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Deprotonation of Arylnitromethanes. Higher Intrinsic Rate Constants with Thiolate Ions than with Oxyanions or Amines as the Proton Acceptors. Hydrogen Bonding in the Transition State and Desolvation of the Base as Competing Factors in Proton Transfer at Carbon

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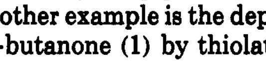
A kinetic study of the deprotonation of arylnitromethanes by alkyl thiolate ions and aryloxide ions in water at 25 °C is reported. Intrinsic rate constants (k_o) were determined for the reactions of phenylnitromethane and (4-nitrophenyl)nitromethane by extrapolating Brønsted plots of log k_1 (k_1 is the deprotonation rate constant) vs $\Delta pK = pK_a^{BH} - pK_a^{CH}$ (BH = RSH or ArOH; CH = $ArCH_2NO_2$) to $\Delta pK = 0$. $k_o^{RS^-}$ for the deprotonation of phenylnitromethane was found to be comparable to $k_o^{ArO^-}$ and also to the previously reported $k_o^{R_2NH}$ (deprotonation by secondary alicyclic amines) but larger than the previously reported $k_o^{RCOO^-}$ (deprotonation by carboxylate ions); for the deprotonation of (4-nitrophenyl)nitromethane $k_o^{RS^-}$ was found to exceed $k_o^{ArO^-}$ as well as $k_o^{R_2NH}$. This is in sharp contrast with the deprotonation of HCN (Bednar and Jencks), 4-(4-nitrophenoxy)-2-butanone (Pohl and Hupe), and acetylacetone (Ahrens et al.) where k_o for thiolate ions is much *lower* than for oxyanions or amines. These conflicting observations are attributed to a change in the relative importance of hydrogen-bonding stabilization of the transition state (favors reactions with oxyanions and amines over thiolate ions) and the requirement for (partial) desolvation of the base as it enters the transition state (favors reactions with thiolate ions). In reactions where the negative charge in the transition state is substantially localized on the carbon, the hydrogen-bonding factor prevails, whereas for the arylnitromethane reactions where the negative charge is significantly delocalized, the desolvation factor dominates. A Brønsted plot for the deprotonation of seven arylnitromethanes (Z = 2-Me, 3-Me, H, 3-Cl, 3-NO_2, 4-NO_2, 3,5-$(NO_2)_2$) by $HOCH_2CH_2S^-$ yields $\alpha_{CH} = 1.30$. In combination with $\beta_B = 0.48$ (from log k_1 vs ΔpK, see above) an imbalance of $\alpha_{CH} - \beta_B = 0.82$ is obtained. This imbalance is not significantly different from that reported for the deprotonation of arylnitromethanes by secondary alicyclic amines. The relevance of this result with respect to imbalances in the nucleophilic addition of thiolate ions to nitroolefins is discussed. The point for the 2-methyl derivative deviates positively, the 4-nitro derivative negatively from the Brønsted line. The positive deviation is attributed to a decrease in the resonance stabilization of the carbanion due to steric hindrance of the π-overlap, the negative deviation to the added resonance stabilization of the carbanion by the 4-nitro substituent.

In contrast to the numerous kinetic studies of the deprotonation of carbon acids by oxyanions and amines,[1,2] the number of such investigations involving thiolate ions as the proton acceptor is small. In the few cases where comparisons are possible, the proton-transfer rates with thiolate ions in aqueous solution are significantly lower than those with oxyanions or amines of equal pK_a, i.e., the *intrinsic* rate constants (k_o)[3] of the proton transfer involving thiolate ions are lower than for the other bases. For example, for the deprotonation of acetylacetone (acac) a log $k_o \approx 2.5$ for RS^- and a log $k_o \approx 3.2$ for ArO^- may be estimated from the data reported by Ahrens et al.,[4] while for the deprotonation by the piperidine/morpholine pair log $k_o \approx 2.7$.[4] Another example is the deprotonation 4-(4-nitrophenoxy)-2-butanone (1) by thiolate ions and oxy-



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anions.[5] This reaction could only be measured in the deprotonation direction,[6] and hence no k_o could be obtained. However, by comparing Brønsted plots for the two families of bases it was shown that the thiolate ions react 30–50 times more slowly than the oxyanions of the same pK_a, suggesting an approximately 30–50-fold difference in the intrinsic rate constants. In a third example, the intrinsic rate constant for the deprotonation of HCN by $HOCH_2CH_2S^-$ in water is approximately 200-fold lower than with oxyanions as bases.[7]

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[1] For reviews, see: (a) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1. (b) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1973; Chapter 10. (c) Crooks, J. E. In *Proton Transfer Reactions*; Caldin, E., Gold, V., Eds.; Wiley: New York, 1975; p 153. (d) Kresge, A. J. *Ibid.* p 179. (e) More O'Ferrall, R. A. *Ibid.* p 201.

[2] (a) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (c) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

[3] For a reaction with a forward rate constant k_1 and a reverse rate constant k_{-1} the intrinsic rate constant k_o is defined as $k_o = k_1 = k_{-1}$ when $\Delta G^\circ = 0$. In proton-transfer reactions it is common practice to include statistical corrections for bases that have more than one equivalent basic site or for the conjugate acids of the bases that have more than one equivalent proton.[1b]

[4] Ahrens, M.-L.; Eigen, M.; Kruse, W.; Maass, G. *Ber. Bunsenges.* **1970**, *74*, 380.

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

[6] The rapid loss of *p*-nitrophenoxide ion from the carbanion provides the driving force for this thermodynamically unfavorable proton transfer.

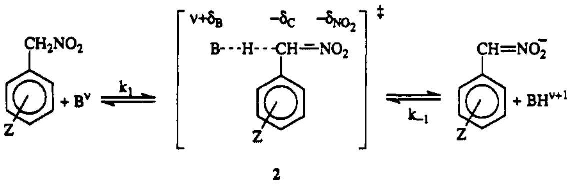
[7] Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7117.

