$\times 10^{-4}$ mol) of triphenylphosphine was heated to 145 °C for 15 h. Distillation of the product mixture gave 4.3 g (82% yield) of cyclohexene and recovery of 1,2-dichlorotetramethyldisilane unreacted.

Reaction of Diphenic Acid Chloride with 1,2-Dichlorotetramethyldisilane. A reaction mixture containing 5.0 g (1.79×10^{-2} mol) of diphenic acid chloride and 7.13 g (3.58×10^{-2} mol) of 1,2-dichlorotetramethyldisilane was heated to 145 °C, neat, under an atmosphere of nitrogen. A catalyst mixture comprising 25 mg of bis(benzonitrile)palladium chloride and 33 mg of triphenylphosphine was introduced, initiating rapid evolution of carbon monoxide from the mixture. After 15 h at 145 °C, gaseous evolution had ceased, and distillation gave 2.1 g of Me_2SiCl_2, bp 68–71 °C, and 3.5 g of unreacted 1,2-dichlorotetramethyldisilane, bp 144–148 °C. Vacuum distillation at 145 °C/1 Torr gave a yellow-orange material which was recrystallized from hexane/toluene to give 3.12 g (97% yield) of fluorenone, mp 78–82 °C (lit. mp 83–85 °C).[29] The structure was further confirmed by high-resolution mass spectroscopy.

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(29) *Handbook of Chemistry and Physics*, 48th ed.; Weast, R. C., Ed.; Chemical Rubber Co.: Cleveland, 1967; p C-325.

Kinetics of Hydrolysis of Substituted β-Nitrostyrenes. Transition-State Imbalances and Intrinsic Rate Constants for Three Different Types of Nitronate Ion Forming Processes. Relevance to the Nitroalkane Anomaly[1]

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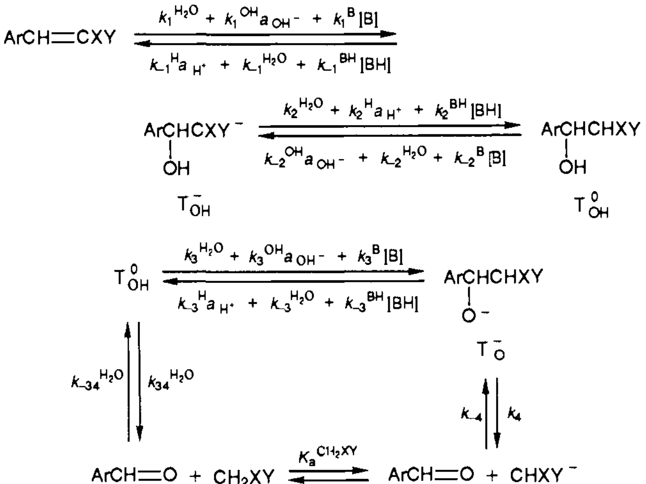
Contribution from the Thimann Laboratories of the University of California, Santa Cruz, California 95064. *Received January 9, 1989*

Abstract: A kinetic study of the hydrolysis of β-nitrostyrene and of the 4-chloro and 3-nitro derivatives in 50% Me_2SO–50% water (v/v) at 20 °C is reported. The mechanism involves four steps: nucleophilic addition of OH^- or water to form $ArCH(OH)CHNO_2^-$ (T_{OH}^-); carbon protonation of T_{OH}^- by water, H^+, and buffer acids to form $ArCH(OH)CH_2NO_2$ (T_{OH}^0); deprotonation of the OH group in T_{OH}^0 to form $ArCH(O^-)CH_2NO_2$ (T_O^-); collapse of T_O^- into ArCHO and $CH_2NO_2^-$. In strongly acidic solution the aci form of T_{OH}^0, $PhCH(OH)CH{=}NO_2H$ ($T_{OH,aci}^0$), which is generated by protonation of T_{OH}^- on the nitro group, could also be detected. All steps are reversible, and the rate and equilibrium constants of most of them could be determined by a combination of kinetic experiments starting with the substrate, the products, the independently synthesized T_{OH}^0, and T_{OH}^- (generated at high pH and then subjected to a pH jump) and by measuring product ratios spectrophotometrically or by HPLC analysis. The intrinsic rate constants of the proton transfer, $T_{OH}^- \rightleftarrows T_{OH}^0$, are close to those for the deprotonation of nitromethane and 2-nitroethanol, and the Brønsted coefficients show a transition-state imbalance ($\alpha_{CH} \gg \beta_{B^-}$) that is typical for the deprotonation of nitroalkanes. The other two processes that lead to the formation of a nitronate ion, i.e., nucleophilic addition to the olefin to form T_{OH}^- and collapse of T_O^- to form $CH_2NO_2^-$, show similar structure–reactivity behavior as the proton transfer, such as transition-state imbalances as manifested by $\alpha_{nuc}^n > \beta_{nuc}^n$ for nucleophilic addition and depressed intrinsic rate constants. However, these imbalances are smaller compared to the one in the proton transfers, especially so for the nucleophilic addition to the olefin. It is suggested that there is an inherent tendency for reactions leading to resonance-stabilized ions to have imbalanced transition states, but in proton transfers there are two imbalance *enhancing* factors, namely sp^3 hybridization of the carbon in the protonated form and hydrogen bonding in the transition state, while in the collapse of T_O^- there is one such factor (sp^3 hybridization of the carbon in T_O^-).

The mechanism of the hydrolysis of activated olefins, ArCH=CXY (X and Y are electron-withdrawing substituents), is shown in Scheme I.[2] During the past several years a number of detailed kinetic studies has been reported[3] which led to the determination of many of the rate constants that are shown in the scheme. Most steps in Scheme I refer to carbanion forming (or carbanion consuming) reactions: k_1 leads to a carbanion by means of nucleophilic addition to the olefin, k_{-2} leads to the same carbanion by a proton transfer, and k_4 generates a carbanion during the collapse of a tetrahedral intermediate. Hence, the determination of the rate and equilibrium constants of these various steps as a function of X and Y can teach us a great deal about structure–reactivity patterns in carbanion-forming processes. With this aim in mind, we have undertaken an investigation of

Scheme I



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(1) This is part 25 in the series Nucleophilic Addition to Olefins. Part 24: Bernasconi, C. F.; Killion, R. B. *J. Org. Chem.* **1989**, *54*, 2878.

(2) For reviews summarizing the earlier literature, see: (a) Patai, S.; Rappoport, Z. In *The Chemistry of the Alkenes*; Patai, S., Ed.; Wiley-Interscience: New York, 1964; Chapter 8. (b) Fyfe, C. A. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Wiley-Interscience: New York, 1971; Chapter 2.

(3) (a) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5133, 5143. (b) Bernasconi, C. F.; Carrē, D. J.; Kanavarioti, A. *Ibid.* **1981**, *103*, 4850. (c) Bernasconi, C. F.; Howard, K. A.; Kanavarioti, A. *Ibid.* **1984**, *106*, 6827. (d) Bernasconi, C. F.; Laibelman, A.; Zitomer, J. L. *Ibid.* **1985**, *107*, 6563. (e) Bernasconi, C. F.; Kanavarioti, A.; Killion, R. B. *Ibid.* **1985**, *107*, 3612. (f) Bernasconi, C. F.; Fox, J. P.; Kanavarioti, A.; Panda, M. *Ibid.* **1986**, *108*, 2372. (g) Bernasconi, C. F.; Stronach, M. *J. Org. Chem.* **1986**, *51*, 2144.

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Table I. Summary of Rate and Equilibrium Constants of the Hydrolysis of Various β-Nitrostyrenes

parameter	50% Me_2SO–50% water (20 °C)[a]			water (25 °C)[b]
	NS	Cl-NS	NO_2-NS	$CH_2(O)_2$-NS (**2**)
k_1^{OH}, $M^{-1}\ s^{-1}$	1.31	2.11	5.48	0.30
$k_1^{H_2O}$, s^{-1}	2.20×10^{-6}	2.40×10^{-6}	3.30×10^{-6}	8.18×10^{-6}
$k_{-1}^{H_2O}$, s^{-1}	3.89×10^{-6}	2.57×10^{-6}	1.00×10^{-6}	6.0×10^{-7}
k_{-1}^{H}, $M^{-1}\ s^{-1}$	5.12×10^{4}	2.34×10^{4}	4.84×10^{3}	1.64×10^{3}
$K_1^{H_2O}(pK_1^{H_2O})$, M	4.30×10^{-11} (10.37)	1.03×10^{-10} (9.99)	6.82×10^{-10} (9.17)	5.0×10^{-9} (8.3)
K_1^{OH}, M^{-1}	3.39×10^{5}	8.13×10^{5}	5.37×10^{6}	5.0×10^{5}
$k_2^{H_2O}$, s^{-1}	1.40×10^{-3}	1.55×10^{-3}	1.90×10^{-3}	1.76×10^{-3}
k_2^{H}, $M^{-1}\ s^{-1}$	3.43×10^{3}	3.22×10^{3}	4.61×10^{3}	1.8×10^{2}
k_{-2}^{OH}, $M^{-1}\ s^{-1}$	3.62×10^{2}	5.50×10^{2}	1.13×10^{3}	2.9×10^{2}
$k_{-2}^{H_2O}$, s^{-1}	1.11×10^{-7}	1.43×10^{-7}	3.42×10^{-7}	3.06×10^{-7}
$K_a^{CH} = k_{-2}^{H_2O}/k_2^{H}$, M ($pK_a^{CH}$)	3.24×10^{-11} (10.49)	4.47×10^{-11} (10.35)	7.41×10^{-11} (10.13)	1.7×10^{-9} (8.77)
pK_a^{OH}	14.80	14.56	14.39	~14.0;[c] ~12.5[d]
k_4, s^{-1}	1.59×10^{2}	1.17×10^{2}	6.24×10^{1}	~2×10^{3}; ~63.2[d]
k_{-4}, $M^{-1}\ s^{-1}$	~1.38×10^{1}[e]	1.89×10^{1}	3.73×10^{1}	0.2
$K_4 = k_4/k_{-4}$, M	~1.15×10^{1}[e]	6.19	1.66	~1.0×10^{4}; 3.16×10^{2}[d]
pK_a^{NOH}	~4.65	~4.44	~4.45	

[a] This work. [b] 3,4-(Methylenedioxy)-β-nitrostyrene; ref 9. [c] Estimated in ref 9. [d] Estimated in this work; see the text. [e] Extrapolated value from a plot of log k_4 vs log K_4.

the hydrolysis of β-nitrostyrene. The nitro group is a particularly interesting activating group because of its large resonance effect. This resonance effect contributes importantly to the stabilization of nitronate ions but its development appears to have made minimal progress in the transition state. This manifests itself in abnormal structure–reactivity coefficients ("nitroalkane anomaly") derived from remote substituents in the nitronate ion, e.g., in unusually high (>1) Brønsted α values in the deprotonation of arylnitroalkanes[4] or unusually low α values (<0) in the deprotonation of certain nitroalkanes[5] and also in low intrinsic rate constants[4-6] (the intrinsic rate constant k_0 is defined as k when $K = 1$).[7]

An interesting question is whether the lag in the development of resonance behind bond formation and its effect on structure–reactivity coefficients and intrinsic rate constants is the same, irrespective of the type of carbanion-forming reaction, or whether it matters if the carbanion is formed via proton transfer (k_{-2}), nucleophilic addition (k_1), or collapse of a tetrahedral intermediate (k_4). In an attempt to answer this question, we set out to study the hydrolysis of β-nitrostyrene and its 4-chloro and 3-nitro derivatives and determine as many rate constants in Scheme I as possible.

