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Kinetics of Reversible Thiolate Ion Addition to Substituted β-Nitrostyrenes in Water. Radicaloid Transition State or Principle of Nonperfect Synchronization?

Claude F. Bernasconi* and David F. Schuck

Department of Chemistry and Biochemistry, University of California, Santa Cruz, California 95064

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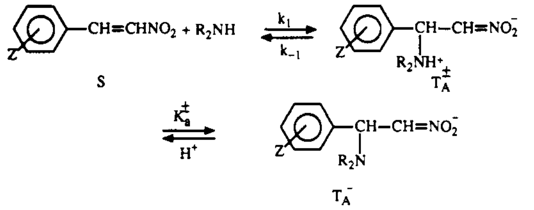
The kinetics of reversible nucleophilic thiolate ion (RS^- with R = *n*-Bu, $HOCH_2CH_2$, $MeO_2CCH_2CH_2$ and MeO_2CCH_2) addition to Z-substituted β-nitrostyrenes (Z = 4-Me_2N, 4-MeO, 4-MeS, 4-Me, H, 3-Cl, 4-Cl, 3-CN, 4-CN, and 3-NO_2), to form $ArCH(RS)CH{=}NO_2^-$, have been measured in water at 20 °C. Rate constants in the forward (k_1) and reverse direction (k_{-1}) and equilibrium constants (K_1) correlate reasonably well with Hammett σ-constants for the non-π-donor substituents but show deviations for the π-donors 4-Me_2N, 4-MeO, and 4-MeS. These deviations are negative for K_1 but positive for k_1 and k_{-1}; the positive deviations for the π-donor substituents are also observed when plotting log k_1 vs log K_1 (Brønsted plots). The negative deviations of K_1 are a consequence of resonance stabilization of the olefin. The positive deviations are attributed to a transition-state stabilization stemming from a preorganization created by the π-donor which leads to a better delocalization of the negative charge into the nitro group. An alternative interpretation of the rate acceleration in terms of a radicaloid transition state (Gross, Z.; Hoz, S. *J. Am. Chem. Soc.* **1988**, *110*, 7489) cannot be ruled out but is shown to be less attractive and unnecessary. Brønsted parameters such as β_{nuc}, β_{eq}, β^n_{nuc}, and β^n_{lg}, and intrinsic rate constants ($k_o = k_1 = k_{-1}$ when $K_1 = 1$) were determined from the dependence on RS^- basicity for β-nitrostyrene and 3-cyano-β-nitrostyrene. β_{eq} is low (0.5), indicating that the carbon basicity of RS^- is less sensitive to electronic effects in R than its proton basicity. β_{nuc} (β^n_{nuc}) is very low, suggesting a transition state with very little C–S bond formation. The low β^n_{nuc} (0.22) contrasts with a large α^n_{nuc} = d log k_1/d log K_1 = 0.74 (variation of Z), indicating a large transition-state imbalance ($\alpha^n_{nuc} - \beta^n_{nuc}$), as previously observed in the reaction of RS^- with α-nitrostilbenes. The intrinsic rate constant (log k_o = 3.5) is also similar to that for the reaction of RS^- with α-nitrostilbenes and significantly higher than for the reaction of amines with β-nitrostyrenes. Most of these features can, at least in part, be attributed to the soft acid-soft base interactions of RS^- with the nitroolefins. Rate constants for carbon protonation of several of the $ArCH(RS)CH{=}NO_2^-$ adducts by acetic acid (k_p^{HA}) were also determined. They display the unusual, but for nitronate ions typical, acceleration when Ar and/or R is made more electron withdrawing.

In 1986 we reported a kinetic study of the reaction of piperidine with substituted β-nitrostyrenes.[1] The reaction can be described by the two-step mechanism of eq 1. The

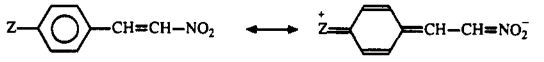


(1)

substituent dependence of k_1, k_{-1}, and K_1 (k_1/k_{-1}) was rather unusual in two respects. (1) With Z = H, 4-Br, 3-Cl, 4-CN, and 4-NO_2, both k_1 and k_{-1} increase slightly with increasing electron-withdrawing strength of the substituent ($\rho(k_1) = 0.27 \pm 0.02$, $\rho(k_{-1}) = 0.33 \pm 0.05$) which results in an equilibrium constant that is essentially substituent-independent ($\rho(K_1) = -0.06 \pm 0.07$). (2) The 4-MeO and 4-$Me_2N$ substituents show substantial positive deviations from the Hammett plots defined by the other substituents for both k_1 and k_{-1}; the deviation is stronger for k_{-1} than for k_1, indicating a negative deviation for K_1 from a corresponding Hammett plot.

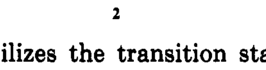
The small ρ-values were attributed to the near cancellation of opposing factors: the combined effect of negative charge development on the $CHNO_2$-moiety and rehybridization of the α-carbon which should be favored by electron-withdrawing substituents and the development of positive charge on the amine nitrogen, which is disfavored.

The positive deviations for 4-MeO and 4-Me_2N from both the k_1 and k_{-1} Hammett plots indicate that the *intrinsic* rate constant ($k_o = k_1 = k_{-1}$ when $K_1 = 1$) of the reaction is enhanced, or the intrinsic barrier lowered, by these substituents. The following interpretation was offered. The π-donor substituents lead to resonance stabilization of the olefin (**1b**) which manifests itself in the



1a **1b**

reduced K_1 values for the 4-MeO and 4-Me_2N derivatives. In the absence of other factors, this resonance effect would also be expected to lower k_1.[2] However, the resonance structure **1b** not only stabilizes the olefin, it also preorganizes the electronic structure toward that of the product, thereby facilitating the delocalization of the incipient negative charge in the transition state, an exaggerated representation of which is shown in **2**. This delocalization



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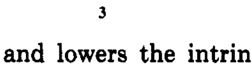

3

stabilizes the transition state and lowers the intrinsic barrier. Without such preorganization, delocalization of the incipient charge into the nitro group lags behind bond formation (**3**). This lag is a major cause for the large intrinsic barriers or low k_o values in nitronate ion forming reactions and is a manifestation of the principle of nonperfect synchronization (PNS).[5] In other words, the effect of the π-donor substituents may be understood as the

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(1) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *108*, 4541.

(2) Such lowering has been observed in the reactions of piperidine with other electrophilic olefins such as benzylidenemalononitriles[3] and benzylidene Meldrum's acids.[4]

(3) Bernasconi, C. F.; Killion, R. B., Jr. *J. Org. Chem.* **1989**, *54*, 2878.

(4) Bernasconi, C. F.; Panda, M. *J. Org. Chem.* **1987**, *52*, 3042.

(5) (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

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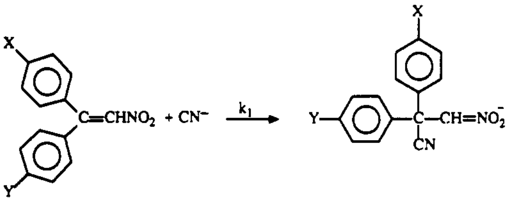
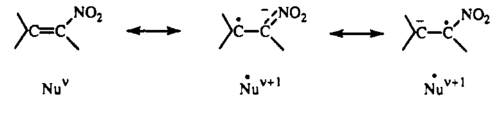
consequence of a partial circumvention of the k_0-lowering PNS effect of delayed delocalization of the negative charge into the nitro group.

In 1988 Gross and Hoz[6] reported kinetic data on the nucleophilic addition of CN^- to substituted 1,1-diaryl-2-nitroethylenes, eq 2. In water, k_1 was shown to correlate



(2)

quite well with σ^0 for seven X, Y combinations, but for X = Y = MeO and X = H, Y = MeO positive deviations from the Hammett plot were observed that were reminiscent of the results we had obtained for reaction 1. When the reaction was conducted in Me_2SO, the positive deviations disappeared. The explanation offered for the enhanced reactivity of the 4-MeO derivatives differed markedly from ours. According to Gross and Hoz these reactions have some of the characteristics of an electron transfer from the nucleophile to the olefin, i.e., the transition state has some radicaloid character which can be understood as a resonance hybrid of **4a–c**. In water **4b** is the major resonance



4a **4b** **4c**

form and rate enhancements arise from mesomeric stabilization of the lone electron on the benzylic carbon by p-MeO or p-Me_2N groups. In Me_2SO **4c** becomes favored and hence there is no special acceleration by the p-MeO and p-Me_2N substituents.