0022-3263/93/1958-0217$04.00/0

These findings, which show that log k_0 decreases in the order $RO^- > R_2NH \gg RS^-$, are most plausibly understood in terms of a reduction in the hydrogen-bonding ability of these bases. According to Bednar and Jencks,[7] hydrogen bonding between the CH-acid and the proton acceptor stabilizes the transition state of proton transfer. Hence, a decrease in the hydrogen-bonding ability of the base should reduce the stabilization of the transition state and lower k_0, as observed. The fact that the difference in k_0 between thiolate and oxyanion reactions increases in the series acac < 1 < HCN supports the hydrogen-bonding explanation. This is because hydrogen-bonding stabilization of the transition state should be most effective when the developing negative charge is mainly localized on the carbon, but less effective if this charge is being (partially) delocalized away from the carbon.[8] Since the reactions that lead to the most strongly delocalized carbanions should also have the most delocalized transition state, one expects the strength of the transition-state hydrogen-bonding stabilization to follow the order HCN > 1 > acac, which is the order suggested by the differences in k_0 between thiolate and oxyanion reactions.

If the above inference is correct, one would expect the difference between k_0 for thiolate ion and oxyanions (or amines) to further decrease or even vanish for a reaction that leads to a more strongly delocalized carbanion than acetylacetonate ion. As will be shown in this paper, this is indeed the case for the deprotonation of arylnitromethanes.

A second objective of the present work was to examine whether the use of thiolate ions has a major effect on the transition-state imbalance in the deprotonation of substituted phenylnitromethanes.[2,10] The transition-state imbalance is believed to be caused by a lag in the charge delocalization behind charge transfer ($\delta_{NO_2} < \delta_B$ in 2) and manifests itself by a Brønsted α_{CH}-value (change in k_1 with the pK_a of the arylnitromethane) that is substantially larger than the Brønsted β_B-value[11] (change in k_1 with the pK_a of the base).



(1)

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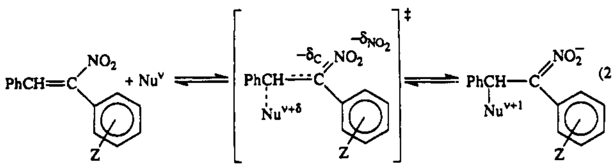
In the nucleophilic additions to substituted α-nitrostilbenes, eq 2, the imbalance $\alpha^n_{nuc} - \beta^n_{nuc}$ (α^n_{nuc} reflects the change in k_1 with the change in the equilibrium constant induced by changes in Z, β^n_{nuc} reflects the change in k_1 with changes in the equilibrium constant induced by a change in the pK_a of the nucleophile), is strongly enhanced when the nucleophile is changed from secondary alicylic amines[14a] to RS^-.[14b] The same is true for nucleophilic addition to substituted β-nitrostyrenes.[15] It has been suggested that soft acid–soft base interactions[16] are responsible for these enhanced imbalances.[14b,15b] Inasmuch as soft acid–soft base interactions should play a much smaller role in proton transfers than in nucleophilic addition reactions, the absence of a significant increase in the imbalance for the deprotonation of arylnitromethanes by thiolate ions would support the above interpretation of the large imbalances in the nucleophilic addition reactions. Our results confirm this expectation.



(2)

Results

General Features. The methodology for obtaining the proton transfer rate constants k_1 and k_{-1} in eq 1 was the same as discussed in an earlier paper[17] and hence is only briefly described here. The reactions were run in aqueous solution at 25 °C and monitored spectrophotometrically. The ionic strength was usually maintained at 0.5 M with KCl; some experiments were run at $\mu = 0.1$ M, with virtually identical results as at $\mu = 0.5$ M. A typical determination of k_1 consisted of running the reaction under pseudo-first-order conditions (base in excess) at 6–10 different concentrations of B^- in a 1:1 $[B^-]$–[BH] buffer; in most cases the pH was substantially higher than the pK_a^{CH} of the carbon acid and hence the slope of k_{obsd} (pseudo-first-order rate constant) vs $[B^-]$ afforded k_1 while k_{-1} was calculated from k_1 and $K_1 = K_a^{CH}/K_a^{BH}$.

In a few cases the contribution from k_{-1} to the slope was significant; in these situations k_1 and k_{-1} were obtained by solving the simultaneous equations slope = $k_1 + k_{-1}$ and $k_1/k_{-1} = K_a^{CH}/K_a^{BH}$. Strong spectral overlap between the phenolate buffers and phenylnitromethane anion made kinetic measurements difficult for this reaction, and only phenoxide ion and 4-cyanophenoxide ion yielded reliable results.

All rate constants determined in this work are summarized in Tables I–III.

Discussion

Brønsted α_{CH} and β_B Values. Imbalances. Figure 1 shows a Brønsted plot of log k_1 vs (− pK_a^{CH}) for the reaction of $HOCH_2CH_2S^-$ with the seven arylnitromethanes listed in Table I. Since the pK_a^{CH} values of the arylnitromethanes have been determined at an ionic strength of 0.1 M,[10] the data in Table I were obtained at the same ionic strength rather than our standard $\mu = 0.5$ M. Control experiments at $\mu = 0.5$ M yielded nearly identical k_1 values. The slope of the line, calculated by omitting the deviating points for the 2-methyl and 4-nitro derivatives (more on

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[8] It is well-known that hydrogen bonding is an important factor in determining k_0 for proton transfers from normal acids (OH, SH, and NH acids) where there is no charge delocalization.[1a,9]

[9] Ahrens, M.-L.; Maass, G. *Angew. Chem., Int. Ed. Engl.* 1968, *7*, 7141.

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

[11] In most proton transfers that lead to the formation of a delocalized carbanion there is such an imbalance with $\alpha_{CH} > \beta_B$.[2] In the case of the arylnitromethanes the imbalance is so large as to lead to $\alpha_{CH} > 1$, e.g., $\alpha_{CH} = 1.54$ with B = OH^- and $\alpha_{CH} = 1.29$ with B = morpholine[10] ("nitroalkane anomaly")[12] which means that the imbalance can be recognized without knowing β_B. It should be noted that in some reactions the lag in the charge delocalization can lead to $\alpha_{CH} < \beta_B$.[2c,13]

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

[13] (a) Stefanidis, D.; Bunting, J. W. *J. Am. Chem. Soc.* 1991, *113*, 991. (b) Bernasconi, C. F.; Fairchild, D. *J. Phys. Org. Chem.* 1992, *5*, 409.

