one assumes that $\log \gamma_{COO^-}$ increases with increasing pK_a of RCOOH, the larger slope of the Brønsted plot (linear part) could simply be a consequence of an increase in $(\alpha_{des}^{COO^-} - \beta) \log \gamma_{COO^-}$ with increasing $\log \gamma_{COO^-}$, even if the underlying β value (as well as $\alpha_{des}^{COO^-}$) remains constant. This is shown schematically in the lower part of Figure 8.

That $\log \gamma_{COO^-}$ indeed increases with increasing pK_a^{COOH}, at least up to methoxyacetate ion, is indicated by the fact that the solvent effect on pK_a^{COOH} increases with increasing pK_a^{COOH}. The relevant data are summarized in Table X. For example, for the change from water to 90% Me$_2$SO, $\Delta pK_{COOH} = pK_a^{COOH}(90\%\ Me_2SO) - pK_a^{COOH}(0\%)$ is 3.45, 3.90, 4.12, 4.77, 4.49, and 4.96 for $Cl_2CHCOOH$, $NCCH_2COOH$, $ClCH_2COOH$, $MeOCH_2COOH$, $ClCH_2CH_2COOH$, and AcOH, respectively; for the change from water to 70% Me$_2$SO, we have ΔpK_{COOH} = 1.64, 1.78, 1.93, 2.27, 2.33, and 2.33, respectively. Since the solvent effect on pK_a^{COOH} is given by eq 20 and γ_{COOH} is likely to have a much smaller pK_a^{COOH} dependence than γ_{COO^-}, the increase in ΔpK_{COOH} with increasing pK_a^{COOH} must be due to an increase in $\log \gamma_{COO^-}$.

$$\Delta pK_{COOH} = \log \gamma_{COO^-} + \log \gamma_{H^+} - \log \gamma_{COOH} \tag{20}$$

The fact that ΔpK_{COOH} and hence $\log \gamma_{COO^-}$ no longer increases with pK_a^{COOH} beyond methoxyacetate indicates the presence of a saturation effect. This provides an explanation of the curvature in the Brønsted plots at high pK_a^{COOH}, since according to eq 19 $\delta \log k_1^B$ no longer increases.

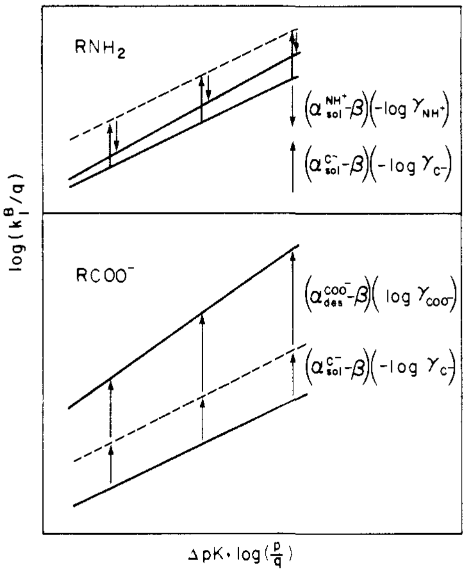

Figure 8. Schematic representations of how the Brønsted plots change with solvent according to eq 19 for RCOO$^-$, according to eq 23 for RNH$_2$.

The stronger negative deviation of the OH$^-$ point from the Brønsted plots in 50% compared to that in 10% Me$_2$SO (Table IX) can be explained along similar lines: $\log \gamma_{OH^-}$ for the change from water to 50% Me$_2$SO (3.40, Table II) is not much larger than $\log \gamma_{AcO^-} = 3.08$ despite the much greater basicity of OH$^-$. Hence $\delta \log k_1^{OH}$ and $\delta \log k_1^{AcO}$ should be quite similar according to eq 19, which leads to a larger negative deviation in 50% Me$_2$SO, mainly because of the larger Brønsted β value in this latter solvent.

