1944 *J. Org. Chem.* **1998,** *63,* 1944−1953

Carbanion Stabilization by Adjacent Sulfur: Polarizability, Resonance, or Negative Hyperconjugation? Experimental Distinction Based on Intrinsic Rate Constants of Proton Transfer from (Phenylthio)nitromethane and 1-Nitro-2-phenylethane

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(Phenylthio)nitromethane, $PhSCH_2NO_2$, is about as acidic as $PhCH_2NO_2$ and about 4 pK_a-units more acidic than CH_3NO_2 in water or aqueous DMSO, showing the well-known acidifying effect of thio substituents in the α-position of carbon acids. Over the years various interpretations have been offered for the acidifying effect of sulfur groups: d−p π-resonance, polarizability, and negative hyperconjugation. Assuming that the nature of the factors that potentially stabilize the transition state of the proton transfer from the carbon acid are the same as those that potentially stabilize the carbanion, we show that a distinction between these interpretations can be based on the effect of the phenylthio group on the *intrinsic* rate constants (k_o) of proton transfer. Such intrinsic rate constants were determined for the deprotonation of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ by amines in water and 90% DMSO−10% water; in both solvents k_o for $PhSCH_2NO_2$ was found to be substantially higher than for $PhCH_2CH_2NO_2$ as well as for other nitroalkanes reported previously. Based on a detailed analysis of how various factors such as resonance, inductive effects, polarizability, and positive and negative hyperconjugation affect the intrinsic rate constants for proton transfer, it is concluded that the high k_o values for $PhSCH_2NO_2$ result from a combination of the inductive and polarizability effect of the PhS group and that d−p π-resonance and negative hyperconjugation play a minor role if any.

Introduction

It is well-known that α-alkylthio or α-arylthio groups increase the acidity of adjacent CH bonds. This increased acidity has led to numerous synthetic applications.[1] The acidifying effect has been attributed to the stabilization of the carbanion by sulfur.[2] The mechanism by which this stabilization occurs has generated much interest. Originally this stabilization was explained in terms of a resonance effect involving the d orbitals of sulfur, i.e., d−p π-bonding between the carbanion lone pair and sulfur 3d orbitals,[2−7] e.g., eq 1. However, theoretical work has challenged this notion, suggesting that the stabilization is mainly due to the polarizability of sulfur.[8−11] A third interaction mechanism, negative hyperconjugation, has also been invoked by several authors.[9,11−13] This mechanism involves double bond−no bond resonance structures (e.g., eq 2).[14]

$$CH_3{-}S{-}CH_2^- \longleftrightarrow CH_3{-}\bar{S}{=}CH_2 \qquad (1)$$

$$CH_3{-}S{-}CH_2^- \longleftrightarrow \bar{C}H_3 \quad S{=}CH_2 \qquad (2)$$

The d−p π-bonding mechanism is no longer strongly advocated; regarding polarizability and negative hyperconjugation, they may well both be important.[9,11−13] However, based on a recent high level ab initio study, Wiberg et al.[15] have concluded that negative hyperconjugation is the main factor in the stabilization of the dimethyl sulfide anion by sulfur. Similar conclusions were reached by Cuevas and Juaristi.[16]

In the present study we attempt to evaluate the relative influence of the various interaction mechanisms by using an approach that combines kinetic and thermodynamic data. It is based on the assumption that the kinds of the factors that potentially stabilize the transition state of the deprotonation of a carbon acid are the same as of those that potentially stabilize the carbanion, i.e., polarizability, d−p π-bonding, negative hyperconjugation, and possibly others (see below). It exploits the

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[1] (a) Corey, E. J.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075. (b) Seebach, D. *Synthesis* **1969**, *1*, 19. (c) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553.

[2] For reviews, see (a) Price, C. C.; Oae, S. *Sulfur Bonding*; Ronald Press: New York, 1962. (b) Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 165; pp 71−84.

[3] Oae, S.; Tagaki, W.; Ohno, A. *Tetrahedron* **1964**, *20*, 417.

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[11] Schleyer, P. v. R.; Clark, T.; Kos, A. J.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 6467.

[12] Hopkinson, A. C.; Lien, M. H. *J. Org. Chem.* **1981**, *46*, 998.

[13] Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141.

[14] Equation 2 can be visualized as donation of the carbanion lone pair to the C−S σ^* antibonding orbital.

[15] Wiberg, K. B.; Castejon, H. *J. Am. Chem. Soc.* **1994**, *116*, 10489.

[16] Cuevas, G.; Juaristi, E. *J. Am. Chem. Soc.* **1997**, *119*, 7545.

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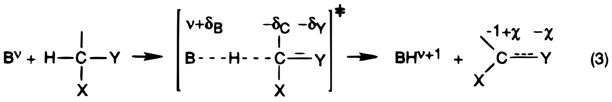
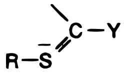
fact that typically the *relative* importance of these factors in stabilizing the transition state is not the same as in stabilizing the carbanion.

The reasoning is as follows. As has been amply demonstrated,[17] the transition state of the deprotonation of carbon acids activated by π-acceptors is imbalanced in the sense that $sp^3 \rightarrow sp^2$ rehybridization of the α-carbon and charge delocalization into the π-acceptor group (Y in eq 3) lag behind proton transfer, i.e., $\delta_Y/\delta_C < \chi/(1 - \chi)$ in eq 3; δ_B is the amount of charge transferred from B to the carbon acid at the transition state, $-\delta_C$ and $-\delta_Y$ are the partial negative charges on C and Y, respectively, at the transition state, while $-\chi$ is the negative charge on Y and $-1 + \chi$ the negative charge on C of the product ion. In a nutshell, the reason for this lag is that the degree of charge delocalization into the Y group is coupled to the degree of C−Y bond formation which in turn depends on the fraction of charge that has been transferred from the base to the carbon acid. Since neither C−Y π-bond formation nor charge transfer are complete at the transition state, the charge delocalized into the Y group is just a fraction of a fraction, and therefore quite small.[17,18] The consequence of this lag is that resonance stabilization of the transition state is disproportionately weak compared to that of the anion, and hence the *intrinsic*[19] rate constant of the reaction is reduced compared to that of a reaction where Y is not a π-acceptor, or a weaker π-acceptor.[17]



(3)

Similar reasoning should be applicable to resonance effects that involve d−p π-bonding (eq 1) or negative hyperconjugation (eq 2), i.e., their development at the transition state is expected to lag behind proton transfer. In other words, if d−p π-bonding or negative hyperconjugation are the dominant carbanion-stabilizing mechanisms of α-thio groups, one expects the intrinsic rate constant of the reaction to be reduced if X in eq 3 is a RS group. This is because the charge delocalization symbolized by the resonance structures **1** (d−p π resonance) or **2** (negative hyperconjugation) will have made minimal progress at the transition state, just as is the case for the resonance structure **3** (p−p π resonance). That *positive* hyperconjugation follows this pattern has been shown by Kresge.[18]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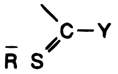
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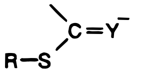
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On the other hand, if carbanion stabilization with X = RS in eq 3 is mainly a polarizability effect, the intrinsic rate constants should be enhanced. This is because polarizability effects do not depend on charge delocalization/resonance development, i.e., they can operate on a pyramidal carbon. Hence, relative to the degree of proton transfer, the transition state with its charge mainly localized on the adjacent carbon benefits more from the stabilizing influence of the sulfur than the carbanion.

(Phenylthio)nitromethane, $PhSCH_2NO_2$, appeared to be a suitable candidate for the study of the effect of an α-thio group along the lines described above because proton transfers from nitroalkanes have strongly imbalanced transition states.[17,18,20] Furthermore, intrinsic rate constants for the deprotonation of several nitroalkanes which would be suitable for purposes of comparison, are already known. With the above reasoning in mind, we studied the proton-transfer kinetics of the reaction of $PhSCH_2NO_2$ and also of 1-nitro-2-phenylethane, $PhCH_2CH_2NO_2$, with amines in water and 90% DMSO−10% water. The latter substrate was not only included to serve as additional reference nitro compound but because, as will become apparent, it displays some interesting features of its own.