The apparent conflict between Hoz' and our interpretation acquires added significance in the context of Hoz' suggestion that transition states with radicaloid character may be a general phenomenon in nucleophilic reactions involving substrates with low-lying LUMOs (alkenes, aromatic compounds, acyl compounds, carbocations, but not S_N2 substrates),[7] a notion that fits in well with proposals by Shaik and Pross,[8] and by Kochi.[9] It is therefore important to find more experimental evidence which would shed light on the relative merits of the two interpretations. The present study was devised with this objective in mind. If nucleophilic additions to nitro-activated olefins indeed go through transition states with radicaloid character, the use of nucleophiles which are stronger electron donors than CN^- or piperidine, for example, thiolate ions,[10] should enhance the radicaloid character, thereby magnifying the positive deviations of the p-MeO and p-Me_2N derivatives. Furthermore, substituents that are particularly effective at stabilizing radicals without being exceptionally good π-donors in the sense of stabilizing the olefin (e.g., **1b**) should lead to larger positive deviations from Hammett correlations than p-MeO or p-Me_2N, while substituents that destabilize radicals should lead to negative deviations.

We have tested these predictions by studying the reactions of a series of substituted β-nitrostyrenes with the anions of mercaptoethanol ($HOCH_2CH_2S^-$) and methyl mercaptoacetate ($MeO_2CCH_2S^-$) in aqueous solution. Our results do not support the notion of a radicaloid transition state.

An additional objective of our study was to determine intrinsic rate constants of thiolate ion addition to β-nitrostyrenes and transition state imbalances[5] in these reactions. A recent determination of these parameters in the reaction of α-nitrostilbenes with thiolate ions[12] suggested that they might be significantly higher than in the reaction of β-nitrostyrenes with amines, a prediction that is borne out by our results.

Results

We determined the kinetics of the reactions of $HOCH_2CH_2S^-$ and $MeO_2CCH_2S^-$ with Z-substituted β-nitrostyrenes (Z = H, 4-Me, 4-MeO, 4-MeS, 4-Me_2N, 3-Cl, 4-Cl, 4-CN, 3-CN, and 3-NO_2) as well as the reactions of methyl 3-mercaptopropionate ion ($MeO_2CCH_2CH_2S^-$) and n-butanethiolate ion (n-BuS^-) with β-nitrostyrene (Z = H) and 3-cyano-β-nitrostyrene (Z = 3-CN). All experiments were conducted in water at 20 °C at an ionic strength of 0.5 M maintained with KCl.

The reversible addition of a thiolate ion to a substituted β-nitrostyrene can be described by eq 3. Kinetics of adduct formation were measured in a stopped-flow spectrophotometer. The reactions, especially for substrates with strongly electron-withdrawing substituents, are quite fast even at modest [RS^-] and hence were conducted in N-methylmorpholine buffers around pH 7.80. At this pH the free [RS^-] of the most reactive (most basic) thiolate ions could be kept very low while still maintaining pseudo-first-order conditions. Excellent first-order plots were obtained in all cases.

(3)

T_{RS}^-

The pseudo-first-order rate constants for equilibrium approach are given by

$$k_{obsd} = k_1[RS^-] + k_{-1} \qquad (4)$$

For a given substrate, k_{obsd} was typically measured at five to seven thiolate ion concentrations. The raw data are summarized elsewhere.[13] Representative plots of k_{obsd} vs [RS^-] are shown in Figure 1. These plots provided accurate k_1 values from the slope but in many cases the intercepts were too small to afford reliable k_{-1} values.

A better method for the determination of k_{-1} was to generate T_{RS}^- in basic solution and subject it to a pH-jump into an acetic acid buffer, as described in the Experimental Section. In these experiments the free thiolate ion concentration was typically negligible, making the breakdown of T_{RS}^- into S virtually irreversible. Due to rapid decomposition of the T_{RS}^- solutions these experiments were subject to complications as detailed in the Experimental Section; with T_{RS}^- derived from n-BuS^- the results were not very reproducible and should only be regarded as giving approximate rate constants.

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[6] Gross, Z.; Hoz, S. *J. Am. Chem. Soc.* **1988**, *110*, 7489.

[7] Hoz, S. In *Nucleophilic Reactivity*; Harris, J. M., McManus, S., Eds.; Advances in Chemistry Series 215; American Chemical Society: Washington, DC, 1987; Chapter 12.

[8] (a) Shaik, S. S. *Prog. Phys. Org. Chem.* **1985**, *15*, 197. (b) Pross, A. *Adv. Phys. Org. Chem.* **1985**, *15*, 99.

[9] Fukuzumi, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 7240.

[10] In water, the oxidation potentials of CN^-, OH^-, and piperidine are estimated to be 2.52, 1.72, and 1.75 V, respectively, while the estimate for n-$C_3H_7S^-$ is 0.74 V.[11]

[11] Pearson, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 6109.

[12] Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506.

[13] Schuck, D. F. Ph.D. Thesis, University of California, Santa Cruz, 1992.

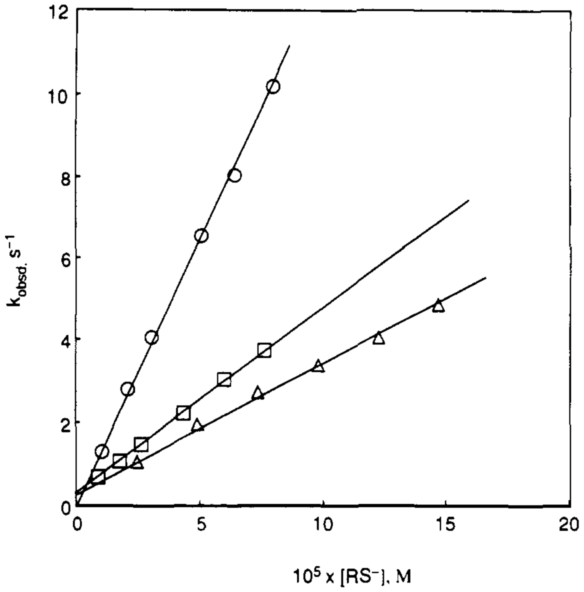


Figure 1. Representative plots of k_{obsd} vs thiolate ion concentration: ○, $HOCH_2CH_2S^-$/3-CN; □, $HOCH_2CH_2S^-$/H; △, $MeO_2CCH_2S^-$/4-MeS (x-axis is $10^4 \times [RS^-]$ for this case).

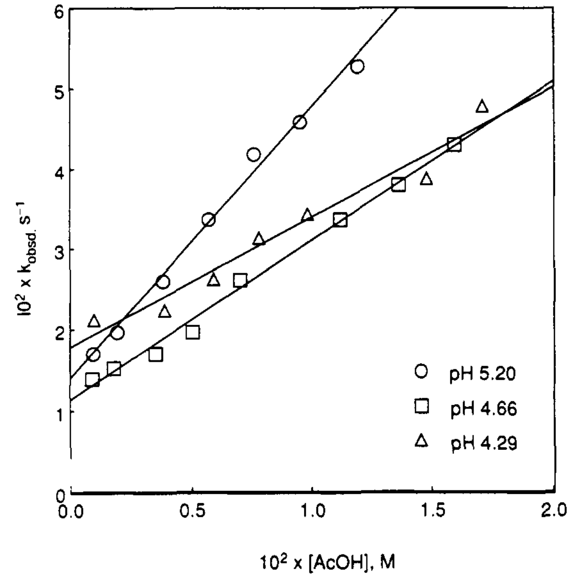
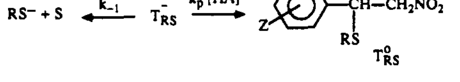


Figure 2. Plots of k_{obsd} vs [AcOH] from pH-jump experiments for the β-nitrostyrene adduct of $HOCH_2CH_2S^-$.

Pseudo-first-order rate constants for the breakdown of T_{RS}^- were measured as a function of acetic acid buffer concentration. The raw data are reported elsewhere.[13] As seen from the three representative plots in Figure 2, k_{obsd} depends significantly on acetic acid concentration. These observations are consistent with a competition between thiolate ion expulsion and carbon protonation of T_{RS}^-, as shown in eq 5. This interpretation is supported by the observation of a decreased yield of S with increasing acetic acid concentration, as revealed by diminishing infinity absorbance values at λ_{max} of the olefin.