It should be noted that the interpretation of the curvature and of the increased negative deviation of the OH$^-$ point with increasing Me$_2$SO content given here differs somewhat from that offered previously.[1] The difference is only apparent, though, and has to do with a different choice of reference states. We recall that in applying eq 19, we use 10% Me$_2$SO as the reference solvent, whereas our previous discussion[1] was based on an equation similar to eq 15; in eq 15 the reference state is a hypothetical solvent in which desolvation of the carboxylate ions does not require energy.

Amines and Water. When the base is an amine, there are no ions on the reactant side but there are two ions on the product side. Hence, the solvent effect on k_0 may be approximated by eq 21 with eq 22, while $\delta \log k_0(C^-)$ is defined as before (eq 18).

$$\delta \log k_0(RNH_2/CH) \approx \delta \log k_0(NH^+) + \delta \log k_0(C^-) \tag{21}$$

$$\delta \log k_0(NH^+) = (\alpha_{sol}^{NH^+} - \beta)[-(\log \gamma_{NH^+})] \tag{22}$$

Ammonium ions are better solvated by Me$_2$SO than by water. This is reflected in negative $\log \gamma_{NH^+}$ values (Table II). Since solvation of the developing positive charge appears to lag behind proton transfer in the transition state,[21a,26] we have $\alpha_{sol}^{NH^+} - \beta$

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(25) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria in Organic Reactions*; Wiley: New York, 1963; pp 156–168.

(26) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969; p 178.

Table XI. Solvent Effects on $pK_a^{NH^+}$ of RNH_2^+ and R_2NH^+

		% Me_2SO			
	water[a]	10	50	70	90
$MeONH_2$	[b]	4.88	[b]	4.70 (−0.18)	5.15 (0.27)
$NCCH_2NH_2$	5.57	5.58	5.39	5.42 (−0.16)	5.95 (0.37)
$EtOOCCH_2NH_2$	7.95	7.97	7.83	7.75 (−0.22)	8.22 (0.25)
$H_2NCOCH_2NH_2$	8.29	8.29	8.28	8.34 (+0.05)	9.19 (0.90)
$MeOCH_2CH_2NH_2$	9.83	9.73	9.63	9.57 (−0.16)	10.20 (0.47)
n-$BuNH_2$	11.12	10.98	10.68	10.49 (−0.49)	10.98 (0.00)
morpholine	8.90	8.84	8.70	8.66 (−0.18)	8.90 (0.06)
piperidine	11.53	11.43	11.05	10.66 (−0.77)	10.72 (−0.61)

[a] From ref 1. [b] Not determined. [c] Numbers in parentheses are $\Delta pK_{NH^+} = pK_a^{NH^+}(X\%\ Me_2SO) - pK_a^{NH^+}(10\%\ Me_2SO)$.

< 0 and $\delta \log k_0(NH^+)$ is negative. This counteracts the positive $\delta \log k_0(C^-)$, and hence the solvent effect on $\log k_0$ for the amines should be smaller than for carboxylate ions, as observed. Note that in the amine reactions, the solvent effect on k_0 is again somewhat smaller than for acetylacetone, reflecting the smaller $\log \gamma_{C^-}$ values (Table II).

The increase (or at least part of it) in the Brønsted slopes with increasing Me_2SO content may, just as with the carboxylate ions, be understood as a solvation effect. If eq 21 is applied to any k_1^B (B = amine), then eq 23 results, and if one assumes that $\log \gamma_{NH^+}$

$$\delta \log k_1^B \approx (\alpha_{sol}^{NH^+} - \beta)[-(\log \gamma_{NH^+})] + (\alpha_{sol}^{C^-} - \beta)[-(\log \gamma_{C^-})] \quad (23)$$

becomes more negative with decreasing $pK_a^{NH^+}$, this will make the $(\alpha_{sol}^{NH^+} - \beta)[-(\log \gamma_{NH^+})]$ term more negative with decreasing $pK_a^{NH^+}$ for constant $\alpha_{sol}^{NH^+} - \beta$. This would indeed lead to a higher slope in the Me_2SO-rich solvents as schematically illustrated in Figure 8 (top).

