J. Org. Chem. **1997,** *62,* 8162−8170

Kinetics of Proton Transfer from Benzoylnitromethane and 1,2-Diphenyl-2-nitroethanone to Various Bases. Resonance, Inductive, Solvation, Steric, and Transition State Hydrogen-Bonding Effects on Intrinsic Rate Constants

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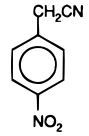
Received July 11, 1997[⊗]

The replacement of a hydrogen in nitromethane and in phenylnitromethane by the PhCO group has a strong acidifying effect, i.e., $PhCOCH_2NO_2$, **5**, is 5.8, 6.6, and 8.6 pK_a units more acidic than CH_3NO_2 in water, 50% DMSO−50% water (v/v), and 90% DMSO−10% water (v/v), respectively, and PhCOCH(Ph)NO_2, **6**, is 2.0, 3.0, and 3.2 pK_a units more acidic than $PhCH_2NO_2$ in the same solvents. A major focus of this paper is an attempt to sort out the relative contributions of resonance, inductive/field, and solvation effects that lead to the increased acidities. To this end rate constants for the reversible deprotonation of **5** by secondary alicyclic amines in water, 50% DMSO−50% water (v/v), and 90% DMSO−10% water (v/v) and for the reversible deprotonation of **6** by secondary alicyclic amines, carboxylate ions, thiolate ions, and aryloxide ions in water, by secondary alicyclic and primary aliphatic amines in 50% DMSO, and by secondary alicyclic anions in 90% DMSO were determined. From Brønsted plots based on these data the intrinsic rate constants (k_o) for the reactions of **5** and **6** with the various buffer families were obtained and compared with previously determined k_o values for the deprotonation of CH_3NO_2 and $PhCH_2NO_2$, respectively. An analysis of the changes in k_o induced by the introduction of the PhCO group, coupled with a comparison of solvent transfer activity coefficients for the transfer of the anions ($\mathbf{5}^-$ and $\mathbf{6}^-$) from water to 50% and 90% DMSO with those for $CH_2{=}NO_2^-$ and $PhCH{=}NO_2^-$, respectively, indicates a substantial increase in the resonance stabilization of $\mathbf{5}^-$ relative to $CH_2{=}NO_2^-$ and a corresponding sharp drop in the solvational stabilization by hydrogen bonding from water; the effects on $\mathbf{6}^-$ are qualitatively similar but quantitatively much smaller. Our study also shows that the intrinsic rate constant for proton transfer from **6** to thiolate ions is higher than for proton transfer to aryl oxide ions and amines. This result indicates that, in contrast to most other proton-transfer reactions, hydrogen-bonding stabilization of the transition state for deprotonation of **6** is not an important factor.

Introduction

The study of proton transfers from carbon acids continues to provide insights into the factors that affect chemical reactivity in reactions that lead to carbanions. The task of identifying these factors has been greatly facilitated by focusing on the intrinsic barriers ($\Delta G_o^{\ddagger}$)[1] or intrinsic rate constants (k_o)[1] of the reaction because these parameters allow a separation between thermodynamic and purely kinetic effects. A recurring theme has been that resonance and solvation effects in the carbanion are among the most important factors that affect intrinsic rate constants or intrinsic barriers.[2] The underlying reason for this phenomenon is that neither resonance development nor solvation of the incipient carbanion are able to keep pace with the progress of proton transfer at the transition state; i.e., the transition state is imbalanced. This means that the stabilization of the transition state is disproportionately weak compared to that of the carbanion and this results in a depressed intrinsic rate constant,[3] the more so the greater the stabilization of the carbanion. This, in a nutshell, explains why the intrinsic rate constants are low for reactions that lead to strongly resonance stabilized and/or highly solvated carbanions but high in situations where there is weak resonance and solvation.

A question that has not received the same level of attention refers to possible synergistic or antagonistic effects of two or more π-acceptors that may all potentially contribute to the resonance stabilization of a carbanion. A case in point is the comparison between CH_3NO_2 and $PhCH_2NO_2$. Here the additional resonance effect provided by the phenyl group manifests itself in a lower intrinsic rate constant for the deprotonation of $PhCH_2NO_2$ compared to that of CH_3NO_2.[4] A similar phenomenon is seen in the comparison among **1**,[5] **2**,[6] and **3**:[5] k_o for **3**



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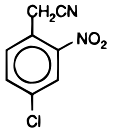

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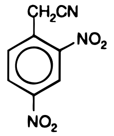

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which has two nitro groups is substantially lower than for **1** and **2** which have only one nitro group.

[⊗] Abstract published in *Advance ACS Abstracts,* October 15, 1997.

(1) The intrinsic barrier (intrinsic rate constant) of a reaction with a forward rate constant k_1 and a reverse rate constant k_{-1} is defined as $\Delta G_o^{\ddagger} = \Delta G_1^{\ddagger} = \Delta G_{-1}^{\ddagger}$ when $\Delta G° = 0$ (as $k_o = k_1 = k_{-1}$ when $K_1 = 1$). For proton transfers, statistical factors are usually included, see below.

(2) For reviews, see: (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20,* 301. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25,* 9. (c) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27,* 119.

(3) The reduction in the intrinsic rate constant by the lag in resonance development or solvation behind proton transfer is a manifestation of a more general phenomenon that has been called the principle of nonperfect synchronization (PNS).[2]

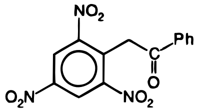
(4) Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J.-X. *J. Org. Chem.* **1988**, *53,* 3342.

(5) Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105,* 4343.

(6) Bernasconi, C. F.; Wenzel, P. J. *J. Am. Chem. Soc.* **1996**, *118,* 11446.

S0022-3263(97)01259-0 CCC: $14.00

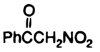
On the other hand, several cases are known where the introduction of an additional π-acceptor leads to an *increase* rather than a decrease in the intrinsic rate constant. Examples include 2,4,6-trinitrotoluene vs **4**,[7]



4

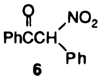
and 2,2′,4,4′,6-pentanitrodiphenylmethane vs 2,2′,4,4′,6,6′-hexanitrodiphenylmethane.[8] In the first example steric crowding prevents the PhCO group from being coplanar with the picryl moiety; in the second example, the 6′-nitro group has a similar effect and turns the second picryl group out of the plane of the first one. Hence the PhCO group in the conjugate base of **4** and the second picryl group in the 2,2′,4,4′,6,6′-hexanitrodiphenylmethide ion cannot act as π-acceptors and therefore do not lead to a lowering of the intrinsic rate constant. The fact that k_o is enhanced can be attributed to a disproportionately large transition state stabilization by the electron-withdrawing *inductive/field* effect of the PhCO and picryl groups, respectively. This is a direct consequence of the lag in charge delocalization behind proton transfer which, at the transition state, leads to a larger fraction of charge on the carbon than in the product anion.

In the present paper we pursue the issue of interplay between resonance, inductive/field, and solvation effects further. To this end we have studied the kinetics of the reversible proton transfer from benzoylnitromethane (**5**)



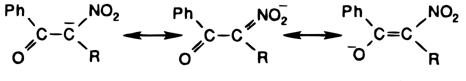
$Ph\overset{\overset{O}{\|}}{C}CH_2NO_2$

5



6

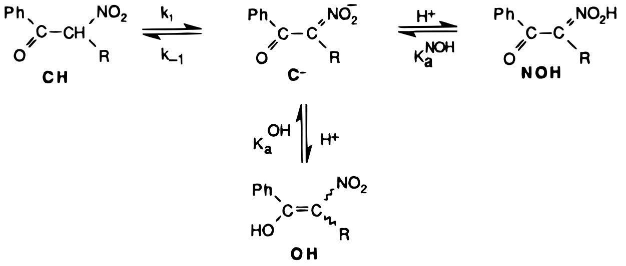
to a series of secondary alicyclic amines and from 1,2-diphenyl-2-nitroethanone (**6**) to primary and secondary amines as well as to aryloxide, carboxylate, and thiolate ions in water, 50% DMSO−50% water, and 90% DMSO−10% water. A specific question we would like to address is whether or not the carbonyl group is a strong participant in the π-delocalization of the respective anions, i.e., whether 5^- (c) and 6^- (c) are major contributors to the



5^- (a) (R = H) 5^- (b) 5^- (c)
6^- (a) (R = Ph) 6^- (b) 6^- (c)

respective resonance hybrids. The PhCO group being almost as good a π-acceptor as the nitro group,[9] one might reasonably expect the resonance effect of the PhCO group to be substantial. According to space-filling molecular models, no significant steric hindrance to coplanarity of the OCCNO$_2$ atoms in 5^- is expected that would impede π-overlap. The situation in 6^- is less clear-cut; here steric congestion forces either the nitro and/or the α-phenyl group somewhat out of the plane, which is likely to reduce the degree of resonance stabilization of 6^- compared to that of 5^-.