[14] (a) Bernasconi, C. F.; Renfrow, R. A. *J. Org. Chem.* 1987, *52*, 3035. (b) Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* 1988, *110*, 7506.

[15] (a) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* 1986, *108*, 4541. (b) Bernasconi, C. F.; Schuck, D. F. *J. Org. Chem.* 1992, *57*, 2365.

[16] (a) Pearson, R. G. *Surv. Prog. Chem.* 1969, *5*, 1. (b) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* 1967, *89*, 1827.

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

Table I. Reaction of Arylnitromethanes with $HOCH_2CH_2S^-$ in Water at 25 °C[a]

Z	pK_a^{CH} [b]	ΔpK [d]	k_1 [e] ($M^{-1}\,s^{-1}$)	k_{-1} [f] ($M^{-1}\,s^{-1}$)
2-Me	7.60	2.01	1.51 (0.02)	1.48×10^{-2}
3-Me	6.97	2.64	4.60 (0.14)	1.05×10^{-2}
H	6.88	2.73	5.33 (0.10)	1.18×10^{-2}
3-Cl	6.63	2.98	14.0 (0.37)	1.47×10^{-2}
3-NO_2	6.30	3.31	32.8 (0.7)	1.61×10^{-2}
4-NO_2	5.89	3.72	72.8 (0.7)	1.39×10^{-2}
3,5-$(NO_2)_2$	5.66[c]	3.89	215 (3)	2.41×10^{-2}

[a] μ = 0.1 M (KCl). [b] Reference 10. [c] This work. [d] $\Delta pK = pK_a^{BH} - pK_a^{CH}$ with $pK_a^{BH} = 9.61$ (ref 5). [e] Numbers in parentheses are standard deviations. [f] $k_{-1} = k_1K_a^{BH}/K_a^{CH}$.

Table II. Reaction of Phenylnitromethane and (4-Nitrophenyl)nitromethane with Thiolate Ions in Water at 25 °C[a]

$B^- = RS^-$	pK_a^{BH} [b]	ΔpK [c]	k_1 [d] ($M^{-1}\,s^{-1}$)	k_{-1} [e] ($M^{-1}\,s^{-1}$)
$C_6H_5CH_2NO_2$ ($pK_a^{CH} = 6.88$)				
EtS^-	10.35	3.47	11.2 (0.8)	3.78×10^{-3}
$HOCH_2CH_2S^-$	9.61	2.73	5.11 (0.09)	9.52×10^{-3}
$MeO_2CCH_2CH_2S^-$	9.33	2.45	3.58 (0.03)	1.27×10^{-3}
$MeO_2CCH_2S^-$	7.91	1.03	0.77 (0.02)	7.19×10^{-2}
4-$NO_2C_6H_4CH_2NO_2$ ($pK_a^{CH} = 5.89$)				
EtS^-	10.35	4.46	206 (12)	7.16×10^{-3}
$HOCH_2CH_2S^-$	9.61	3.72	110 (8)	2.10×10^{-2}
$MeO_2CCH_2CH_2S^-$	9.33	3.44	91 (5)	3.30×10^{-2}
$MeO_2CCH_2S^-$	7.91	2.02	19.2 (0.5)	1.83×10^{-1}

[a] μ = 0.5 M (KCl). [b] Reference 5. [c] $\Delta pK = pK_a^{BH} - pK_a^{CH}$. [d] Numbers in parentheses are standard deviations. [e] $k_{-1} = k_1K_a^{BH}/K_a^{CH}$.

Table III. Reaction of Phenylnitromethane and (4-Nitrophenyl)nitromethane with Phenolate Ions in Water at 25 °C[a]

$B^- = ArO^-$	pK_a^{BH} [b]	ΔpK [c]	k_1 [d] ($M^{-1}\,s^{-1}$)	k_{-1} [e] ($M^{-1}\,s^{-1}$)
$C_6H_5CH_2NO_2$ (pK_a^{CH} = 6.88)				
$C_6H_5O^-$	9.95	3.07	8.65	7.40×10^{-3}
4-$CNC_6H_4O^-$	7.95	1.07	0.57	4.90×10^{-2}
4-$NO_2C_6H_4CH_2NO_2$ (pK_a^{CH} = 5.89)				
4-$MeOC_6H_4O^-$	10.20	4.31	186	9.12×10^{-3}
$C_6H_5O^-$	9.95	4.06	132	1.15×10^{-2}
3-$ClC_6H_4O^-$	9.02	3.13	46.5	3.44×10^{-2}
4-$CNC_6H_4O^-$	7.95	2.06	9.37	8.16×10^{-2}

[a] μ = 0.5 M (KCl). [b] *Handbook of Biochemistry and Molecular Biology*; Fasman, G. D., Ed.; CRC Press: Cleveland, 1975. [c] $\Delta pK = pK_a^{BH} - pK_a^{CH}$ with $pK_a^{CH} = 5.89$. [d] Standard deviations ±3% or better. [e] $k_{-1} = k_1K_a^{BH}/K_a^{CH}$.

these deviations below) yields $\alpha_{CH} = 1.30 \pm 0.06$. This α_{CH} value is indistinguishable from $\alpha_{CH} = 1.29 \pm 0.06$ and 1.30 ± 0.05 determined by Bordwell and Boyle[10] for the reactions of the same arylnitromethanes with morpholine and 2,4-lutidine, respectively.

Figure 2 shows two Brønsted-type plots[18] for the deprotonation of phenylnitromethane and (4-nitrophenyl)nitromethane by various thiolate ions, while Figure 3 shows similar plots for the reactions with phenolate ions. The Brønsted β_B values are reported in Table IV, along with β_B for the reactions with secondary cyclic amines and carboxylate ions from the literature. We note that the β_B values for the thiolate ion reactions are slightly lower than those for the amine reactions although, considering the error limits in these coefficients, the differences are hardly significant. Since α_{CH} is the same for the thiolate ion and amine reactions (Table IV), the imbalance, $\alpha_{CH} - \beta_B$, is at best marginally larger for the thiolate ion reactions.