The assumption that $\log \gamma_{NH^+}$ becomes more negative with increasing acidity is supported by the fact that the solvent effect on $pK_a^{NH^+}$, which can be expressed as eq 24, has a tendency to increase with decreasing $pK_a^{NH^+}$ (Table XI). Assuming that the dependence of $\log \gamma_N$ on $pK_a^{NH^+}$ is negligible, this increased solvent effect with decreasing $pK_a^{NH^+}$ must come from an increase in $-(\log \gamma_{NH^+})$.

$$\Delta pK_{NH^+} = \log \gamma_N + \log \gamma_{H^+} - \log \gamma_{NH^+} \quad (24)$$

It should be noted, though, that the trend of increasing ΔpK_{NH^+} with decreasing $pK_a^{NH^+}$ is only clearly manifested for the pip/mor pair and for n-$BuNH_2$ vs. the whole group of the other primary amines. The somewhat random ΔpK_{NH^+} values for the primary amines may be the reason for the deviation of several of the points from the Brønsted line or, more precisely, for the change in these deviations from one solvent to another. For example, the excellent adherence of glycine amide to the Brønsted plot in 10% Me_2SO, and its negative deviation in the other solvents, may be traced to a large $-(\log \gamma_{NH^+})$, as suggested by the unusually large ΔpK_{NH^+} (e.g., 0.90 in 90% Me_2SO which is larger than for any amine). In contrast, the negative deviation of methoxyamine in 10% Me_2SO, but its excellent fit on the Brønsted plot in 90% Me_2SO, may be attributed to an abnormally small ΔpK_{NH^+} value (0.27 in 90% Me_2SO which is the smallest of all ΔpK_{NH^+} values of primary amines except for n-butylamine).

Possibly because of the many deviant points (or for other reasons), no clear leveling off in the increase in ΔpK_{NH^+} is detectable, and hence the Brønsted plots do not show any clear-cut curvature, which contrasts with the carboxylate case. Note, though, if there was a leveling off in the increase of ΔpK_{NH^+} with decreasing acidity of RNH_3^+, this would lead to *upward* curvature in the Brønsted plot. In fact, the reduced negative deviation of the water points with increasing Me_2SO content of the solvent (Table IX) may be understood in terms of a "leveling off" since $-(\log \gamma_{H^+})$ is only slightly larger than $-(\log \gamma_{NH^+})$ (Table II).

Solvation Effects of the Uncharged Reactants and Products. Even though it is reasonable to assume that solvation effects of the uncharged CH, RNH_2, and RCOOH play a minor role, their effect may not be altogether negligible. In this section, we examine how these effects may affect k_0.

For the reaction of CH with $RCOO^-$, eq 16 becomes eq 25, while for the reaction of CH with an amine, eq 21 expands to eq 26, with eq 27–29 applying.

$$\delta \log k_0(RCOO^-/CH) = \delta \log k_0(COO^-) + \delta \log k_0(C^-) + \delta \log k_0(COOH) + \delta \log k_0(CH) \quad (25)$$

$$\delta \log k_0(RNH_2/CH) = \delta \log k_0(NH^+) + \delta \log k_0(C^-) + \delta \log k_0(N) + \delta \log k_0(CH) \quad (26)$$

$$\delta \log k_0(COOH) = (\alpha_{sol}^{COOH} - \beta)[-(\log \gamma_{COOH})] \quad (27)$$

$$\delta \log k_0(N) = (\alpha_{des}^{N} - \beta) \log \gamma_N \quad (28)$$

$$\delta \log k_0(CH) = (\alpha_{des}^{CH} - \beta) \log \gamma_{CH} \quad (29)$$

Estimates of $\log \gamma_{COOH}$, $\log \gamma_N$, and $\log \gamma_{CH}$ are included in Table II.

Since solvation of *ions* always seems to be late (desolvation early),[24] it is probably a good assumption that the same holds ture for uncharged species as well. Recent results by Jencks et al.,[27] which show that desolvation of amines is ahead of nucleophilic attack in phosphoryl-transfer reactions, support our assumption. This implies $\alpha_{sol}^{COOH} < \beta$, $\alpha_{des}^{CH} > \beta$, and $\alpha_{des}^{N} > \beta$ and hence

$$\delta \log k_0(COOH) < 0$$

$$\delta \log k_0(CH) < 0$$

$$\delta \log k_0(N) \approx 0$$

Note the fact that $\delta \log k_0(N) \approx 0$ is a consequence of $\log \gamma_N \approx 0$ not of $\alpha_{des}^N - \beta \approx 0$; i.e., there is not contradiction with Jencks's[27] results.