Scheme 1



Our approach to this question will primarily be based on comparisons of pK_a values and intrinsic rate constants for proton transfer between **5** and CH$_3$NO$_2$ and between **6** and PhCH$_2$NO$_2$, respectively, and on solvent transfer activity coefficients of 5^- and 6^-, respectively.

Another problem to be discussed in this paper is the relative importance of hydrogen-bonding stabilization of the transition state of proton transfers from carbon acids. The fact that the intrinsic rate constant for the deprotonation of carbon acids by thiolate ions is usually lower than for the deprotonation by oxyanions or amines[11−13] has been interpreted to mean that hydrogen bonding is a significant factor in transition state stabilization.[13] However, the intrinsic rate constant for the deprotonation of phenylnitromethane and (4-nitrophenyl)nitromethane by thiolate ions has recently been shown to be *higher* than for the reaction with oxyanions and amines,[14] implying that transition state stabilization by hydrogen bonding may not be important here. Our results, based on a determination of intrinsic rate constants for the deprotonation of **6** by amines and thiolate, aryl oxide, and carboxylate ions in water, will show that the behavior of **6** is similar to that of phenylnitromethane in this respect.

Results

Rate and pK_a Determinations. Proton-transfer rates were determined in water, 50% DMSO−50% water (v/v), and 90% DMSO−10% water (v/v) at 20 °C. The reaction can be described by Scheme 1,[15]

$$k_1 = k_1^{\mathrm{H_2O}} + k_1^{\mathrm{OH}} a_{\mathrm{OH^-}} + k_1^{\mathrm{B}}[\mathrm{B}] \tag{1}$$

$$k_{-1} = k_{-1}^{\mathrm{H}} a_{\mathrm{H^+}} + k_{-1}^{\mathrm{H_2O}} + k_{-1}^{\mathrm{BH}}[\mathrm{BH}] \tag{2}$$

where B and BH stand for the buffer base and buffer acid, respectively; charges have been omitted for simplicity. Note that the enol (**OH**) and nitronic acid form (**NOH**) only play a role in the reactions of **6** performed in carboxylate buffers.

Rate constants, k_1^{B} and k_{-1}^{BH}, for the reaction of **5** with secondary alicyclic amines in water, 50% DMSO, and 90% DMSO are summarized in Table 1; the k_1^{B} and k_{-1}^{BH} values for the reaction of **6** with a variety of buffers are reported in Tables 2 (water) and 3 (50% and 90% DMSO). Spectrophotometrically determined pK_a^{CH} and pK_a^{app} values are reported in Table 4; pK_a^{CH} refers to the acidity

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[7] Moutiers, G.; El Fahid, B.; Collot, A.-G.; Terrier, F. *J. Chem. Soc., Perkin Trans. 2* **1996**, 49.

[8] Terrier, F.; Xie, H.-Q.; Farrell, P. G. *J. Org. Chem.* **1990**, *55*, 2610.

[9] For example, $\sigma_R(\mathrm{NO_2}) = 0.16$, $\sigma_R(\mathrm{PhCO}) = 0.16$; $R^-(\mathrm{NO_2}) = 0.62$, $R^-(\mathrm{PhCO}) = 0.52$; $(\sigma_P^- - \sigma_m)(\mathrm{NO_2}) = 0.56$, $(\sigma_P^- - \sigma_m)(\mathrm{PhCO}) = 0.45$.[10]

[10] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

[11] Ahrens, M.-L.; Eigen, M.; Kruse, W.; Maass, G. *Ber. Bunsen-Ges.* **1970**, *74*, 380.

[12] Pohl, E. R., Hupe, D. *J. Am. Chem. Soc.* **1978**, *100*, 8130.

[13] Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7117.

[14] Bernasconi, C. F.; Wiersema, D.; Stronach, M. W. *J. Org. Chem.* **1993**, *58*, 217.

[15] For simplicity only one of the resonance structures of C^- is shown in the scheme.

Table 1. Proton Transfer Rate Constants for the Reaction of 5 with Secondary Alicyclic Amines at 20 °C

base	pK_a^{BH}	k_1^B,[a] $M^{-1} s^{-1}$	k_{-1}^{BH},[b] $M^{-1} s^{-1}$
	Water, $\mu = 0.5$ M (KCl)[c]		
morpholine	8.90	4.97×10^3	0.29
PZ-CH_2CH_2OH[d]	9.45	1.27×10^4	0.21
piperazine	10.12	2.94×10^4	0.10
piperidine	11.53	8.32×10^4	0.011
	50% DMSO−50% Water, $\mu = 0.5$ M (KCl)[e]		
morpholine	8.72	7.88×10^3	1.11
PZ-CH_2CH_2OH[d]	9.51	2.19×10^4	0.50
piperazine	9.90	3.63×10^4	0.34
piperidine	11.02	8.69×10^4	0.061
	90% DMSO−10% Water, $\mu = 0.06$ M (KCl)[f]		
morpholine	8.91	2.27×10^4	6.85×10^1
PZ-CH_2CH_2OH[d]	9.53	5.08×10^4	3.68×10^1
piperazine	10.23	1.87×10^5	2.70×10^1
piperidine	10.74	2.06×10^5	9.19

[a] k_1^B was determined from slopes according to eq 15; experimental error was 2−4% based on standard deviations. [b] k_{-1}^{BH} determined as $k_1^B K_a^{BH}/K_a^{CH}$. [c] $pK_a^{CH} = 4.67 \pm 0.02$. [d] 1-(2-Hydroxyethyl)piperazine. [e] $pK_a^{CH} = 4.87 \pm 0.02$. [f] $pK_a^{CH} = 6.39 \pm 0.07$.

Table 2. Proton Transfer Rate Constants for the Reaction of 6[a] with Various Bases in Water at 20 °C, μ = 0.5 M (KCl)

base	pK_a^{BH}	k_1^B,[b] $M^{-1} s^{-1}$	k_{-1}^{BH},[c] $M^{-1} s^{-1}$
$NCCH_2COO^-$	2.35	2.61×10^{-2}	1.28×10^1
$ClCH_2COO^-$	2.72	5.24×10^{-2}	1.09×10^1
$MeOCH_2COO^-$	3.40	1.24×10^{-1}	5.41
$ClCH_2CH_2COO^-$	3.90	2.88×10^{-1}	3.79
CH_3COO^-	4.57	5.90×10^{-1}	1.74
morpholine	8.90	7.14×10^1	9.86×10^{-3}
PZ-CH_2CH_2OH[d]	9.45	1.58×10^2	6.15×10^{-3}
piperazine	10.12	4.63×10^2	3.85×10^{-3}
piperidine	11.53	1.76×10^3	5.69×10^{-4}
$CF_3CH_2S^-$	7.51	8.83×10^1	2.99×10^{-1}
$MeO_2CCH_2S^-$	7.90	2.64×10^2	3.64×10^{-1}
$MeO_2CCH_2CH_2S^-$	9.33	1.04×10^3	5.21×10^{-1}
$HOCH_2CH_2S^-$	9.65	1.30×10^3	3.19×10^{-2}
4-$NCC_6H_4O^-$	8.04	2.60×10^2	2.60×10^{-1}
3-$ClC_6H_4O^-$	9.13	1.31×10^3	1.10×10^{-1}
$C_6H_5O^-$	10.02	3.22×10^3	3.40×10^{-2}
4-$MeOC_6H_4O^-$	10.21	5.08×10^3	3.40×10^{-2}

[a] $pK_a^{CH} = 5.04 \pm 0.06$. [b] k_1^B was determined from slopes according to eq 15 for all bases except carboxylate ions; experimental error was 3−5% based on standard deviations. For the carboxylate ions, k_1^B was obtained as $k_1^B = k_{-1}^{BH}K_a^{CH}/K_a^{BH}$. [c] k_{-1}^{BH} was determined from slopes according to eq 16 and to eq 17 for the carboxylate ions, with K_a^{app} obtained as explained in the Experimental Section; experimental error was 4−6% based on standard deviations. For all the other bases k_{-1}^{BH} was obtained as $k_1^B K_a^{BH}/K_a^{CH}$. [d] 1-(2-Hydroxyethyl)piperazine.