Results

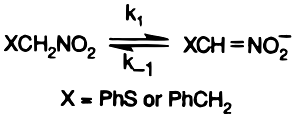
General Features. Proton-transfer rates and pK_a values of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ were determined in water at 25 °C and in 90% DMSO−10% water (v/v) at 20 °C. The reason for choosing two different temperatures was that in water there are more literature data available for comparisons at 25 °C, while in 90% DMSO, 20 °C has been the standard temperature used in previous studies.

Most measurements were made in amine buffers and KOH solutions. Pseudo-first-order conditions with the nitroalkanes as the minor component were used throughout. The ionic strength was kept constant with KCl at 0.5 M in water and at 0.06 M in 90% DMSO. The pK_a^{CH} values for $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ as carbon acids were determined by classic spectrophotometric methodology according to eq 4 where A, A_{C^-} and A_{CH} are the absorbances at pH $\sim pK_a^{CH}$, pH $\gg pK_a^{CH}$ and pH $\ll pK_a^{CH}$, respectively.

$$pK_a^{CH} = pH + \log\frac{A_{C^-} - A}{A - A_{CH}} \qquad (4)$$

The pK_a^{NOH} values of the aci-forms were only determined in 90% DMSO−10% water; they were obtained kinetically as described below.

Kinetics in Water. Proton-transfer rates were measured for the reactions of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ with primary aliphatic and secondary alicyclic amines. The reactions can be described by eq 5



$$XCH_2NO_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} XCH{=}NO_2^- \qquad (5)$$

X = PhS or $PhCH_2$

with

$$k_1 = k_1^{H_2O} + k_1^{B}[B] + k_1^{OH}a_{OH^-} \qquad (6)$$

$$k_{-1} = k_{-1}^{H}a_{H^+} + k_{-1}^{BH}[BH^+] + k_{-1}^{H_2O} \qquad (7)$$

where B is the amine. All measurements were carried

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[17] For recent 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.

[18] Kresge, A. J. *Can. J. Chem.* **1974**, *52*, 1897.

[19] The intrinsic rate constant, k_o, for a reaction with a forward rate constant k_1 and a reverse rate constant k_{-1} is defined as $k_o = k_1 = k_{-1}$ when $K_1 = 1$ ($\Delta G° = 0$); in proton transfers statistical factors are usually included.

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

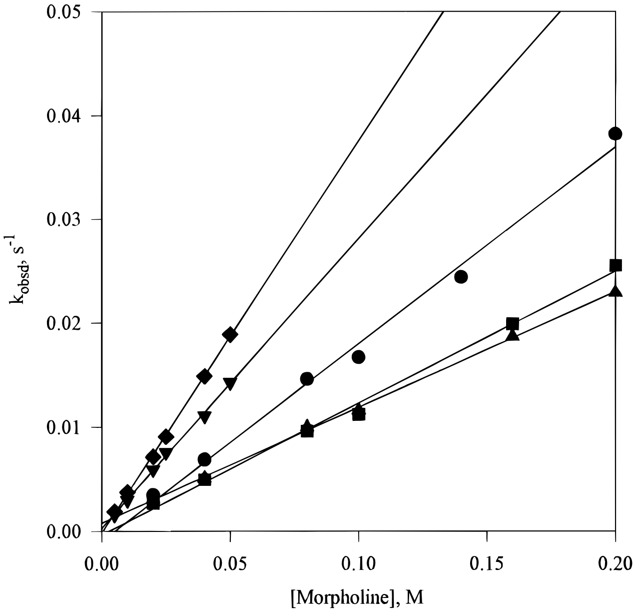

Figure 1. Plots of k_{obsd} vs amine concentration for the reaction of $PhCH_2CH_2NO_2$ with morpholine in water at 25 °C. ◆: pH 8.18; ▼: pH 8.30; ●: pH 8.78; ■: pH 9.08; ▲: pH 9.38. Data at pH 8.48 and 9.26 omitted for clarity.

out at pH values considerably above the estimated pK_a^{NOH} of the aci-form of XCH_2NO_2 (see Discussion) and hence protonation of $XCH{=}NO_2^-$ on the nitro group is not included in eq 5.

The pseudo-first-order rate constant for equilibrium approach is given by eq 8. Kinetic determinations were

$$k_{obsd} = k_1 + k_{-1} \tag{8}$$

made in amine buffers at a pH near pK_a^{BH} of the buffer. Typically k_{obsd} was measured at 5–7 buffer concentrations for a given pH; the raw data are reported in Table S1 of the Supporting Information.[21] Plots of k_{obsd} vs [B] or [BH$^+$] gave excellent straight lines; the rate constants k_1^B and k_{-1}^{BH} which are the main focus of this work were obtained from the slopes of these plots given by eqs 9 and 10, respectively, where K_a^{CH} is the acidity constant of the carbon acid and K_a^{BH} the acidity constant of the buffer acid.

$$\text{slope}([\text{B}]) = k_1^B + k_{-1}^{BH}\frac{a_{H^+}}{K_a^{BH}} = k_1^B\left(1 + \frac{a_{H^+}}{K_a^{CH}}\right) \tag{9}$$

$$\text{slope}([\text{BH}]) = k_1^B\frac{K_a^{BH}}{a_{H^+}} + k_{-1}^{BH} = k_{-1}^{BH}\left(1 + \frac{K_a^{CH}}{a_{H^+}}\right) \tag{10}$$

At pH $\gtrsim pK_a^{CH}$ the equilibrium was approached from the carbon acid side, eq 9 was solved for k_1^B using K_a^{CH} determined spectrophotometrically, and k_{-1}^{BH} was obtained as $k_{-1}^{BH} = k_1^B K_a^{BH}/K_a^{CH}$. At pH $\lesssim pK_a^{CH}$ the equilibrium was approached from the carbanion side, eq 10 was solved for k_{-1}^{BH} and k_1^B was obtained as $k_1^B = k_{-1}^{BH} K_a^{CH}/K_a^{BH}$. In the case of $PhCH_2CH_2NO_2$ with morpholine, pK_a^{CH} is close to pK_a^{BH} which allowed a kinetic determination of pK_a^{CH} from the pH-dependence of the slopes.

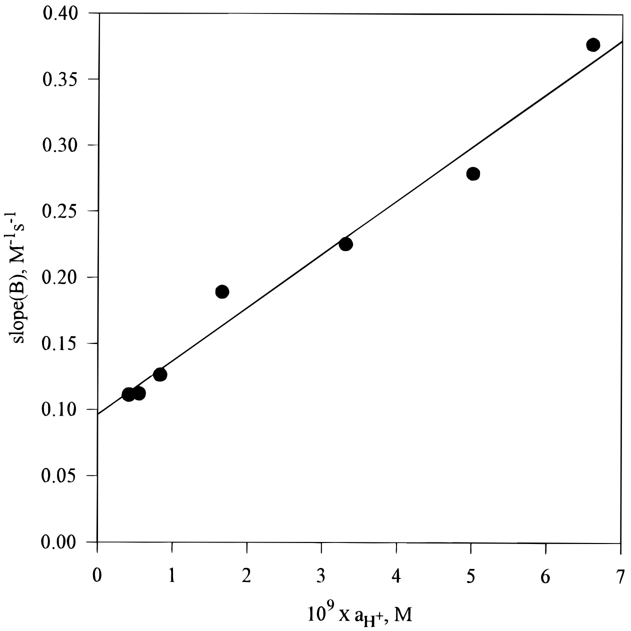

Figure 2. Plot of slope(B) vs a_{H^+} according to eq 9 for the reaction of $PhCH_2CH_2NO_2$ with morpholine in water at 25 °C. Note this plot includes points from data that were omitted from Figure 1.