There has been an earlier report on the kinetics of the hydrolysis of a β-nitrostyrene derivative, 3,4-(methylenedioxy)-β-nitrostyrene, in water.[9] However, we wanted to carry out our investigation in 50% Me_2SO–50% water, a solvent used for most of our comparative studies,[3] and we also wanted to vary the phenyl substituent in order to determine structure–reactivity coefficients.

Results

General Features. All experiments were carried out in 50% Me_2SO–50% water (v/v) at 20 °C and at a constant ionic strength of 0.5 M maintained with KCl. Pseudo-first-order conditions, achieved by having KOH or HCl in excess or by working in buffered solutions, were used throughout; for measurements of the reaction in the reverse direction nitromethane was used in large excess over benzaldehyde.

The general methodology was basically the same for the three compounds β-nitrostyrene (NS), 4-chloro-β-nitrostyrene (Cl-NS), and 3-nitro-β-nitrostyrene (NO_2-NS). This methodology involved primarily the study of the kinetic behavior of the substrate (S), of the reaction products, of T_{OH}^- (after generating it from substrate and KOH), and of T_{OH}^0 (synthesized independently). It also included spectrophotometric and HPLC determinations of products or product ratios generated by the reactions of T_{OH}^- and T_{OH}^0 in acidic and/or basic solution. The combination of the results of all these experiments yielded most of the rate and equilibrium constants shown in Scheme II. Note that Scheme II differs from Scheme I in that it includes an additional equilibrium, the formation of the aci form of T_{OH}^0 ($T_{OH,aci}^0$), and in that the $k_{34}^{H_2O}$

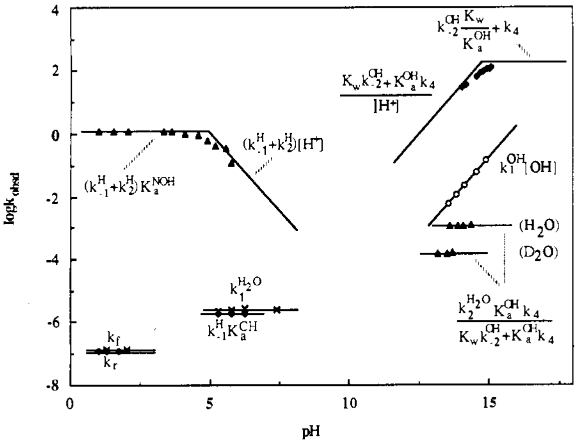
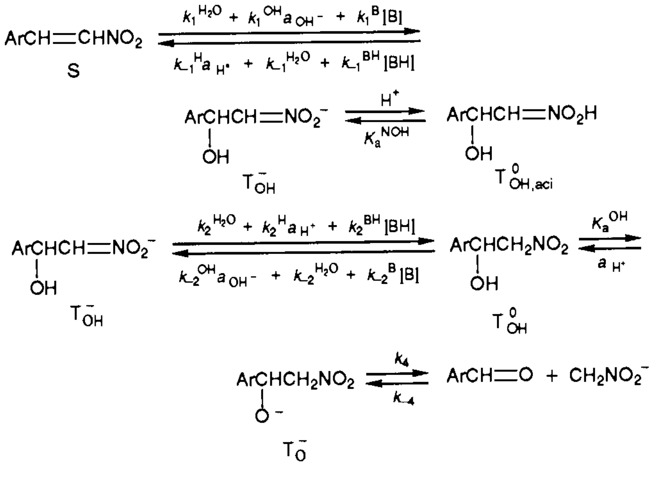


Figure 1. pH–rate profiles for various processes of Scheme II for NS.

Scheme II



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(4) (a) Fukyama, M.; Flanagan, P. W. K.; Williams, F. T., Jr.; Frainer, L.; Miller, S. A.; Schechter, H. *J. Am. Chem. Soc.* **1970**, *92*, 4689. (b) Bordwell, F. G.; Boyle, W. J., Jr. *Ibid.* **1972**, *94*, 3907; **1975**, *97*, 3447.

(5) Kresge, A. J. *Can. J. Chem.* **1974**, *52*, 1897.

(6) Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.

(7) In proton transfers it is commom to make statistical corrections; i.e., for $CH + B \rightleftharpoons C^- + BH$, $\log k_0 = \log (k/q) = \log (k/p)$ when $pK_a^{BH} - pK_a^{CH} + \log (p/q) = 0$, with CH being the carbon acid, q being the number of protonation sites on B^-, and p being the number of protons on BH.[8]

(8) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University: Ithaca, 1973; Chapter 10.

(9) Crowell, T. K.; Kim, T.-R. *J. Am. Chem. Soc.* **1973**, *95*, 6781.

step, for which no evidence was found, has been omitted.[10]

Figure 1 shows the pH–rate profiles for various processes of Scheme II for NS. Similar pH–rate profiles were obtained for Cl-NS and NO_2-NS. In the following we describe how the various rate and equilibrium constants were obtained; they are summarized in Table I.

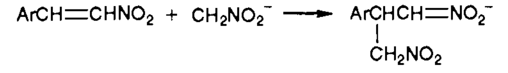
1. Reaction of Substrate with KOH. In KOH solutions, T_{OH}^- is thermodynamically strongly favored over the substrate and its formation is faster than its further reaction to T_{OH}^0 and products. k_1^{OH} is therefore easily obtained from

$$k_{obsd} = k_1^{OH} a_{OH^-} \tag{1}$$

by monitoring the disappearance of the substrate which has a distinctly different spectrum (λ_{max} = 320 nm for NS, 326 nm for Cl-NS, and 280 nm for NO_2-NS) than T_{OH}^- (λ_{max} = 250 nm for NS, ≤250 nm for Cl-NS, and 250 nm for NO_2-NS). This process was measured in the stopped-flow apparatus. The raw data are summarized in Table S1.[11]

2. Reaction of Substrate with Buffers. In an attempt to determine $k_1^{H_2O}$ for water addition, the β-nitrostyrenes were placed into acetate, cacodylate, DABCO, and triethylamine buffers spanning a pH range from ~5 to ~10.5. Between pH ~7 and ~10.5 none of the intermediates accumulates and the reaction can, in a first approximation, be understood as a conversion of S to benzaldehyde and $CH_2NO_2^-$ via T_{OH}^-, T_{OH}^0, and T_O^- as steady-state intermediates, with nucleophilic attack by water and OH^- being rate limiting. Between pH ~5 and ~7, conversion of T_{OH}^0 to benzaldehyde and nitromethane becomes very slow, so T_{OH}^0 is now the "product" of the reaction, with water addition to S being rate limiting.

In most of the experiments the reaction was not first order but showed logarithmic plots of ΔOD vs time that curved downward. This suggests an autocatalytic process which may be attributed to reaction of $CH_2NO_2^-$ with the substrate to form the adduct **1**. This adduct can then lead to an isoxazole[12] or to polymerization



$$ArCH{=}CHNO_2 + CH_2NO_2^- \longrightarrow Ar\underset{\displaystyle CH_2NO_2}{\underset{|}{C}}HCH{=}NO_2^- \tag{2}$$

1

products by reaction with further molecules of β-nitrostyrene. The known rate constant for reaction 2 with NS (17.6 $M^{-1}\,s^{-1}$)[12] is consistent with this interpretation under the reaction conditions used in these studies. The problem caused by reaction 2 could be partially circumvented by using the method of initial rates, with k_{obsd} being determined as

$$k_{obsd} = -\frac{\Delta OD/\Delta t}{\epsilon_s[S]_0} \tag{3}^{13}$$

This method worked well below pH 6.5 since little nitromethane is generated (T_{OH}^0 is the product) and only a small fraction is in the reactive anionic form (eq 2). k_{obsd} is given by

$$k_{obsd} = k_1^{H_2O} + k_1^B[B] \tag{4}$$

with $k_1^B[B]$ referring to general-base catalysis of water addition. This catalysis was generally quite weak, but it was corrected for in calculating $k_1^{H_2O}$. A representative buffer plot (NO_2-NS, B^- = AcO^-, pH 6.26) is shown in Figure 2 (circles). In some cases the buffer plots were characterized by an initial steep rise followed by a more shallow dependence as shown in Figure 2 (crosses) for the example of NS, B^- = AcO^-, pH 5.78. The initial steep rise can be attributed to the reverse of water addition, $k_{-1}^H a_{H^+} + k_{-1}^{BH}[BH]$, being faster than or comparable with carbon protonation of T_{OH}^- ($k_2^H a_{H^+} + k_2^{BH}[BH]$) at low [BH], which leads to a k_{obsd} according to eq 5.

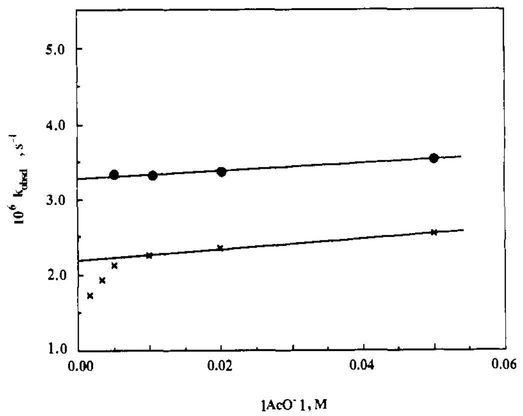


Figure 2. Hydrolysis in acetate buffers: (●) NO_2-NS, pH 6.26, eq 4; (×) NS, pH 5.78, eq 5.

$$k_{obsd} = \frac{k_2^H a_{H^+} + k_2^{BH}[BH]}{k_{-1}^H a_{H^+} + k_{-1}^{BH}[BH] + k_2^H a_{H^+} + k_2^{BH}[BH]}(k_1^{H_2O} + k_1^B[B]) \tag{5}$$

Equation 5 simplifies to eq 4 at high [BH] when $k_2^{BH}[BH] + k_2^H a_{H^+} \gg k_{-1}^H a_{H^+} + k_{-1}^{BH}[BH]$. The raw data are summarized in Tables S2–S4.[11]

