Hydrolysis of Substituted α-Nitrostilbenes: Dissection of Rate Coefficients for Individual Steps in the Four-Step Mechanism. Estimates of Intrinsic Rate Constants and Transition-State Imbalances

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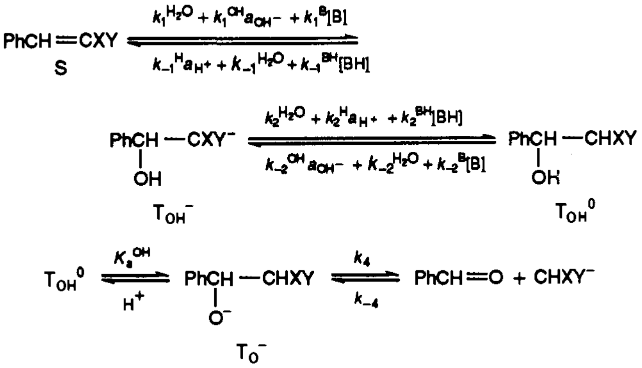
Abstract: A kinetic study of the hydrolysis of substituted α-nitrostilbenes (NS–Z with Z = 4-Me, H, 4-Br, 3-NO$_2$, and 4-NO$_2$) in 50% Me$_2$SO–50% water (v/v) at 20 °C is reported. The mechanism consists of four steps: nucleophilic addition to NS–Z of water ($k_1^{H_2O}$) and OH$^-$ (k_1^{OH}) to form PhCH(OH)C(Ar)NO$_2^-$ (T$_{OH}^-$); carbon protonation of T$_{OH}^-$ by water ($k_2^{H_2O}$), H$_3$O$^+$ (k_2^{H}), and buffer acids (k_2^{BH}) to form PhCH(OH)CH(Ar)NO$_2$ (T$_{OH}^0$); rapid oxygen deprotonation of T$_{OH}^0$ (K_a^{OH}) to form PhCH(O$^-$)CH(Ar)NO$_2$ (T$_O^-$); collapse of T$_O^-$ (k_4) into benzaldehyde and arylnitromethane anion. The aci-form of T$_{OH}^0$, PhCH(OH)CH(Ar)NO$_2$H (T$_{OH,aci}^0$), can also be generated as a transient by reaction of T$_{OH}^-$ with strong acid. A combination of kinetic experiments involving the reaction of the olefin with water and OH$^-$, the reaction of T$_{OH}^-$ with acid, and the reaction of independently synthesized T$_{OH}^0$ with base allowed the dissection of the rate coefficients of most of the individual steps. From the substituent dependence of these rate coefficients, it is concluded that water and OH$^-$ addition to NS–Z ($k_1^{H_2O}$ and k_1^{OH}) as well as the collapse of T$_O^-$ to benzaldehyde and ArCH=NO$_2^-$ (k_4) is characterized by substantial transition-state imbalances, reminiscent of the imbalance observed in the deprotonation of ArCH$_2$NO$_2$. It is also shown that the intrinsic rate constants for the k_1^{OH} and k_4 steps are low compared to those for the corresponding steps in the hydrolysis of other olefins of the type PhCH=CXY (XY = (H, NO$_2$), (CO)$_2$C$_6$H$_4$, (COO)$_2$C(CH$_3$)$_2$, and (CN)$_2$). This again parallels the behavior in the deprotonation of ArCH$_2$NO$_2$.

The hydrolysis of activated olefins involves the multistep mechanism shown in Scheme 1 for a generalized substrate PhCH=CXY where X and Y are electron-withdrawing substituents.[1] The detailed kinetic study of the various steps in Scheme 1 is a fairly arduous task but worthwhile because, in favorable cases, it can provide valuable structure–reactivity information on three processes that lead to the creation or destruction of related carbanions of the general structure RCXY$^-$.[1c] The first process is the formation of the carbanionic adduct T$_{OH}^-$ by nucleophilic addition to the olefin, the second is the protonation of T$_{OH}^-$, and the third is the generation of CHXY$^-$ in the product-forming step. Evidence has been presented which shows that the *intrinsic* rate constant, k_0,[2] for the three types of carbanion reactions depends on X and Y in a qualitatively similar way.[4] Most notably, k_0 decreases with the π-acceptor strength of X and Y.