These considerations suggest that, if anything, the solvation/desolvation of the neutrals should make a *negative* contribution to $\delta \log k_0$, and hence the effect from the late solvation/early desolvation of ions may actually be larger than implied by eq 16 and 21.

Comparison with Acetylacetone. It is instructive to compare the k_0 values for the ionization of ID with those of the ionization of acetylacetone (AA). We shall restrict our comparisons to the amine reactions (Table VII) because the k_0 values for the deprotonation of AA by carboxylate ions are very uncertain, due to long extrapolations.[1]

We note that k_0 for ID is larger than for AA by about 0.4 log units in 10% and 50% Me_2SO and by about 0.1 (primary amines) to 0.2 log units (pip/mor) in 90% Me_2SO. One can think of several possible reasons for these differences in k_0.

(1) The approach of the base to ID might be slightly less obstructed than with AA. However, if steric hindrance indeed played a significant role in the AA reaction, the amount by which k_0 for the pip/mor pair is generally larger than k_0 for the primary amines should be smaller with AA than with ID. This is becasue of the greater bulk of pip/mor. This is not borne out by the results. Furthermore, the solvent dependence of the k_0^{ID}/k_0^{AA} ratios cannot be explained by a steric effect either.

(2) The factors which lead to the higher acidity of ID compared to AA may at the same time be responsible for the increased k_0. One of these factors is the coplanarity of ID which facilitates the

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[27] Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

π-overlap in the anion. Another is the electron-withdrawing effect of the benzene ring compared to the methyl groups in AA. That this electronic effect must play a significant role in determining the pK_a values is seen by the fact that the pK_a *difference* between ID and AA becomes larger with increasing Me_2SO content, showing the decrease in the attenuation of the electronic effect on the anion in the less solvating medium.

If coplanarity were the reason for the higher k_0 with ID, one would not expect the k_0^{ID}/k_0^{AA} ratio to depend on the solvent. If the electronic effect were the *direct* cause of the difference in k_0, the k_0^{ID}/k_0^{AA} ratio should become larger rather than smaller in the Me_2SO-rich solvents, due to the reduced attenuation of the electronic effect.

(3) A more satisfactory way to explain the enhanced k_0 for ID is that it is related to the electron-withdrawing effect in an *indirect* way. That is, the electronic effect can be viewed as a stabilization of the developing negative charge which in the transition state is to a significant extent localized on carbon. In other words, it is the retarded delocalization of the negative charge into the carbonyl groups (imbalanced transition state) that leads to the substituent effect on k_0. According to this view, the substituent effect on k_0 is a *response* to the imbalance rather than a primary *cause*, as discussed in more detail elsewhere.[24]

The usual manifestation of this imbalance is that the Brønsted α value obtained by varying the pK_a of the carbon acid is larger than the β value obtained by varying pK_a^{BH}. The substituent dependence of k_0 is just a different manifestation of the same phenomenon.[24,28]

That the Brønsted α value indeed exceeds β in our system is seen by defining α as log $[k_1^B(ID)/k_1^B(AA)]/(pK_a^{AA} - pK_a^{ID})$ for a given base B. For example, with piperidine one obtains $\alpha = 0.55$ in 50% Me_2SO and $\alpha = 0.56$ in 90% Me_2SO. Hence the imbalances are $\alpha - \beta = 0.55 - 0.41$[29] $= 0.14$ in 50% and $\alpha - \beta = 0.56–0.49$[29] $= 0.07$ in 90% Me_2SO. Note that the reduction in the imbalance in the Me_2SO-rich solvent of course parallels the decrease in the k_0^{ID}/k_0^{AA} ratio.