(5)

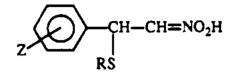
According to eq 5, k_{obsd} is given by

$$k_{obsd} = k_{-1} + k_p^H[HA] \qquad (6)$$

Hence, plots of k_{obsd} vs [HA] should yield k_{-1}(intercept) and k_p^{HA}(slope). At pH ≥5.38 where a majority of our experiments were conducted, eq 6 indeed represents a very good approximation of the true situation, but at lower pH both the slopes and intercepts become pH dependent, as indicated in Figure 2. This is because rapid equilibrium protonation of the nitro group of T_{RS}^- becomes significant and carbon protonation of T_{RS}^- by the hydronium ion starts to make a major contribution to the rate. This requires modification of eq 6 into eq 7 with K_a^{NOH} being the acid

$$k_{obsd} = \frac{K_a^{NOH}}{K_a^{NOH} + a_{H^+}}(k_{-1} + k_p^H a_{H^+} + k_p^{HA}[HA]) \qquad (7)$$

dissociation constant of the nitronic acid $T^o_{RS,NOH}$ and k_p^H the rate constant for carbon protonation of T_{RS}^- by the hydronium ion.[14] The pH-dependence of the slopes and intercepts of Figure 2 are easily understood in terms of eq 7.



$T^o_{RS,NOH}$

The decrease in the slopes with decreasing pH reflects the $K_a^{NOH}k_p^{HA}/(K_a^{NOH} + a_{H^+})$ term; the intercept also decreases from pH 5.20 to 4.66 but then increases from pH 4.66 to 4.29 because $k_a^H a_{H^+}$ becomes dominant at low pH. From a limited set of experiments approximate pK_a^{NOH} values in the range from 3.9 (Z = H, R = $HOCH_2CH_2S$) to 4.8 (Z = Me_2N, R = $HOCH_2CH_2S$) were determined,[17] which indicated that at pH ≥5.38 we have indeed pH ≫ pK_a^{NOH}.

Both k_{-1} and k_p^{HA} values could easily be determined for Z = 4-Me, H, 3-Cl, 4-Cl, 3-CN, 4-CN, and 3-NO_2. On the other hand, with Z = 4-Me_2N, 4-MeO, and 4-MeS the k_p^{HA}/k_{-1} ratios are quite small and hence the slopes of plots of k_{obsd} vs [HA] were too shallow and too uncertain to yield reliable k_p^{HA} values. Hence, no k_p^{HA} values are reported for these compounds.

Discussion

Table I provides a summary of k_1, k_{-1}, and K_1 for the addition of four thiolate ions to various substituted β-nitrostyrenes and k_p^{HA} for carbon protonation of the adducts by acetic acid. The K_1 values were calculated as k_1/k_{-1}.

Substituent Dependence of k_1, k_{-1}, and K_1. A. Hammett Plots. Hammett plots for mercaptoethanol anion ($HOCH_2CH_2S^-$) addition are shown in Figure 3 and for methylmercaptoacetate anion ($MeO_2CCH_2S^-$) addition in Figure 4. The various ρ-values are reported in Table II. The general features of the Hammett plots are very much the same for both nucleophiles and can be summarized as follows.

(1) log K_1 correlates well with σ[18] for Z = H, 3-Cl, 3-CN,

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[14] The contribution by the $k_p^H a_{H^+}$ term may be estimated as follows. The k_p^H/k_p^{HA} ratio for the protonation of $PhCH{=}NO_2^-$ [15] and $HOCH_2CH{=}NO_2^-$ [16] is around 30 and suggests a similar k_p^H/k_p^{HA} ratio for T_{RS}^-. At [HA] = 0.004 M and pH 5.38 the k_p^{HA}[HA] term contributes typically ≈50% to k_{obsd} in most cases, i.e., $k_p^{HA}[HA] \approx k_{-1} + k_p^H a_{H^+}$. Under these conditions the $k_p^H a_{H^+}/k_p^{HA}[HA]$ ratio becomes ≈0.04, i.e., the $k_p^H a_{H^+}$ term contributes about 4% to the proton transfer rate. This is undetectable within our limits of precision but at lower pH this contribution is no longer negligible.

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

[16] Bernasconi, C. F.; Panda, M. Unpublished results.

[17] These determinations were made from the slopes given by $k_p^{HA}K_a^{NOH}/(K_a^{NOH} + a_{H^+})$.

[18] Taken from Hine:[19] 4-Me_2N (−0.83), 4-MeO (−0.27), 4-Me (−0.17), 4-MeS (0.0), H (0.0), 4-Cl (0.23), 3-Cl (0.37), 3-CN (0.56), 4-CN (0.66), 3-NO_2 (0.71). The alternative σ value for 4-Me_2N (−0.63) is preferred by Exner.[20]

[19] Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; p 55.

Table I. Summary of Rate and Equilibrium Constants for the Reaction of Thiolate Ions with Substituted β-Nitrostyrenes in Water at 20 °C, $\mu = 0.5$

Z	k_1[a] ($M^{-1}\,s^{-1}$)	k_{-1}[b] (s^{-1})	$K_1 = k_1/k_{-1}$[c] (M^{-1})	k_p^{HA}[d] ($M^{-1}\,s^{-1}$)
$MeO_2CCH_2S^-$ ($pK_a^{RSH} = 7.90 \pm 0.02$)				
4-Me_2N	2.47×10^4	6.26×10^{-1}	3.95×10^4	
4-MeO	2.26×10^4	1.85×10^{-1}	1.22×10^5	
4-Me	2.34×10^4	1.01×10^{-1}	2.31×10^5	3.38
4-MeS	3.03×10^4	1.36×10^{-1}	2.23×10^5	
H	2.95×10^4	6.31×10^{-2}	4.68×10^5	3.70
4-Cl	3.95×10^4	7.15×10^{-2}	5.52×10^5	3.98
3-Cl	5.18×10^4	4.87×10^{-2}	1.07×10^6	4.81
3-CN	7.46×10^4	4.21×10^{-2}	1.77×10^6	5.44
4-CN	9.02×10^4	4.48×10^{-2}	2.01×10^6	5.10
3-NO_2	8.71×10^4	4.30×10^{-2}	2.03×10^6	5.39
$MeO_2CCH_2CH_2S^-$ ($pK_a^{RSH} = 9.33 \pm 0.04$)				
H	3.08×10^4	1.64×10^{-2}	1.88×10^6	2.59
3-CN	9.56×10^4	9.78×10^{-3}	9.80×10^6	3.32
$HOCH_2CH_2S^-$ ($pK_a^{RSH} = 9.65 \pm 0.02$)				
4-Me_2N	2.45×10^4	1.11×10^{-1}	2.21×10^5	
4-MeO	3.41×10^4	2.91×10^{-2}	1.17×10^6	
4-Me	3.70×10^4	1.83×10^{-2}	1.99×10^6	1.73
4-MeS	4.52×10^4	2.30×10^{-2}	1.96×10^6	
H	4.57×10^4	1.15×10^{-2}	4.00×10^6	2.00
4-Cl	6.39×10^4	1.52×10^{-2}	4.20×10^6	2.46
3-Cl	7.41×10^4	1.30×10^{-2}	5.70×10^6	2.75
3-CN	1.23×10^5	9.60×10^{-3}	1.28×10^7	2.60
4-CN	1.70×10^5	1.05×10^{-2}	1.63×10^7	2.84
3-NO_2	1.40×10^5	8.15×10^{-3}	1.72×10^7	3.14
n-BuS^- ($pK_a^{RSH} \approx 10.49$[f])				
H	3.32×10^4	$\approx 0.8 \times 10^{-2}$[e]	$\approx 4 \times 10^6$[e]	≈2[e]
3-CN	8.46×10^4	$\approx 0.6 \times 10^{-2}$[e]	$\approx 1.4 \times 10^7$[e]	≈3[e]

[a] Estimated error ±5%. [b] Estimated error ±10%. [c] Estimated error ±15%. [d] Estimated error ±10%. [e] Estimated error ±50%; these values were not used in the Brønsted or Hammett plots, see text. [f] Estimated from pK_a measured in 50% Me_2SO–50% water, see Experimental Section.

Table II. Hammett ρ-Values for the Reactions of $HOCH_2CH_2S^-$ and $MeO_2CCH_2S^-$ with Substituted β-Nitrostyrenes

	$HOCH_2CH_2S^-$	$MeO_2CCH_2S^-$
$\rho(k_1)$	0.74 ± 0.06	0.69 ± 0.03
$\rho(k_{-1})$	-0.18 ± 0.12	-0.25 ± 0.04
$\rho(K_1)$	0.96 ± 0.16	0.95 ± 0.06
$\rho^{nor}(k_1) = \rho(k_1)/\rho(K_1)$	0.77 ± 0.14	0.73 ± 0.06
$\alpha_{nuc}^{n} = d \log k_1/d \log K_1$	0.79 ± 0.10	0.68 ± 0.06
$\rho(k_p^{HA})$[a]	0.19 ± 0.05	0.24 ± 0.03

[a] Protonation of T_{RS}^- by acetic acid.