Scheme 1



Broadly speaking there seems to be a consensus that this decrease is a consequence of the greater structural and solvational reorganization which characterizes reactions that lead to resonance-stabilized carbanions. This greater need for reorganization enhances the intrinsic barrier.[3,5–11] Our own view has been that it is not so much the need for reorganization *but the fact that this reorganization lags behind charge transfer or bond formation* ("transition-state imbalance") which leads to higher intrinsic barriers.[4,11] The transition-state imbalances manifest themselves by Brønsted α-values, obtained from varying the remote substituents in the substrate, that typically exceed Brønsted β-values measured by varying the pK_a of the base or nucleophile.[12–15]

Despite the mentioned qualitative similarities in the way k_0 is affected by X and Y for the various carbanion reactions, there

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(1) For reviews, see: (a) Patai, S.; Rappoport, Z. In *The Chemistry of Alkenes*; Patai, S., Ed.; Interscience: New York, 1964; p 496. (b) Fyfe, C. A. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Interscience: New York, 1971; p 51. (c) Bernasconi, C. F. *Tetrahedron* **1989**, *45*, 4017.

(2) For a reaction with forward and reverse rate constants k_1 and k_{-1}, the intrinsic rate constant is defined as $k_0 = k_1 = k_{-1}$ when $K_1 = 1$, the intrinsic barrier as $\Delta G_0^{\ddagger} = \Delta G_1^{\ddagger} = \Delta G_{-1}^{\ddagger}$ when $\Delta G° = 0$; in proton transfers, statistical factors are usually included.[3]

(3) Bell, R. P. *The Proton in Chemistry*; Cornell University: Ithaca, New York, 1973; Chapter 10.

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(12) Proton transfers ($\alpha_{CH} > \beta_B$):[13] (a) Bordwell, F. G.; Boyle, W. J. *J. Am. Chem. Soc.* **1972**, *94*, 3907. (b) Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *Ibid.* **1979**, *101*, 1295. (c) Bell, R. P.; Grainger, S. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1367. (d) Bowden, K.; Hirani, S. I. *J. Ibid.* **1990**, 885. (e) Gandler, J. R.; Bernasconi, C. F. *J. Am. Chem. Soc.* **1991**, *113*, 631. (f) Bernasconi, C. F.; Wiersema, D.; Stronach, M. W. *J. Org. Chem.* **1993**, *58*, 217.

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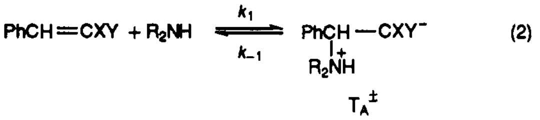
are significant *quantitative* differences. This is best documented for the comparison of proton transfers to amines (eq 1)with

$$CH_2XY + R_2NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CHXY^- + R_2NH_2^+ \qquad (1)$$



$$PhCH{=}CXY + R_2NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\underset{R_2NH}{|+}}{PhCH}{-}CXY^- \qquad (2)$$

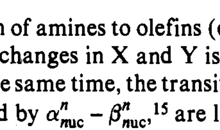
$$T_A^{\pm}$$

nucleophilic addition of amines to olefins (eq 2). The sensitivity of log k_0 for eq 2 to changes in X and Y is only about 45% that of log k_0 in eq 1; at the same time, the transition-state imbalances for eq 2, as measured by $\alpha^n_{nuc} - \beta^n_{nuc}$,[15] are less than half those of eq 1 as measured by $\alpha_{CH} - \beta_B$.[1c,4a,b,13]