Table 3. Proton Transfer Rate Constants for the Reaction of 6 with Various Bases in DMSO−Water Mixtures at 20 °C

base	pK_a^{BH}	k_1^B,[a] $M^{-1} s^{-1}$	k_{-1}^{BH},[b] $M^{-1} s^{-1}$
	50% DMSO−50% Water, $\mu = 0.5$ M (KCl)[c]		
$EtOOCCH_2NH_2$	7.83	2.24×10^1	5.37×10^{-2}
$H_2NCOCH_2NH_2$	8.28	2.30×10^1	1.95×10^{-2}
$MeOCH_2CH_2NH_2$	9.63	1.88×10^2	7.14×10^{-3}
n-$BuNH_2$	10.68	7.65×10^2	2.59×10^{-3}
PZ-CHO[d]	7.97	3.26×10^1	5.70×10^{-2}
morpholine	8.72	1.15×10^2	3.60×10^{-2}
PZ-CH_2CH_2OH[e]	9.51	2.23×10^2	1.12×10^{-2}
piperazine	9.90	5.64×10^2	1.15×10^{-2}
piperidine	11.02	1.66×10^3	2.60×10^{-3}
	90% DMSO−10% Water, $\mu = 0.06$ M (KCl)[f]		
morpholine	8.91	3.82×10^2	2.77×10^1
PZ-CH_2CH_2OH[e]	9.53	9.25×10^2	1.61×10^1
piperazine	10.23	3.00×10^3	1.04×10^1
piperidine	10.74	3.65×10^3	4.58

[a] See footnote *a* in Table 1. [b] See footnote *b* in Table 1. [c] $pK_a^{CH} = 5.21 \pm 0.10$. [d] 1-Formylpiperazine. [e] 1-(2-Hydroxyethyl)piperazine. [f] $pK_a^{CH} = 7.77 \pm 0.09$.

constant of **CH** while pK_a^{app} refers to an apparent acidity constant defined by $1/K_a^{app} = 1/K_a^{OH} + 1/K_a^{NOH}$ with K_a^{OH} and K_a^{NOH} being the acidity constants of **OH** and **NOH**, respectively. In water, pK_a^{app} for **6** was determined with cyanoacetate buffers, in 50% DMSO with chloroacetate and in 90% DMSO in dichloroacetate buffers. The procedures for obtaining the various rate constants and pK_a values are described in the Experimental Section.

Solvent Activity Coefficients. To assess the various contributions to the solvent effect on pK_a^{CH}, such as changes in the solvation of **CH**, **C**$^-$, and the hydronium ion, we determined the solvent transfer activity coefficients,[16] ${}^{I}\gamma^{II}_{CH}$ for the transfer of **CH** from solvent I to solvent II, e.g., I = water, II = 90% DMSO. From these ${}^{I}\gamma^{II}_{CH}$ values, the solvent activity coefficients, ${}^{I}\gamma^{II}_{C^-}$, for the transfer of **C**$^-$ from solvent I to solvent II, could then be obtained by applying the Parker[16] formalism of eq 3.

$$ {}^{I}\Delta^{II}pK_a^{CH} = \log {}^{I}\gamma^{II}_{C^-} + \log {}^{I}\gamma^{II}_{H^+} - \log {}^{I}\gamma^{II}_{CH} \quad (3) $$

In this equation ${}^{I}\Delta^{II}pK_a^{CH}$ represents the difference between the pK_a^{CH} values in the two solvents, i.e., ${}^{I}\Delta^{II}pK_a^{CH} = pK_a^{CH}(II) - pK_a^{CH}(I)$ while $\log {}^{I}\gamma^{II}_{CH}$, $\log {}^{I}\gamma^{II}_{C^-}$, and $\log {}^{I}\gamma^{II}_{H^+}$ are related to the standard free energies of transfer by eqs 4−6, respectively;[17] $\log {}^{I}\gamma^{II}_{H^+}$ is known from Wells' work.[18]

$$ {}^{I}\delta^{II}\Delta G^{\circ}_{tr}(CH) = 2.303RT \log {}^{I}\gamma^{II}_{CH} \quad (4) $$

$$ {}^{I}\delta^{II}\Delta G^{\circ}_{tr}(C^-) = 2.303RT \log {}^{I}\gamma^{II}_{C^-} \quad (5) $$

$$ {}^{I}\delta^{II}\Delta G^{\circ}_{tr}(H^+) = 2.303RT \log {}^{I}\gamma^{II}_{H^+} \quad (6) $$

We determined $\log {}^{I}\gamma^{II}_{CH}$ by carrying out distribution experiments between n-heptane and the various solvents of interest, as described by Watarai[19] and by Bernasconi and Bunnell.[20] These experiments provided partition coefficients from which $\log {}^{I}\gamma^{II}_{CH}$ and $\log {}^{I}\gamma^{II}_{C^-}$ were calculated as described in the Experimental Section. They are reported in Table 5. Note that a positive $\log {}^{I}\gamma^{II}_{X}$ value means that X is less strongly solvated in solvent II compared to solvent I, and a negative $\log {}^{I}\gamma^{II}_{X}$ value means the opposite.

Discussion

Acidity Constants, UV Spectra, and Solvent Transfer Activity Coefficients. pK_a^{CH} values are reported in Table 4 along with the pK_a^{CH} of CH_3NO_2 and $PhCH_2NO_2$. Comparison between **5** and CH_3NO_2 shows a strong acidifying effect of the benzoyl group which amounts to 5.8, 6.6, and 8.6 pK_a units in water, 50% DMSO, and 90% DMSO, respectively. This contrasts

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

(17) The standard state refers to an arbitrarily chosen reference solvent,[16] i.e., solvent I in our case.

(18) Wells, C. F. In *Thermodynamic Behavior of Electrolytes in Mixed Solvents*; Furter, W. F., Ed.; Advances in Chemistry 177; American Chemical Society: Washington, DC, 1979; p 53.

(19) (a) Watarai, H.; Suzuki, N. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1848. (b) Watarai, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3019.

(20) Bernasconi, C. F.; Bunnell, R. D. *J. Am. Chem. Soc.* **1988**, *110*, 2900.

Table 4. pK_a Values of 5 and 6 at 20 °C[a]

solvent	pK_a^{CH}	pK_a^{app}	pK_a^{CH} − pK_a^{app}
	$PhCOCH_2NO_2$ (**5**)		
water	4.97[b] (10.76)[c]		
50% DMSO−50% water	5.17[b] (11.80)[c]		
90% DMSO−10% water	6.69[b] (15.28)[c]		
	$PhCOCH(Ph)NO_2$ (**6**)		
water	5.04 ± 0.06 (7.07)[d]	2.38 ± 0.05 (3.64)[e]	2.66 ± 0.11 (3.43)[f]
50% DMSO−50% Water	5.21 ± 0.10 (8.23)[d]	3.42 ± 0.05 (4.75)[e]	1.79 ± 0.15 (3.48)[f]
90% DMSO−50% Water	7.77 ± 0.09 (10.98)[d]	4.78 ± 0.07 (7.73)[e]	2.99 ± 0.16 (3.25)[f]

[a] $\mu = 0.5$ M (KCl) in water and 50% DMSO−50% water; $\mu = 0.06$ M (KCl) in 90% DMSO−10% water. [b] Statistically corrected for two equivalent protons. [c] pK_a^{CH} of CH_3NO_2 after statistical correction for three equivalent protons, from ref 4. [d] pK_a^{CH} of $PhCH_2NO_2$ after statistical correction, from ref 4. [e] pK_a^{NOH} of $PhCH{=}NO_2H$, from ref 4. [f] pK_a^{CH} − pK_a^{NOH} for $PhCH_2NO_2$.