3. Reaction of Substrate and T_{OH}^0 in HCl Solution. If the substrate is placed into an HCl solution, a slow partial conversion into T_{OH}^0 is observed. In a similar way an acidic solution of T_{OH}^0 is partially converted into substrate. These observations indicate that S and T_{OH}^0 are of comparable thermodynamic stability, and that under these conditions the reaction of T_{OH}^0 to form products is immeasurably slow. The interconversion of S and T_{OH}^0 under these conditions can be described by eq 6 with T_{OH}^- acting as a

$$S \underset{k_{-1}^H a_{H^+}}{\overset{k_1^{H_2O}}{\rightleftharpoons}} T_{OH}^- \underset{k_{-2}^{H_2O}}{\overset{k_2^H a_{H^+}}{\rightleftharpoons}} T_{OH}^0 \tag{6}$$

steady-state intermediate. Rates were measured in both directions. Due to the slowness of the reaction the method of initial rates was used. The steady-state rate constants in the forward (k_f) and reverse directions (k_r) are given by eq 7 and 8, respectively. The results of these measurements are summarized in Tables S5 and S6[11] while k_f and k_r are shown in Figure 1.

$$-\frac{\Delta OD/\Delta t}{(\epsilon_s - \epsilon_{T^0_{OH}})[S]_0} = k_f = \frac{k_1^{H_2O} k_2^H}{k_{-1}^H + k_2^H} \tag{7}$$

$$\frac{\Delta OD/\Delta t}{(\epsilon_s - \epsilon_{T^0_{OH}})[T_{OH}^0]_0} = k_r = \frac{k_{-2}^{H_2O} k_{-1}^H}{k_{-1}^H + k_2^H} \tag{8}$$

By combining k_f with $k_1^{H_2O}$ (vide supra) we now obtain k_2^H/k_{-1}^H by virtue of eq 9. Furthermore, since according to eq

$$\frac{k_2^H}{k_{-1}^H} = \frac{k_f}{k_f + k_1^{H_2O}} \tag{9}$$

7 and 8 k_f/k_r is given by

$$\frac{k_f}{k_r} = \frac{k_1^{H_2O} k_2^H}{k_{-2}^{H_2O} k_{-1}^H} \tag{10}$$

a knowledge of k_2^H/k_{-1}^H allows us now to calculate $k_{-2}^{H_2O}$ as

$$k_{-2}^{H_2O} = \frac{k_r}{k_f}\frac{k_2^H}{k_{-1}^H} k_1^{H_2O} \tag{11}$$

4. Reaction of T_{OH}^0 in Acetate Buffer Solutions. In the presence of an acetate buffer in the pH range between 5.3 and 6.3 the equilibration between S and T_{OH}^0 is still much faster than the

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[10] The $k_{34}^{H_2O}$ step was observed as a very slow process in strongly acidic solution in the hydrolysis of benzylidenemalononitrile[3c] and benzylidene-1,3-indandione.[3d] The $k_{34}^{H_2O}$ pathway is probably also present in the hydrolysis of β-nitrostyrene, but it is too slow for kinetic measurements to be practical.

[11] See the paragraph concerning supplementary material at the end of this paper.

[12] Bernasconi, C. F.; Zitomer, J. L. Unpublished results.

[13] The products do not absorb at λ_{max} of S.

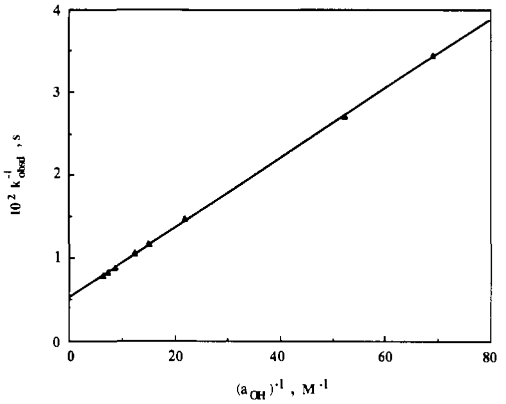


Figure 3. Reaction of T^0_{OH} in KOH solution plotted according to eq 17 for NS.

conversion of T^0_{OH} to products and this equilibration can be written as

$$S \underset{k_{-1}{}^{H}a_{H^+}}{\overset{k_1{}^{H_2O}}{\rightleftarrows}} T^-_{OH} \underset{k_{-2}{}^{H_2O} + k_{-2}{}^{B}[B]}{\overset{k_2{}^{H}a_{H^+} + k_2{}^{BH}[BH]}{\rightleftarrows}} T^0_{OH} \qquad (12)$$

The $k_1{}^{B}[B]$ and $k_{-1}{}^{BH}[BH]$ terms (see Scheme II) are negligible and have been omitted.

Initial rate experiments of the conversion of T^0_{OH} to S provide k_r given by

$$k_r = \frac{(k_{-2}{}^{H_2O} + k_{-2}{}^{B}[B])k_{-1}{}^{H}a_{H^+}}{(k_2{}^{H} + k_{-1}{}^{H})a_{H^+} + k_2{}^{BH}[BH]} \qquad (13)$$

which at high buffer concentration ($k_2{}^{BH}[BH] \gg (k_2{}^{H} + k_{-1}{}^{H})a_{H^+}$ and $k_{-2}{}^{B}[B] \gg k_{-2}{}^{H_2O}$) simplifies to

$$k_r = \frac{k_{-2}{}^{B}[B]}{k_2{}^{BH}[BH]} k_{-1}{}^{H}a_{H^+} = K_a{}^{CH}k_{-1}{}^{H} \qquad (14)$$

with $K_a{}^{CH}$ being the CH acidity constant of T^0_{OH}. Such experiments were performed with NS and NO_2-NS, with the results summarized in Table S7.[11]

5. Reaction of T^0_{OH} in KOH Solution. In basic solution, T^0_{OH} is rapidly converted into a mixture of T^-_{OH} and products according to eq 15. k_{obsd} values observed in the stopped-flow apparatus as

$$T^-_{OH} \xleftarrow{k_{-2}{}^{OH}a_{OH^-}} T^0_{OH} \underset{a_{H^+}}{\overset{K_a{}^{OH}}{\rightleftarrows}} T^-_{O} \xrightarrow{k_4} ArCH{=}O + CH_2NO_2^- \qquad (15)$$

a function of pH are summarized in Table S8;[11] eq 16 shows the

$$k_{obsd} = k_{-2}{}^{OH}a_{OH^-}\frac{a_{H^+}}{K_a{}^{OH} + a_{H^+}} + k_4\frac{K_a{}^{OH}}{K_a{}^{OH} + a_{H^+}} \qquad (16)$$

relationship of k_{obsd} to the parameters of eq 15. After inverting and substituting K_w/a_{OH^-} for a_{H^+} ($K_w = a_{H^+}a_{OH^-}$) eq 16 becomes eq 17. Figure 3 shows a representative plot of k_{obsd}^{-1} vs $a_{OH^-}^{-1}$. From the ratio intercept/slope = $K_a{}^{OH}/K_w$ one obtains $K_a{}^{OH}$.

$$k_{obsd}^{-1} = \frac{K_a{}^{OH}}{k_4K_a{}^{OH} + k_{-2}{}^{OH}K_w} + \frac{K_w}{k_4K_a{}^{OH} + k_{-2}{}^{OH}K_w}a_{OH^-}^{-1} \qquad (17)$$

Further information can be gained from the determination of the ratio $[T^-_{OH}]/[CH_2NO_2^-]$ or $[T^-_{OH}]/[ArCH{=}O]$ formed in reaction 15. Since the first term on the right side of eq 16 refers to formation of T^-_{OH} and the second term to formation of the products, we obtain

$$\frac{[T^-_{OH}]}{[CH_2NO_2^-]} = \frac{[T^-_{OH}]}{[ArCH{=}O]} = \frac{k_{-2}{}^{OH}K_w}{k_4K_a{}^{OH}} \qquad (18)$$

The ratios obtained spectrophotometrically (see the Experimental Section) are 0.181 for NS, 0.224 for Cl-NS, and 0.558 for NO_2-NS. Combining eq 18 with the intercept of Figure 3 (first term on the right side of eq 17) and $K_a{}^{OH}$ affords k_4. With k_4 being known, $k_{-2}{}^{OH}$ could also be calculated from eq 18.

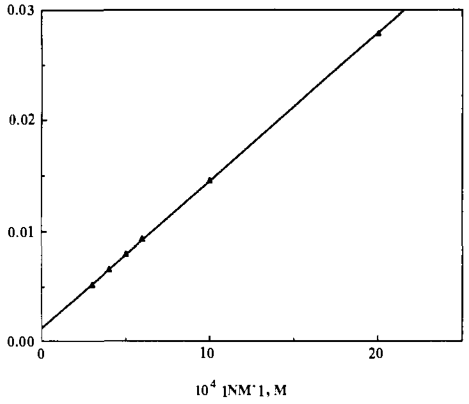


Figure 4. Reaction of 3-nitrobenzaldehyde with $CH_2NO_2^-$(NM^-) plotted according to eq 20.

It should be noted that the ratio given by eq 18 is a kinetic rather than a thermodynamic ratio. The latter is reached on a much slower time scale. This slow process which is kinetically the same as that measured when T^-_{OH}, generated by reaction of the substrate with KOH, is converted to products is discussed in the next section.

6. Reaction of T^-_{OH} in KOH Solution. T^-_{OH}, generated by reaction of the substrate with KOH, is slowly converted to products. With NS, there is 100% conversion to benzaldehyde and $CH_2NO_2^-$. With Cl-NS and NO_2-NS, the plots of log ΔOD vs time showed upward curvature, indicating that the reaction is significantly reversible. Using very low substrate concentration led to linear log plots with Cl-NS but not with NO_2-NS.

The observed reactions correspond to eq 19; with NS, and Cl-NS at low concentrations, contribution by the k_{-4} step is

$$T^-_{OH} \underset{k_{-2}{}^{OH}a_{OH^-}}{\overset{k_2{}^{H_2O}}{\rightleftarrows}} T^0_{OH} \underset{a_{H^+}}{\overset{K_a{}^{OH}}{\rightleftarrows}} T^-_{O} \underset{k_{-4}}{\overset{k_4}{\rightleftarrows}} ArCH{=}O + CH_2NO_2^- \qquad (19)$$

negligible while with NO_2-NS it is significant under all experimental conditions. k_{obsd} is given by

$$k_{obsd} = \frac{k_2{}^{H_2O}k_4K_a{}^{OH}}{k_4K_a{}^{OH} + k_{-2}{}^{OH}K_w} + \frac{k_{-2}{}^{OH}k_{-4}K_w}{k_4K_a{}^{OH} + k_{-2}K_w}([ArCH{=}O]_e + [CH_2NO_2^-]_e) \qquad (20)$$

with $[ArCH{=}O]_e$ and $[CH_2NO_2^-]_e$ being equilibrium concentrations.

The measurable reversibility of the reaction with the two substituted β-nitorstyrenes was exploited by conducting the reaction in the reverse direction, with $[CH_2NO_2^-]_0 \gg [ArCHO]_0$.