Much less quantitative information is available regarding the formation of carbanions by expulsion from a tetrahedral intermediate such as that in the k_4 step in Scheme 1. In particular, data relating to transition-state imbalances and intrinsic rate constants are scarce. Part of the work to be discussed here addresses this problem. The major thrust of the present study is to evaluate or estimate intrinsic rate constants and transition-state imbalances for the three carbanion reactions of Scheme 1 with XY = (Ar, NO_2). On the basis of what is known about the deprotonation of arylnitromethanes,[12a,4] one would expect particularly large imbalances and particularly low intrinsic rate constants for all three reactions with this XY combination. This expectation is borne out by the results.

Results

General Features. The hydrolysis of the *E*-isomer of five α-nitrostilbenes, NS-Z(Z = 4-Me, H, 4-Br, 3-NO_2, and 4-NO_2),

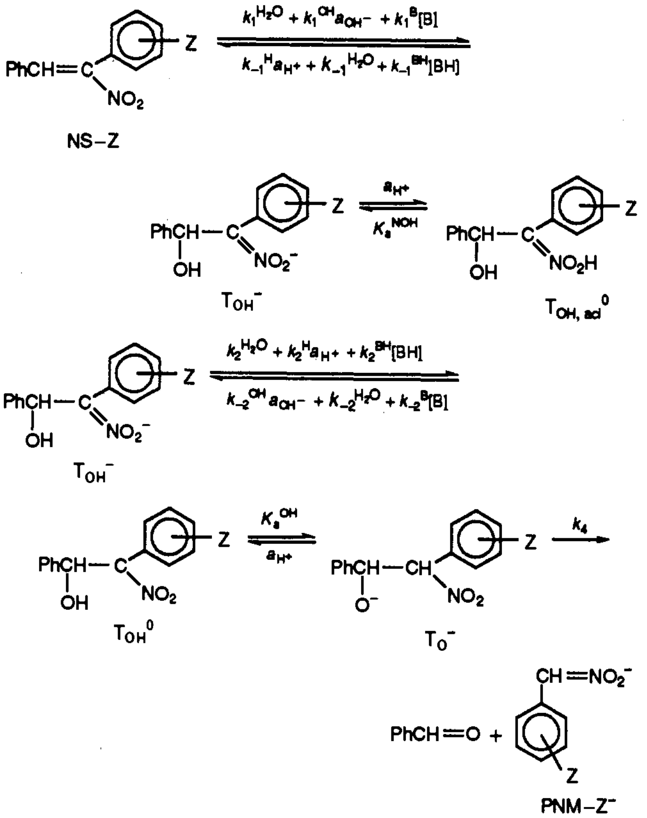


NS–Z

was examined in 50% Me_2SO–50% water (v/v) at 20 °C. All experiments were run under pseudo-first-order conditions[16] in KOH, HCl, or buffer solutions and at a constant ionic strength of 0.5 M maintained with KCl. The kinetic results are consistent with Scheme 2, which is quite similar to Scheme 1 except that it includes an additional acid–base equilibrium involving protonation of the nitro group of the adduct (T_{OH}^-) to generate the aci-form $T_{OH,aci}^0$; it also shows the k_4 step is irreversible because even at relatively high concentrations of benzaldehyde and arylnitromethane anion (0.005 M) the reaction was not measurably reversible.[17]

Four types of experiments were performed. (1) The substrate was reacted with KOH to generate T_{OH}^-, which then slowly decomposed to benzaldehyde and PNM–Z⁻. (2) T_{OH}^- in KOH solution is long-lived enough to allow it to be reacted with HCl or carboxylic acid solutions. These "pH-jump" experiments led to a mixture of regenerated substrate and some T_{OH}^0. (3) The substrate was reacted with carboxylate buffers; in these runs, none of the intermediates are detectable and the reaction leads to the formation of benzaldehyde and PNM–Z⁻. (4) T_{OH}^0 intermediates were synthesized separately and reacted with KOH and carboxylate and amine buffers. The reaction leads exclusively to benzaldehyde and PNM–Z⁻.