Table 5. Solvent Transfer Activity Coefficients, log $^{I}\gamma^{II}_{X}$, for the Transfer of Various Species X from Solvent I to Solvent II[a]

	log $^{0}\gamma^{50}_{X}$ [b]	log $^{0}\gamma^{90}_{X}$ [c]	log $^{50}\gamma^{90}_{X}$ [d]
H^+ [e]	−1.93	−3.05	−1.12
5[f]	−1.13	−3.10	−1.97
5$^-$	1.00	1.67	0.67
CH_3NO_2 [g]	−0.10	−0.87	−0.77
$CH_2{=}NO_2^-$	2.87	6.70	3.83
6[h]	−0.81	−2.88	−2.07
6$^-$	1.29	2.90	1.61
$PhCH_2NO_2$[g]	−1.11	−2.86	−1.75
$PhCH{=}NO_2^-$	1.99	4.09	2.10

[a] Experimental uncertainty in log $^{I}\gamma^{II}_{X}$ is better than ±0.06. [b] I = water, II = 50% DMSO. [c] I = water, II = 90% DMSO. [d] I = 50% DMSO, II = 90% DMSO. [e] Reference 18. [f] $^{0}P^{H} = 7.58$, $^{50}P^{H} = 0.558$, $^{90}P^{H} = 0.006$ (see eqs 19 and 20). [g] Reference 20. [h] $^{0}P^{H} = 13.4$, $^{50}P^{H} = 2.09$, $^{90}P^{H} = 1.76 \times 10^{-2}$ (see eqs 18 and 19).

with the much more modest acidifying effect of the benzoyl group in **6** when compared to $PhCH_2NO_2$; here the pK_a^{CH} value decreases by only 2.0, 3.0, and 3.2 units, respectively. As a result the absolute acidity of **5** is about the same as that of **6** in water and 50% DMSO and about 1.1 pK_a units higher than that of **6** in 90% DMSO.

The PhCO group is both a strong π-acceptor and inductively electron withdrawing, and hence its acidifying influence on **5** and **6** must be the combined result of these two effects. The fact that the acidifying effect on **6** is much weaker than that on **5** suggests that the charge delocalization into the carbonyl group of **6**$^-$ (**6**$^-$**(c)**) is less effective than into the carbonyl group of **5**$^-$ (**5**$^-$**(c)**), presumably because of steric hindrance of π-overlap in **6**$^-$**(c)**. Alternatively and/or additionally, the steric crowding around the α-carbon suggested by molecular models may prevent the nitro and/or the phenyl group from being coplanar with the rest of the π-system, thereby diminishing the resonance effect of these groups.

The notion that the resonance structure **5**$^-$**(c)** plays an important role, thereby leading to a greater dispersion of the negative charge in **5**$^-$ than in $CH_2{=}NO_2^-$, is supported by the solvent transfer activity coefficients summarized in Table 5. The log $^{I}\gamma^{II}_{C^-}$ values for **5**$^-$ are much smaller than for $CH_2{=}NO_2^-$; e.g., log $^{0}\gamma^{90}_{C^-} = 1.67$ for **5**$^-$ contrasts with log $^{0}\gamma^{90}_{C^-} = 6.70$ for $CH_2{=}NO_2^-$. The large value for $CH_2{=}NO_2^-$ reflects the much stronger solvation of this anion by water than by DMSO, a consequence of the highly concentrated negative charge on the nitro group which in water leads to hydrogen bonding. The much smaller log $^{0}\gamma^{90}_{C^-}$ value for **5**$^-$ indicates that hydrogen-bonding solvation is less important, as expected for an anion whose charge is much more dispersed; part of the reduction in log $^{0}\gamma^{90}_{C^-}$ may also be the result of better solvation in DMSO of **5**$^-$ compared to $CH_2{=}NO_2^-$.

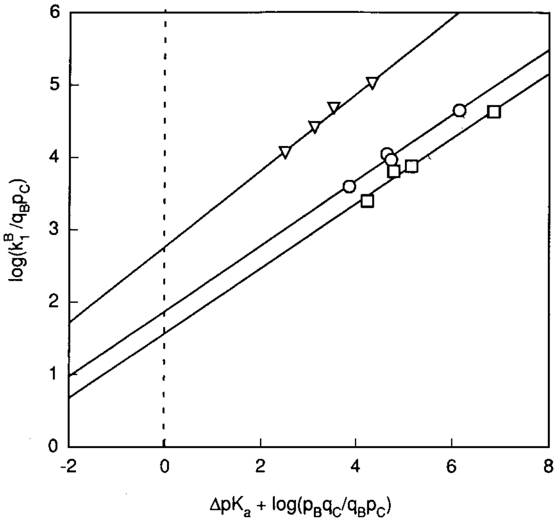

Figure 1. Brønsted plots for the deprotonation of $PhCOCH_2NO_2$ (**5**) by secondary alicyclic amines in water (□), 50% DMSO (○), and 90% DMSO (△); ΔpK_a = pK_a^{BH} − pK_a^{CH}, p_B and p_C = number of equivalent protons on BH and **CH**, respectively, and q_B and q_C = number of basic sites on B and **C**$^-$, respectively.

For **6**$^-$ the log $^{I}\gamma^{II}_{C^-}$ values are all larger than for **5**$^-$, suggesting that **6**$^-$ is more strongly solvated by water than **5**$^-$. This implies that in **6**$^-$ the charge is more concentrated on one group (presumably the nitro group) than is the case for **5**$^-$. On the other hand, the log $^{I}\gamma^{II}_{C^-}$ values for **6**$^-$ are somewhat smaller than for $PhCH{=}NO_2^-$, e.g., log $^{I}\gamma^{II}_{C^-} = 2.90$ for **6**$^-$ and 4.09 for $PhCH{=}NO_2^-$. This difference is not nearly as dramatic as the difference between log $^{I}\gamma^{II}_{C^-}$ for **5**$^-$ and $CH_2{=}NO_2^-$; nevertheless, it suggests more effective charge dispersion in **6**$^-$ than in $PhCH{=}NO_2^-$ which is consistent with *some* contribution by **6**$^-$**(c)**.

The conclusions drawn from the pK_a^{CH} values and solvent transfer activity coefficients are supported by the UV spectra. λ_{max} for **5**$^-$ is red-shifted by more than 100 nm compared to λ_{max} for $CH_2{=}NO_2^-$, e.g., from 248[4] to 352 nm in 50% DMSO. The red-shift in the spectrum of **6**$^-$ compared to that of $PhCH{=}NO_2^-$ is less dramatic; in 50% DMSO λ_{max} for $PhCH{=}NO_2^-$ is 303 nm[4] while there is a shoulder in the spectrum of **6**$^-$ in the range of 350−380 nm.[21]

Effect of the PhCO Group on Intrinsic Rate Constants. Brønsted plots constructed from the data in Tables 1−3 are shown in Figures 1−3. Brønsted β_B values [$\delta(\log k_1^B)/\delta pK_a^{BH}$] values are summarized in Table

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[21] Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Schuck, D. F.; Rappoport, Z. *J. Am. Chem. Soc.* **1991**, *113*, 4937.

Table 6. Brønsted β_B Values

	water	50% DMSO–50% water	90% DMSO–10% water
		$PhCOCH_2NO_2$ (**5**)	
R_2NH	0.45 ± 0.04 (0.59)[a]	0.45 ± 0.04 (0.62)[a]	0.53 ± 0.04 (0.69)[a]
		PhCOCH(Ph)NO_2 (**6**)	
RS^-	0.51 ± 0.08 (0.48)[b]		
ArO^-	0.58 ± 0.04 (0.59)[b]		
$RCOO^-$	0.61 ± 0.03 (0.54)[c]		
R_2NH	0.52 ± 0.05 (0.48)[c]	0.54 ± 0.03 (0.52)[c]	0.53 ± 0.03 (0.69)[c]
RNH_2		0.59 ± 0.05	

[a] CH_3NO_2 at 20 °C, ref 4. [b] $PhCH_2NO_2$ at 25 °C, ref 14. [c] $PhCH_2NO_2$ at 20 °C, ref 4.