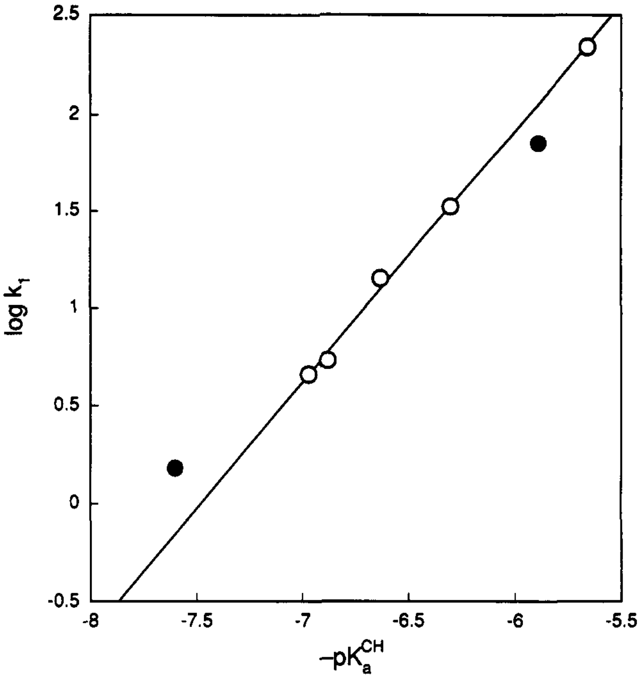

Figure 1. Brønsted plot for the deprotonation of various arylnitromethanes by $HOCH_2CH_2S^-$ in water (data from Table I). The slope (α_{CH}) was calculated without including the deviating points (2-CH_3, positive deviation; 4-NO_2, negative deviation); see text.

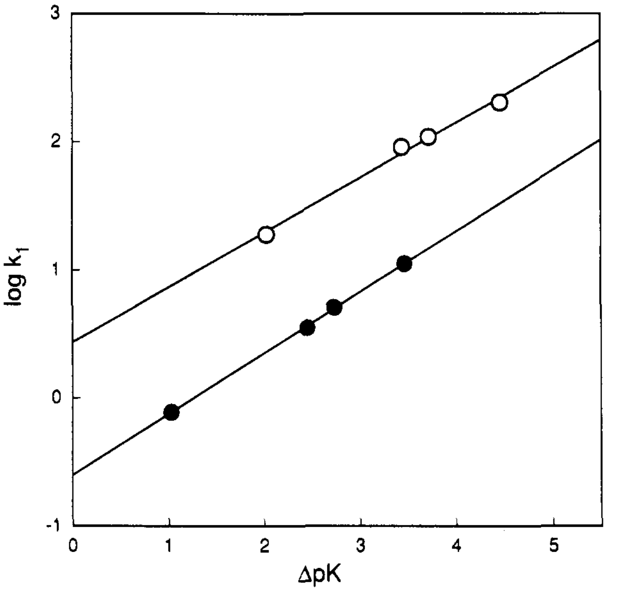

Figure 2. Brønsted (Eigen) plots for the deprotonation of phenylnitromethane (●) and (4-nitrophenyl)nitromethane (○) by thiolate ions in water (data from Table II). Extrapolation to $\Delta pK = 0$ yields the intrinsic rate constant, k_o.

The small and probably insignificant dependence of the imbalance on the type of base in the proton transfer contrasts with a sharp increase in $\alpha_{nuc}^{n} - \beta_{nuc}^{n}$ in the nucleophilic addition of thiolate ions to α-nitrostilbenes[14b] and β-nitrostyrenes[15b] compared to the corresponding nucleophilic additions by piperidine/morpholine[14a,15a] (Table IV). As mentioned in the introduction, this increase in the imbalance has, at least in part, been attributed to soft acid–soft base interactions between the thiolate ion

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[18] Strictly speaking these are Eigen[1a] plots; they have the same slopes as the corresponding Brønsted plots.

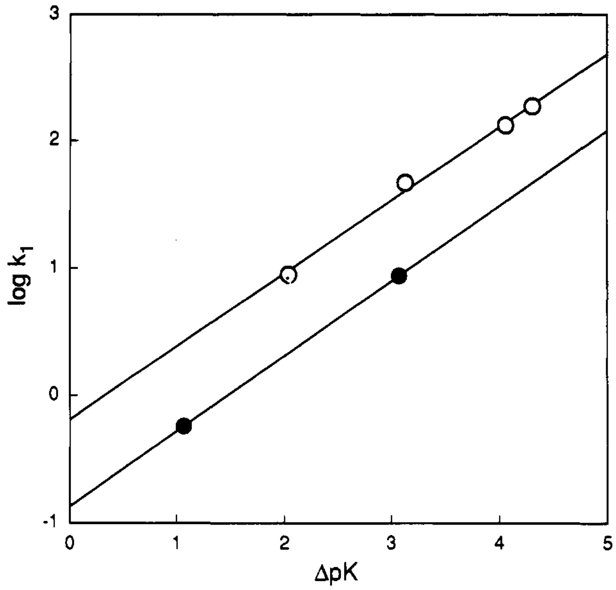

Figure 3. Brønsted (Eigen) plots for the deprotonation of phenylnitromethane (●) and (4-nitrophenyl)nitromethane (○) by phenoxide ions in water (data from Table III). Extrapolation to $\Delta pK = 0$ yields the intrinsic rate constants, k_o.