From k_{obsd} in the reaction of NS (Table S9)[11] or from the intercept of a plot of k_{obsd} vs $[CH_2NO_2^-]_0$ in the reactions of Cl-NS and NO_2-NS (Tables S10 and S11),[11] $k_2{}^{H_2O}$ was obtained since all the other terms in the expression $k_2{}^{H_2O}k_4K_a{}^{OH}/(k_4K_a{}^{OH} + k_{-2}{}^{OH}K_w)$ are known (see reaction of T^0_{OH} in KOH solution). From the slope of the plot k_{obsd} vs $[CH_2NO_2^-]_0$, k_{-4} was also accessible. Such a plot is shown in Figure 4 for NO_2-NS.

By combining $k_2{}^{H_2O}$ with $k_{-2}{}^{OH}$ determined as described in the previous section, we now also obtain the CH acidity constant of T^0_{OH}, $K_a{}^{CH}$, as

$$K_a{}^{CH} = \frac{k_{-2}{}^{OH}}{k_2{}^{H_2O}}K_w \qquad (21)$$

7. Reaction of T^-_{OH} in KOD Solution in 50% Me_2SO–50% D_2O. As discussed in the previous section, conversion of T^-_{OH} to products is irreversible with NS and also with Cl-NS as long as low substrate concentrations are used. Hence, eq 20 simplifies to

$$k_{obsd} = \frac{k_2{}^{H_2O}k_4K_a{}^{OH}}{k_4K_a{}^{OH} + k_{-2}{}^{OH}K_w} \qquad (22)$$

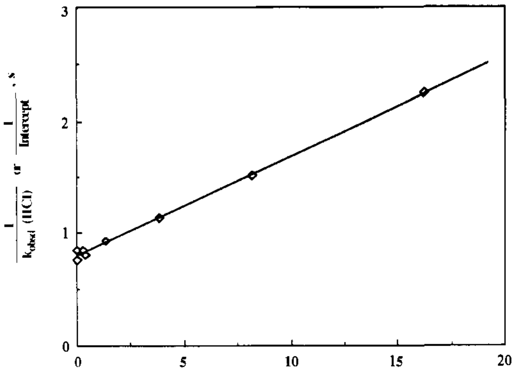
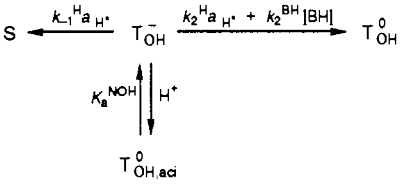


Figure 5. Reaction of T_{OH}^- with acid plotted according to eq 24 for NS.

Scheme III



The results of experiments conducted in 50% Me_2SO–50 D_2O are summarized in Tables S9[11] and S10.[11] They yield $k_{obsd}^{H_2O}/k_{obsd}^{D_2O}$ = 8.00 for NS and 7.65 for Cl-NS. These rather large kinetic isotope effects[14] suggest that the $k_2^{H_2O}$ step (carbon protonation of T_{OH}^- by water) is essentially rate limiting, requiring that $k_4K_a^{OH} \gg k_{-2}^{OH}K_w$ in eq 22. This conclusion is consistent with the small ratios $k_{-2}^{OH}K_w/k_4K_a^{OH}$ of 0.181 (NS) and 0.224 (Cl-NS) derived in section 4.

8. Reaction of T_{OH}^- with Acid. When T_{OH}^- is mixed with an acidic buffer or an HCl solution in the stopped-flow apparatus, a mixture of substrate and T_{OH}^0 is formed according to Scheme III. At low buffer concentrations the $k_{-1}^{BH}[BH]$ term (see Scheme II) is negligible and hence has been omitted. k_{obsd} is given by

$$k_{obsd} = \{(k_{-1}^H + k_2^H)a_{H^+} + k_2^{BH}[BH]\}\frac{K_a^{NOH}}{K_a^{NOH} + a_{H^+}} \qquad (23)$$

with K_a^{NOH} being the acid-dissociation constant of the aci form of T_{OH}^0. For NS, an extensive series of measurements was carried out in acetate, methoxyacetate, chloroacetate, and cyanoacetate buffers. The intercepts and slopes of the buffer plots are summarized in Table S12.[11] The intercepts are shown, along with data in HCl solution, in Figure 1. The inverse of these intercepts and of k_{obsd} in HCl are given by eq 24. A plot according to eq

$$\frac{1}{k_{obsd}(\mathrm{HCl})} \text{ or } \frac{1}{\text{intercept}} = \frac{1}{(k_{-1}^H + k_2^H)K_a^{NOH}} + \frac{1}{(k_{-1}^H + k_2^H)a_{H^+}} \qquad (24)$$

24 is shown in Figure 5. It yields $k_{-1}^H + k_2^H = 1.12 \times 10^5$ M^{-1} s^{-1} and $pK_a^{NOH} = 4.96$. We consider these values to be only approximate because of the rather large uncertainty in the intercepts of the buffer plots according to eq 23. This uncertainty stems from the smallness of the $(k_{-1}^H + k_2^H)a_{H^+}$ term compared to the $k_2^{BH}[BH]$ term at pH values close to pK_a^{NOH} or above. With Cl-NS and NO_2-NS, this problem was even more severe and a different method had to be used to determine $k_{-1}^H + k_2^H$ and K_a^{NOH} (see below).

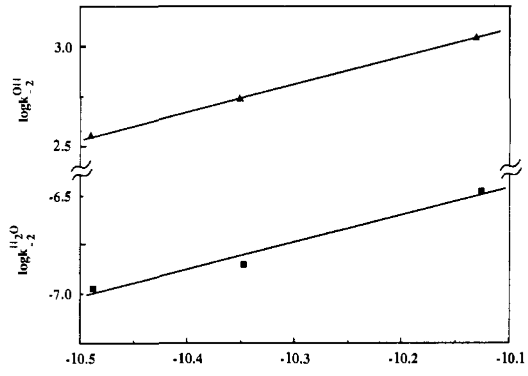


Figure 6. Brønsted plots of k_{-2}^{OH} (▲) and $k_{-2}^{H_2O}$ (■) vs log K_a^{CH} for the carbon deprotonation of T_{OH}^0 by OH^- and water, respectively.

The *slopes* of the buffer plots allow calculation of k_2^{BH} from eq 25. The more accurate K_a^{NOH} value determined by the alternative method discussed below was used in these calculations.

$$k_2^{BH} = \text{slope}\,\frac{K_a^{NOH} + a_{H^+}}{K_a^{NOH}} \qquad (25)$$

The ratio k_2^H/k_{-1}^H was calculated by two independent methods. In the first, k_2^H/k_{-1}^H was equated with the ratio $[T_{OH}^0]/[S]$, which was obtained by quenching T_{OH}^- with HCl and measured spectrophotometrically (see the Experimental Section). This method yielded $k_2^H/k_{-1}^H = 0.116$. The second method is based on eq 9, where k_f is defined in eq 7. This yields $k_2^H/k_{-1}^H = 0.063$. The agreement between the two methods is only fair. There are at least three factors that are likely to contribute to the less than perfect agreement. (a) The spectrophotometric determination had to be made by measuring [S] at λ_{max} of S, and $[T_{OH}^0]$ was calculated as $[S]_0 - [S]$. Since $[S]_0 - [S]$ is a small difference between two large numbers there is the potential for a relatively large experimental error. (b) Heating effects during the quenching of the rather strongly basic T_{OH}^- solution (0.1 M KOH) with HCl (>0.1 M) may slightly alter the k_2^H/k_{-1}^H ratio. (c) Both k_f and $k_1^{H_2O}$ were measured by the method of initial rates which is potentially subject to larger experimental errors than conventional rate measurements.

Using the average value from the two determinations affords $k_2^H/k_{-1}^H = 0.089$. In conjunction with $k_{-1}^H + k_2^H = 1.12 \times 10^5$ M^{-1} s^{-1}, this yields $k_{-1}^H = 1.03 \times 10^5$ M^{-1} s^{-1} and $k_2^H = 9.15 \times 10^3$ M^{-1} s^{-1}.

As indicated above for Cl-NS and NO_2-NS, the $k_2^{BH}[BH]$ term in eq 23 was so large in the pH range close to and above pK_a^{NOH} that the intercepts of plots of k_{obsd} vs [BH] became experimentally difficult to determine. Hence a different method was used to evaluate k_{-1}^H, k_2^H, and pK_a^{NOH}. Experiments in HCl solution at pH $\ll pK_a^{NOH}$ afforded k_{obsd} given by

$$k_{obsd} = (k_{-1}^H + k_2^H)K_a^{NOH} \qquad (26)$$

The results are summarized in Table S12.[11] The k_2^H/k_{-1}^H ratio was obtained in the same way as that for NS (from the $[T_{OH}^0]/[S]$ ratio and from eq 9). k_2^H could be calculated as

$$k_2^H = \frac{K_a^{CH}}{k_{-2}^{H_2O}} \qquad (27)$$

since $k_{-2}^{H_2O}$ is known from eq 11 and K_a^{CH} is known from eq 21. With k_2^H known, k_{-1}^H is now also obtained and eq 26 can be solved for K_a^{NOH}. This method of determining k_{-1}^H, k_2^H, and K_a^{NOH} was also applied to NS and yielded somewhat different values than the method based on eq 24: $k_{-1}^H = 5.12 \times 10^4$ M^{-1} s^{-1}, $k_2^H = 3.43 \times 10^3$ M^{-1} s^{-1}, and $pK_a^{NOH} = 4.65$. We believe that this second method affords more reliable results than the one based on eq 24 and hence it is these values which are reported in Table I. Our preference for the latter values is supported by the close agreement between $k_{-1}^H = 5.12 \times 10^4$ M^{-1} s^{-1} calculated above

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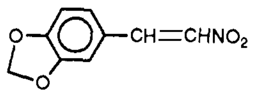
[14] (a) More O'Ferrall, R. A. In *Proton Transfer Reactions*, Caldin, E., Gold, V., Eds.; Wiley: New York, 1975; p 201. (b) Melander, L.; Saunders, W. J., Jr. *Reaction Rates of Isotopic Molecules*, Wiley-Interscience: New York, 1980; Chapter 5.

and $k_{-1}^{H} = 5.89 \times 10^4$ M^{-1} s^{-1} determined from eq 14 with K_a^{CH} from eq 21.

Finally from k_{-1}^{H} and $k_1^{H_2O}$ we obtain $K_1^{H_2O} = k_1^{H_2O}/k_{-1}^{H}$ as well as $K_1^{OH} = K_1^{H_2O}/K_w$.

Discussion

The rate and equilibrium constants defined in Scheme II are summarized in Table I for the reactions of NS, Cl-NS, and NO_2-NS in 50% Me_2SO–50% water; the table also includes similar data for the hydrolysis of 3,4-methylenedioxy-β-nitrostyrene ($CH_2(O)_2$-NS, **2**) in water reported by Crowell and Kim.[9]



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Most parameters in Table I were determined by combining results of different kinetic measurements or of kinetic measurements with product ratios. As a consequence, the unavoidable propagation of errors may adversely affect some of the parameters. The k_1^{OH} values are afflicted with the smallest experimental error, estimated at ±2%, since they were determined directly (eq 1) and were measurable with excellent reproducibility. $k_1^{H_2O}$ was obtained from intercepts of very weakly sloping straight lines (eq 4) and should, in principle, be quite accurate. Due to the complications by reaction 2, the method of initial rates had to be used, though, which we estimate yielded $k_1^{H_2O}$ with an error of ±15%.