Table 1. Summary of Rate Constants and pK_a^{CH} Values for the Reactions of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ with Amines and OH$^-$ in Water at 25 °C[a]

B	pK_a^{BH}	k_1^B (M^{-1} s^{-1})[b]	k_{-1}^{BH} (M^{-1} s^{-1})[b]
$PhSCH_2NO_2$ ($pK_a^{CH} = 6.67 \pm 0.02$)			
piperidine	11.24	3.16×10^3	0.083
piperazine	9.94	1.05×10^3	0.564
PZ-CH_2CH_2OH[c]	9.34	4.18×10^2	0.814
morpholine	8.78	1.53×10^2	1.19
n-butylamine	10.87	5.92×10^2	0.0374
2-methoxyethylamine	9.64	1.15×10^2	0.123
glycinamide	8.21	1.3×10^1	0.387
cyanomethylamine	5.50	0.36	5.33
methoxyamine	4.70	0.067	6.26
OH$^-$		4.59×10^4	
$PhCH_2CH_2NO_2$ ($pK_a^{CH} = 8.55 \pm 0.02$)			
piperidine	11.24	3.24	6.61×10^{-3}
piperazine	9.94	0.854	3.48×10^{-2}
PZ-CH_2CH_2OH[c]	9.34	0.292	4.73×10^{-2}
morpholine	8.78	0.129	7.62×10^{-2}
n-butylamine	10.87	4.70×10^{-1}	2.25×10^{-3}
2-methoxyethylamine	9.64	6.94×10^{-2}	5.64×10^{-3}
cyanomethylamine	5.50	3.47×10^{-4}	3.90×10^{-1}
methoxyamine	4.70	5.97×10^{-5}	4.23×10^{-1}
OH$^-$		19.7	

[a] Ionic strength 0.5 M (KCl). [b] Estimated experimental error 3–5%. [c] 1-(2-hydroxyethyl)piperazine.

Figure 1 shows plots of k_{obsd} vs morpholine concentration at various pH values while Figure 2 shows a plot of slope(B) vs a_{H^+} according to eq 9. The pK_a^{CH} value of 8.63 obtained from this plot is in excellent agreement with the spectrophotometric value of 8.55.

We also determined k_1^{OH} by measuring k_{obsd} as function of [KOH] in the absence of amine buffers where eq 8 simplifies to $k_{obsd} = k_1^{OH} a_{OH^-}$. All rate constants are summarized in Table 1.

Kinetics in 90% DMSO–10% Water. Rates were measured for reactions with secondary alicyclic amines only. The experimental methodology was the same as in water. However, most of the plots of k_{obsd} vs [B] or

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[21] See paragraph concerning Supporting Information at the end of this paper.

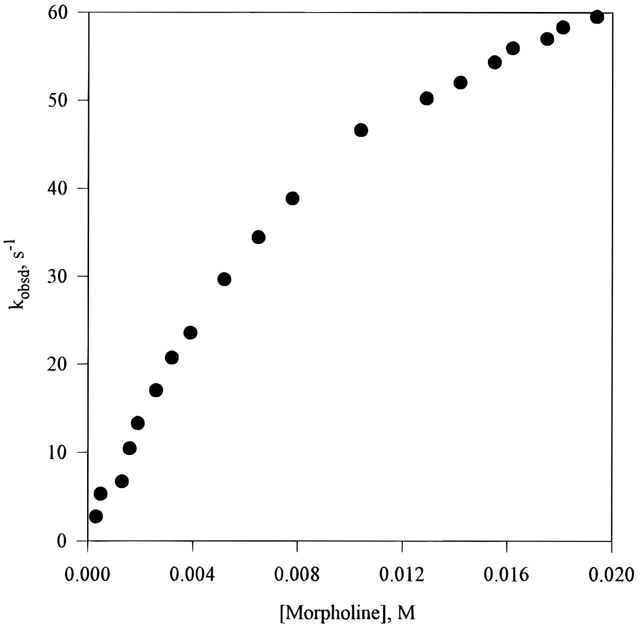


Figure 3. Plot of k_{obsd} vs ammonium ion concentration for the reaction of $PhCH_2CH{=}NO_2^-$ with morpholinium ion in 90% DMSO−10% water at 20 °C, pH 8.59.

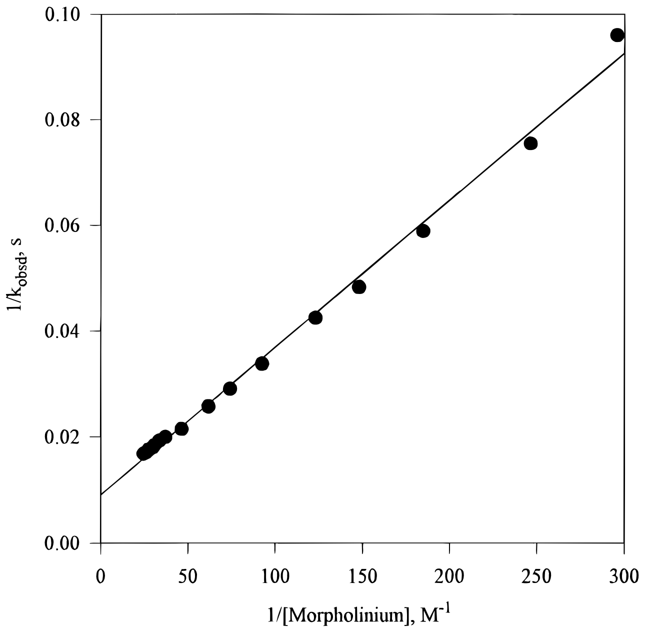
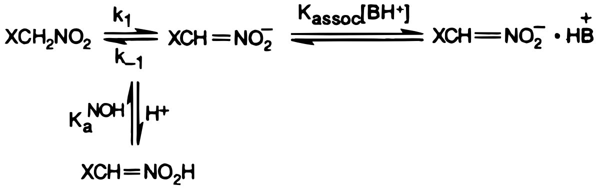


Figure 4. Inversion plot according to eq 14 for the reaction of $PhCH_2CH{=}NO_2^-$ with morpholinium ion in 90% DMSO−10% water at 20 °C, pH 8.59.

Scheme 1



[BH^+] were curved; Figure 3 shows a representative example. The curvature is reminiscent of similar observations reported for the reactions of nitromethane and phenylnitromethane with amines in 90% DMSO−10% water.[22] It can be attributed to an association between the nitronate ion and the protonated amine to form a hydrogen bonded complex as shown in Scheme 1; note that the scheme also includes the aci-form of the nitroalkanes because pK_a^{NOH} is much higher in 90% DMSO−10% water than in water and played a significant role in some of the kinetic runs with $PhCH_2CH_2NO_2$.

Based in Scheme 1, k_{obsd} is given by eq 11; in this solvent the intercepts of plots of k_{obsd} vs [B] or [BH^+] were

$$k_{obsd} = k_1 + \frac{k_{-1}}{1 + \frac{a_{H^+}}{K_a^{NOH}} + K_{assoc}[BH^+]} \tag{11}$$

very small and usually negligible which means that k_{obsd} can be approximated by eq 12. In the case of $PhCH_2CH_2NO_2$ all experiments were done at pH ≪ pK_a^{CH}

$$k_{obsd} = k_1^{B}[B] + \frac{k_{-1}^{BH}[BH^+]}{1 + \frac{a_{H^+}}{K_a^{NOH}} + K_{assoc}[BH^+]} \tag{12}$$

(13.63) so that eq 12 simplifies to eq 13. Inversion plots of $1/k_{obsd}$ vs $1/[BH^+]$ according to eq 14 afforded values for K_{assoc}/k_{-1}^{BH} and $(1+ a_{H^+}/K_a^{NOH}))/k_{-1}^{BH}$. A representative example is shown in Figure 4. In principle, a pH-

$$k_{obsd} = \frac{k_{-1}^{BH}[BH^+]}{1 + \frac{a_{H^+}}{K_a^{NOH}} + K_{assoc}[BH^+]} \tag{13}$$

$$\frac{1}{k_{obsd}} = \frac{1 + \frac{a_{H^+}}{K_a^{NOH}}}{k_{-1}^{BH}[BH^+]} + \frac{K_{assoc}}{k_{-1}^{BH}} \tag{14}$$

dependence of the $(1 + a_{H^+}/K_a^{NOH}))/k_{-1}^{BH}$ term would then yield K_a^{NOH} and k_{-1}^{BH} separately from which K_{assoc} could finally be obtained. However, the relatively low value of pK_a^{NOH} made this method unsuitable for an accurate determination of this acidity constant and pK_a^{NOH} was therefore obtained from kinetic data for the protonation of $PhCH_2CH{=}NO_2^-$ in methoxyacetic acid buffers.