Table IV. Brønsted Coefficients for the Deprotonation of Arylnitromethanes and Nucleophilic Addition to Nitroolefins in Aqueous Solution at 25 °C

B^{ν} or Nu^{ν}	α_{CH} or α^{n}_{nuc}	β_B or β^{n}_{nuc}	$\alpha_{CH} - \beta_B$ or $\alpha^{n}_{nuc} - \beta^{n}_{nuc}$
		$C_6H_5CH_2NO_2 + B^{\nu}$	
R_2NH[a]	1.29 ± 0.06	0.55 ± 0.06[j]	0.74 ± 0.12
RS^-[b]	1.30 ± 0.06	0.48 ± 0.02	0.82 ± 0.06
ArO^-[b]		0.59[k]	
$RCOO^-$[c]		0.60[k]	
OH^-[a]	1.54		
		$4\text{-}NO_2\text{-}C_6H_4CH_2NO_2 + B^{\nu}$	
R_2NH[a]		0.52 ± 0.06[j]	
RS^-[b]		0.43 ± 0.04	
ArO^-[b]		0.57 ± 0.03	
		$PhCH{=}C(Ar)NO_2 + Nu^{\nu}$[d]	
R_2NH[e]	0.67[i]	0.37	0.30
RS^-[f]	0.87	0.19	0.68
		$ArCH{=}CHNO_2 + Nu^{\nu}$	
R_2NH[g]	0.51[i]	0.25	0.26
RS^-[h]	0.70	0.20	0.50

[a] Reference 10. [b] This work. [c] Based on acetate and chloroacetate ion: Keeffe, J. R.; Munderloh, N. H. *J. Chem. Soc., Chem. Commun.* 1974, 17. [d] In 50% Me_2SO–50% water at 20 °C. [e] Reference 14a. [f] Reference 14b. [g] Reference 15a. [h] Reference 15b. [i] α^{n}_{nuc} has been corrected for the effect of the positive charge on the developing zwitterion; see refs 14a and 15a. [j] Based on reactions of $C_6H_5CH(CH_3)NO_2$. [k] Based on two points only, no standard deviation available.

and the olefin.[14b,15b] These interactions greatly increase the stability of the thiolate ion adducts compared to amine adducts derived from amines of the same basicity as the thiolate ions.[19] More importantly, the intrinsic rate constants for thiolate ion addition is also enhanced compared to that for amine addition, indicating that at the transition state the soft acid–soft base interactions have made more progress than C–S bond formation.[14b,15b] This disproportionately large development of the soft acid–soft base interactions may allow the development of substantial negative charge density on the α-carbon (large α^{n}_{nuc}) without extensive C–S bond formation (low β_{nuc}) which could explain the large $\alpha^{n}_{nuc} - \beta^{n}_{nuc}$ values.

Our results for the proton transfer reaction add support to the above interpretation of the exalted $\alpha^{n}_{nuc} - \beta^{n}_{nuc}$ values for the thiolate ion addition to nitro-activated olefins. In the transition state of the proton transfer the soft acid–soft base interactions should be much smaller or nonexistent because of the hardness of the proton[16] and because the distance between the sulfur base and the (soft) developing carbanion is too large.[20] Hence, the imbalance in the proton transfer should depend little on the type of base, as observed.[21]

Deviations of 2-Methyl- and (4-Nitrophenyl)nitromethane from the Brønsted Line. The point for the 2-methyl derivative deviates positively by 0.38 log units from the Brønsted plot in Figure 1. A similar, even larger positive deviation (ca. 0.85 log units) was noted in the deprotonation of the same series of arylnitromethanes by OH^- in water.[24]

These deviations can be attributed to a steric effect by the methyl group which reduces the resonance stabilization of the nitronate ion by hindering coplanarity of the nitro group. This effect leads to a substantial decrease in the acidity of (2-methylphenyl)nitromethane ($pK_a^{CH} = 7.60$) compared to that of the 3-methyl derivative $pK_a^{CH} = 6.97$.) However, the concomitant decrease in k_1 is disproportionately small because, according to the rules of the principle of nonperfect synchronization (PNS),[25] the reduced resonance stabilization of the product ion leads to an increase in the *intrinsic* rate constant. This increase in the intrinsic rate constant counteracts the reduction in k_1 caused by the thermodynamic effect of the lower acidity of the 2-methyl derivative and results in a positive deviation from the Brønsted plot.

It should be noted that just as a reduction of the resonance stabilization of the nitronate ion enhances k_o, an increase in the resonance stabilization by a substituent lowers k_0 and leads to a negative deviation from a Brønsted plot. Such a negative deviation is seen for the 4-nitro derivative in Figure 1 but it is quite small. A larger deviation has been observed with OH^- as the base in water[24] and an even larger one with $PhCOO^-$ as the base in Me_2SO solution.[26]

Intrinsic Rate Constants. The intrinsic rate constants, k_o,[3] for the deprotonation of phenylnitromethane

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[19] For example, the equilibrium constant for addition of EtS^- to α-nitrostilbene is about 4×10^5 fold higher than for addition of piperidine which has approximately the same pK_a as EtS^-.[14]

[20] Polarizability effects which are at the root of the softness of sulfur bases fall off very rapidly with distance; see, e.g.: Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* 1987, *16*, 1.

[21] It should be noted that the above discussion is based on the traditional interpretation of β_B and β^{n}_{nuc},[22] i.e., that these parameters represent at least an approximate measure of charge transfer at the transition state and hence the deviation of α_{CH} from β_B or of α^{n}_{nuc} from β^{n}_{nuc} can be taken as a measure of transition-state imbalance. This interpretation is not universally accepted.[23]

[22] (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; p 156. (b) Kresge, A. J. *Acc. Chem. Res.* 1975, *8*, 354. (c) Jencks, W. P. *Chem. Rev.* 1985, *85*, 511.

[23] (a) Pross, A. *J. Org. Chem.* 1984, *49*, 1811. (b) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* 1985, *107*, 4737. (c) Pross, A.; Shaik, S. S. *New J. Chem.* 1989, *13*, 427.

[24] Data from ref 10 discussed in ref 2c.

[25] The PNS[2] states that a product-stabilizing factor lowers the intrinsic rate constant (k_o) if its development lags behind bond changes or charge transfer at the transition state but raises the intrinsic rate constant if it develops ahead of bond changes or charge transfer. Resonance is a product-stabilizing factor that typically lags behind charge transfer and hence lowers the intrinsic rate constant.[2] A corollary of the PNS is that a reactant stabilizing factor lowers k_o if its loss is ahead of charge transfer but increases k_o if its loss lags behind charge transfer.

[26] Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *J. Am. Chem. Soc.* 1979, *101*, 1295.