An accurate evaluation of the errors in the other parameters is more difficult to come by and some of them may well be in the order of ±50%. However, the sources of error for most of the parameters are probably similar for the three substrates, so that in assessing the substituent effects on these parameters substantial cancellation of errors may be expected. This expectation is borne out by our observations, discussed below, that structure–reactivity plots are linear with rather little scatter and that the substituent effects are generally "reasonable" and consistent with what is known about such substituent effects in nitronate ion forming reactions.

Equilibrium Constants. Five independent equilibrium constants were determined in this study: $K_1^{H_2O}$ ($pK_1^{H_2O}$) for the nucleophilic addition $S + H_2O \rightleftarrows T_{OH}^- + H^+$, pK_a^{CH} for the CH acidity of T_{OH}^0, pK_a^{OH} for the OH acidity of T_{OH}^0, pK_a^{NOH} for the acidity of the nitronic acid or aci form of T_{OH}^0, and K_4 for the breakdown of T_O^- into ArCH=O and $CH_2NO_2^-$. The following points are noteworthy.

(1) The pK_a^{CH} values (10.49–10.13) are between 0.83 and 1.21 pK_a units lower than $pK_a^{CH} = 11.32$ for nitromethane in the same solvent,[15] reflecting the electron-withdrawing effect of the ArCH(OH) moiety of T_{OH}^0. The observed pK_a differences between T_{OH}^0 and nitromethane actually slightly underestimate this electronic effect because of a statistical factor of $^3/_2$ favoring ionization of nitromethane over T_{OH}^0. The pK_a^{CH} values in 50% Me_2SO are higher than that for T_{OH}^0 derived from $CH_2(O)_2$-NS (**2**)[9] in water by 1.36–1.72 pK_a units, reflecting mainly the reduced hydrogen-bonding solvation of the nitronate ions (T_{OH}^-) in 50% Me_2SO; for nitromethane the pK_a change from water to 50% Me_2SO amounts to 1.04 units.[15]

The substituent effect on pK_a^{CH} is quite small ($\rho \approx 0.50 \pm 0.04$)[16] because the negative charge in T_{OH}^- is undoubtedly largely delocalized into the nitro group. The somewhat larger ρ value reported for the pK_a^{CH} of arylnitromethanes in water[4] is a consequence of the aryl group being one carbon atom closer to the center of negative charge compared to T_{OH}^-.

(2) The $pK_1^{H_2O}$ values determined in this study (9.17–10.37) are significantly higher than $pK_1^{H_2O} = 8.3$ for $CH_2(O)_2$-NS (**2**) in water, again reflecting the diminished solvation of T_{OH}^- in the presence of Me_2SO. It is interesting that the substituent effect on $pK_1^{H_2O}$ ($\rho = 1.69 \pm 0.01$)[16] is much larger than that on pK_a^{CH} ($\rho \approx 0.50$). If one assumes that the substituent effect on pK_a^{CH} is mainly the result of stabilization of the negative charge in T_{OH}^- and that this effect should be the same regardless of whether T_{OH}^- is formed by the reaction of the β-nitrostyrene with water (or OH^-) or by deprotonation of T_{OH}^0, the enhanced ρ value for $pK_1^{H_2O}$ implies a large substituent effect on the stability of the *olefin*. A similar result was reported for the formation of T_{OH}^- derived from phenyl substituted benzylidene Meldrum's acids.[3a] This effect is in the direction of stabilizing the olefin by electron-donating groups, a common phenomenon observed in several other cases.[1,17]

(3) Our pK_a^{OH} values for T_{OH}^0 in 50% Me_2SO are only slighlty higher than the reported value for T_{OH}^0 derived from $CH_2(O)_2$-NS (**2**) in water. In contrast to our pK_a^{OH} values, which were experimentally determined, the one for $CH_2(O)_2$-NS is an estimate.[9] In view of the fact that the pK_a of weakly acidic alcohols increases roughly parallel with pK_w upon addition of Me_2SO,[18] the pK_a^{OH} of T_{OH}^0 derived from $CH_2(O)_2$-NS in water would be expected to be in the order of 12.5 rather than 14.0. We have therefore also listed this alternative pK_a^{OH} value in Table I.

The substituent effect on pK_a^{OH} ($\rho = 0.54 \pm 0.17$)[16] is comparable to that on pK_a^{CH} (≈ 0.50). The roughly equal substituent effects on the two pK_a's is consistent with the strong delocalization of the charge into the nitro group of T_{OH}^-, which compensates for the inherently much stronger substituent dependence of a carbanion compared to any oxyanion.

(4) The K_4 values determined in this study (6.19 for Cl-NS, 1.66 for NO_2-NS) are more than 3 orders of magnitude lower than that reported for the breakdown of T_O^- derived from $CH_2(O)_2$-NS (**2**) in water. One would expect K_4 to be larger in water than in 50% Me_2SO because of the greater stability of $CH_2NO_2^-$ in the former solvent, but an effect of 1–2 orders of magnitude would seem more reasonable. The reason for the unusually large apparent solvent effect can be traced to the inaccurate estimate of pK_a^{OH} in water mentioned earlier: k_4 from which K_4 was calculated as k_4/k_{-4} was obtained from the measured $K_a^{OH}k_4$ value and the expected K_a^{OH}.[9] A reduction in pK_a^{OH} from 14.0 to 12.5 implies a reduction in k_4 and K_4 by the same amount, which leads to a much more reasonable estimate for K_4 (see alternative value in Table I).

The substituent effect on K_4 is substantial with $\rho = -1.19$ based on the 4-Cl and 3-NO_2 substituents. This effect is significantly larger than the effect on pK_a^{OH} ($\rho = 0.54$), which is reminiscent of the comparison between substituent effects on pK_a^{CH} and $pK_1^{H_2O}$. It suggests that about half of the effect reflects stabilization of the negative charge in T_O^- by electron-withdrawing substituents; the other half reflect *de*stabilization of the benzaldehyde being formed.

(5) The experimental error in the pK_a^{NOH} values is larger than for most other parameters obtained in this study and hence it is not surprising that no meaningful ρ value can be obtained. Nevertheless, it appears that the substituent effect is quite small, which is consistent with the small substituent effect on pK_a^{CH} and also with the small difference in pK_a^{NOH} between nitromethane and phenylnitromethane in water.[19] The absolute values of pK_a^{NOH} on the order of 4.5 are also consistent with $pK_a^{NOH} = 4.75$ for phenylnitromethane in 50% Me_2SO.[15]

Rates of Proton Transfer at Carbon, $T_{OH}^- \rightleftarrows T_{OH}^0$. The rate constants for protonation of T_{OH}^- by water ($k_2^{H_2O}$) and by the hydronium ion (k_2^{H}) and the rate constants for the corresponding reverse processes (k_{-2}^{OH} and $k_{-2}^{H_2O}$) are summarized in Table I, along with similar rate constants for 3,4-(methylenedioxy)-β-nitrostyrene ($CH_2(O)_2$-NS). For NS we have also determined proton-transfer rate constants involving carboxylate buffers (k_2^{BH} and k_{-2}^{B}); they are summarized in Table II, along with similar

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

[16] Sign of ρ defined for log K_a^{CH}, log $K_1^{H_2O}$, etc. rather than pK_a^{CH}, $pK_1^{H_2O}$, etc.

[17] (a) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *108*, 4541. (b) Bernasconi, C. F.; Panda, M. *J. Org. Chem.* **1987**, *52*, 3042.

[18] Hallé, J.-C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1969**, 1851.

[19] $pK_a^{NOH} = 3.25$ for CH_3NO_2 at 25 °C,[20] and 3.64 for $PhCH_2NO_2$ at 20 °C.[15]

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

Table II. Rate Constants of Proton Transfer at Carbon, T^-_{OH} + BH $\rightleftarrows$ T^0_{OH} + B^-, for β-Nitrostyrene, 3,4-Methylene-β-nitrostyrene, and 2-Nitroethanol

B	(pK_a^{BH})	k_2^{BH}, M^{-1} s^{-1}	k_{-2}^{B}, M^{-1} s^{-1}	ΔpK^a + log p/q
NS,[b] 50% Me_2SO–50% Water, 20 °C (pK_a^{CH} = 10.49)				
$NCCH_2COO^-$	(3.29)	6.13×10^2	4.15×10^{-5}	−7.47
$MeOCH_2COO^-$	(4.56)	2.43×10^2	2.99×10^{-4}	−6.21
$ClCH_2CH_2COO^-$	(5.20)	1.28×10^2	6.74×10^{-4}	−5.58
CH_3COO^-	(5.78)	4.22×10^1	8.23×10^{-4}	−5.01
$CH_2(O)_2$-NS,[c] Water, 25 °C (pK_a^{CH} = 8.77)				
$ClCH_2COO^-$	(2.66)	2.1×10^1	1.63×10^{-5}	−6.41
CH_3COO^-	(4.61)	4.9	3.39×10^{-4}	−4.46
$HOCH_2CH_2NO_2$,[d] Water, 25 °C (pK_a^{CH} = 9.39)				
$ClCH_2COO^-$	(2.66)	4.79×10^1	9.13×10^{-6}	−7.03
$MeOCH_2COO^-$	(3.40)	2.39×10^1	2.44×10^{-5}	−6.29
CH_3COO^-	(4.61)	9.32	1.55×10^{-4}	−5.08

[a] $\Delta pK = pK_a^{BH} - pK_a^{CH}$. [b] This work. [c] Reference 9. [d] Reference 21.

Table III. Brønsted β_B Values and Intrinsic Rate Constants (log k_0) for Deprotonation of Various Nitroalkanes

reaction	β_B	log k_0	ref
T^0_{OH} + $RCOO^-$ (NS, 50% Me_2SO, 20 °C)	0.65	0.16	this work
T^0_{OH} + $RCOO^-$ ($CH_2(O)_2$-NS, H_2O, 25 °C)	0.68	−0.74	9
$HOCH_2CH_2NO_2$ + $RCOO^-$ (H_2O, 25 °C)	0.63	−1.00	21
$HOCH_2CH_2NO_2$ + R_2NH (H_2O, 25 °C)	0.63	−0.45	21
CH_3NO_2 + R_2NH (H_2O, 20 °C)	0.59	−0.59	15
CH_3NO_2 + R_2NH (50% Me_2SO, 20 °C)	0.62	0.73	15

rate constants for $CH_2(O)_2$-NS. For comparison purposes, proton-transfer rate constants for 2-nitroethanol[21] are also included.