4-CN, and 3-NO_2, i.e., substituents that have no π-donor capabilities. The least-squares $\rho(K_1)$ values based on these points are 0.96 ± 0.16 for $HOCH_2CH_2S^-$ and 0.95 ± 0.06 for $MeO_2CCH_2S^-$. These ρ-values are much larger than $\rho(K_1) = -0.06 \pm 0.07$ for the piperidine addition[1] mentioned in the introduction. This is reasonable since the thiolate reaction leads to an anionic rather than a zwitterionic adduct. In fact, our $\rho(K_1)$ values for thiolate ion addition are close to $\rho(K_1) = 1.16$ for hydroxide ion addition,[21] as one might expect.

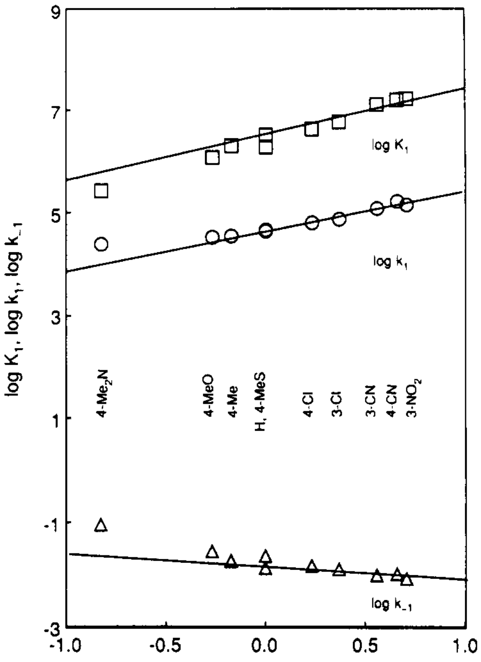

Figure 3. Hammett plots for the reaction of $HOCH_2CH_2S^-$ with substituted β-nitrostyrenes.

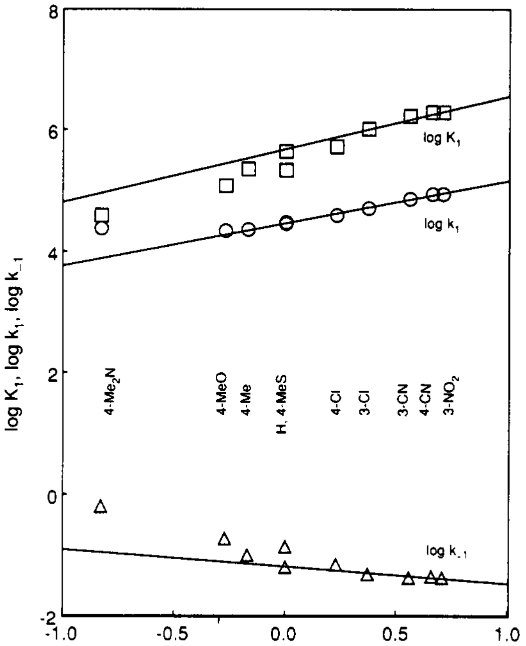

Figure 4. Hammett plots for the reaction of $MeO_2CCH_2S^-$ with substituted β-nitrostyrenes.

(2) The π-donor substituents 4-Me_2N, 4-MeO, 4-MeS, 4-Me, and 4-Cl, but mainly the first three, cause significant negative deviations from the least-squares lines of the K_1 Hammett plots. For 4-MeO and 4-MeS these deviations are of the order of 0.25 log units while for 4-Me_2N the average deviation amounts to ≈0.35 log units if Hine's[18,19] $\sigma = -0.83$ is used, or to about ≈0.55 log units with Exner's preferred[18,20] $\sigma = -0.63$. Similar or even larger negative deviations were observed for 4-Me_2N and 4-MeO in the reactions of β-nitrostyrenes with piperidine[1] and hydroxide ion.[21] These deviations can be attributed to an extra stabilization of the olefin by through-resonance (**1b**). As suggested by a reviewer, an alternative way of treating the data is to plot log K_1 vs σ^+. Such a plot (not shown) gives a satisfactory correlation with *all* substituents, including the π-donors. The conclusion to be drawn is the same, namely that the π-donor substituents provide extra resonance stabilization to the olefin.

It is perhaps surprising that the negative deviation for 4-MeS is about as large as for 4-MeO since 4-MeS is a

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

(21) Bernasconi, C. F.; Zitomer, J. L.; Schuck, D. F. *J. Org. Chem.* **1992**, *57*, 1132.

weaker π-donor than 4-MeO (e.g., $\sigma^+ = -0.62$ for MeS, -0.79 for MeO).[19] Our result may be an artifact stemming from the choice of σ-value for 4-MeS ($\sigma = 0.0$); according to Exner,[20] σ for 4-MeS is very uncertain and could well be slightly negative which would have the effect of reducing the negative deviation from the Hammett line.

(3) log k_1 correlates well with σ for all substituents except for 4-Me_2N and 4-MeO; $\rho(k_1)$ calculated by excluding the deviating points affords 0.74 ± 0.06 for $HOCH_2CH_2S^-$ and 0.69 ± 0.03 for $MeO_2CCH_2S^-$. Two of the π-donor substituents that showed negative deviations from the log K_1 Hammett plots, 4-MeO, and especially 4-Me_2N, have *positive* deviations (average of ≈0.45 log units for 4-Me_2N with $\sigma = -0.83$, and ≈0.3 log units with $\sigma = -0.63$). These deviations are similar to those observed in the reactions of substituted β-nitrostyrenes with piperidine,[1] hydroxide ion,[21] and nitromethide ion.[21] They are most easily understood in terms of an enhanced intrinsic rate constant induced by the preorganization effect of resonance structure **1b** discussed in the introduction.

It should be noted that the rate enhancement caused by the preorganization effect is significantly larger than the size of the positive deviations from the Hammett line implies. This is because in the absence of preorganization, log k_1 for the π-donor should show a *negative* deviation from the line due to the depressed equilibrium constant, as will become more apparent when considering Brønsted plots (see below).[22] The absence of an observable positive deviation for 4-MeS is related to the seemingly exaggerated negative deviation from the log K_1 plot for this substituent, again probably due to a too high σ-value. This interpretation gains further support when considering the log k_{-1} plots and Brønsted plots.

(4) log k_{-1} correlates well only with the strictly non-π-donor substituents Z = H, 3-Cl, 3-CN, 4-CN, and 3-NO_2, with $\rho(k_{-1}) = -0.18 \pm 0.12$ for $HOCH_2CH_2S^-$, and $\rho(k_{-1}) = -0.25 \pm 0.04$ for $MeO_2CCH_2S^-$. There are relatively strong positive deviations for 4-Me_2N, 4-MeO, and 4-MeS and weak ones for 4-Me and 4-Cl. The deviations for 4-Me_2N and 4-MeO are larger than the corresponding positive deviations from the log k_1 plots, e.g., approximately 0.8 log units for k_{-1} vs ≈0.45 log units for k_1 with Z = 4-Me_2N ($\sigma = -0.83$). This is because the π-donor substituents exert two independent effects on the reaction. One is stabilization of the olefin (reduction of k_1 and increase in k_{-1} with resulting reduction in K_1), the other is a stabilization of the transition state (equal increase in k_1 and k_{-1} with no effect on K_1).

The relatively strong positive deviation for 4-MeS is again most easily understood as an artifact resulting from a too high σ value; a lower σ would imply a smaller positive deviation that would be more in keeping with a π-donor effect that should be smaller than for 4-MeO. Whether the slight deviations for 4-Me and 4-Cl are a true reflection of a small π-donor effect (especially 4-Me), or caused by an inappropriate σ-value, or simply due to experimental error cannot be decided on the basis of our data.

B. Brønsted Plots. The preceding analysis of the Hammett correlations provides some useful qualitative insights, but the uncertainties in the choice of the appropriate σ-values, especially for the π-donor substituents, make a reliable *quantitative* assessment of the deviations of these substituents impossible. However, by plotting log k_1 vs log K_1 (Brønsted plots), these ambiguities can be avoided. Thus, only changes in the *intrinsic* rate constant (k_o) lead to deviations from Brønsted plots, and these deviations are not "contaminated" with thermodynamic effects but give a direct measure of the change in k_o. Such Brønsted plots are displayed in Figure 5 for the $HOCH_2CH_2S^-$ reaction and in Figure 6 for the $MeO_2CCH_2S^-$ reaction. These plots show excellent correlations for all substituents except for 4-Me_2N, 4-MeO, and 4-MeS. The latter points deviate positively by an average of ≈0.75 log units for 4-Me_2N, of ≈0.25 log units for 4-MeO, and ≈0.22 log units for 4-MeS. It is these deviations rather than those from the Hammett plots that should be regarded as a quantitative measure of the rate enhancement caused by the π-donor substituents. It is interesting that these deviations correlate quite well with the σ^+ constants which are -1.67, -0.79, and -0.62,[19] respectively. This correlation is consistent with the notion that the enhancement of the intrinsic rate constant is caused by the transition-state preorganization through the π-donor effect.