Scheme 2



These experiments which are now described in detail allowed the determination of the rate and equilibrium constants summarized in Table 1.

1. Reaction of NS–Z with KOH. Two kinetic processes were observed. The pseudo-first-order rate constant, k_{obsd}^{I}, of the faster process is linearly dependent on [KOH] as shown in Figure 1. It is associated with the formation of T_{OH}^- as confirmed by UV spectra that are quite similar to the spectra of the corresponding phenylnitromethane anions (PNM–Z⁻), but different from those of NS–Z; e.g., with Z = H, λ_{max} = 293 nm for T_{OH}^-, 300 nm for PNM–H⁻, and 325 nm for NS–H.[21] In the concentration range used, neither $k_1^{H_2O}$ nor $k_{-1}^{H_2O}$ contributes significantly to k_{obsd}^{I}, which is thus given by eq 3.

$$k_{obsd}^{I} = k_1 a_{OH^-} \qquad (3)$$

The slow process refers to the conversion of T_{OH}^- to benzaldehyde and PNM–Z⁻, as demonstrated by HPLC analysis. Its rate constant, k_{obsd}^{II}, is pH-independent between [KOH] = 0.002 and 0.20 M,[22] which, in principle, is consistent with either the $k_2^{H_2O}$ step or the k_4 step (T_{OH}^0 as steady-state intermediate) being rate limiting. Strong general acid catalysis by piperidinium ion (Figure 2) and a large kinetic solvent isotope effect, $k_{obsd}^{II}(H_2O)/k_{obsd}^{II}(D_2O)$ = 4.9 ± 0.5 for the NS-4-NO_2 derivative, indicate that carbon protonation of T_{OH}^- by water is rate limiting, i.e.

$$k_{obsd}^{II} = k_2^{H_2O} \qquad (4)$$

The $k_2^{H_2O}$ values are summarized in Table 1.

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(13) α_{CH} is the Brønsted coefficient obtained by varying the acidity of the CH acid, β_B the Brønsted coefficient obtained by varying the basicity of the base. When the substituent in the substrate is closer to the negative charge in the transition state, $\alpha_{CH} > \beta_B$; when the opposite is the case, $\alpha_{CH} < \beta_B$.[14]

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(15) Nucleophilic addition ($\alpha^n_{nuc} > \beta^n_{nuc}$), with $\alpha^n_{nuc} = d \log k_1/d \log K_1$ obtained by varying the olefin and $\beta^n_{nuc} = d \log k_1/d \log K_1$ obtained by varying the nucleophile. See ref 1c.

(16) With NS–Z as the minor component.

(17) In the hydrolysis of benzylidene-1,3-indandione,[18] benzylidenemalononitrile,[19] and β-nitrostyrene,[20] the k_4 step *is* measurably reversible.

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(21) All spectral information is summarized in ref 22.

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Table 1. Summary of Rate and Equilibrium Constants According to Scheme 2 for the Hydrolysis of Substituted α-Nitrostilbenes in 50% Me_2SO–50% Water at 20 °C[a]