Table V. Intrinsic Rate Constants, Expressed as log k_o,[a] for the Deprotonation of Arylnitromethanes by Various Bases in Water at 25 °C

base	$C_6H_5CH_2NO_2$	$4\text{-}NO_2C_6H_5CH_2NO_2$
RS^-	-0.61 ± 0.02^b	0.45 ± 0.15^b
ArO^-	-0.87 ± 0.15^b	-0.17 ± 0.10^b
$RCOO^-$	-1.74 ± 0.10^c	
R_2NH	-0.86 ± 0.10^e	-0.12^e

[a] k_o in units of $M^{-1} s^{-1}$. [b] This work. [c] Based on data from: Keeffe, J. R.; Munderloh, N. H. *J. Chem. Soc., Chem. Commun.* 1974, 17. [d] Based on data of ref 10.

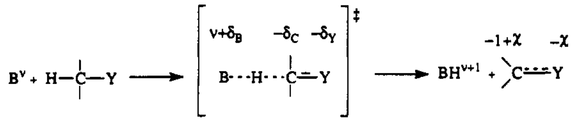
and (4-nitrophenyl)nitromethane by thiolate and phenolate ions were obtained by extrapolation of the corresponding Brønsted plots of Figure 2 and 3 to $\Delta pK = 0$. These k_o values, along with those previously determined for the reactions with carboxylate ions and amines, are reported in Table V. It should be noted that, for reasons detailed under Results, the Brønsted plot for the reaction of phenylnitromethane with phenolate ions consists of only two points which may render the intrinsic rate constants derived from this plot somewhat less certain. A conservative error limit of ±0.15 log units has therefore been assigned to this k_o value.

The most noteworthy feature of our results is that for the reactions of phenylnitromethane with thiolate ions k_o is comparable with that for the corresponding reactions with aryloxide ions and amines and higher than k_o for the reaction with carboxylate ions; with (4-nitrophenyl)nitromethane the intrinsic rate constant for thiolate is even higher than k_o for the aryloxide ions and amines. This contrasts with HCN, 4-(4-nitrophenoxy)-2-butanone (1) and acac where k_o for the deprotonation by thiolate ions is *lower* than with the other types of bases. This is clearly seen in Table VI which compares the ratios $k_o^{RS^-}/k_o^{ArO^-}$, $k_o^{RS^-}/k_o^{RCOO^-}$, and $k_o^{RS^-}/k_o^{R_2NH}$ for $C_6H_5CH_2NO_2$ and $4\text{-}NO_2C_6H_4CH_2NO_2$ with those for HCN, 1, and acac. These ratios increase along the sequence HCN < 1 < acac < $C_6H_5CH_2NO_2$ < $4\text{-}NO_2C_6H_4CH_2NO_2$; i.e., the arylnitromethanes continue the trend expected for transition states with decreasing charge density on the carbon. In other words, as pointed out in the introduction, the disadvantage of the thiolate ions in terms of their inferior hydrogen bonding capabilities compared to oxyanions or amines becomes less and less important as the negative charge on the developing carbanion in the transition state becomes more delocalized. This phenomenon can even be seen when comparing (4-nitrophenyl)nitromethane with phenylnitromethane: the larger log $(k_o^{RS^-}/k_o^{ArO^-})$ and log $(k_o^{RS^-}/k_o^{R_2NH})$ for the former apparently reflects a further increase in charge delocalization due to the *p*-nitrophenyl group.

A comment aimed at dispelling a point of potential confusion is in order here. Since in reactions that lead to delocalized carbanions the delocalization lags behind charge transfer at the transition state, one might infer that the degree of delocalization at the transition state should be about equally small for all reactions, irrespective of the amount of delocalization in the carbanion. Our results along with the data on HCN, 1, and acac show that this is not the case; i.e., despite the lag, the delocalization at the transition state increases with the degree of delocalization in the carbanion. This conclusion is consistent with a recently proposed model[2c] which relates the charge on the carbon in the transition state to the Brønsted β_B-value and the degree of charge delocalization in the carbanion. According to this model, which is derived from a proposal by Kresge,[12] the charge on the carbon, δ_C, is given by eq 3 with δ_B being the charge transferred from

$$\delta_C = \delta_B - \delta_Y = \delta_B - \chi(\delta_B)^n \tag{3}$$

the base to the carbon acid, δ_Y the charge on the π-acceptor Y in the transition state, χ the charge delocalized into Y in the carbanion, and n having a value between 2 and 3.



(4)

If one equates δ_B with the Brønsted β_B value,[27] eq 3 becomes

$$\delta_C = \beta_B - \chi(\beta_B)^n \tag{5}$$

In applying eq 5 to obtain crude estimates of δ_C we shall use $\beta_B = 0.5$; this is close to the experimental values for the reactions of $PhCH_2NO_2$ (0.48), 1 (0.59),[5] and acac (0.59)[28] and probably also close to β_B in reaction of HCN,[7] and δ_C is not very sensitive to small deviations from β_B.[29] Assuming $n = 2.5$ then leads to

$$\delta_C = 0.50 - 0.18\chi \tag{6}$$

For the reaction of HCN we can assume $\chi \approx 0$ and hence $\delta_C \approx 0.50$. At the other extreme, the reaction of phenylnitromethane, χ is likely to be close to unity and hence $\delta_C \approx 0.32$. For the reactions of 1 and acac χ is more difficult to estimate but it is reasonable to assume $1 > \chi(\text{acac}) > \chi(1) > 0$. For the sake of argument we shall use $\chi(\text{acac}) \approx 0.75$ and $\chi(1) \approx 0.50$, which leads to $\delta_C(\text{acac}) \approx 0.37$ and $\delta_C(1) \approx 0.41$.