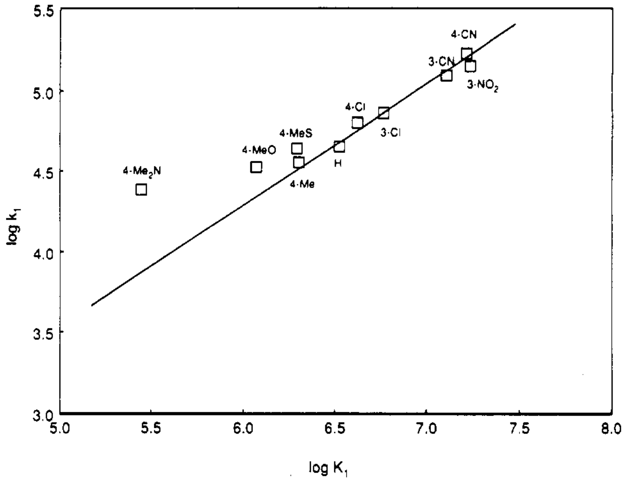

Figure 5. Brønsted-type plots for the reaction of $HOCH_2CH_2S^-$ with substituted β-nitrostyrenes (dependence on Z).

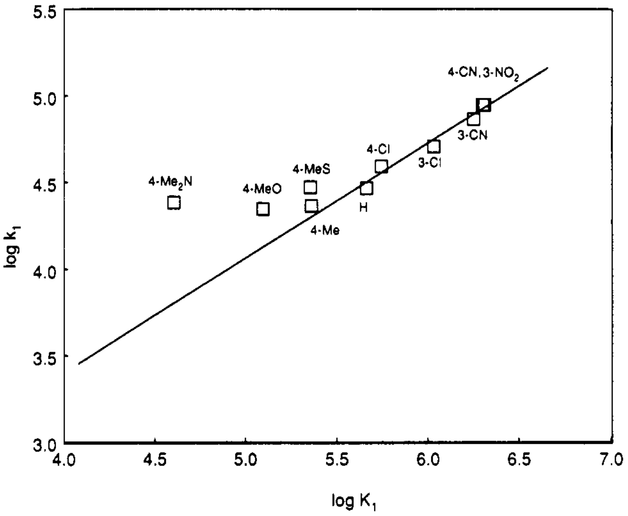

Figure 6. Brønsted-type plots for the reaction $MeO_2CCH_2S^-$ with substituted β-nitrostyrenes (dependence on Z).

Radicaloid Transition State? The foregoing discussion has demonstrated that the rate enhancements induced by 4-Me_2N, 4-MeO, and 4-MeS are easily accounted for by the π-donor properties of these substituents. This is particularly evident on the basis of the Brønsted plots which do not suffer from possible ambiguities that arise from uncertain σ-values and show a direct correlation between rate enhancement and π-donor strength. We now must ask whether Gross and Hoz'[6] alternative interpre-

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[22] The conclusion that the rate enhancements are actually larger than the positive deviations from our Hammett plots could also be derived by plotting log k_1 vs σ^+.

Table III. $\sigma^\bullet_C$ **and** $\sigma^\bullet_\alpha$ **Substituent Constants for Benzyl Radical Stabilization**

Z	$\sigma^{\bullet\,a}_C$	$\sigma^{\bullet\,b}_\alpha$
4-Me_2N	0.90	
4-MeO	0.24	0.018
4-MeS	0.43	0.063
4-Me	0.11	0.015
H	0	0
4-Cl	0.12	0.011
3-Cl	−0.04	−0.007
3-CN	−0.12	−0.026
4-CN	0.46	0.040
3-NO_2	−0.11	

[a] Reference 25. [b] Reference 24.

tation of the rate accelerations in terms of a stabilization of a radicaloid transition state (**4b**) is equally satisfactory. It is our contention that it is not, for the following reasons.

If the transition state had radicaloid character, it is unlikely that the seven β-nitrostyrenes with substituents that are either weakly or not at all π-donating would adhere so well to the Brønsted lines in Figures 5 and 6 as they do and that the positive deviations for 4-Me_2N, 4-MeO, and 4-MeS would show a correlation with σ^+ as observed in this study. This is because the substituent effects on the stability of radicals do not correlate closely with the classical polar and resonance effects; this is true even though different methods to evaluate substituent effects on radicals or define relevant substituent constants ($\sigma^\bullet$) give somewhat conflicting results.[23]

Two sets of substituent constants that are particularly relevant with respect to our system are the $\sigma^\bullet_C$ and $\sigma^\bullet_\alpha$ scales.[24] They are both based on benzylic radicals, $\sigma^\bullet_C$ being derived from rates of a benzylic radical forming reaction[25] and $\sigma^\bullet_\alpha$ from ESR hyperfine coupling constants.[24] $\sigma^\bullet_C$ and $\sigma^\bullet_\alpha$ values for substituents used in the present study are summarized in Table III. According to both scales, 4-MeS is substantially more stabilizing than 4-MeO and hence should show larger rather than smaller positive deviations from the Brønsted lines; 4-CN should also strongly deviate positively from the lines, and significantly more so than 4-MeO. None of these predictions are observed, either in the reactions reported in this study or in the reaction of piperidine with β-nitrostyrenes[1] or of CN^- with 1,1-diaryl-2-nitroethylenes.[6]

Similar discrepancies arise when radical-stabilizing energies estimated by Bordwell[23] are used as criterion. For example, for fluorenyl radicals the 3-MeS group is somewhat more stabilizing than the 3-MeO groups while 2-CN is destabilizing[26] (note that here the 3-position is roughly equivalent to a "para" position, the 2-position to a "meta" position); for arylacetonitrile radicals the stabilization by 4-CN is even larger than by 4-MeO and 4-Cl is also strongly stabilizing,[27] which is again inconsistent with our results.

The absence of a better correlation with measures of radical stabilization in the present study is all the more significant because thiolate ion nucleophiles are much stronger reductants than oxyanions, amines, or $CN^{-\,10}$ and hence would be expected to imbue the transition state with significantly more radicaloid character.[28] This should not only have accentuated the expected correlation with $\sigma^\bullet$ constants but should have also been reflected in substantially greater rate enhancements by π-donor substituents in the thiolate reactions compared to the reactions with piperidine, OH^-, or CN^-. On the basis of deviations from log k_1 – Hammett plots (Brønsted plots are not available[29]) for the reactions of OH^- and piperidine with β-nitrostyrenes, this greater enhancement does not manifest itself. For example, for 4-(dimethylamino)-β-nitrostyrene, the positive deviations are ca. 0.35 log units with piperidine,[1] ca. 0.30 log units with OH^-,[21] and ca. 0.45 log units for the thiolate ion reactions. Since the same σ-constant is used in all reactions, uncertainties in these deviations arising from the choice of σ should cancel and hence the above numbers may serve as basis for comparison between the three reactions. We consider the differences among these deviations too small to be significant.[30]

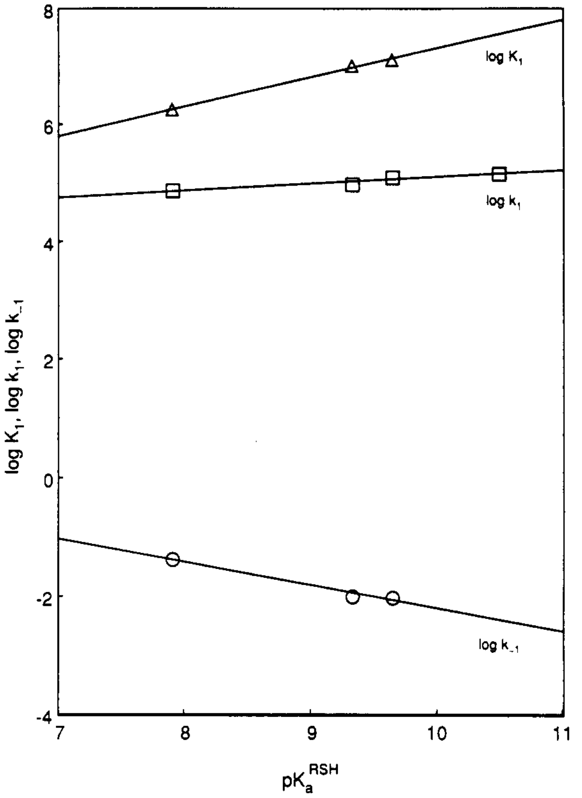

Figure 7. Brønsted plots for the reaction of 3-cyano-β-nitrostyrene with thiolate ions (dependence on thiolate ion).