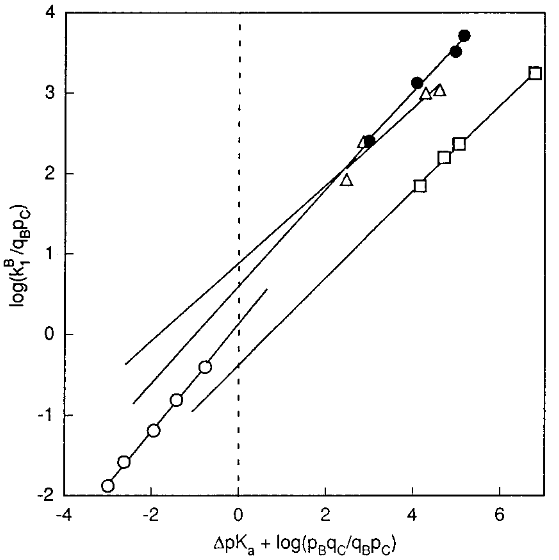

Figure 2. Brønsted plots for the deprotonation of PhCOCH(Ph)NO_2 (**6**) by carboxylate ions (○), secondary alicyclic amines (□), thiolate ions (△) and aryl oxide ions (●) in water; $\Delta pK_a = pK_a^{BH} - pK_a^{CH}$, p_B and p_C = number of equivalent protons on BH and **CH**, respectively, and q_B and q_C = number of basic sites on B and $\mathbf{C}^-$, respectively.

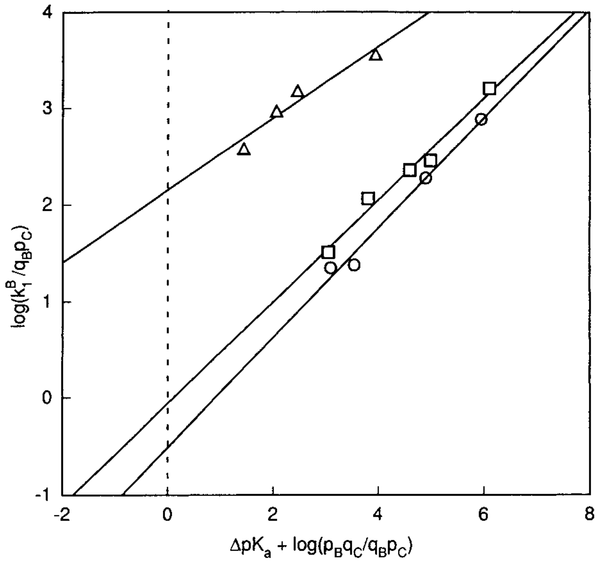

Figure 3. Brønsted plots for the deprotonation of PhCOCH(Ph)NO_2 (**6**) by primary aliphatic amines in 50% DMSO (○) and by secondary alicyclic amines in 50% DMSO (□) and 90% DMSO (△); $\Delta pK_a = pK_a^{BH} - pK_a^{CH}$, p_B and p_C = number of equivalent protons on BH and **CH**, respectively, and q_B and q_C = number of basic sites on B and $\mathbf{C}^-$, respectively.

6 and intrinsic rate constants are reported in Table 7; these latter are defined as $k_o = k_1^B/q_Bp_C$, when $pK_a^{BH} - pK_a^{CH} + \log(p_Bq_C/q_Bp_B) = 0$.[22] The Brønsted β_B values require little comment; they all fall within the typical range observed for the deprotonation of most nitroalkanes[4,23,24–27] and many other carbon acids.[28] On the other hand, the intrinsic rate constants reveal a number of interesting features.

We shall first focus on the reactions of **5** and **6** with secondary alicyclic amines for which we have the most complete set of data. The following points are noteworthy.

(1) In water log k_o for **5** is substantially higher than for CH_3NO_2 [$\Delta(\log k_o)^{29} = 2.36$]; in 50% Me_2SO log k_o for **5** still exceeds that for CH_3NO_2 but by a smaller amount [$\Delta(\log k_o)^{29} = 1.32$] while in 90% DMSO the log k_o values are quite comparable with that for **5** being slightly smaller than for CH_3NO_2 [$\Delta(\log k_o)^{29} = -0.16$].

(2) log k_o for **6** relative to log k_o for $PhCH_2NO_2$ shows a similar pattern, but the $\Delta(\log k_o)$ values[29] in water (1.06) and 50% DMSO (0.38) are significantly smaller than in the comparison between **5** and CH_3NO_2, while in 90% DMSO log k_o for **6** and $PhCH_2NO_2$ are comparable but with log k_o for **6** still slightly exceeding log k_o for $PhCH_2NO_2$ [$\Delta(\log k_o) = 0.18$].

(3) The log k_o values for **6** are smaller than for **5** in all solvents, with the differences being larger in water and 50% DMSO than in 90% DMSO.

Just as is the case for the pK_a^{CH} values, the trends in the intrinsic rate constants may be understood mainly as the result of an interplay of resonance, inductive/field, and solvation effects. An additional factor that has no influence on pK_a^{CH} but may affect the log k_o values is steric hindrance to the approach of the base at the transition state.

The discussion of how these four factors affect log k_o can be based on eq 7;[29]

$$\Delta(\log k_o) = \delta(\log k_o^R) + \delta(\log k_o^I) + \delta(\log k_o^S) + \delta(\log k_o^{st}) \quad (7)$$

$\delta(\log k_o^R)$, $\delta(\log k_o^I)$, $\delta(\log k_o^S)$ and $\delta(\log k_o^{st})$ refer to the contribution to $\Delta(\log k_o)$ that comes from the difference

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[22] p_B, p_C, q_B, and q_C are statistical factors; p_B refers to the number of equivalent protons on BH, p_C to the number of equivalent protons on the **CH** acid, q_B to the number of equivalent basic sites on B, and q_C to the number of equivalent basic sites on the nitronate ion.

[23] Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907.

[24] (a) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3447. (b) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3107.

[25] Keeffe, J. R.; Munderloh, N. H. *J. Chem. Soc., Chem. Commun.* **1974**, 17.

[26] Gandler, J. R.; Bernasconi, C. F. *J. Am. Chem. Soc.* **1992**, *114*, 631.

[27] (a) Gregory, M. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1967**, *89*, 2397. (b) Bruice, P. Y. *J. Am. Chem. Soc.* **1984**, *106*, 5959.

[28] For a recent review, see ref 2c.

[29] $\Delta(\log k_o)$ is defined in footnotes *f* and *h* of Table 7.

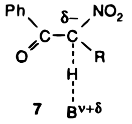
Table 7. Intrinsic Rate Constants Expressed as log k_o at 20 °C[a]

	water	50% DMSO−50% water	90% DMSO−10% water
		$PhCOCH_2NO_2$ (**5**)	
R_2NH	1.57 ± 0.23 (−0.79)[b] *2.36*[f]	1.87 ± 0.19 (0.55)[b] *1.32*[f]	2.75 ± 0.13 (2.91)[b] *−0.16*[f]
		$PhCOCH(Ph)NO_2$ (**6**)	
R_2NH[c]	−0.32 ± 0.27 (−1.38)[d] *1.06*[h]	−0.01 ±0.13 (−0.39)[d] *0.38*[h]	1.84 ± 0.07 (1.66)[d] *0.18*[h]
RNH_2[e]		−0.62 ± 0.10	
RS^-	0.83 ± 0.29 (−0.77)[g] >*1.60*[h]		
ArO^-	0.71 ± 0.17 (−0.99)[g] >*1.70*[h]		
$RCOO^-$	−0.02 ± 0.06 (−2.22)[d] *2.20*[h]		

[a] All k_o values are statistically corrected for the number of protons on **CH** and BH and the number of equivalent basic sides on B. [b] Deprotonation of CH_3NO_2 at 20 °C, ref 4. [c] Secondary alicyclic amines. [d] Deprotonation of phenylnitromethane at 20 °C, ref 4. [e] Primary aliphatic amines. [f] $\Delta(\log k_o) = \log k_o^{\mathbf{5}} - \log k_o^{(CH_3NO_2)}$. [g] Deprotonation of phenylnitromethane at 25 °C, ref 14. [h] $\Delta(\log k_o) = \log k_o^{\mathbf{6}} - \log k_o^{(PhCH_2NO_2)}$.

in the resonance, inductive, solvation, and steric effects, respectively, for the two reactions that are being compared. For example, $\delta(\log k_o^R)$ is the change in log k_o that results from the increase in the resonance stabilization in $\mathbf{5}^-$ compared to $CH_2{=}NO_2^-$ or in $\mathbf{6}^-$ compared to $PhCH{=}NO_2^-$, etc. It should be noted that the use of eq 7 is based on the premise that the four factors are additive and independent of each other. This is probably an oversimplification, but as will become apparent, it leads to intuitively reasonable conclusions.