Why Are Thiolate Ions the Most Reactive Bases with $ArCH_2NO_2$? Referring back to Table VI we note that $k_o^{RS^-}$ for the deprotonation of (4-nitrophenyl)nitromethane has not just become similar to $k_o^{ArO^-}$ and $k_o^{R_2NH}$ but is significantly larger than these latter values, and for the deprotonation of phenylnitromethane $k_o^{RS^-} \gtrsim k_o^{ArO^-} \gg k_o^{RCOO^-}$. This suggests the presence of one or more other factors which, for strongly hydrogen-bonded transition states, are overshadowed by the hydrogen-bonding effect but which manifest themselves when hydrogen bonding becomes negligible. One such factor is probably the solvation of the respective bases. In order to enter the transition state, the base needs to be partially desolvated. There exists substantial evidence that in the transition state this desolvation process is more advanced ("early desolvation") than the proton or charge transfer.[2,30,31] According to the rules of the PNS[25] this lowers the intrinsic rate constant of the reaction and the more so the more strongly the base is solvated. This PNS-effect can be understood in terms of eq 7 in which $\delta \log k_o^{des}(B)$ is the decrease in

$$\delta \log k_o^{des}(B) = (\lambda_{des}^{B} - \beta_B)\delta \log K_1^{des}(B) \tag{7}$$

log k_o caused by the desolvation requirement, $\delta \log K_1^{des}(B)$ is the reduction in the equilibrium constant (K_1) of the reaction brought about by the solvation of B,

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[27] Again this is the traditional interpretation.[21]

[28] Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* 1985, *26*, 420.

[29] For example, with $\chi = 1.0$ and $n = 2.5$ eq 5 yields $\delta_C = 0.31, 0.32$, and 0.32 for $\beta_B = 0.45, 0.50$, and 0.60, respectively. With $\chi = 0.5$ and $n = 2.5$ one obtains $\delta_C = 0.38, 0.41$, and 0.44 for $\beta_B = 0.45, 0.50$, and 0.60, respectively.

Table VI. Relative Intrinsic Rate Constants for the Deprotonation of Different Carbon Acids by Thiolate Ions, Aryl Oxide Ions, Carboxylate Ions, and Amines in Water at 25 °C

	HCN[a]	1[b]	acac[c]	$C_6H_5CH_2NO_2$[d]	$4\text{-}NO_2C_6H_4CH_2NO_2$[d]
$\log (k_o^{RS^-}/k_o^{ArO^-})$	≤ -2.4[e]	ca. -1.6[f]	ca. -0.7[g]	0.26 ± 0.26	0.62 ± 0.25
$\log (k_o^{RS^-}/k_o^{RCOO^-})$			ca. -0.5[h]	1.13 ± 0.25	
$\log (k_o^{RS^-}/k_o^{R_2NH})$	≤ -1.9[i]		ca. -0.2[j]	0.25 ± 0.20	0.57 ± 0.25

[a] Reference 7. [b] Reference 5. [c] Reference 4. [d] This work. [e] Based on $\log k_o^{RS^-} \lesssim 5.7$ ($RS^- = HOCH_2CH_2S^-$) and $\log k_o^{ArO^-} \approx 8.1$ ($ArO^- = 3\text{-}NO_2C_6H_4O^-$). [f] Based on an average distance between Brønsted plots in the pK_a^{BH} range of 7–10. [g] Based on $\log k_o^{RS^-} \approx 2.5$ and $\log k_o^{ArO^-} \approx 3.2$ determined from Eigen plots. [h] Based on $\log k_o^{RS^-} \approx 2.5$ determined from an Eigen plot and $\log k_o^{RCOO^-} \approx 3.0$ estimated from data at 20 °C reported in ref 28. [i] Based on $\log k_o^{RS^-} \lesssim 5.7$ ($RS^- = HOCH_2CH_2S^-$) and $\log k_o^{RR'NH} \approx 7.6$ ($RR'NH = ClCH_2CH_2NH_2$). [j] Based on $\log k_o^{RS^-} \approx 2.5$ and $\log k_o^{RR'NH} \approx 2.7$ determined from Eigen plots.

λ_{des}^{B} is a measure of the progress of the desolvation of B at the transition state, and β_B has its usual meaning. Since the reduction of K_1 implies $\delta \log K_1^{des}(B) < 0$ and early desolvation means $\lambda_{des}^{B} > \beta_B$ we obtain $\delta \log k_o^{des}(B) < 0$.[32]

In the context of eq 7, the reason why $k_o^{RS^-}$ is larger than $k_o^{ArO^-}$ and $k_o^{RCOO^-}$ is that $\delta \log k_o^{des}(B)$ is less negative for the thiolate ion reactions compared to the oxyanion reactions, presumably because $|\delta \log K_1^{des}(B)|$ is smaller for the thiolate ions. This conclusion is consistent with the weaker solvation by water of thiolate ions compared to oxyanions.[33]

Turning to the amine bases, the fact that for the deprotonation of $ArCH_2NO_2$ $k_o^{R_2NH}$ is smaller than $k_o^{RS^-}$ may seem puzzling. Since the solvation of amines is weaker than that of thiolate ions, one would expect that the PNS-effect of early desolvation of the base should depress $k_o^{R_2NH}$ even less than $k_o^{RS^-}$ and, hence, in the absence of significant transition-state hydrogen bonding, $k_o^{R_2NH}$ should be larger than $k_o^{RS^-}$, i.e., $\log (k_o^{RS^-}/k_o^{R_2NH}) < 0$. An additional feature that should tend to accelerate the reactions with amines is a favorable electrostatic interaction in the transition state which contrasts with an unfavorable one in the reactions with anionic bases. Such electrostatic effects can be quite significant.[34]

There are at least two factors that may contribute to the unexpectedly small $k_o^{R_2NH}$. The first is that even though the solvation of amines is weaker than that of thiolate ions, their desolvation at the transition state needs to be essentially complete because they only have one electron pair available for reaction.[35] This contrasts with thiolate ions (and oxyanions) which have three electron pairs; since only one such pair needs to be desolvated, this may be energetically less costly; i.e., $|\delta \log K_1^{des}(B)|$ in eq 7 may be smaller for thiolate ions than for amines. Hence, the PNS effect of early desolvation of the amines is not necessarily smaller than that of the early desolvation of the thiolate ions.