To summarize, we see none of the experimental manifestations that would be expected if there was a radicaloid

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(23) For a recent paper reviewing such attempts see: Bordwell, F. G.; Cheng, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 1736.

(24) (a) Dust, J. M.; Arnold, D. R. *J. Am. Chem. Soc.* **1983**, *105*, 1221, 6531. (b) Wayner, D. D. M.; Arnold, D. R. *Can. J. Chem.* **1985**, *63*, 2378.

(25) (a) Creary, X. *J. Org. Chem.* **1980**, *45*, 280. (b) Creary, X.; Mehrsheikh-Mohammadi, M. E.; McDonald, S. *Ibid.* **1987**, *52*, 3254.

(26) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1979.

(27) Bordwell, F. G.; Cheng, J.-P.; Bausch, M. J.; Bares, J. E. *J. Phys. Org. Chem.* **1988**, *1*, 209.

(28) A reviewer has suggested that more definite conclusions could be drawn by including a discussion of the one-electron reduction potential of β-nitrostyrene. A literature search for this parameter proved unsuccessful. However, inasmuch as our comparisons refer to reactions of the same olefin, it is the relative oxidation potentials of the *nucleophiles* which are the critical issue here, irrespective of the reduction potential of the olefin.

(29) For the $OH^{-\,21}$ and $CN^{-\,6}$ reactions the equilibrium constants are not known; for the piperidine reaction[1] the virtual independence of K_1 on the substituent for non π-donor substituents makes the Brønsted plot extremely inaccurate.

(30) It might be argued that the reason why the expected greater rate enhancement with the thiolate nucleophiles is not observed is an earlier transition state than in the piperidine or OH^- reactions. However, if β^n_{nuc} is accepted as an approximate measure of the interaction of the nucleophile with the substrate at the transition state, the transition states for the two reactions are about equally early ($\beta^n_{nuc} = 0.25$ for piperidine,[1] 0.22 ± 0.08 for RS^-, see below).[31]

(31) According to Gross and Hoz[32] the diradical character is actually greater for an early than for a late transition state.

(32) Gross, Z.; Hoz, Z. Paper presented at Second European Symposium on Organic Reactivity (ESOR II), Padua, Italy, 1989.

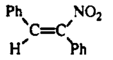
Table IV. Brønsted β-Values for the Reaction of Nitro-Activated Olefins with Thiolate Ions

	β-nitrostyrene[a] H_2O	3-cyano-β-nitrostyrene[a] H_2O	α-nitrostilbene[b] 50% Me_2SO–50% H_2O	β-methoxy-α-nitrostilbene[c] 50% Me_2SO–50% H_2O
$\beta_{nuc} = d \log k_1/d\, pK_a^{RSH}$	0.11 ± 0.04	0.11 ± 0.02	0.16 ± 0.02	0.09 ± 0.01
$\beta_{lg} = d \log k_{-1}/d\, pK_a^{RSH}$	−0.42 ± 0.09[d]	−0.39 ± 0.06[d]	−0.68 ± 0.06	−0.71 ± 0.14
$\beta_{eq} = d \log K_1/d\, pK_a^{RSH}$	0.50 ± 0.02[d]	0.50 ± 0.02[d]	0.84 ± 0.07	0.80 ± 0.13
$\beta^n_{nuc} = \beta_{nuc}/\beta_{eq}$	0.22 ± 0.08	0.22 ± 0.04	0.19 ± 0.03	0.11 ± 0.02
$\beta^n_{lg} = \beta_{lg}/\beta_{eq}$	−0.84 ± 0.18	−0.78 ± 0.12	−0.81 ± 0.10	−0.89 ± 0.02
$\log k_o$	3.5 ± 1.0	3.5 ± 0.6	3.43 ± 0.10	2.16 ± 0.09

[a] This work. [b] Reference 12. [c] Reference 33. [d] Based on correlation without *n*-BuS$^-$, see text.

transition state. On the other hand, all experimental observations are easily accommodated by our preorganization model. Does this exclude any radicaloid character of the transition state? We think not, but it makes the hypothesis look contrived and unnecessary. It is conceivable that a radicaloid transition state could benefit in a similar way from the preorganization induced by π-donor substituents as the classical transition state and that this preorganization is energetically more significant than the stabilization of the radicaloid portion of the transition state. Such a situation would also be consistent with our findings, but inasmuch as the interpretation of the results does not *require* such a hypothesis we see no need to invoke it.

Dependence on Thiolate Ion Basicity and Intrinsic Rate Constants. Brønsted plots as a function of thiol pK_a are shown in Figure 7 for the reaction of 3-cyano-β-nitrostyrene; the corresponding plots (not shown) for the reaction of β-nitrostyrene are very similar. In view of the large uncertainty in k_{-1} for the reaction with *n*-BuS$^-$ (see Experimental Section), the points for this nucleophile have not been included in the k_{-1} and K_1 correlations. The various Brønsted parameters are summarized in Table IV. The table includes the log of the intrinsic rate constants (k_o), obtained by extrapolation of log k_1 vs log K_1 plots (variation of RS$^-$) to log K_1 = 0 (plots not shown). For comparison purposes, the corresponding parameters for the reactions of thiolate ions with α-nitrostilbene (5)[12] and β-methoxy-α-nitrostilbene (6)[33] in 50% Me_2SO–50% water are also included in the table. The following points are noteworthy.



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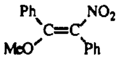

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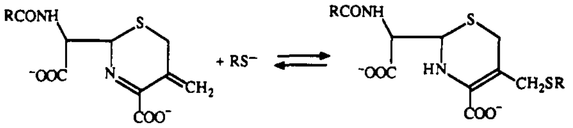
(1) β_{nuc} is very low (0.11), as was observed for thiolate addition to 5 (0.16) and 6 (0.09); for the normalized β^n_{nuc} a value of 0.22 is obtained (0.19 for 5, 0.11 for 6). These low β_{nuc} (β^n_{nuc}) values suggest a transition state with little C–S bond formation or little charge transfer.[34] It is possible that some back-bonding which would shift electron density from the incipient carbanion to a d-orbital of the sulfur could depress β_{nuc} (β^n_{nuc}) and thus partially account for the low values.[37] However, the high α^n_{nuc} values to be discussed under "Transition State Imbalance" suggest that this cannot be an important factor.

(2) The β_{eq} value of 0.5 is quite low, indicating that the electronic effect of R on the *carbon* basicity of RS$^-$ is considerably attenuated compared to that on the *proton* basicity. β_{eq} values lower than unity have previously been reported for thiolate ion addition to 5 (0.84),[9] 6 (0.80),[33] and the imine 7 derived from cephalosporin (0.71).[38] Since all these β_{eq} values are subject to substantial experimental error, it is not clear whether the differences in β_{eq} between the various systems are very significant. Especially in the case of β-nitrostyrene and 3-cyano-β-nitrostyrene, the low standard deviations (Table IV) may be misleading and the true experimental error may be larger, due to the small pK_a range of the available thiolate ions and the small number of experimental points on the Brønsted plots. Be it as it may, there can be little doubt that the β_{eq} values are all smaller than unity. This contrasts with the addition of amines to electrophilic olefins for which β_{eq} tends to be closer to unity, e.g., 1.04 for piperidine/morpholine addition to β-nitrostyrene in water[1] (0.95 in 50% Me_2SO–50% water),[1] an average of 0.95 for piperidine/morpholine addition to six substituted benzylidene Meldrum's acids in 50% Me_2SO–50% water[4] and 0.93, 0.90, and 0.85 for addition of the same amines to α-nitrostilbene,[39] benzylidene-1,3-indandione,[40a] and benzylidenemalondialdehyde,[40b] respectively.[41]



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The smaller β_{eq} values for thiolate ion compared to amine addition is probably related to the same soft acid-soft base[42] interactions that enhance the affinity (both kinetic and thermodynamic, see below) of thiolate ions toward electrophilic olefins compared to that of amines of the same pK_a.[43] In other words, the stabilization provided by the soft acid–soft base interactions, which are absent in the reaction of RS$^-$ with the proton, may be thought of as attenuating the demand for stabilization by

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(33) Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Rappoport, Z. *J. Am. Chem. Soc.* **1990**, *112*, 3169.

(34) The assumption of a correlation of β_{nuc} or β^n_{nuc} with degree of bond formation or charge transfer which represents the "traditional" view[35] has been questioned.[36] Hence, we shall refrain from drawing very *quantitative* conclusions from these parameters.

(35) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; pp 128–170. (b) Kresge, A. J. In *Proton Transfer Reactions*; Caldin, E. F., Gold, V., Eds.; Wiley: New York, 1975; p 179. (c) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.