The increase in resonance stabilization of the carbanion that results from the introduction of the PhCO group is expected to make $\delta(\log k_o^R)$ negative. As alluded to in the Introduction, this reduction in k_o is the well-known consequence of the lag in the charge delocalization behind proton transfer at the transition state (**7**)[30] and is a manifestation of the PNS.[3] In contrast, the electron-withdrawing inductive effect of the PhCO group should lead to a positive $\delta(\log k_o^I)$ term. This effect is also the result of the lag in charge delocalization: the accumulation of the charge on the carbon leads to a disproportionately strong stabilization of the transition state relative to that of the anion and hence enhances k_o.[2] Regarding $\delta(\log k_o^S)$, solvation of the incipient carbanion at the transition state lags behind proton transfer in a similar way as is the case for resonance development,[2] and hence stronger solvation must lead to a negative $\delta(\log k_o^S)$ term.[31] Finally, $\delta(\log k_o^{st})$ can be expected to be negative because replacing a hydrogen by the PhCO group will invariably increase the bulkiness of the substrate and lead to a more crowded transition state.



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On the basis of the above considerations, the following interpretation of the log k_o values can be offered. In 90% DMSO the solvation of the various carbanions is relatively weak (see discussion of pK_a^{CH}) and hence the $\delta(\log k_o^S)$ term can be assumed to be small. This means that in this solvent $\Delta(\log k_o)$ can be approximated by eq 8.

$$\Delta(\log k_o) \approx \delta(\log k_o^R) + \delta(\log k_o^I) + \delta(\log k_o^{st}) \quad (8)$$

For the reaction of **5** the steric effect is likely to be negligible,[32] implying $\delta(\log k_o^{st}) \approx 0$, which leads to a further simplification of eq 8 to eq 9 for the case of **5**.

$$\Delta(\log k_o) \approx \delta(\log k_o^R) + \delta(\log k_o^I) \quad (9)$$

The observed $\Delta(\log k_o)$ value of −0.16 indicates that the positive $\delta(\log k_o^I)$ and negative $\delta(\log k_o^R)$ term essentially offset each other, with a slightly larger contribution by the $\delta(\log k_o^R)$ term.

For the reaction of the much bulkier **6**, $\delta(\log k_o^{st})$ is not negligible. Evidence for such a steric effect comes from a comparison with the reaction of **6** involving *primary* aliphatic amines. Specifically, the difference between log k_o for secondary alicyclic amines and log k_o for primary aliphatic amines can serve as a measure of the importance of the steric effect.[5,28,33,34] In the absence of significant steric hindrance, this difference is typically 0.8−1.0[35] log units, while a smaller difference indicates significant steric hindrance. On the basis of the 0.61 units difference between log $k_o^{R_2NH}$ and log $k_o^{RNH_2}$ in the reactions of **6** in 50% DMSO, we conclude that there is a moderate steric effect which is probably only significant with the relatively bulky secondary amines but of minor importance with the other bases; this latter point will be taken up below.

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[30] The representation of **7** which implies that all the negative charge is localized on carbon is an exaggeration; it is likely that some of the charge is being delocalized into the nitro and carbonyl groups.

[31] The desolvation of the neutral carbon acid also contributes to the solvent effect on k_o because this desolvation is ahead of proton transfer at the transition state.[2] However, this effect is usually small[2] and should contribute minimally to $\delta(\log k_o^S)$. The effect of the early desolvation of the amine and of the late solvation of the developing ammonium ion affect k_o as well, but these effects should be about the same for the various carbon acids[28] and hence should not contribute significantly to $\Delta(\log k_o)$.

[32] In general, steric effects on proton transfers from carbon acids are only substantial when the α-carbon has three substituents (CHXYZ) but not when it has only two (CH_2XY) or one substituent (CH_3X).[28]

[33] (a) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (b) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969. (c) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115. (d) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1990**, *112*, 8448.

[34] (a) Bernasconi, C. F.; Bunnell, R. D.; Terrier, F. *J. Am. Chem. Soc.* **1988**, *110*, 6514. (b) Farrell, P. G.; Terrier, F.; Xie, H.-Q.; Boubaker, T. *J. Org. Chem.* **1990**, *55*, 2546. (c) Bernasconi, C. F.; Fairchild, D. E. *J. Phys. Org. Chem.* **1992**, *5*, 409. (d) Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **1993**, *115*, 12526.

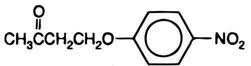
[35] The higher k_o values for secondary amines is a well-known phenomenon caused by differences in the solvation energies of the respective protonated amines and the fact that at the transition solvation of the incipient protonated amine lags behind proton transfer.[28,36]

Despite the negative contribution of the $\delta(\log k_o^{st})$ term to $\Delta(\log k_o)$ for the reaction of **6**, $\Delta(\log k_o)$ is slightly positive (0.18). Assuming that the $\delta(\log k_o^{I})$ term is comparable to that for the reaction of **5**, the positive $\Delta(\log k_o)$ for the reaction of **6** must then be the result of a significantly less negative $\delta(\log k_o^{R})$ term, due to a smaller resonance effect on **6**$^-$. This is consistent with the conclusions based on the pK_a^{CH} values and the solvent transfer activity coefficients, according to which charge delocalization into the carbonyl group of **6**$^-$ is less effective than in **5**$^-$.

In water the $\delta(\log k_o^{S})$ term becomes important, particularly for the comparison between **5**$^-$ and $CH_2{=}NO_2^-$, as indicated by the large difference in the $\log {}^{0}\gamma^{90}_{C^-}$ values (1.67 for **5**$^-$, 6.70 for $CH_2{=}NO_2^-$, Table 5). The much stronger solvation of $CH_2{=}NO_2^-$ compared to that of **5**$^-$ depresses k_o for the deprotonation of CH_3NO_2 much more than k_o for the deprotonation of **5**. This translates into a large positive $\delta(\log k_o^{S})$ term and is the reason for the increase in $\Delta(\log k_o)$ from -0.16 in 90% DMSO to 2.36 in water (Table 7). In accordance with the reduced difference between $\log {}^{0}\gamma^{50}_{C^-}$ for **5**$^-$ (1.00) and $CH_2{=}NO_2^-$ (2.87) in 50% DMSO (Table 5), the $\delta(\log k_o^{S})$ term in this solvent is expected to be smaller than in water, in agreement with the smaller increase in the $\Delta(\log k_o)$ value (from -0.16 to 1.32). The situation in the comparison between **6**$^-$ and $PhCH{=}NO_2^-$ is similar, but due to the smaller differences in the $\log {}^{0}\gamma^{90}_{C^-}$ and ${}^{0}\gamma^{50}_{C^-}$ values between the two anions, the $\delta(\log k_o^{S})$ terms are expected to be smaller than for the **5**/CH_3NO_2 comparison. This is borne out by the smaller increases in $\Delta(\log k_o)$ upon changing from 90% DMSO (0.18) to 50% DMSO (0.38) or to water (1.06).