The Brønsted β_B values defined as d log k_{-2}^B/dpK_a^{BH} are summarized in Table III. In view of the fact that they are derived from only two or three data points in each case, their uncertainty is probably as large as the variation among them, i.e., we consider the three values to be indistinguishable within experimental error. We also note that the β_B values derived from the piperidine/morpholine pair in the deprotonation of nitromethane (last two entries in Table III) are in the same range as the values for the various nitro alcohols.

By extrapolation of the Brønsted plots of log (k_{-2}^B/q) vs ΔpK + log (p/q) to ΔpK + log (p/q) = 0, one obtains the *intrinsic rate constants*, k_0, of proton transfer which are included in Table III. In comparing the various systems the following points can be made. (1) log k_0 for T^0_{OH} + $RCOO^-$ (NS, 50% Me_2SO, 20 °C) is approximately 0.9 log unit higher than for T^0_{OH} + $RCOO^-$ ($CH_2(O)_2$-NS, water, 25 °C). This reflects the well-known increase in the intrinsic rate constant of the deprotonation of nitroalkanes in the presence of Me_2SO as cosolvent.[15] The observed change of 0.9 log unit actually underestimates this increase because of the lower temperature in the Me_2SO-containing solvent. For example, the increase in k_0 for the reaction of the piperidine/morpholine pair with nitromethane from water to 50% Me_2SO at the same temperature is 1.32 log units, and this solvent effect is expected to be even larger with carboxylate ions as the base.[15,22,23]

(2) log k_0 for T^0_{OH} + $RCOO^-$ ($CH_2(O)_2$-NS, H_2O, 25 °C) is roughly the same as for $HOCH_2CH_2NO_2$ + $RCOO^-$ (H_2O, 25 °C). This result suggests that in these reactions the steric effect of replacing a hydrogen by an aryl group on a carbon adjacent to the carbanionic center is minimal. A similar conclusion is reached when comparing T^0_{OH} + $RCOO^-$ (NS, 50% Me_2SO, 20 °C) with CH_3NO_2 + R_2NH (50% Me_2SO, 20 °C): log k_0 for the former is 0.57 log units lower, but this reduction in log k_0 may be attributed to the change in base from R_2NH to $RCOO^-$, which seems to lower log k_0 by about 0.55 log unit if the reactions of $HOCH_2CH_2NO_2$ can serve as a model. Thus even the replacement of a hydrogen on the carbanionic carbon by the rather bulky ArCH(OH) moiety seems to have a minimal effect on k_0.

Table IV. Brønsted α Values from Phenyl-Substituent Dependence

$T^0_{OH} + OH^- \xrightarrow{k_{-2}^{OH}} T^-_{OH} + H_2O$	$\alpha_{CH} = \dfrac{d \log k_{-2}^{OH}}{d \log K_a^{CH}} = 1.38 \pm 0.02$
$T^0_{OH} + H_2O \xrightarrow{k_{-2}^{H_2O}} T^-_{OH} + H_3O^+$	$\alpha_{CH} = \dfrac{d \log k_{-2}^{H_2O}}{d \log K_a^{CH}} = 1.39 \pm 0.25$
$S + H_2O \xrightarrow{k_1^{H_2O}} T^-_{OH} + H^+$	$\alpha^n_{nuc} = \dfrac{d \log k_1^{H_2O}}{d \log K_1^{H_2O}} = 0.15 \pm 0.02$
$S + OH^- \xrightarrow{k_1^{OH}} T^-_{OH}$	$\alpha^n_{nuc} = \dfrac{d \log k_1^{OH}}{d \log K_1^{H_2O}} = 0.52 \pm 0.01$
$T^-_{O} \xrightarrow{k_4} ArCHO + CH_2{=}NO_2^-$	$\alpha^n_{C=O} = \dfrac{d \log k_4}{d \log K_4} = 0.48 \pm 0.10$

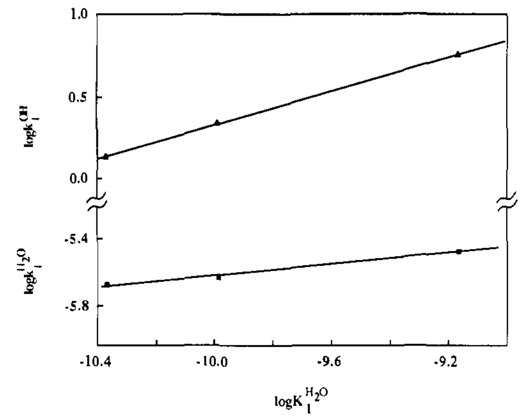

Figure 7. Plots of log k_1^{OH} (▲) and log $k_1^{H_2O}$ (■) vs log $K_1^{H_2O}$ for addition of OH^- and H_2O, respectively, to the olefin.

Turning to the proton-transfer rate constants involving OH^-/H_2O and H_2O/H_3O^+ (Table I), we note that the rate of protonation of T^-_{OH} increases slightly with *decreasing* basicity of the nitronate ion, e.g., $k_2^{H_2O}$ = 1.40×10^{-3} s^{-1}, 1.55×10^{-3} s^{-1}, and 1.90×10^{-3} s^{-1} for NS, Cl-NS, and NO_2-NS, respectively. This trend is reminiscent of the results with arylnitroalkanes;[4] it implies a negative Brønsted β_{C^-} value (β_{C^-} = d log $k_2^{H_2O}/dpK_a^{CH}$ or d log k_2^{H}/dpK_a^{CH}) and an α_{CH} value (α_{CH} = d log $k_{-2}^{H_2O}$/d log K_a^{CH} or d log k_{-2}^{OH}/d log K_a^{CH}) that is greater than unity. On the basis of three-point Brønsted plots (Figure 6), we obtain α_{CH} = 1.38 ± 0.03 (k_{-2}^{OH}), α_{CH} = 1.39 ± 0.25 ($k_{-2}^{H_2O}$), β_{C^-} = −0.38 ± 0.03 ($k_2^{H_2O}$), and β_{C^-} = −0.39 ± 0.25 (k_2^{H}) (see also Table IV). In view of the fact that these α_{CH} and β_B values are derived from only three points and that the pK_a^{CH} range is quite small, these parameters can only be regarded as approximate despite the fact that the standard deviation for α_{CH} and β_B-derived from k_{-2}^{OH} and $k_2^{H_2O}$, respectively, is quite small. They do, however, correctly reflect the unusual Brønsted behavior of nitroalkanes which has been attributed to a transition state in which charge delocalization into the nitro group lags behind proton transfer.[4,23]

Rates of Nucleophilic Addition. A plot of log k_1^{OH} vs log $K_1^{H_2O}$ (or log K_1^{OH}) for OH^- addition to β-nitrostyrenes to form T^-_{OH} (Figure 7) yields an excellent straight line of slope α^n_{nuc} = d log k_1^{OH}/d log $K_1^{H_2O}$ = 0.52 ± 0.01 (Table IV). This α value is much smaller than $\alpha_{CH} \approx$ 1.38 for the formation of T^-_{OH} by deprotonation of T^0_{OH} with OH^- (k_{-2}^{OH}), but it is similar to α^n_{nuc} = 0.51 for piperidine addition to a series of β-nitrostyrenes after correction for electrostatic effects.[17a] These α^n_{nuc} values suggest that charge delocalization into the nitro group in the transition state is not as strongly delayed as in the proton-transfer reaction; in fact, taken by themselves they do not give an indication whether there is any lag at all in charge delocalization behind bond formation. However, on the basis of comparable results for the reaction of

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[21] Bernasconi, C. F.; Panda, M.; Stronach, M. W. Unpublished results.

[22] (a) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (b) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969. (c) Bernasconi, C. F.; Terrier, F. *Ibid.* **1987**, *109*, 7115. (d) Bernasconi, C. F.; Bunnell, R. D.; Terrier, F. *Ibid.* **1988**, *110*, 6514.

[23] Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219.

β-nitrostyrenes with piperidine and morpholine,[17a] we believe there is a delay in delocalization. The β^n_{nuc} value (β^n_{nuc} = d log $k_1^{R_2NH}$/d log $K_1^{R_2NH}$) of 0.25 in the piperidine/morpholine reaction was taken as an approximate measure of bond formation between the nucleophile and the substrate and hence the fact that α^n_{nuc} is greater than β^n_{nuc} was taken as evidence for an imbalanced transition state, i.e., one in which charge delocalization or resonance development lag behind bond formation. It would be difficult to argue that only the transition state for amine addition but not the one for OH^- addition is imbalanced. Hence we conclude that C–O bond formation has made significantly less than 50% progress in the transition state for OH^- addition and that α^n_{nuc} reflects a similar degree of imbalance as in the amine reaction. This conclusion is supported by a comparison of intrinsic rate constants discussed below.

Possible reasons for the much smaller imbalances in the addition reactions compared to the proton transfer have been discussed previously.[24] We have taken the differences between α and β ($\alpha^n_{nuc} - \beta^n_{nuc}$ in nucleophilic additions, $\alpha_{CH} - \beta_B$ in proton transfer) as a crude indicator of these imbalances, assuming that β is a rough measure of bond formation or charge transfer at the transition state. One important factor believed to contribute to the smaller imbalances in nucleophilic additions is the difference in the hybridization of the carbon on which the negative charge develops. In the proton transfer this carbon is sp^3-hybridized (in the acid form) while in the addition reaction it is sp^2-hybridized (in the olefin). In the transition state of the latter reaction the sp^2 carbon is likely to keep its hybridization and maintain its π-overlap with the nitro group, thereby facilitating the shift of the charge into the nitro group and reducing the imbalance. On the other hand, in the deprotonation reaction the carbon can more easily accomodate the negative charge in the transition state by maintaining its sp^3 hybridization, which may enhance the imbalance.

Support for our conclusions regarding the transition state imbalances comes from a comparison of k_1^{OH} for OH^- addition to β-nitrostyrenes with k_1^{OH} for OH^- addition to benzylidenemalononitrile.[3f] Since $K_1^{OH} = 2.50 \times 10^6$ M^{-1} for the latter is close to $K_1^{OH} = 5.37 \times 10^6$ M^{-1} for NO_2-NS, the ratio $(k_1^{OH})_{CN}/(k_1^{OH})_{NO_2} = 3.18 \times 10^2$ is a rough measure of the ratio of the *intrinsic* rate constants. If $(k_1^{OH})_{NO_2}$ is corrected for the slightly higher K_1^{OH} value by assuming a $\beta^n_{nuc} = 0.25$, the ratio $(k_1^{OH})_{CN}/(k_1^{OH})_{NO_2}$ becomes 3.84×10^2, which we shall take as a good approximation to the true ratio of the intrinsic rate constants, $(k_0)_{CN}/(k_0)_{NO_2}$.[25,26] This ratio is about the same as the ratio of 2.45×10^2 for the intrinsic rate constants for piperidine/morpholine addition to benzylidenemalononitrile[1] and β-nitrostyrene[17a] in the same solvent. It is noteworthy that these ratios are much lower than the ratio $(k_0)_{CN}/(k_0)_{NO_2} \approx 2 \times 10^6$ for deprotonation of malononitrile vs nitromethane.[24] As discussed extensively elsewhere,[23,24] the lower intrinsic rate constants for formation of nitro-stabilized carbanions compared to that of cyano-stabilized carbanions may, to a large extent, be attributed to the fact that the nitronate ion derives a greater fraction of its stability from resonance than the malononitrile anions, but the transition state is not able to benefit from this resonance because its development lags behind bond formation (imbalance). The lower $(k_0)_{CN}/(k_0)_{NO_2}$ ratios for nucleophilic addition compared to proton transfer are thus consistent with the smaller imbalance for nucleophilic addition that is indicated by $\alpha^n_{nuc} - \beta^n_{nuc} \ll \alpha_{CH} - \beta_B$. The fact that $(k_0)_{CN}/(k_0)_{NO_2}$ is about the same for OH^- and piperidine/morpholine addition to β-nitrostyrene supports our contention (vide supra) that the imbalances in the two reactions must be of similar magnitude.