parameter	4-Me	H	4-Br	3-Cl	3-CN	3-NO_2	4-NO_2
$k_1^{H_2O}$, s^{-1} [b]	3.46×10^{-7}	5.88×10^{-7}	1.26×10^{-6}			3.72×10^{-6}	4.20×10^{-6}
k_{-1}^{H}, $M^{-1} s^{-1}$ [c]	2.37×10^{3}	1.99×10^{3}	2.00×10^{3}			1.91×10^{3}	1.32×10^{3}
$K_1^{H_2O}$, M[d]	1.46×10^{-10}	2.95×10^{-10}	6.30×10^{-10}			1.95×10^{-9}	3.18×10^{-9}
k_1^{OH}, $M^{-1} s^{-1}$ [e]	0.161	0.219	0.568			2.00	2.36
$K_1^{OH} = K_1^{H_2O}/K_w$, M^{-1} [d,f]	1.16×10^{6}	2.34×10^{6}	5.00×10^{6}			1.55×10^{7}	2.52×10^{7}
$k_2^{H_2O}$, s^{-1} [g]	1.64×10^{-5}	2.05×10^{-5}	3.21×10^{-5}			4.53×10^{-5}	2.75×10^{-5}
k_2^{H}, $M^{-1} s^{-1}$ [h]	1.2×10^{2}	0.85×10^{2}	2.2×10^{2}			2.9×10^{2}	1.8×10^{2}
k_1^{PipH}, $M^{-1} s^{-1}$ [i]							9.20×10^{-3}
k_2^{AcOH}, $M^{-1} s^{-1}$ [j]	1.03	1.02	1.08			2.12	1.66
$k_2^{MeOAcOH}$, $M^{-1} s^{-1}$ [j]	2.77	2.53	3.62			6.31	4.86
k_2^{ClAcOH}, $M^{-1} s^{-1}$ [j]	5.12	4.56	7.62			16.8	13.0
$K_a^{OH}k_4$, $M^{-1} s^{-1}$ [k]		4.10×10^{-11}		3.46×10^{-10}	1.33×10^{-9}	2.61×10^{-9}	3.74×10^{-9}
pK_a^{NOH} [l]	5.08	4.85	4.72			4.41	4.27

[a] $\mu = 0.5$ M (KCl). [b] Estimated error ±4%. [c] Estimated error ±10%. [d] Estimated error ±14%. [e] Estimated error ±4%. [f] $pK_w = 15.9$. [g] Estimated error ±20%. [h] Estimated error ±20%. [i] Estimated error ±6%. [j] Estimated error ±20%. [k] Estimated error ±5%. [l] Estimated error ±0.08 units.

Table 2. Reaction of T_{OH}^- with 0.05 M HCl in 50% Me_2SO–50% Water at 20 °C[a,b]

Z	% NS–Z	% T_{OH}^0	[NS–Z]/[T_{OH}^0]
4-Me	95[c]	5.0[d]	19
H	95[c]	4.1[e]	23.2
4-Br	90[f]	10.0[d]	9.0
3-NO_2	86[c]	13.2[g]	6.5
4-NO_2	87[c]	12.2[h]	7.1

[a] Product distribution from HPLC analysis. [b] $\mu = 0.5$ M (KCl). [c] All *E*-isomer. [d] All threo isomer. [e] ~1.3% threo, ~2.8% erythro. [f] ~85% *E*-isomer, ~5% *Z*-isomer. [g] 5.5% threo, 7.7% erythro. [h] 5.3% threo, 6.9% erythro.

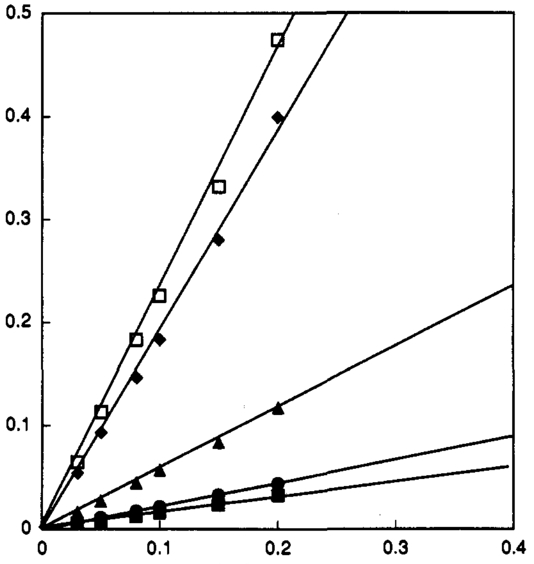


Figure 1. Pseudo-first-order rate constants for nucleophilic addition of OH^- to NS-Z: ■, 4-Me; ●, H; ▲, 4-Br; ◆, 3-NO_2; □, 4-NO_2.