Turning to the reactions of **6** with carboxylate, aryl oxide, and thiolate ions, their $\log k_o$ as well as the $\Delta(\log k_o)$ values have been determined in water (Table 7). The $\Delta(\log k_o)$ values are all significantly larger than for the reaction with the secondary alicyclic amines. (In the case of RS^- and ArO^-, the values given for $\Delta(\log k_o)$ are lower limits because $\log k_o$ for $PhCH_2NO_2$ was determined at 25 °C rather than 20 °C). This increase in $\Delta(\log k_o)$ appears to reflect the reduced steric effect [less negative $\delta(\log k_o^{S})$ term] in the reactions of **6** with the anions compared to the reaction with the bulkier secondary alicyclic amines.

High Intrinsic Rate Constants with Thiolate Ions. Inspection of Table 7 reveals that $\log k_o$ for the deprotonation of **6** by thiolate ions is higher than for deprotonation by any of the other bases. This is the same result obtained for the deprotonation of $PhCH_2NO_2$.[14] These findings contrast with the more common observation that, for proton transfers, k_o is typically substantially *lower* for thiolate ions than for oxyanions or amines as the proton acceptor. This is not only true for the deprotonation of normal acids[37] but for carbon acids[11-13] as well. For example, for HCN,[13] $\log(k_o^{RS^-})/(k_o^{R_2NH}) \leqslant -1.9$ and $\log(k_o^{RS^-}/k_o^{ArO^-}) \leq -2.4$; for acetylacetone,[11] $\log(k_o^{RS^-}/k_o^{R_2NH}) \approx -0.2$, $\log(k_o^{RS^-}/k_o^{RCOO^-}) \approx -0.5$ and $\log(k_o^{RS^-}/k_o^{ArO^-}) \approx -0.7$; for **8**,[12] $\log(k_o^{RS^-}/k_o^{ArO^-}) \approx -1.6$. The relatively high intrinsic rate constant observed for the deprotonation of $PhCH_2NO_2$ by thiolate ion [$\log(k_o^{RS^-}/k_o^{ArO^-}) = 0.26$, $\log(k_o^{RS^-}/k_o^{RCOO^-}) = 1.13$, $\log k_o^{RS^-}/k_o^{R_2NH}) = 0.25$] has been attributed to a change in the relative importance of hydrogen-bonding stabilization of the transition state and the requirement for partial desolvation of the base as it enters the transition state.[14] This partial desolvation which is ahead of proton transfer at the transition state leads to a lowering of k_o in proportion to the degree of solvation of the base.



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These points have been discussed in considerable detail in ref 14. The conclusion was that hydrogen bonding is the overriding factor with normal acids and with carbon acids where the charge in the conjugate carbanion is not too strongly delocalized. On the other hand, when there is more complete delocalization, as is the case for nitronate ions, hydrogen bonding becomes a minor factor because more delocalization in the carbanion implies more delocalization in the transition state and therefore less negative charge on the α-carbon of the transition state. As elaborated upon in ref 14, this is true despite the imbalance.[38] Hence the energetically less demanding desolvation of thiolate ions compared to oxyanions or amines results in a higher intrinsic rate constant for the reaction with thiolate ions. The same explanation undoubtedly holds for the relatively high intrinsic rate constant in the deprotonation of **6** with thiolate ions: $\log(k_o^{RS^-}/k_o^{ArO^-}) = 0.12$, $\log(k_o^{RS^-}/k_o^{RCOO^-}) = 0.85$, $\log(k_o^{RS^-}/k_o^{R_2NH})) = 1.15$.

pK_a^{app} and $pK_a^{NOH^-}$. With regard to pK_a^{app} of **6**, the major question is whether it refers to the acidity of the **OH** or **NOH** form. In general, of the three possible tautomeric forms of α-nitro ketones (keto, enol, and aci form), the aci form is typically the least favored.[39,40] This suggests that **OH** should be favored over **NOH**, i.e., $1/K_a^{NOH} < (\ll)\ 1/K_a^{OH}$ and hence $1/K_a^{app} = 1/K_a^{OH}$ (eq 12, Experimental Section) or $pK_a^{app} = pK_a^{OH} > (\gg)\ pK_a^{NOH}$.

Even though pK_a^{NOH} is experimentally inaccessible, a lower limit may be estimated on the basis of the following reasoning. Electron-withdrawing groups generally increase the CH acidity of nitro compounds more than their nitronic acid acidity, i.e., the difference between pK_a^{CH} and pK_a^{NOH} decreases with decreasing pK_a^{CH}. For $PhCH_2NO_2$, $pK_a^{CH} - pK_a^{NOH} = 3.43$, 3.48, and 3.25 in water, 50% DMSO, and 90% DMSO, respectively (Table 4). This allows bracketing of pK_a^{NOH} between pK_a^{app} and $pK_a^{CH} - (pK_a^{CH} - pK_a^{NOH})_{PhCH_2NO_2}$, i.e., $2.38 > pK_a^{NOH} > 1.61$ in water, $3.42 > pK_a^{NOH} > 1.73$ in 50% DMSO, and $4.78 > pK_a^{NOH} > 4.52$ in 90% DMSO.

Conclusions

(1) The replacement of one hydrogen in CH_3NO_2 by the PhCO group has a strong acidifying effect which is the combined result of increased charge dispersion (resonance) in **5**$^-$ compared to $CH_2{=}NO_2^-$ and the electron withdrawing inductive/field effect of the PhCO group. The increased charge dispersion lessens the hydrogen-bonding solvation by water which manifests itself by $\log {}^{0}\gamma^{50}_{C^-}$,

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(36) (a) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University: Ithaca, New York, 1973; Chapter 10. (b) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1968; p 178.

(37) (a) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1. (b) *Proton-Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Wiley & Sons: New York, 1975.

(38) See also ref 30.

(39) Nielsen, A. T. In *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Wiley-Interscience: New York, 1969; p 349.

(40) Toullec, J. In *The Chemistry of Enols*; Rappoport, Z., Ed.; Wiley & Sons: New York, 1990; p 323.

log ${}^{0}\gamma^{90}{}_{C^-}$, and log ${}^{50}\gamma^{90}{}_{C^-}$ values for 5^- that are much smaller than for $CH_2{=}NO_2^-$. Strong confirmation of this interpretation comes from a comparison of intrinsic rate constants. In 90% DMSO, where solvation of the nitronate ions is much weaker than in water, the difference in log k_o between **5** and CH_3NO_2, $\Delta(\log k_o)$, is dominated by $\delta(\log k_o^I)$ and $\delta(\log k_o^R)$; $\Delta(\log k_o)$ is seen to be close to zero (−0.16) because the decrease in k_o expected from the enhanced resonance in 5^- ($\delta(\log k_p^R) < 0$) is nearly offset by the positive $\delta(\log k_o^I)$. In the water-rich solvents, the $\delta(\log k_o^S)$ term becomes important, which leads to large positive $\Delta(\log k_o)$ values because the reduced solvation of 5^- compared to $CH_2{=}NO_2^-$ results in a strongly positive $\delta(\log k_o^S)$ term.

(2) Qualitatively the replacement of one hydrogen in $PhCH_2NO_2$ by the PhCO group has the same effect as on CH_3NO_2, but its magnitude is much smaller due to steric crowding, which reduces π-overlap and charge dispersion in 6^-. This manifests itself in a smaller acidity enhancement and log ${}^{0}\gamma^{50}{}_{C^-}$, log ${}^{0}\gamma^{90}{}_{C^-}$, and log ${}^{50}\gamma^{90}{}_{C^-}$ values for 6^- that are only slightly smaller than for $PhCH{=}NO_2^-$. The relatively small increase in the resonance stabilization of 6^- relative to that of $PhCH{=}NO_2^-$ also leads to a slightly *positive* $\Delta(\log k_o)$ in 90% DMSO, presumably because the $\delta(\log k_o^R)$ term is less negative; and to smaller $\Delta(\log k_o)$ values in 50% DMSO and water than for **5**, because the reduction in hydrogen bonding solvation of 6^- compared to that of $PhCH{=}NO_2^-$ is relatively small and results in a relatively small $\delta(\log k_o^S)$ term.

(3) The much stronger red-shift in the UV spectrum of 5^- relative to that of $CH_2{=}NO_2^-$ compared to the red shift in the spectrum of 6^- relative to that of $PhCH{=}NO_2^-$ is consistent with the above conclusions.