Conclusions. (1) The intrinsic rate constant for ionization of ID by carboxylate ions increases strongly upon addition of Me_2SO to the solvent. This increase can be attributed to the combination of two effects: one is the late solvation of the carbanion, the other the early desolvation of the carboxylate ion. These effects can be described by eq 16.

(2) The increase in k_0 for the reaction with amines is much smaller because the rate-enhancing contribution of the carboxylate ions is replaced by a rate-*retarding* effect which arises from the late solvation of the protonated amine. This is described by eq 21.

(3) The Brønsted β values increase with Me_2SO content of the solvent. At least part of the reason for this increase may be the larger solvent effect on the stability of the carboxylate ions with increasing pK_a^{COOH} (larger log γ_{COO^-}) and a larger solvent effect on the stability of the protonated amines with decreasing p$K_a^{NH^+}$ (more negative log γ_{NH^+}), respectively.

(4) With the carboxylate ions, the increase in log γ_{COO^-} levels off at high pK_a^{COOH} which is the probable cause for the downward curvature of the Brønsted plots in the Me_2SO-rich solvents.

(5) The value of log γ_{OH^-} is disproportionately small relative to p$K_a^{H_2O}$ when compared with log γ_{COO^-}. This is the probable reason why the OH^- point deviates more negatively from the Brønsted line defined by the carboxylate ions when the Me_2SO content of the solvent increases. In a similar way, the increasingly less negative deviation of the water point from a Brønsted line defined by the amines can be arttributed to a disproportionately small $-(\log\gamma_{H^+})$ value (relative to p$K_a^{H_3O^+}$).

(6) The fact that the identity of the deviating points from the Brønsted plots defined by the primary amines changes with solvent may be attributed to differences in log γ_{NH^+} for certain amines.

(7) The larger k_0 value for the ID compared to the AA system is a consequence of an exalted substituent effect on the transition state which is caused by the lag of charge delocalization behind proton transfer. Another manifestation of the same phenomenon is that $\alpha > \beta$ ("imbalance").

Experimental Section

Materials. 1,3-Indandione (Aldrich) was recrystallized from ethanol, mp 131–132 °C (130 °C).[30] The 1,3-indandione anion (ID^-) has a $\lambda_{max} = 421$ nm (ϵ 2190) in 10% Me_2SO and of 414 ± 1 nm (ϵ 2400 ± 100) in the other solvent mixtures used in this study. The purification, where needed, of the amines and the carboxylic acids has been described in a previous paper.[1] Phenol was recrystallized from petroleum ether, 3,5-dimethylphenol and 4-chlorophenol from hexanes, and 4-cyanophenol from water, while 3-chloro- and 3,5-dichlorophenol were used without further purification. Me_2SO was stored over 4-Å molecular sieves prior to use.

Kinetic Experiments and pK_a Determinations. The methods used were basically the same as described before.[1] Due to the relatively low extinction coefficient of ID^- at the wavelength used for the kinetic measurements (415–420 nm), the excess of the buffer over the ID or ID^- concentration was sometimes less than 10-fold. When this was the case, a small correction was applied in the calculation of k_{obsd}.

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(28) Marcus, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 7224.

(29) Average β value for ID and AA.

(30) Sieglitz, A. *Chem. Ber.* **1951**, *84*, 607.

Singlet Oxygen Production in Superoxide Ion–Halocarbon Systems

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Abstract: A search for singlet oxygen chemiluminescence at 1268 nm was made in a number of reactions of superoxide ion. Carbon tetrachloride and carbon tetrabromide reacted with suspended potassium superoxide to produce 1268-nm emission consistent with singlet oxygen. Chloroform was less reactive but produced 1268-nm emission when the concentration of superoxide ion in the halocarbon phase was increased with 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6). The dismutation of superoxide ion in deuterium oxide was not accompanied by 1268-nm chemiluminescence. Less than 0.02 mol of singlet oxygen was produced per mole of superoxide ion between p^{2}H 6 and 9.

The suggestion of Khan that some electron-transfer reactions of superoxide ion (O_2^-) produce singlet oxygen ($^1O_2$)[1] has stimulated many investigators to search for $^1O_2$ as a product of the spontaneous dismutation of O_2^- in H_2O. Most studies using

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