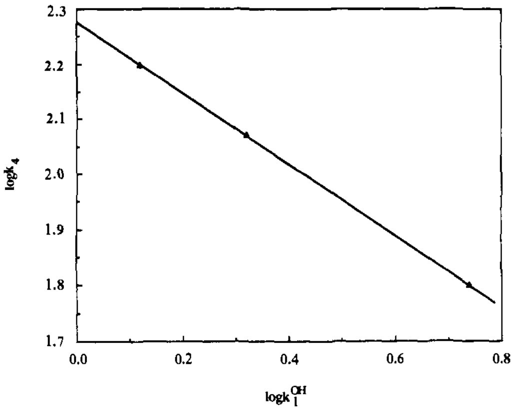
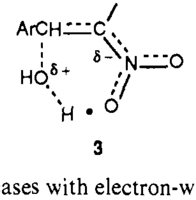


Figure 8. Plot of log k_4 for collapse of T_O^- vs log k_1^{OH} for OH^- addition to the olefin.

In comparing $k_1^{H_2O}$ for *water* addition to NO_2-NS with $k_1^{H_2O}$ for water addition to benzylidenemalononitrile,[3f] we obtain $(k_1^{H_2O})_{CN}/(k_1^{H_2O})_{NO_2} = 3.18 \times 10^2$ or, after correction for the slight differences in $pK_1^{H_2O}$, 3.62×10^2 as an approximate measure of the ratio of the intrinsic rate constants. This ratio is, within experimental error, identical with that for the k_1^{OH} values which implies a similar transition-state imbalance as for OH^- addition. It is therefore surprising that $\alpha^n_{nuc} = 0.15 \pm 0.02$ for water addition is so much smaller than $\alpha^n_{nuc} = 0.52$ for OH^- addition since this would suggest a very different charge distribution in the transition state for water addition. Unless one assumes that the experimental error which arises from initial rate measurements in the determination of $k_1^{H_2O}$ is so large as to give a distorted α^n_{nuc} value, the low α^n_{nuc} must result from the superposition of an inverse substituent effect (negative contribution to α^n_{nuc}) on the regular substituent effect. This inverse substituent effect may be caused by intramolecular hydrogen bonding in the transition state as shown in **3**. Inasmuch as the basicity of the nitronate oxygen decreases with electron-withdrawing phenyl substituents, this will reduce the strength of the hydrogen bond and hence attenuate the regular substituent effect, i.e., decrease α^n_{nuc}. It is not clear, though, whether this hydrogen bonding, if it exists at all, is strong enough to account for our results. In the reaction of water with benzylidene-1,3-indandione[3d] such hydrogen bonding (**4**) appears to be quite strong and manifests itself in an enhanced intrinsic rate constant for water attack. No such enhanced intrinsic rate constant is seen for water addition to β-nitrostyrenes since $(k_0)_{CN}/(k_0)_{NO_2}$ for water addition is the same as that for OH^- addition.



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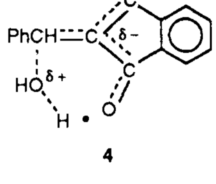

4

Rates of Reaction $T_O^- \rightleftarrows$ ArCHO + $CH_2NO_2^-$. The rate constant for collapse of T_O^- into ArCHO and $CH_2NO_2^-$ (k_4) could be determined for all three substrates, but k_{-4} and hence K_4 was only accessible for Cl-NS and NO_2-NS. The estimated K_4 and k_{-4} values given in Table I were obtained by assuming that a plot of log k_4 vs log K_4 would be linear. In view of the excellent linearity of the plot of log k_1^{OH} vs log $K_1^{H_2O}$ (Figure 7) and the fact that a plot of log k_4 vs log k_1^{OH} is also linear (Figure 8), our assumption seems very sound.

On the basis of the above data, an approximate $\alpha^n_{C=O}$ = d log k_4/d log K_4 of 0.48 ± 0.10 (Table IV) is obtained for the collapse

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(24) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.

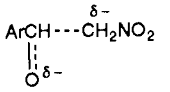
(25) The use of the ratio $(k_1^{OH})_{CN}/(k_1^{OH})_{NO_2}$ at equal K_1^{OH} of the two substrates as an approximate measure of the ratio of the *intrinsic* rate constants is based on the assumption that the (hypothetical) plots of log k_1^{OR} (R = H and alkyl) vs log K_1^{OR} (K_1^{OR} refers to substrate + $RO^- \rightleftarrows T_{OR}^-$) have the same slope, β^n_{nuc}, for both substrates. In such a case, $(k_1^{OR})_{CN}(k_1^{OR})_{NO_2}$ is independent of K_1^{OR} and is equal to $(k_0)_{CN}(k_0)_{NO_2}$, the ratio at $K_1^{OR} = 1$. If β^n_{nuc} is not the same for the two substrates, $(k_1^{OH})_{CN}/(k_1^{OH})_{NO_2}$ has to be regarded as an approximation of $(k_0)_{CN}/(k_0)_{NO_2}$.

(26) This is somewhat lower than an earlier estimate derived from data for $CH_2(O)_2$-NS.[3d] The present value is considered much more reliable.

(27) The collapse of $ArCH(O^-)C(NO_2)(CH_3)_2$ into ArCHO and $(CH_3)_2{=}NO_2^-$ also appears to have a rather small $\alpha^n_{C=O}$ value, which was attributed to a transition state with little C–C bond cleavage.[28]

(28) Guanti, G.; Petrillo, G.; Thea, S.; Cevasco, G.; Stirling, C. J. M. *Tetrahedron Lett.* **1980**, *21*, 4735.

of T_O^- into ArCHO and $CH_2NO_2^-$. This structure–reactivity coefficient is defined in a similar way as α_{CH} and α^n_{nuc} for proton transfer and nucleophilic addition, respectively, i.e., as a normalized substituent effect in the direction of carbanion formation. $\alpha^n_{C=O}$ is difficult to interpret in terms of a transition-state structure because no independent measure of bond formation (e.g., C–O → C=O) or bond cleavage (C- - -C) is available such as for β_B or β^n_{nuc} in the other reactions. Nevertheless, the following qualitative considerations should hold. Since the transition state of the k_4 step (**5**) is expected to suffer from the same lag in charge delocalization which is characteristic for the other nitronate ion forming processes, $\alpha^n_{C=O}$ is likely to *under*estimate the amount of C=O double bond formation or the degree of C–C bond cleavage, just as α_{CH} and α^n_{nuc} *over*estimate the degree of proton transfer and the degree of bond formation between the nucleophile and the olefin, respectively. This is because the lag in the delocalization keeps the negative charge closer to the aryl group than if delocalization had made normal progress, and hence the difference in charge between T_O^- and the transition state seen by the aryl group is diminished. Direct evidence for this phenomenon was reported for the k_4 step in the hydrolysis of benzylidene Meldrum's acid,[3a] where an $\alpha^n_{C=O}$ of ~0.33 was found while the secondary kinetic hydrogen isotope effect suggested >50% C–C bond cleavage at the transition state.[26]



$$\mathrm{Ar\overset{}{C}H\cdots\overset{\delta-}{C}H_2NO_2},\ \mathrm{C{\cdots}O^{\delta-}}$$

5

Complementary conclusions can be drawn based on a comparison of intrinsic rate constants between the k_4 step in the hydrolysis of β-nitrostyrenes and that of benzylidenemalononitrile. In this latter system, $k_4 \approx 5.9 \times 10^5\ s^{-1}$ and $K_4 \approx 4.3 \times 10^1$ M.[3e] Since $K_4 \approx 1.15 \times 10^1$ M for NS is quite similar to K_4 for benzylidenemalononitrile, the ratio $(k_4)_{CN}/(k_4)_{NO_2} \approx 3.71 \times 10^3$ should be a fairly good approximation of the ratio of the intrinsic rate constants. If k_4 for NS is adjusted to the K_4 value for benzylidenemalononitrile by using $\alpha^n_{C=O} = 0.48$, the $(k_4)_{CN}/(k_4)_{NO_2}$ ratio becomes $\sim 1.97 \times 10^3$, which we shall adopt as the best approximation of $(k_0)_{CN}/(k_0)_{NO_2}$ for the ratio of the intrinsic rate constants. We note that this ratio is roughly 5-fold larger than $(k_0)_{CN}/(k_0)_{NO_2} = 3.84 \times 10^2$ for OH^- addition to olefins, but it is still much lower than $(k_0)_{CN}/(k_0)_{NO_2} \approx 2 \times 10^6$ for proton transfer. In keeping with the notion that the ratios of the intrinsic rate constants are related to the degree of imbalance in the transition state, our results suggest that the lag in resonance development at the transition state of the k_4 step is somewhat greater than in the transition state of the k_1^{OH} step, but not nearly as large as in the proton transfer.

In a previous section we argued that the smaller imbalance in the nucleophilic addition to the C=C double bond compared to the proton transfer is, in part, due to sp^2-hybridization of the central carbon in the olefin, which allows for easier delocalization of the charge into the nitro group. If this were the whole explanation, one would expect that the imbalance for the k_4 process is not only larger than for the k_1^{OH} process but approximately as large as for the proton transfer. Since this is not the case, an additional factor must be invoked which enhances the imbalance in the proton transfer. A plausible candidate is hydrogen bonding between the base and the proton which is in flight. This hydrogen bond would be strongest in a situation where the negative charge is mostly localized on the carbon both in the transition state and the carbanion. Such hydrogen bonding is expected to have a stabilizing effect on the transition state, thereby increasing the intrinsic rate constant of the proton transfer. A well-documented example demonstrating this effect is the deprotonation of HCN.[29]

It is likely that the transition state for the deprotonation of malononitrile by normal bases also benefits from hydrogen bonding although probably to a lesser extent than in the HCN reaction since the more delocalized malononitrile anion implies also a less localized charge in the transition state. In the deprotonation of a nitroalkane, hydrogen bonding is further reduced and hence the effect on k_0 is small. This can explain why $(k_0)_{CN}/(k_0)_{NO_2}$ is larger for proton transfer than for the k_4 process.