(4) In the reaction of **6** with secondary alicyclic amines there is a steric effect that reduces the intrinsic rate constants. This effect is most pronounced with secondary alicyclic amines as the proton acceptor but probably of minor importance in the reactions with primary amines as well as carboxylate, aryl oxide, and thiolate ions.

(5) The intrinsic rate constant for deprotonation of **6** by thiolate ions is greater than for the reactions with the other bases. This is attributed to the reduced importance of hydrogen-bonding stabilization of the transition state coupled with the fact that desolvation of thiolate ions is energetically less demanding than desolvation of amines or oxyanions.

Experimental Section

Materials. Benzoylnitromethane (**5**) was available from Aldrich. 1,2-Diphenyl-2-nitroethanone (**6**) was prepared as described previously[21] except that 1-iodo-2-nitrostilbene or 1,2-dinitrostilbene rather than 1-chloro-2-nitrostilbene was used as starting material and the product was purified on a silica gel column three times.

2-Mercaptoethanol, methyl 3-mercaptopropionate, methyl mercaptoacetate, and 3-chlorophenol were purified by vacuum distillation. Phenol and 4-methylphenol were recrystallized from hexane, whereas 2,2,2-trifluoroethanethiol, 4-cyanophenol, acetic acid, methoxyacetic acid, chloroacetic acid, and piperazine were used without further purification. Cyanoacetic acid and 3-chloropropionic acid were recrystallized from pentane and dichloroacetic acid was distilled under vacuum. Piperidine, morpholine, *n*-butylamine, 1-(2-hydroxyethyl)piperazine, and DMSO were refluxed over CaH_2 and then distilled under vacuum. KOH and HCl were prepared from J. T. Baker's "Dilute-it" Analytical Concentrates. Water was obtained from a Millipore Water System.

Solutions and pH Measurements. Reaction solutions were prepared essentially as described before.[4,33] For the 50% DMSO solutions, appropriate amounts of aqueous stock solutions were added to the DMSO, and the volumetric flasks were topped off with water. For the 90% DMSO solutions, Me_2SO was added to the aqueous phase, and the flasks were topped off with DMSO. Compound **5** or **6** was introduced by injecting a few microliters of a concentrated stock solution prepared in acetonitrile. All pH measurements were performed with an Orion 611 Research Digital pH-meter. Calibration in water was with standard Fisher buffers, in DMSO−water mixtures with Hallé[41] buffers. The ionic strength was maintained with KCl at 0.5 M in water and in 50% DMSO and at 0.06 M in 90% DMSO.

pK_a Determinations. The pK_a of most buffers in our solvent systems are known from previous studies.[14,33b,c] The pK_a values of piperazine, 1-(2-hydroxyethyl)piperazine, and 1-formylpiperazine were determined by standard potentiometric methodology. The pK_a^{CH} values of the carbon acids in the various solvents were determined by classical spectrophotometric methodology via eq 10, where A, A_{C^-} and A_{CH} are the absorbances at pH ∼ pK_a^{CH}, pH ≫ pK_a^{CH}, and pH ≪ pK_a^{CH}, respectively.

$$pK_a^{CH} = pH + \log \frac{A_{C^-} - A}{A - A_{CH}} \qquad (10)$$

UV Spectra and Kinetic Experiments. UV spectra were taken with a Lambda 2 Perkin-Elmer or Hewlett-Packard diode array spectrophotometer. The kinetic experiments were performed either on Durrum-Gibson model 110 stopped-flow spectrophotometer or an Applied Photophysics DX-17MV stopped-flow spectrofluorimeter. All rates were measured by monitoring the appearance or disappearance of the anion at 348, 352, and 358 nm in water, 50% DMSO, and 90% DMSO, respectively, for 5^- and at 356, 300, and 328 nm in the three respective solvents for 6^-. Pseudo-first-order conditions, with the carbon acid as the minor component, were used throughout.

The pseudo-first-order rate constant for equilibrium approach is given by eq 11; K_a^{app} is an apparent acidity constant

$$k_{osbd} = k_1 + k_{-1}\frac{K_a^{app}}{K_a^{app} + a_{H^+}} \qquad (11)$$

$$\frac{1}{K_a^{app}} = \frac{1}{K_a^{NOH}} + \frac{1}{K_a^{OH}} \qquad (12)$$

whose relationship to K_a^{NOH} and K_a^{OH} is given in eq 12. The kinetics were followed by approaching the equilibrium either from the carbon acid side (pH > pK_a^{CH} with pK_a^{CH} referring to the pK_a of **CH**) or from the anion side (pH < pK_a^{CH}). In most cases the rates were measured in 1:1 buffers (pH = pK_a^{BH}) at five to seven buffer concentrations. All plots of k_{obsd} vs [B] or vs [BH] gave excellent straight lines whose slopes are given by eq 13 or 14, respectively.

$$\text{slope}([B]) = k_1^{B}\left(1 + \frac{a_{H^+}}{K_a^{CH}}\frac{K_a^{app}}{K_a^{app} + a_{H^+}}\right) \qquad (13)$$

$$\text{slope}([BH]) = k_{-1}^{BH}\left(\frac{K_a^{CH}}{a_{H^+}} + \frac{K_a^{app}}{K_a^{app} + a_{H^+}}\right) \qquad (14)$$

Since pK_a^{CH} > pK_a^{app}, eq 13 simplifies to eq 15 at pH ≫ pK_a^{CH}

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[41] Hallé, J.-C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1970**, 2047.

$$\text{slope}([\text{B}]) = k_1^{\text{B}} \tag{15}$$

$$\text{slope}([\text{BH}]) = k_{-1}^{\text{BH}} \tag{16}$$

and eq 14 to eq 16 at $\text{p}K_a^{\text{app}} \ll \text{pH} \ll \text{p}K_a^{\text{CH}}$. In highly acidic carboxylate buffers where $\text{pH} \leqslant \text{p}K_a^{\text{app}}$, eq 14 becomes eq 17.

$$\text{slope}([\text{BH}]) = k_{-1}^{\text{BH}} \frac{K_a^{\text{app}}}{K_a^{\text{app}} + a_{\text{H}^+}} \tag{17}$$

$\text{p}K_a^{\text{app}}$ in water was obtained from a determination of slope ([BH]) as a function of pH for the cyanoacetate buffer and by performing a nonlinear least-squares analysis according to eq 17. This also yielded a k_{-1}^{BH} value for this buffer; k_{-1}^{BH} values for the other carboxylic acids were then obtained by applying eq 17 in which k_{-1}^{BH} was the only unknown. K_a^{app} in 50% and 90% DMSO was obtained in a similar manner using chloroacetate and dichloroacetate buffers, respectively.

Solvent Transfer Activity Coefficients. log $^{\text{I}}\gamma^{\text{II}}_{\text{CH}}$ was determined from distribution experiments between *n*-heptane and the various solvents of interest, as described by Watarai[19] and by Bernasconi and Bunnell.[20] The partition coefficient of **CH** between *n*-heptane (H) and solvent I is defined as the ratio of the equilibrium concentrations of the carbon acid, [CH], in the two solvents (eq 18).

$$^{\text{I}}P^{\text{H}} = [\text{CH}]_{\text{H}}/[\text{CH}]_{\text{I}} \tag{18}$$

In a similar way, the partition coefficient between *n*-heptane (H) and solvent II is defined by eq 19.

$$^{\text{II}}P^{\text{H}} = [\text{CH}]_{\text{H}}/[\text{CH}]_{\text{II}} \tag{19}$$

The partition coefficient between solvents II and I is then given by eq 20,

$$^{\text{I}}P^{\text{II}} = [\text{CH}]_{\text{II}}/[\text{CH}]_{\text{I}} = {}^{\text{I}}P^{\text{H}}/{}^{\text{II}}P^{\text{H}} \tag{20}$$

while the solvent activity coefficient for the transfer from solvent I to solvent II is the inverse of $^{\text{I}}P^{\text{II}}$ (eq 21).

$$^{\text{I}}\gamma^{\text{II}} = {}^{\text{II}}P^{\text{H}}/{}^{\text{I}}P^{\text{H}} \tag{21}$$

More details can be found in ref 20.

Acknowledgment. This research was supported by Grant No. CHE-9307659 from the National Science Foundation.

JO971259B