For these experiments eq 11 becomes eq 15 (no association of the acid with the nitronate ion was observed)

$$k_{obsd} = \frac{k_{-1}}{1 + \frac{a_{H^+}}{K_a^{NOH}}} \tag{15}$$

and the reciprocal slopes of plots of k_{obsd} vs methoxyacetic acid concentration are given by eq 16. Such slopes were determined at 10 different pH values; they afforded $pK_a^{NOH} = 8.55 \pm 0.03$ and $k_{-1}^{RCOOH} = (3.88 \pm 0.10) \times 10^3$ M^{-1} s^{-1}.

$$\frac{1}{\text{slope}[(\text{RCOOH})]} = \frac{1}{k_{-1}^{RCOOH}} + \frac{a_{H^+}}{k_{-1}^{RCOOH} K_a^{NOH}} \tag{16}$$

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[22] Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J.-X. *J. Org. Chem.* **1988**, *53*, 3342.

Table 2. Summary of Rate Constants, pK_a^{CH}, pK_a^{NOH}, and K_{Assoc} Values for the Reactions of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ with Amines in 90% DMSO−10% Water at 20 °C[a]

B	pK_a^{BH}	k_1^B (M^{-1} s^{-1})[b]	k_{-1}^{BH} (M^{-1} s^{-1})[b]	K_{assoc} (M^{-1} s^{-1})[c]
		$PhSCH_2NO_2$ ($pK_a^{CH} = 10.65 \pm 0.02$; $pK_a^{NOH} = 6.79 \pm 0.09$)		
piperidine	10.74	2.49×10^4	2.02×10^4	
piperazine	10.23	1.15×10^4	3.02×10^4	
PZ-CH_2CH_2OH[d]	9.53	2.35×10^3	3.10×10^4	
morpholine	8.91	6.82×10^2	3.75×10^4	
		$PhCH_2CH_2NO_2$ ($pK_a^{CH} = 13.68 \pm 0.02$; $pK_a^{NOH} = 8.55 \pm 0.03$)		
piperidine	10.74	2.88	2.52×10^4	50
piperazine	10.23	1.84	5.17×10^3	64
PZ-CH_2CH_2OH[d]	9.53	0.447	6.31×10^3	82
morpholine	8.91	0.117	6.86×10^3	62

[a] Ionic strength 0.06 M (KCl). [b] Estimated experimental error 8−12%; this error is significantly higher than in water because of the curved buffer plots and additional uncertainty introduced by the K_a^{NOH} equilibrium in the reaction of $PhCH_2CH_2NO_2$. [c] Estimated experimental error 20 to 30%. [d] 1-(2-hydroxyethyl)piperazine.

With $PhSCH_2NO_2$ all experiments with amine buffers were performed at pH $\gg pK_a^{NOH}$ so that eq 12 simplifies to eq 17. K_{assoc} is relatively small and hence at low buffer concentrations $K_{assoc}[BH^+] \ll 1$. This allowed determination of k_1^B and k_{-1}^{BH} from the slopes according to eqs 9 or 10. K_{assoc} was then found via eq 18 based on data at high $[BH^+]$. To determine pK_a^{NOH}, rates of protonation

$$k_{obsd} = k_1^B[B] + \frac{k_{-1}^{BH}[BH^+]}{1 + K_{assoc}[BH^+]} \qquad (17)$$

$$\frac{1}{k_{obsd} - k_1^B[B]} = \frac{1}{k_{-1}^{BH}[BH^+]} + \frac{K_{assoc}}{k_{-1}^{BH}} \qquad (18)$$

of $PhSCH{=}NO_2^-$ in chloroacetate buffers were measured and the data treated using eq 16; they yield $pK_a^{NOH} = 6.79 \pm 0.09$ and $k_{-1}^{RCOOH} = (2.99 \pm 0.19) \times 10^3$ M^{-1} s^{-1}.

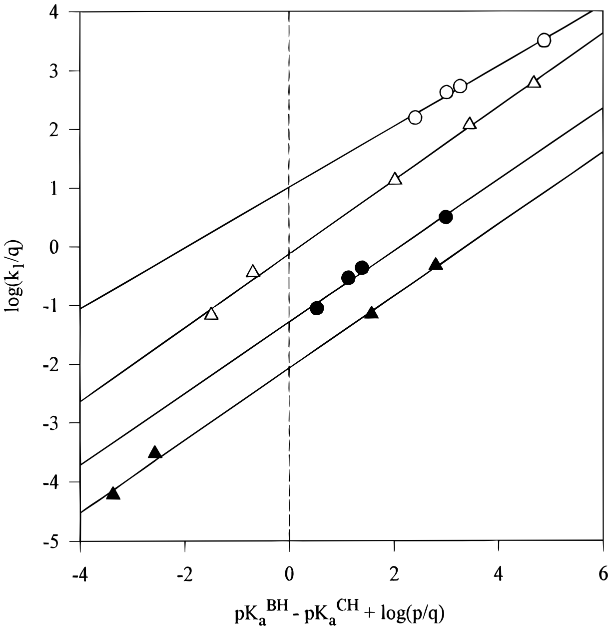

Figure 5. Statistically corrected Brønsted plots for the reactions in water at 25 °C. ○: $PhSCH_2NO_2 + R_2NH$; △: $PhSCH_2NO_2 + RNH_2$; ●: $PhCH_2CH_2NO_2 + R_2NH$; ▲: $PhCH_2CH_2NO_2 + RNH_2$. The points of intersection between the Brønsted lines and the dashed vertical line correspond to log k_o.

Discussion

Rate constants and pK_a values are summarized in Table 1 for the reactions in water and in Table 2 for the reactions in 90% DMSO−10% water; the latter includes K_{assoc} values. Figures 5 and 6 show Brønsted plots while the Brønsted β_B values ($d\log k_1^B/dpK_a^{BH}$)) and intrinsic rate constants ($k_o = k_1^B/q = k_{-1}^{BH}/p$ at $pK_a^{BH} - pK_a^{CH} + \log(p/q) = 0$)[23] are reported in Table 3. Table 3 also includes previously determined β_B and log k_o values for $PhCH_2NO_2$[22] and $HOCH_2CH_2NO_2$.[24]

pK_a Values. The acidifying effect of the α-phenylthio group on carbon acids has been extensively documented by Bordwell et al.[12] For carbon acids whose conjugate base has the negative charge substantially localized on the α-carbon the effect of the phenylthio group is quite dramatic. For example, in DMSO $PhSCH_2CN$ is 11.7 p*K*-units more acidic that CH_3CH_2CN, and $PhSCH_2SO_2Ph$ is 10.5 p*K*-units more acidic than $CH_3CH_2SO_2Ph$. Less than half of the acidifying effect, which is larger than that of an α-phenyl group, could be attributed to inductive electron withdrawal. Similar conclusions were reached with carbon acids that lead to more delocalized anions such as $PhSCH_2COPh$ vs CH_3CH_2COPh and 9-PhS-fluorene vs 9-*tert*-butylfluorene although the effect in these cases is less dramatic. Further attenuation of the acidifying influence of the PhS group was found for nitroalkanes but the effects are still substantial, e.g., $PhSCH_2NO_2$ in DMSO is 5.6 p*K*-units more acidic than CH_3NO_2.