Is hydrogen bonding also a plausible reason why the imbalance measured by $\alpha - \beta$ is so much larger for the proton transfer than for the other nitronate ion forming processes? A possible affirmative answer is in terms of a competition between resonance and hydrogen bonding as transition state stabilizing factors: localization of the charge on carbon reduces the resonance stabilization but enhances hydrogen bonding and hence the resulting transition-state structure is the one for which these two effects cancel. In other words, hydrogen bonding may well lead to a transition state in which the charge is more localized on carbon than would be the case without hydrogen bonding. It may be noted that our proposal has some resemblance to Bordwell's[4a] view that the deprotonation of nitroalkanes by a base, B, proceeds through an intermediate with a completely localized charge on the carbon and hydrogen bonding to BH. In view of Saunders[30] ^{14}C kinetic isotope effect experiments the notion of an intermediate has become unattractive, though.

Summary and Conclusions

The formation of T_{OH}^- by nucleophilic addition of OH^- to β-nitrostyrenes (k_1^{OH}), the deprotonation of T_{OH}^0 by OH^- to form T_{OH}^- (k_{-2}^{OH}), and the collapse of T_O^- into benzaldehyde and $CH_2NO_2^-$ (k_4) shown in Scheme II represent three different types of nitronate ion forming reactions. We have demonstrated in this paper that there are both similarities and differences in the structure–reactivity behavior of these processes. The reactions are similar in that they all have imbalanced transition states in which the delocalization of the negative charge into the nitro group lags behind bond changes. A direct manifestation of these imbalances is that in the proton transfer $\alpha_{C^-} > \beta_{B^-}$, in the nucleophilic addition $\alpha^n_{nuc} > \beta^n_{nuc}$. For the k_4 step no such direct evidence is available, but the imbalance manifests itself indirectly; it is seen in the fact that $(k_0)_{NO_2}$ is much smaller than $(k_0)_{CN}$.

What is different among the three types of reaction is the *quantitative* expression of the imbalances. Thus $(k_0)_{CN}/(k_0)_{NO_2}$ decreases in the order proton transfer ≫ collapse of T_O^- > nucleophilic addition to olefin, while $\alpha - \beta$ decreases similarly in the order proton transfer ≫ nucleophilic addition to olefin. These quantitative differences arise because on top of an inherent tendency for reactions leading to resonance-stabilized ions to have imbalanced transition states,[24] in the proton transfer there are two imbalance-enhancing factors (sp^3 carbon and hydrogen bonding) and in the collapse of T_O^- there is one such factor (sp^3 carbon).

Experimental Section

Materials. β-Nitrostyrene (NS) was available from Aldrich and recrystallized from ethanol, mp 57–58 °C. 4-Chloro-β-nitrosytrene (Cl-NS) and 3-nitro-β-nitrostyrene (NO_2-NS) were prepared by condensing nitromethane with the appropriate benzaldehyde according to the method of Worrall.[31] Nitromethane and benzaldehyde were obtained from Aldrich and purified by distillation. 4-Chlorobenzaldehyde (98% pure) and 3-nitrobenzaldehyde (99% pure) from Aldrich were used without further purification. 1-Phenyl-2-nitroethanol (T_{OH}^0 derived from NS) was prepared by the method of Bordwell and Garbisch.[32]

For the preparation of 1-(4-chlorophenyl)-2-nitroethanol and 1-(3-nitrophenyl)-2-nitroethanol, the following modification of Worrall's[31] procedure was used. Nitromethane (0.25 mol) and 0.25 mol of X-PhCHO were dissolved in methanol. A solution of 0.26 mol of NaOH in 25 mL of ice water was slowly added to the above mixture under stirring and with cooling in a NaCl–ice bath. After 15 min 165 mL of ice water was added, and the contents were poured into a mixture of 4 mol of acetic acid and 8 mol of NaOAc in the absence of solvent. The nitro alcohol formed immediately as a yellow oil, which was extracted with dichloromethane. After washing with water and drying, the solvent

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

[30] Wilson, J. C.; Källsson, I.; Saunders, W. J., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 4780.

[31] Worrall, D. E. In *Organic Syntheses*; Gilman, H., Blatt, A., Eds.; Wiley: New York, 1941; Collect. Vol. 1, p 413.

[32] Bordwell, F. G.; Garbisch, E. G., Jr. *J. Org. Chem.* **1962**, *27*, 2322.

was evaporated, yielding 16 g of crude $T^0_{OH}(NO_2\text{-NS})$ and 19.5 g of crude $T^0_{OH}(\text{Cl-NS})$. The crude products were purified by column chromatography with silica and hexane–ethyl acetate as eluent. The nitro alcohols derived from NS and Cl-NS were ≥98% pure on the basis of the proton NMR; the one derived from NO_2-NS was ≥96%. The latter has mp 65–69 °C; the others remained as pale oils.

Triethylamine and DABCO were obtained from Aldrich. The former was refluxed over CaH_2 and distilled under nitrogen while the latter was recrystallized from hexanes. The other buffers were analytical grade and were used without further purification.

Reactions Solutions and pH Measurements. The methodology was similar to the one used before.[3d,f] pH measurements were conducted in thermally equilibrated solutions (20 °C) by using an Orion 611 pH meter with a Corning No. 476022 glass electrode and a Beckman No. 39400 calomel reference electrode. The pH meter was calibrated with Hallē[18] buffers.

Kinetic Measurements. Fast reactions were monitored in a Durrum-Gibson stopped-flow apparatus, slow reactions were monitored in a Perkin-Elmer 559A spectrophotometer, and both were equipped for computerized data acquisition and analysis. In reactions where T^-_{OH} was used as starting material, T^-_{OH} was generated by placing the substrate into a 0.5 M KOH solution; this base concentration assured rapid, complete formation of T^-_{OH} before signficant conversion to products occurred. This solution was then diluted to 5×10^{-3} M KOH before it was used in pH-jump experiments.

Spectrophotometric and HPLC Product-Ratio Determinations. The ratio $[T^-_{OH}]/[CH_2NO_2^-] = [T^-_{OH}]/[ArCHO]$ (eq 18) was obtained after reacting T^0_{OH} in KOH solution by measuring the apparent extinction coefficient, ϵ_{app}, of the resulting solution at a wavelength where the extinction coefficient of T^-_{OH} ($\epsilon_{T_{OH}^-}$) and the sum of the extinction coefficients of ArCHO and $CH_2NO_2^-$ (ϵ_P) show a maximum difference (250 nm for NS, 265 nm for Cl-NS, and 268 nm for NO_2-NS). From eq 28 and 29, where x and y are the mole fractions of T^-_{OH} and products,

$$\epsilon_{app} = x\epsilon_{T^-_{OH}} + y\epsilon_P \tag{28}$$

$$x + y = 1 \tag{29}$$

respectively, $[T^-_{OH}]/[CH_2NO_2^-] = x/y$ is easily found. Since x/y was relatively small, at least for NS (0.181) and Cl-NS (0.224), and the fact that both T^-_{OH} and P absorb, the x/y ratios may be subject to relatively high experimental error. We therefore also used an HPLC method to determine these ratios, which circumvents the problem that both T^-_{OH} and P are absorbing. All experiments were done on a Hewlett-Packard 1090M chromatograph, using a Hypersil ODS 5-μm (100 × 45 mm) column and a 30% methanol–70% water mobile phase. Unfortunately, the gain in precision with the HPLC method was more than counteracted by the necessity to use higher substrate concentrations, which in basic solution leads to some condensation of $CH_2NO_2^-$ with the substrate despite precautionary measures. Nevertheless, the spectrophotometric and HPLC results were in fair agreement with each other.

In a similar way, the k_2^H/k_{-1}^H ratios were found as $[T^0_{OH}]/[S]$ after acidifying a solution of T^-_{OH}. Here the fact that only S had a significant extinction coefficient at λ_{max} of S facilitated the spectrophotometric measurements. The HPLC results were again in fair agreement with the spectrophotometric ones, but they are deemed less reliable than the latter.

Acknowledgment. This research was supported by Grant CHE-8617370 from the National Science Foundation.

Supplementary Material Available: Tables S1–S13 listing kinetic data (13 pages). Ordering information is given on any current masthead page.

Palladium-Catalyzed Trimethylenemethane Reaction To Form Methylenetetrahydrofurans. Aldehyde and Ketone Substrates and the Tin Effect[1]

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Received January 30, 1989

Abstract: The palladium-catalyzed trimethylenemethane (TMM) cycloaddition of carbonyl compounds has been shown to have a strong dependence upon the presence of cocatalysts such as tri-*n*-butyltin acetate, di-*n*-butyltin diacetate, or trimethyltin acetate. High-yielding annulations of aldehydes were accomplished either by using TMM precursors that contain the elements of trialkyltin acetate (which is then generated in situ) or by using silicon-based precursors and an exogenous cocatalyst. Synthetically, the latter was greatly preferable. Trimethyltin acetate was the best cocatalyst found, being effective at levels of 3–5 mol %. Under these conditions, aldehydes were cleanly converted to 2-substituted 4-methylenetetrahydrofurans in 88–99% yield. Stereogenic aldehydes have good diastereoselectivity. Polyoxygenated α-alkoxy aldehydes generated a single diastereomer in excellent yield. Although many ketones were unreactive (e.g., *tert*-butylcyclohexanone), the 5-oxacyclohexenones, 5-oxacyclohexanones, a 2-acylfuran, and an alkynyl ketone were also shown to be subject to carbonyl cycloaddition when sterically unencumbered. The starting materials for the first two types of substrates were prepared either in optically active form from commercially available glucose derivatives or as racemic mixtures by oxidation of 2-(hydroxymethyl)furans. Some generated a single diastereomer in good yields when a tin cocatalyst was present. In simple systems, the stereochemistry of the major isomer was shown by nuclear Overhauser effect difference spectroscopy to be that derived from axial attack on the carbonyl group. The enones were also subject to methylenecyclopentane formation by olefin cycloaddition. In every case these products are a single diastereomer. The mechanism of the cocatalysis by trialkyltin acetate is briefly discussed and a stannyl ether is suggested as the critical intermediate.

Five-membered oxygen heterocycles are among the most common structures in biologically active compounds. The stable form of many sugars, including many antineoplastic and antiviral agents including the AIDS drug azidothymidine (AZT),[3] is or contains a polyhydroxylated tetrahydrofuran. Nearly the entire class of compounds called ionophores,[4] because of their ion-chelating ability, include at least one tetrahydrofuran ring. Monensin,[5] for

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[1] Taken in part from: King ,S. A. Ph.D. Thesis, Stanford University, Stanford, CA, 1988.

[2] NSF Graduate Fellow, 1985–1988.

[3] Mitsuya, H. *Med. Immunol.* **1987**, *14*, 297.

[4] Westley, J. W. *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Marcel Dekker: New York, 1982; Vol. 1, 11.

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