The second factor is the solvation of the developing $BH^{\nu+1}$ which lags behind proton transfer[2,36] and, according to the PNS,[25] lowers k_o. Since the solvation of $BH^{\nu+1} = RR'NH_2^+$ is undoubtedly stonger than that of $BH^{\nu+1} = RSH$, $k_o^{R_2NH}$ should be reduced more than $k_o^{RS^-}$ by this effect. Note that in the case of $BH^{\nu+1} = RCOOH$ solvation is also quite strong[37] and probably stronger than that of RSH, which may contribute to the large $\log (k_o^{RS^-}/k_o^{RCOO^-}) \approx 1.13$. This k_o-lowering PNS-effect of the strong solvation of carboxylic acids also manifests itself in $k_o^{RCOO^-}$ being lower than $k_o^{ArO^-}$ not only in the deprotonation of arylnitromethanes (Table VI) but in the deprotonation of various nitro-substituted diphenylmethanes[38] and 1,3-indandione.[39]

Conclusions

The present study has addressed two main issues. The first, our major focus, concerns the factors that determine which is the most effective base (at constant pK_a^{BH}) in abstracting a proton from a carbon acid in aqueous solution. The two most important ones appear to be the hydrogen-bonding ability of the central atom, and the solvation of the base, or more precisely, the requirement for partial desolvation of the base at the transition state. With respect to the former, the better hydrogen-bonding ability in the order O > N > S increases k_o in the same order; this effect is quite strong as long as the negative charge in the transition state is mainly localized on the carbon but becomes weak for substantially delocalized transition states.

The requirement of (partial) desolvation of the base reduces k_o irrespective of the degree of charge delocalization in the transition state and becomes a dominant factor in reactions where hydrogen bonding is negligible, i.e., in the deprotonation of arylnitromethanes. This reduction in k_o should parallel the solvation energies of the bases in water ($RO^- > RS^- > R_2NH$) and is clearly seen in the $k_o^{RS^-}/k_o^{ArO^-}$ and $k_o^{RS^-}/k_o^{RCOO^-}$ ratios for the deprotonation of $ArCH_2NO_2$. However, the $k_o^{RS^-}/k_o^{R_2NH}$ ratio is abnormally large which is attributed to the requirement of *complete* desolvation of the only electron pair of the amine as it enters the transition state and/or to the k_o-lowering PNS-effect of the late solvation of the protonated amine.

The second point of interest is related to transition-state imbalances. We have shown that the imbalance, $\alpha_{CH} - \beta_B$, in the deprotonation of arylnitromethanes by

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[30] (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7653. (b) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *Ibid.* **1982**, *104*, 7045.

[31] Terrier, F.; Degorre, F.; Kiffer, D.; Laloi, M. *Bull. Soc. Chim. Fr.* **1988**, 415.

[32] A more extreme assumption is that the desolvation of the base occurs in a separate, preequilibrium step rather than being part of the proton transfer process. This implies that λ_{des}^{β} in eq 7 is not just larger than β_B but has a value of unity, a point of view advocated by Jencks.[30b]

[33] (a) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1. (b) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224. (c) Taft, R. W. *Prog. Phys. Org. Chem.* **1983**, *14*, 247.

[34] Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803.

[35] Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479. See also: Berg, U.; Jencks, W. P. *J. Am. Chem. Soc.* **1991**, *113*, 6997.

[36] Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969; p 178.

[37] Murray, C. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1990**, *112*, 1880.

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

[39] Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969.

thiolate ions is not significantly different from the imbalance in the reaction with amines. This result suggests that the strongly enhanced imbalances, $\alpha^{n}_{nuc} - \beta^{n}_{nuc}$, in the nucleophilic addition of thiolate ions to nitroolefins are not an inherent characteristic of the thiolate ions but probably a consequence of the soft acid–soft base interactions that affect nucleophilic addition reactions but not proton transfers.

Experimental Section

Materials. Phenylnitromethane and (3,5-dinitrophenyl)nitromethane were available from previous studies.[17,40] (3-Nitrophenyl)- and (4-nitrophenyl)nitromethane were synthesized as described elsewhere.[41] (2-Methylphenyl)-, (3-methylphenyl), and (3-chlorophenyl)nitromethane were prepared by the reaction of $AgNO_2$ with 2-methyl, 3-methyl-, and 3-chlorobenzyl bromide (Aldrich), respectively, according to the method of Avery and Butler.[42] These compounds are all liquids and were identified by ^1H NMR (100 MHz, $CDCl_3$) and MS: (2-methylphenyl)nitromethane, δ 2.41 (s, 3 H, CH_3), 5.50 (s, 2 H, CH_2), 7.32 (s, 4 H, Ph); MS (*m*/*e*) 151; (3-methylphenyl)nitromethane, δ 2.37 (s, 3 H, CH_3), 5.40 (s, 2 H, CH_2), 7.36 (s, 4 H, Ph); MS (*m*/*e*) 151; (3-chlorophenyl)nitromethane, δ 5.40 (s, 2 H, CH_2), 7.37 (m, 4 H, Ph); MS (*m*/*e*) 171.

Ethanethiol, 2-mercaptoethanol, methyl 3-mercaptopropionate, and methyl mercaptoacetate (all from Aldrich) were distilled under vacuum and stored under nitrogen. Phenol (Mallinckrodt) and 4-methoxyphenol (Aldrich) were recrystallized from hexane; all the other phenols were from Aldrich and were used without further purification.

pK_a^{CH} of Arylnitromethanes. All pK_a^{CH} have been previously reported except for the pK_a^{CH} of (3,5-dinitrophenyl)nitromethane. It was determined spectrophotometrically from eq 8 by measuring the absorbance values at 294 nm in a series of

$$pK_a^{CH} = pH + \log (A_B - A)/(A - A_A) \qquad (8)$$

acetate buffers ((3,5-dinitrophenyl)nitromethane $pK_a^{CH} = 5.66 \pm 0.03$). A_B, A_A, and A are the absorbance values of pH $\gg$ pK_a^{CH}, pH $\ll$ pK_a^{CH}, and pH $\sim$ pK_a^{CH}.

Reaction Solutions and Kinetic Experiments. The procedures were essentially the same as in previous work.[17] The fastest reactions were measured in an Applied Photophysics DX.17MV stopped-flow spectrophotometer, the slowest in a Lambda 2 Perkin-Elmer spectrophotometer. For reactions with intermediate rates an RX-1000 Rapid Kinetics Accessory connected to a Hewlett-Packard 8452A diode array spectrophotometer was used.

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(40) Gandler, J. R.; Bernasconi, C. F. *J. Am. Chem. Soc.* **1992**, *114*, 631.
(41) Bernasconi, C. F.; Ni, J.-X. To be published.
(42) Avery, S.; Butler, A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1110.