Our own results show that in 90% DMSO−10% water and in water the pK_a^{CH} of $PhSCH_2NO_2$ is about the same as for $PhCH_2NO_2$, or 4.15 p*K*-units more acidic than CH_3NO_2 in 90% DMSO−10% water and 3.53 p*K*-units more acidic than CH_3NO_2 in water (Table 3). The reduction in the p*K*-difference upon making the solvent aqueous is undoubtedly the result of stronger solvation of the nitronate ion which diminishes the influence of the PhS group.

The pK_a^{CH} of $PhCH_2CH_2NO_2$ in water is about the same as the pK_a of $CH_3CH_2NO_2$ (8.60),[25] 1.67 units lower than that of CH_3NO_2 and 0.85 units lower than that of

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(23) *p* and *q* are statistical factors: *p* is the number of equivalent protons on BH^+ while *q* is the number of equivalent basic sites on B.

(24) Bernasconi, C. F.; Panda, M.; Stronach, M. W. *J. Am. Chem. Soc.* **1995**, *117*, 9206.

(25) Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439.

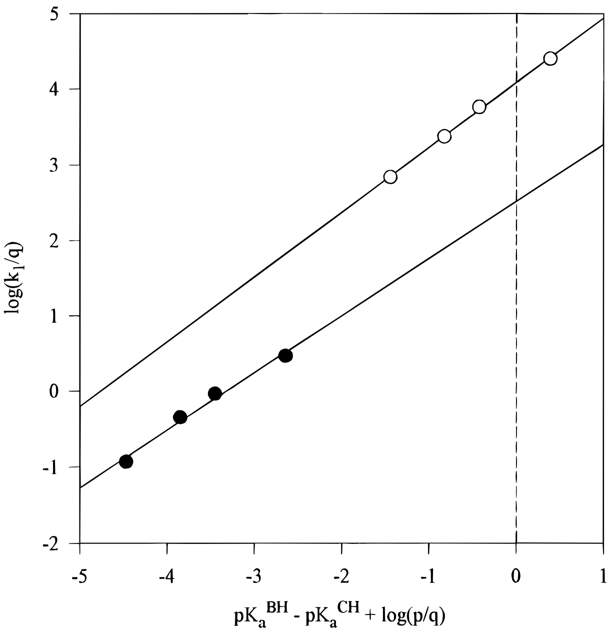
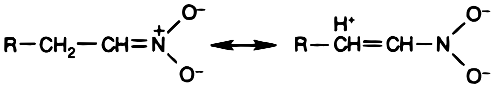


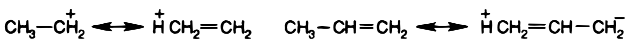
Figure 6. Statistically corrected Brønsted plots for the reactions in 90% DMSO−10% water at 20 °C. ○: $PhSCH_2NO_2 + R_2NH$; ●: $PhCH_2CH_2NO_2 + R_2NH$. The points of intersection between the Brønsted lines and the dashed vertical line correspond to log k_o.

$HOCH_2CH_2NO_2$ (Table 3). The reason for the low pK_a^{CH} of $PhCH_2CH_2NO_2$ is probably the same as the reason for the high acidity of $CH_3CH_2NO_2$ and $HOCH_2CH_2NO_2$ compared to CH_3NO_2, i.e., stabilization of the nitronate ion by the CH_3, $PhCH_2$, and $HOCH_2$ groups, respectively, attached to the sp^2 α-carbon. The classical interpretation of this stabilization is in terms of hyperconjugation[18,26] (**4b**) although an alternative explanation in terms of a strengthening of the bond between the RCH_2 carbon and the α-carbon upon rehybridization of the α-carbon from sp^3 in the acid to sp^2 in the anion (**4a**) is possible. The bond strength argument appears now to be the preferred explanation for the stabilization of alkenes by alkyl groups[27] but this does not necessarily exclude hyperconjugation as a contributing factor in the stabilization of nitronate ions. This is because the hyperconjugative structure (**4b**) is more akin to that of a carbocation (**5b**) where charge is merely delocalized whereas the hyperconjugative structure of an alkyl-substituted alkene (**6b**) leads to the creation and separation of two opposite charges which is energetically unfavorable. The fact that in 90% DMSO the p*K* difference between $PhCH_2CH_2NO_2$ and CH_3NO_2 is reduced from 1.67 to 1.12 units is consistent with the notion that hyperconjugation is at least a contributing factor: because of the large charge separation, **4b** is expected to be less stable in the less polar DMSO than in water.



4a **4b**

R= H, HO, Ph



$$CH_3{-}\overset{+}{C}H_2 \longleftrightarrow \overset{+}{H}\,CH_2{=}CH_2 \qquad CH_3{-}CH{=}CH_2 \longleftrightarrow \overset{+}{H}\,CH_2{=}CH{-}CH_2^-$$

5a **5b** **6a** **6b**

The pK_a^{NOH} values of the aci forms of $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ were only determined in 90% DMSO. Just as is the case with CH_3NO_2 and $PhCH_2NO_2$, pK_a^{NOH} is several p*K*-units lower than the corresponding pK_a^{CH} values but the difference, $pK_a^{CH} - pK_a^{NOH}$ varies considerably from compound to compound (Table 3). There is decreasing trend in $pK_a^{CH} - pK_a^{NOH}$ with increasing acidity which seems to be a general pattern for nitro compounds;[28] the particularly low $pK_a^{CH} - pK_a^{NOH}$ for $PhCH_2NO_2$ has been attributed to the possibility of resonance stabilization of the aci form.[22]

Based on $pK_a^{NOH} = 3.25$ for CH_3NO_2 and 3.90 for $PhCH_2NO_2$ in water,[28] the pK_a^{NOH} values for $PhSCH_2NO_2$ and $PhCH_2CH_2NO_2$ can be expected to be below 4.0 in this solvent. This is confirmed by the fact that the rate constants for deprotonation of these compounds by methoxyamine ($pK_a^{BH} = 4.70$) obtained via eq 10 lie on the Brønsted line defined by the other primary aliphatic amines; if equilibrium protonation on the nitro group had been significant in the kinetic runs with methoxyamine buffers, use of eq 10 would have led to a depressed rate constant.

Intrinsic Rate Constants. The log k_o value for $PhSCH_2NO_2$ is much larger than for all the other nitroalkanes listed in Table 3. Based on the reasoning outlined in the Introduction, this result implies that the extra stabilization of $PhSCH{=}NO_2^-$ compared to say $CH_2{=}NO_2^-$ or $PhCH_2CH{=}NO_2^-$ must be mainly the result of a polarizability effect of the phenylthio group rather than due to d−p π-bonding (eq 1) or negative hyperconjugation (eq 2). This is the main *qualitative* conclusion of our study. This conclusion is particularly interesting in view of Wiberg and Castejon's[15] recent ab initio study and of Cuevas and Juaristi's DFT study[16] which led them to regard negative hyperconjugation as the main stabilizing factor exerted by an α-alkylthio group.

It is not clear at this point why there is disagreement between our conclusions and those reached by Wiberg et al.[15] and Juaristi et al.[16] That negative hyperconjugation plays a significant role can be based on stereoelectronic[9,16] as well as bond lengths[15] arguments but this does not necessarily mean that it is the dominant factor. In other words, even though the calculated geometric parameters are consistent with negative hyperconjugation, the actual stabilization of the carbanions derived from the hyperconjugation may be smaller than that derived from the polarizability effect. Another view has been offered by a referee. According to this referee, negative hyperconjugation should only operate on pyramidal but not on planar carbons. This means that negative hyperconjugation, just like polarizability, should mainly stabilize the transition state and lead to an increase rather than decrease in log k_o. This view appears to be based on the fact that some of the studies showing the stabilizing effect of sulfur involved pyrami-

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(26) Streitwieser, A., Jr.; Hammons, J. H. *Prog. Phys. Org. Chem.* **1965**, *3*, 43.