(36) (a) Pross, A. *J. Org. Chem.* **1984**, *49*, 1811. (b) Bordwell, F. G.; Hughes, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 4737; **1986**, *108*, 7300. (c) Johnson, C. D. *Tetrahedron* **1980**, *36*, 3461. (d) Pross, A.; Shaik, S. S. *New. J. Chem.* **1989**, *13*, 427.

(37) (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Brown, K. L.; Kallen, R. G. *Ibid.* **1972**, *94*, 1894.

(38) Buckwell, S.; Page, M. I.; Longridge, J. L. *J. Chem. Soc., Chem. Commun.* **1986**, 1039.

(39) Bernasconi, C. F.; Renfrow, R. A. *J. Org. Chem.* **1987**, *52*, 3035.

(40) (a) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1991**, *113*, 2222. (b) Bernasconi, C. F.; Stronach, M. W. *J. Org. Chem.* **1991**, *56*, 1993.

(41) A possible exception is the piperidine/morpholine addition to the sterically crowded PhCH═C(COR)$_2$ with R = Et, *i*-Pr, and Ph for which β_{eq} = 0.70–0.71,[40a] but these low values may have more to do with experimental uncertainties than with a real chemical phenomena.

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

(43) See also: (a) Sander, E. G.; Jencks, W. P. *J. Am. Chem. Soc.* **1968**, *90*, 6154. (b) Hine, J.; Weimar, R. D., Jr. *Ibid.* **1965**, *87*, 3387. (c) Hine, J. ref. 19, p 225.

the electron donating effect of R.

(3) The intrinsic rate constant is of the order of log $k_o \approx 3.5$ although the standard deviations (±1.0 for Z = H, ±0.6 for Z = 3-CN) suggest a high uncertainty in this value. However, these large standard deviations are, to some considerable extent, an artifact caused by the absence of a reliable point for the most basic thiolate ion (n-BuS^-) and the rather lengthy extrapolation needed to obtain log k_o as log k_1 when log $K_1 = 0$. That log k_o must be much closer to 3.5 than is suggested by the standard deviations follows from a comparison of $k_1 - K_1$ pairs in Table I with the same parameters in the reaction of thiolate ions with α-nitrostilbene (**5**).[9] By and large the k_1 values associated with a particular K_1 value are very similar for the β-nitrostyrenes and α-nitrostilbene (**5**), indicating that k_o is also very similar in both systems.[44] Since a reasonably accurate log $k_o = 3.4 \pm 0.1$ was obtained for **5**, it follows that our value of 3.5 for the two β-nitrostyrenes must be much more reliable than is suggested by the standard deviation.

The log $k_o = 3.5$ is substantially higher than log $k_o = 2.10$ for piperidine/morpholine addition to β-nitrostyrene[1] under the same conditions. This result parallels the finding that log $k_o = 3.43$ for thiolate ion addition to α-nitrostilbene[12] is much higher than log $k_o = 1.42$ for piperidine/morpholine addition.[33] These results show that the much higher nucleophilic reactivity of thiolate ions compared to amines of the same pK_a are not only a reflection of their higher equilibrium affinities[45] but also stem in large measure from a higher intrinsic rate constant. As discussed in more detail elsewhere,[12] the enhanced k_o values are likely to arise, at least in part, from a development of the product stabilizing soft acid–soft base interactions that is ahead of C–S bond formation at the transition state.

An enhancement of the intrinsic rate constant for thiolate ion nucleophiles over that for amine nucleophiles has recently also been observed for the formation of Meisenheimer complexes derived from 1,3,5-trinitrobenzene (TNB). For example, log $k_o = 4.75$ for the addition of $^-O_2CCH_2S^-$ to TNB in 10% dioxane–90% water at 25 °C.[46] Under the same conditions, a log $k_o \approx 3.80$ may be estimated from data for piperidine addition to TNB.[47] The smaller difference between log $k_o(RS^-)$ and log $k_o(R_2NH)$ in the 1,3,5-trinitrobenzene reaction compared to the reactions of β-nitrostyrene or α-nitrostilbene may be related to a smaller stabilization of the thiolate Meisenheimer complex by soft acid–soft base interactions.[48] This is because, according to the PNS, the enhancement of log k_o should be proportional to the degree of stabilization resulting from the soft acid–soft base interaction, provided that the degree by which these interactions develop ahead of C–S bond formation are the same in the two systems that are being compared.

Table V. α^n_{nuc}, β^n_{nuc}, **and Imbalances for Reactions of Nucleophiles with Nitro-Activated Olefins**

olefin	nucleophile	solvent	α^n_{nuc}	β^n_{nuc}	$\alpha^n_{nuc} - \beta^n_{nuc}$
ArCH=CHNO$_2$[a]	RS^-	H_2O	0.74[b]	0.22[c]	0.52
PhCH=C(Ar)NO$_2$[d]	RS^-	50% Me_2SO	0.87	0.19	0.68
ArCH=CHNO$_2$[e]	R_2NH	H_2O	0.51	0.25	0.26
PhCH=C(Ar)NO$_2$[f]	R_2NH	50% Me_2SO	0.67	0.37	0.30

[a] This work. [b] Average value from $HOCH_2CH_2S^-$ and $MeO_2CCH_2S^-$. [c] Average value from Z = H and 3-CN. [d] Reference 12. [e] Reference 1. [f] Reference 39.

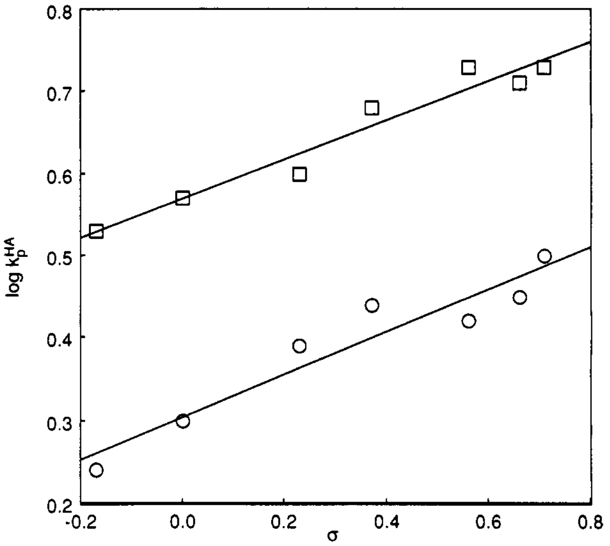

Figure 8. Hammett plots for the protonation of the $HOCH_2CH_2S^-$ adducts (○) and $MeO_2CCH_2S^-$ adducts (□) of substituted β-nitrostyrenes.

Transition State Imbalance. The normalized $\rho(k_1)$ values defined as $\rho(k_1)/\rho(K_1)$ may be regarded as Brønsted-type coefficients which we have called α^n_{nuc} and can also be obtained directly as the slope of a plot of log k_1 vs log K_1 (variation of Z). α^n_{nuc} values for the reactions of $HOCH_2CH_2S^-$ and $MeO_2CCH_2S^-$ with β-nitrostyrenes are reported in Table II; a comparison with α^n_{nuc} values in related systems is given in Table V. Table V also reports the imbalances,[5] $\alpha^n_{nuc} - \beta^n_{nuc}$, for various systems.

The present results which show a much larger imbalance for reactions with thiolate ions compared to that in reactions with piperidine/morpholine are in agreement with previous findings for the substituted α-nitrostilbenes. Both a higher α^n_{nuc} and a lower β^n_{nuc} contribute to the enhanced imbalances. As mentioned earlier in discussing the low β^n_{nuc} values, the rather high α^n_{nuc} values are difficult to reconcile with significant back-bonding to a sulfur d-orbital since such back-bonding would tend to *decrease* α^n_{nuc}, just as it decreases β^n_{nuc}.