(27) Streitwieser, A.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Macmillan: New York, 1992; p 258. (b) McMurry, J. *Organic Chemistry*, 4th ed.; Brooks/Cole: Pacific Grove, CA, 1996; p 197. (c) Jones, M., Jr. *Organic Chemistry*; Norton and Co.: New York, 1997; p 134.

(28) Nielsen, A. T. In *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Wiley: New York, 1969; Part 1, p 349.

Table 3. Brønsted β_B Values and Intrinsic Rate Constants for the Reactions of Nitroalkanes with Amines

	$PhSCH_2NO_2$	$PhCH_2CH_2NO_2$	$HOCH_2CH_2NO_2$[a]	$PhCH_2NO_2$[b]	CH_3NO_2[b]
		Water, 25 °C			
pK_a^{CH}	6.67	8.55	9.40	6.88	10.22 (10.40)[e]
$\beta_B(R_2NH)$[c]	0.52 ± 0.04	0.56 ± 0.01	0.62	0.48	0.64
$\log k_o(R_2NH)$[c]	1.02 ± 0.15	−1.16 ± 0.02	−0.59	−0.86	−0.19 (−0.25)[e]
$\beta_B(RNH_2)$[d]	0.63 ± 0.02	0.61 ± 0.03	0.57		
$\log k_o(RNH_2)$[d]	−0.13 ± 0.05	−2.06 ± 0.07	−1.30		
		90% DMSO−10% Water, 20 °C			
pK_a^{CH}	10.65	13.68		10.68	14.80 (14.98)[e]
pK_a^{NOH}	6.79	8.55		7.73	8.65
$pK_a^{CH} - pK_a^{NOH}$	3.86	5.13		2.95	6.15
$\beta_B(R_2NH)$[c]	0.85 ± 0.03	0.76 ± 0.06		0.69	0.69
$\log k_o(R_2NH)$[c]	4.08 ± 0.02	2.51 ± 0.23		1.75	3.06 (3.01)[e]
$\log(k_o^D/k_o^W)$[f,g]	3.06	3.79		2.61	3.26
$^W\Delta^D pK_a^{CH}$[f,h]	3.89	5.13		3.80	4.58

[a] Reference 24. [b] Reference 22. [c] Secondary alicyclic amines. [d] Primary aliphatic amines. [e] Statistically corrected to make CH_3NO_2 comparable to nitroalkanes with only two α-protons. [f] D = 90% DMSO, W = water. [g] Ratio refers to k_o for R_2NH. [h] $^W\Delta^D pK_a^{CH} = pK_a^{CH}(D) - pK_a^{CH}(W)$.

Table 4. Acidities and Intrinsic Rate Constants of XCH_2NO_2 Relative to CH_3NO_2. Dissection of Relative Intrinsic Rate Constants into Contributions by Resonance, Inductive, Hyperconjugation, and Polarizability Effects

	$PhSCH_2NO_2$	$PhCH_2CH_2NO_2$	$HOCH_2CH_2NO_2$	$PhCH_2NO_2$
		Water		
$\Delta\log K_a^{XCH_2NO_2}$	3.73	1.85	1.00	3.52
$\Delta\log k_o^{XCH_2NO_2}$ (obsd)[a]	1.27	−0.91	−0.34	−0.61
$\delta\log k_o^{R}$				<−0.61
$\delta\log k_o^{I}$	>0	≈0 (small)	>0 (small)	>0 (small)
$\delta\log k_o^{h^+}$		≈−0.91	>0 (small)	
$\delta\log k_o^{dR} + \delta\log k_o^{h^-}$	≤0			
$\delta\log k_o^{P}$	>0			
		90% DMSO		
$\Delta\log K_a^{XCH_2NO_2}$	4.33	1.30		4.30
$\Delta\log k_o^{XCH_2NO_2}$ (obsd)	1.07	−0.50		−1.26
$\delta\log k_o^{R}$				−1.25
$\delta\log k_o^{I}$	>0	<0 (small)		>0 (small)
$\delta\log k_o^{h^+}$		>−0.50		
$\delta\log k_o^{dR} + \delta\log k_o^{h^-}$	≤0			
$\delta\log k_o^{P}$	>0			

[a] Based on statistically corrected pK_a^{CH} and $\log k_o$ for CH_3NO_2.

dal carbons in conformationally rigid systems.[4,9,16] However, it contradicts the premise, elaborated upon in the Introduction, that negative hyperconjugation is akin to a resonance effect as described by eq 2 and, by its very nature, leads to a partial planarization of the α-carbon.[15] We therefore respectfully disagree with this referee.

One question that we have not yet addressed is how one may assess the *magnitude* of the polarizability effect on $\log k_o$. This is not a trivial task because there is a complex interplay of other factors that affect the intrinsic rate constants of proton transfers, as can be seen from the large differences in the $\log k_o$ values among the four nitroalkanes used in the comparison with $PhSCH_2NO_2$.

In the following section these factors will be analyzed in some detail. This analysis will focus on the reactions with secondary alicyclic amines because there is a more complete set of data available. However comparable conclusions would be reached on the basis of the reactions with the primary amines. Incidentally, the intrinsic rate constants for these latter reactions ($\log k_o(RNH_2)$) are substantially lower than $\log k_o(R_2NH)$ for the secondary alicyclic amines, a common finding for proton transfers from carbon acids in situations where the rates are not significantly affected by steric effects.[17c,29,30]

Analysis of Main Factors Affecting the Intrinsic Rate Constants. We choose CH_3NO_2 as reference compound. This allows us to define $\Delta\log k_o^{XCH_2NO_2}$ by eq 19 and $\Delta\log K_a^{XCH_2NO_2}$ by eq 20. The observed $\Delta\log k_o^{XCH_2NO_2}$ and $\Delta\log K_a^{XCH_2NO_2}$ values are summarized in Table 4; they are based on statistically corrected pK_a^{CH} and $\log k_o$ values for CH_3NO_2.[32] The relevant factors that can affect $\Delta\log k_o^{XCH_2NO_2}$ include p−p π resonance (R), inductive effects (I), positive hyperconjugation and/or bond strength effects elaborated upon in the section on pK_a values (h^+),[33] negative hyperconjugation (h^-), d−p π resonance (dR), and polarizability (P). This may be expressed by eq 21 but it should be noted

$$\Delta\log k_o^{XCH_2NO_2} = \log k_o^{XCH_2NO_2} - \log k_o^{CH_3NO_2} \quad (19)$$

$$\Delta\log K_a^{XCH_2NO_2} = \log K_a^{XCH_2NO_2} - \log K_a^{CH_3NO_2} = pK_a^{CH_3NO_2} - pK_a^{XCH_2NO_2} \quad (20)$$

that typically only a few terms in eq 21 are simultaneously operative in any given case. Steric effects are probably of minor importance in this study[34] and have not been included.

$$\Delta\log k_o^{XCH_2NO_2} = \delta\log k_o^{R} + \delta\log k_o^{I} + \delta\log k_o^{h^+} + \delta\log k_o^{h^-} + \delta\log k_o^{dR} + \delta\log k_o^{P} \quad (21)$$

We now analyze the relevant contributions to $\Delta\log k_o^{XCH_2NO_2}$ for the four compounds listed in Table 4.

$PhCH_2NO_2$. This is a familiar case[20,22] but $\Delta\log k_o^{PhCH_2NO_2}$ has not been analyzed by means of eq 21. The factors to consider here are p−p π resonance and the electron-withdrawing inductive effect of the phenyl group, i.e., eq 21 reduces to eq 22.

$$\Delta\log k_o^{PhCH_2NO_2} = \delta\log k_o^{R} + \delta\log k_o^{I} \quad (22)$$

As has been amply documented, resonance in the product ion lowers the intrinsic rate constant.[17] This is a consequence of the imbalance which prevents the resonance effect from stabilizing the transition state in proportion to the degree of proton transfer. This means $\delta\log k_o^{R} < 0$.[35]

The electron-withdrawing inductive effect of the phenyl group is expected to increase k_o, i.e., $\delta\log k_o^{I} > 0$ because, due to the imbalance, the negative charge at the transition state is mainly localized on the α-carbon (δ_C in eq 3), i.e., close to the phenyl group. This allows a particularly effective stabilization of the transition state by this group. In contrast, because in the nitronate ion the charge is mainly delocalized into the nitro group and far away from the phenyl group, stabilization of the nitronate ion by this latter group is relatively ineffective.[17,36]

Since the observed $\Delta\log k_o^{XCH_2NO_2}$ for $PhCH_2NO_2$ is negative (−0.61 in water and −1.26 in 90% DMSO) it is clear that the resonance effect is dominant.

$HOCH_2CH_2NO_2$. For this compound the inductive effect and positive hyperconjugation/bond strength effects are the main factors[24] so that eq 21 takes on the form of eq 23. The inductive effect of the $HOCH_2$ group is slightly electron withdrawing, although less than that

$$\Delta\log k_o^{HOCH_2CH_2NO_2} = \delta\log k_o^{I} + \delta\log k_o^{h^+} \quad (23)$$

of the phenyl group in $PhCH_2NO_2$.[37] Hence $\delta\log k_o^{I}$ should be slightly positive. The net decrease in log k_o compared to that for CH_3NO_2 ($\Delta\log k_o^{XCH_2NO_2} = -0.34$ in water) is thus the result of a negative $\delta\log k_o^{h^+}$. The negative value of $\delta\log k_o^{h^+}$ arises from the fact that the transition state benefits very little from hyperconjugation and/or the bond strength effect because $sp^3 \rightarrow sp^2$ hybridization of the α-carbon has made little progress.[40]

$PhCH_2CH_2NO_2$. The situation with this compound is similar to that with $HOCH_2CH_2NO_2$, i.e., eq 24 applies. However, here $\delta\log k_o^{I}$ is very small because the $PhCH_2$

$$\Delta\log k_o^{PhCH_2CH_2NO_2} = \delta\log k_o^{I} + \delta\log k_o^{h^+} \quad (24)$$

group has a very small inductive effect; in fact, depending on which substituent constant is taken as a measure of the inductive effect, it may either be considered slightly electron withdrawing or electron donating.[37] We shall assume that $\delta\log k_o^{I} \approx 0$ and hence $\Delta\log k_o^{PhCH_2CH_2NO_2} \approx \delta\log k_o^{h^+}$. This is consistent with our finding that $\delta\log k_o^{XCH_2NO_2}$ for $PhCH_2CH_2NO_2$ is more negative than for $HOCH_2CH_2NO_2$.

$PhSCH_2NO_2$. This compound represents the most complex case because, apart from the inductive effect, it is not clear *a priori* which of the potential factors associated with the phenylthio group, such as d−p π resonance, negative hyperconjugation, and polarizability, are important. If all factors were to contribute, eq 25 would apply. In eq 25 $\delta\log k_o^{dR}$ and $\delta\log k_o^{h^-}$ are expected to be negative while $\delta\log k_o^{I}$ and $\delta\log k_o^{P}$ are expected to

$$\Delta\log k_o^{PhSCH_2NO_2} = \delta\log k_o^{I} + \delta\log k_o^{dR} + \delta\log k_o^{h^-} + \delta\log k_o^{P} \quad (25)$$

be positive. Since the experimental $\Delta\log k_o^{XCH_2NO_2}$ is strongly positive (1.27 in water and 1.07 in 90% DMSO) the latter two terms are clearly dominant. However, it is difficult to evaluate the relative magnitude of $\delta\log k_o^{I}$ and $\delta\log k_o^{P}$. From the analysis of $\Delta\log k_o^{XCH_2NO_2}$ for $PhCH_2NO_2$, $HOCH_2NO_2$, and $PhCH_2CH_2NO_2$, it appears that $\delta\log k_o^{I}$ is typically quite small, as pointed out previously.[17a,b] For $PhSCH_2NO_2$ one expects a somewhat larger $\delta\log k_o^{I}$ term because the inductive effect of the PhS group is larger than that of the other X

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(29) (a) Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 4343. (b) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (c) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969. (d) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115. (e) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1990**, *112*, 8448.

(30) 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 state solvation of the incipient protonated amine lags behind proton transfer.[17c,31]

(31) (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.

(32) Statistically corrected for the fact that CH_3NO_2 has three while XCH_2NO_2 has only two acidic protons.

(33) h^+ is symbolizing positive hyperconjugation; this symbol is used for simplicity and is meant to include bond strength effects.

(34) The previously mentioned fact that log $k_o(R_2NH)$ is significantly larger than log $k_o(RNH_2)$ is a clear indication that steric effects are not important.[29]

(35) It may be useful to remind ourselves that it is the *intrinsic* rate constant, not the *actual* rate constant which is lowered; the latter is actually somewhat enhanced.[22] It is the fact that the experimental rate constant is not enhanced as much as one would expect if the resonance effect were developed in proportion to the degree of proton transfers which leads to the reduction in the *intrinsic* rate constant. We add this clarification in response to a referee's comment.

(36) Incidentally, this is also the reason in the deprotonation of substituted phenylnitromethanes by amines the α_{CH} Brønsted value (variation of the phenyl substituent) is much larger than the Brønsted β_B value (variation of the amine).[20]

(37) For example, the σ_I values for Ph, $HOCH_2$, $PhCH_2$, and PhS are 0.12, 0.05, 0.03, and 0.30, respectively,[38] while the *F* values are 0.12, 0.03, −0.04, and 0.30, respectively.[39]

(38) Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439.

(39) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(40) A referee has suggested that "important solvation changes between neutral and anion are bound to complicate analysis". In view of the fact that the OH group does not get ionized, we do not believe this to be an important issue. However, as has been discussed in ref 24, intramolecular hydrogen bonding between the OH and NO_2 group in $HOCH_2CH{=}NO_2^-$ might possibly play a role in stabilizing the nitronate ion. This effect would lag behind proton transfer at the transition state in a similar way as hyperconjugation and bond strength effects and hence would have a similar effect on log k_o. It can therefore be regarded as included in the $\delta\log k_o^{h^+}$ term.

groups.[37] Based on Bordwell's[7] analysis of the relative contribution of the inductive effect to the acidifying effect of the α-phenylthio group in a number of carbon acids, we estimate that close to a third or half of the $\Delta\log k_o^{XCH_2NO_2}$ value could be due to the $\delta\log k_o^{I}$ term. This implies that the $\delta\log k_o^{P}$ term is at least half to two-thirds of the $\Delta\log k_o^{XCH_2NO_2}$ value if $\delta\log k_o^{dR}$ and $\delta\log k_o^{h^-}$ are negligible, and larger than that if the $\delta\log k_o^{dR}$ and/or $\delta\log k_o^{h^-}$ terms are significant.