A number of contributing factors to the enhanced imbalances with thiolate ion nucleophiles have previously been discussed in detail.[12] A major factor may be related to the disproportionately large progress in the soft acid-soft base interactions at the transition state which enhances the intrinsic rate constant of the thiolate reactions. Ac-

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(44) For example, the k_1–K_1 pairs 1.23×10^5 M^{-1} s^{-1}–1.28×10^7 M^{-1} and 9.56×10^4 M^{-1} s^{-1}–9.80×10^6 M^{-1} for the reaction of 3-cyano-β-nitrostyrene with $HOCH_2CH_2S^-$ and $MeO_2CCH_2CH_2S^-$, respectively (Table I), are quite similar to the k_1–K_1 pairs 6.68×10^4 M^{-1} s^{-1}–1.91×10^7 M^{-1} and 5.81×10^4 M^{-1} s^{-1}–8.16×10^6 M^{-1} for the reaction of α-nitrostilbene with $CH_3CH_2S^-$ and $HOCH_2CH_2S^-$, respectively[12]; another set of approximately matching k_1–K_1 pairs are 4.57×10^4 M^{-1} s^{-1}–4.00×10^6 M^{-1} for the reaction of β-nitrostyrene with $HOCH_2CH_2S^-$ and 4.82×10^4 M^{-1} s^{-1}–5.09×10^6 M^{-1} for the reaction of α-nitrostilbene with $MeO_2CCH_2CH_2S^-$.[12]

(45) For example, K_1 for morpholine addition to β-nitrostyrene is 1.44 M^{-1}[1] while K_1 for $MeO_2CCH_2CH_2S^-$ addition is 1.88×10^6 M^{-1} (Table I), even though the pK_a of the thiolate ion (9.33) is comparable to that of morpholine (8.90). The corresponding k_1 values are 1.37×10^2 M^{-1} s^{-1} for morpholine[1] and 3.08×10^4 M^{-1} s^{-1} for $MeO_2CCH_2CH_2S^-$ (Table I).

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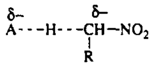
(48) $K_1(RS^-)/K_1(R_2NH) \approx 6 \times 10^3$ for addition to TNB with $RS^- = {}^-O_2CCH_2S^-$ and R_2NH being a hypothetical secondary alicyclic amine of the same pK_a (10.7) as $^-O_2CCH_2S^-$. This compares with $K_1(RS^-)/K_1(R_2NH) \approx 5 \times 10^5$ for addition to β-nitrostyrene with $RS^- = MeO_2CCH_2CH_2S^-$ and R_2NH being a hypothetical secondary alicyclic amine of the same pK_a (9.33) as $MeO_2CCH_2CH_2S^-$.

cording to this notion, the strong polarizability of the thiolate ion may allow substantial negative charge density to develop in the olefin (large α^{n}_{nuc}) without extensive loss of charge from the nucleophile or extensive C–S bond formation (low β^{n}_{nuc}).

The view that the large imbalances with thiolate nucleophiles is related to the soft acid–soft base interaction with the olefin is supported by the fact that in proton transfers, where soft acid–soft base interactions should play a minor role if any, the imbalances are less sensitive to the base. For example, for the deprotonation of substituted phenylnitromethanes by secondary alicyclic amines α = 1.29 and β = 0.56[49] which yields an imbalance $\alpha - \beta$ = 0.73. For the corresponding reaction with thiolate ions, α = 1.32, β = 0.43, and $\alpha - \beta$ = 0.89.[50]

Rates of Protonation of T^-_{RS}. The rate constants for carbon protonation of T^-_{RS} by acetic acid (k_p^{HA} in Table I) show a weak increasing trend with increasing electron withdrawing strength of Z. Hammett plots are shown in Figure 8 and yield $\rho(k_p)$ = 0.19 ± 0.05 for the $HOCH_2CH_2S^-$, adducts and $\rho(k_p)$ = 0.24 ± 0.03 for the $MeO_2CCH_2S^-$ adducts, indicating that k_p is slightly enhanced by electron-withdrawing substituents. The k_p^{HA}-enhancing effect of acidifying groups is also seen in the fact that for a given Z substituent, the k_p^{HA} values increase in the order $MeO_2CCH_2S > MeO_2CCH_2CH_2S > HOCH_2CH_2S$. This result which implies that a decrease in carbanion basicity leads to a faster protonation is unusual but parallels similar observations made in our laboratory.[12,51] It is qualitatively the same phenomenon which was first observed by Bordwell[49] and others[52] for the protonation of phenylnitroalkane anions. It is the consequence of an extensive shift of the negative charge from the nitro group in $RCH{=}NO_2^-$ to the carbon in the transition state 8.



$$\overset{\delta-}{A}\text{- - -}H\text{- - -}\underset{R}{\overset{\delta-}{C}H}{-}NO_2$$

8

Experimental Section

Materials. β-nitrostyrene was obtained from Aldrich and recrystallized from ethanol, mp 56–57 °C (lit.[53] 58 °C). The 4-Me_2N, 4-MeO, 3-Cl, and 4-CN derivatives were available from a previous study[1] while the others were prepared by condensation of the corresponding benzaldehyde with nitromethane according to Worrall[54] and recrystallized from ethanol: 4-methyl-β-nitrostyrene, mp 101–102 °C (lit.[55] 102 °C); 4-chloro-β-nitrostyrene, mp 112–113 °C (lit.[56] 112–112.5 °C); 3-nitro-β-nitrostyrene, mp 124–125 °C (lit.[56] 124.5–125.5 °C); 4-(methylthio)-β-nitrostyrene, mp 84–86 °C,[57] ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.52 (s, 3 H, CH_3S), 7.26 (d, 8.5 Hz, 2 H, Ar), 7.45 (d, 8.5 Hz, 2 H, Ar), 7.56 (d, 13.6 Hz, 1 H, vinyl), 7.96 (d, 13.6 Hz, 1 H, vinyl); MS (m/e) 195 (M^+); 3-cyano-β-nitrostyrene, mp 127–129 °C,[58] ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.60 (m, 2 H, vinyl, Ar), 7.77 (d, 1.3 Hz, 1 H, Ar), 7.80 (d, 1.3 Hz, 1 H, Ar), 7.83 (d, 1.4 Hz, 1 H, Ar), 7.98 (d, 13.7 Hz, 1 H vinyl); MS (m/e) 174 (M^+).

2-Mercaptoethanol, n-butanethiol, methyl mercaptoacetate, and methyl 3-mercaptopropionate (Aldrich) were distilled under reduced pressure and stored under nitrogen. N-methylmorpholine (Aldrich) and triethylamine (Aldrich) were refluxed over CaH_2 and distilled. Glacial acetic acid (Mallinckrodt), acetonitrile (Alltech, HPLC/spectrograde), and KCl (Fisher Scientific) were used without further purification. KOH and HCl solutions were Dilut-it (Baker) diluted to appropriate values with deionized water.

pK_a Determinations. The pK_a of 2-mercaptoethanol, methyl mercaptoacetate, and methyl 3-mercaptopropionate were measured by standard potentiometric procedures. n-Butanethiol was not soluble enough for a pK_a determination, and hence the pK_a was measured in 50% Me_2SO–50% water, and its value in water estimated by assuming that the difference between pK_a (50% Me_2SO) and pK_a (H_2O) for n-butanethiol is the same as for ethanethiol (0.91).[12,37a]

Reaction Solutions and Kinetics. Solutions used in experiments with n-BuSH and methyl mercaptoacetate were degassed by sonication and/or purged with argon prior to addition of the thiol. Such precautions were not necessary with 2-mercaptoethanol and methyl 3-mercaptopropionate. All pH measurements were performed on a 611 Orion pH meter. The pH of the reaction solutions was determined by mock mixing experiments simulating a stopped-flow run. The thiolate ion solutions were prepared by addition of small volumes of a 0.2 M thiol stock solution in acetonitrile to a 0.05/0.05 M N-methylmorpholine buffer. This solution was then mixed in a 1:1 ratio with a 5 × 10^{-5} M substrate solution (prepared by diluting a 0.05 M stock solution in acetonitrile with aqueous 10^{-3} M HCl) in a Durrum–Gibson stopped-flow spectrophotometer. All solutions had an ionic strength of 0.5 M maintained by KCl, and all experiments were run at 20 °C.

Generation of Thiolate Adducts and pH-Jump Experiments. A stock solution of the thiolate adduct T^-_{RS} was generated by preparing a 0.05 M solution of the respective β-nitrostyrene, 0.1 triethylamine, and 0.1 M thiol in acetonitrile. For the pH-jump experiments, a solution of T^-_{RS} was prepared by diluting a 10 μL aliquot of the stock solution into 10 mL of 10^{-3} M or 10^{-4} M KOH/0.5 M KCl in water. This solution was then mixed in the stopped-flow apparatus with acetate buffers to give a pH of the reaction solution varying from 4.29 to 5.53 (and a few experiments at pH 6.25). The final nominal thiol concentration was 5 × 10^{-5} M and the T^-_{RS} concentration 2.5 × 10^{-5} M. All of the thiolate ion adducts were fairly stable in acetonitrile, but much less so in aqueous base. This necessitated the frequent preparation of fresh reaction solutions. In the case of the n-BuS$^-$ adduct, the aqueous solutions were particularly unstable, and the kinetic data obtained from them were not very reproducible.

The analysis of the first-order kinetic plots often involved a sloping infinity line, reflecting a slow decomposition of the reaction solutions.

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(57) No mp could be found in the literature.

(58) Slotta[59] gives mp 50 °C which seems erroneous.

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