A comment regarding the circumstances under which the polarizability effect enhances k_o is in order. As outlined in the Introduction this enhancement is a consequence of the accumulation of negative charge on the α-carbon of the imbalanced transition state which allows a disproportionately strong stabilization of the transition state by the adjacent sulfur. This is similar to the explanation of why electron-withdrawing inductive effects enhance k_o. However, there are some important differences between the two effects that result from the fact that polarizability effects are proportional to the *square* of the charge ($(\delta_C)^2$ in eq 3) and drop off very steeply with the fourth power of distance, whereas inductive effects are simply proportional to the charge and drop off only with the square of the distance.[41] With respect to the inductive effect, this means that, as long as the transition state is imbalanced in the sense that charge delocalization lags behind proton transfer, $\delta\log k_o^{I}$ will always be positive. In contrast, as discussed in more detail elsewhere,[17b] $\delta\log k_o^{P}$ is positive only if the imbalance is substantial and proton transfer at the transition state has made significant progress. Both conditions are amply met in the deprotonation of nitroalkanes.[17b]

Solvent Effect on $\mathbf{p}K_a^{CH}$ and log k_o. All nitro compounds in Table 3 show the typical increase in pK_a^{CH} as the solvent is changed from water to 90% DMSO, reflecting mainly the loss of hydrogen bonding solvation of the nitronate ion by water. The magnitude of the solvent effect on pK_a^{CH} varies somewhat depending on the X group in XCH_2NO_2 (see ${}^{W}\Delta^{D}pK_a^{CH}$ in Table 3). For $PhSCH_2NO_2$ and $PhCH_2NO_2$ ${}^{W}\Delta^{D}pK_a^{CH}$ is smaller than for CH_3NO_2; apparently part of the loss in solvation of the respective nitronate ion in 90% DMSO is offset by enhanced inductive and polarizability effects in the former case, and enhanced inductive and resonance effects in the latter. For $PhCH_2CH_2NO_2$ ${}^{W}\Delta^{D}pK_a^{CH}$ is *larger* than for CH_3NO_2; in this case the extra stabilization of the anion by positive hyperconjugation is *less* effective in 90% DMSO than in water which, as mentioned earlier, must be the result of destabilization of the charge separated structure **4b** in DMSO.

As to the intrinsic rate constants, they are all considerably larger in 90% DMSO than in water, with log (k_o^{D}/k_o^{W})[42] values varying between 2.61 and 3.79 (Table 3). As discussed in detail elsewhere,[17c,43] there are several factors that contribute to the solvent effect on k_o for deprotonation of carbon acids. The main one is the lag in the solvation of the incipient nitronate ion behind proton transfer at the transition state coupled with the fact that nitronate ions are much less solvated by DMSO than by water. If one regards the ${}^{W}\Delta^{D}pK_a^{CH}$ values discussed above as an approximate measure of the strength of solvation of the nitronate ion by water, there is indeed a rough correlation between $\log(k_o^{D}/k_o^{W})$ and ${}^{W}\Delta^{D}pK_a^{CH}$, consistent with the above notion about the origin of the solvent effect.

Association between Nitronate Ions and $\mathbf{R_2NH_2^+}$. In 90% DMSO−10% water there is measurable association between the ammonium ions and the nitronate ions (Scheme 1). The association is strong enough with $PhCH_2CH{=}NO_2^-$ to allow a determination of K_{assoc} for all $R_2NH_2^+$ although the K_{assoc} values suffer from large experimental uncertainty (Table 2). In the case of $PhSCH{=}NO_2^-$ the association is weaker and only allows crude K_{assoc} values to be obtained with morpholinium and 1-(2-hydroxyethyl)piperazinium ion.

The dependence of K_{assoc} on $R_2NH_2^+$ and nitronate ion appears to follow the expected trend for hydrogen bonded complexes, i.e., K_{assoc} increases with increasing oxygen basicity of the nitronate ion (pK_a^{NOH}) and increasing acidity of $R_2NH_2^+$ although the latter trend is quite weak, perhaps on account of the large experimental uncertainties. The same dependencies were observed for K_{assoc} in the case of $CH_2{=}NO_2^-$ and $PhCH{=}NO_2^-$.[22]

Conclusions

The main objective of the present study has been to identify the principal interaction mechanism that can explain the strong acidifying effect of the thiophenoxy group on $PhSCH_2NO_2$. Apart from an inductive effect, the possible interaction mechanisms include d−p π-resonance, negative hyperconjugation, and polarizability. On the basis of our findings that the intrinsic rate constant (k_o) for the deprotonation of $PhSCH_2NO_2$ by amines is substantially higher than for the deprotonation of other nitroalkanes, it was concluded that the dominant interaction mechanism is the polarizability of the sulfur group. This conclusion follows from an analysis which shows that, because of the imbalanced nature of the transition state its stabilization by the thiophenoxy group is disproportionately strong compared to the stabilization of the nitronate ion; this is what causes the increase in k_o. This contrasts with the expectation that d−p π-resonance or negative hyperconjugation should *depress* k_o.

Experimental Section

${}^{1}H$ NMR spectra were recorded on a Bruker 250-MHz spectrometer. Kinetic experiments were carried out on a Durrum-Gibson stopped-flow spectrophotometer equipped with OLIS computerized software. UV−vis spectra were obtained on a Perkin-Elmer Lambda 2 or Hewlett-Packard 8562 diode array spectrophotometer. pH measurements were made on an Orion 611 pH meter.

Materials. Water was taken from a Milli-Q water purification system. Piperidine, 1-(2-hydroxyethyl)piperazine, piperazine, morpholine, 2-methoxyethylamine, and *n*-butylamine were refluxed over CaH_2 and freshly distilled prior to use. Methoxyacetic acid was distilled prior to use. Chloroacetic acid, cyanomethylamine, glycinamide, and methoxyamine were recrystallized from ethanol. KOH and HCl solutions were prepared from "dilut-it" from Baker Analytical. DMSO was distilled from CaH_2 and stored over 4 Å molecular sieves.

1-Nitro-2-phenylethane is a yellow oil that was synthesized by the procedure of Varma and Kabalka[44] by reducing β-ni-

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[41] Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

[42] The $\log(k_o^{D}/k_o^{W})$ in Table 3 are for the reactions with secondary alicyclic amines, with k_o^{D} referring to 90% DMSO. Note that if the temperatures in the two solvents were the same, the $\log(k_o^{D}/k_o^{W})$ values would be slightly higher.

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

trostyrene with $NaBH_4$. ^1H NMR (250 MHz, $CDCl_3$): δ3.31 (2H, t, phenyl-CH_2), 4.60 (2H, t, CH_2NO_2), 7.35 (5H, m, ArH).

(Phenylthio)nitromethane is a clear oil that was synthesized by the procedure of Barrett et al.[45] ^1H NMR (250 MHz, $CDCl_3$): δ5.44 (2H, s, CH_2), 7.35 (5H, m, ArH); lit.[45] 5.45 (2H, s, CH_2), 7.25−7.5 (5H, m, ArH).

Kinetic Runs and Spectra. The kinetic experiments were run under pseudo-first-order conditions with the substrate as the minor component. The reactions were monitored spectrophotometrically at the λ_{max} of the anion of the substrate. For reactions at pH < pK_a^{CH}, the carbon acid was placed in a 10^{-3} M KOH solution and then mixed in the stopped-flow apparatus with the respective amine buffer containing 10^{-3} M HCl.

Reaction Solutions: pH and pK_a Measurements. The pK_a^{BH} values of the amines and pK_a^{AH} of the acids were determined by measuring the pH of various buffer ratios and plotting log([B]/[BH$^+$]) vs pH according to the Henderson−Hasselbach equation pH = pK_a + log([B]/[BH$^+$]) where the intercept is the pK_a and the slope is unity. The pH of reaction solutions for stopped-flow runs was measured in mock-mixing experiments that simulated the stopped-flow runs. Water solutions were prepared at an ionic strength of 0.50 M by addition of KCl, and pH measurements were performed with an Orion Ross electrode and an Orion no. 800500 reference electrode. The solutions of 90% Me_2SO−10% water were prepared by adding 10 mL of aqueous solution to a 100-mL volumetric flask and topping off with Me_2SO. The reaction mixtures were adjusted to have an ionic strength of 0.06 M by addition of KCl. pH measurements were made with an Orion Ross electrode and an Orion 80-03 Sure-Flow reference electrode. For 90% Me_2SO−10% water, the pH meter was calibrated according to Hallé et al.[46] The pK_a values of the carbon acids were determined in chloroacetate (for $PhSCH_2NO_2$) and methoxyacetate buffer (for $PhCH_2CH_2NO_2$) by classical spectrophotometric procedures at the λ_{max} of the anion of the substrate.

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Supporting Information Available: Table S1−S29, kinetic data (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(45) Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Org. Synth.* **1990**, *68*, 8.

(46) Hallé, J. C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1970**, 2047.