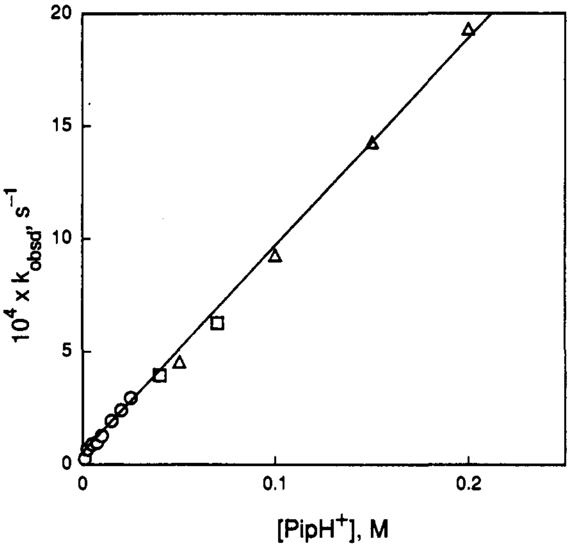


Figure 2. Pseudo-first-order rate constants for piperidinium ion catalyzed conversion of T_{OH}^- (Z = 4-NO_2) to benzaldehyde and PNM–Z$^-$: ○, pH 12.02; □, pH 11.52; △, pH 11.02. The slope of the line yields k_2^{PipH} for the carbon protonation of T_{OH}^- by the piperidinium ion.

Table 3. Reaction of T_{OH}^- with HCl in 50% Me_2SO–50% Water at 20 °C[a,b]

4-Me	H	4-Br	3-NO_2	4-NO_2
2.03 ± 0.04[c]	3.01 ± 0.08[c]	4.26 ± 0.08[c]	8.62 ± 0.09[d]	8.96 ± 0.17[c]

[a] k_{obsd} at pH 1.0–3.0. [b] $\mu = 0.5$ M (KCl), k_{obsd} in units of s^{-1}. [c] Average of 4 runs (pH 1.0, 1.3, 2.0, and 3.0). [d] Average of three runs (pH 1.0, 1.3, and 2.0).

2. Reaction of T_{OH}^- with Acid (pH-Jumps). The reaction of T_{OH}^- with HCl mainly regenerates NS-Z although small amounts of T_{OH}^0 are also formed. HPLC analysis of runs in 0.05 M HCl showed yields of ≥86% of NS–Z, mostly the *E*-isomer, which was also the starting material (Table 3); T_{OH}^0 was formed as a mixture of erythro and threo isomers in most cases.

Between pH 1.0 and 3.0, k_{obsd} is pH-independent (Table 3). This is consistent with hydronium ion catalyzed breakdown of T_{OH}^- to NS-Z ($k_{-1}^{H}a_{H^+}$), concurrent protonation of T_{OH}^- on carbon ($k_2^{H}a_{H^+}$), and the K_a^{NOH} equilibrium strongly favoring the $T_{OH,aci}^0$ side, i.e., k_{obsd} is given by eq 5 which for $K_a^{NOH} \ll a_{H^+}$ simplifies to eq 6.

$$k_{obsd} = \frac{K_a^{NOH}}{K_a^{NOH} + a_{H^+}}(k_{-1}^{H} + k_2^{H})a_{H^+} \quad (5)$$

$$k_{obsd} = K_a^{NOH}(k_{-1}^{H} + k_2^{H}) \quad (6)$$

The reaction is also subject to buffer catalysis in carboxylate buffers and by piperidinium ions. This catalysis is principally due to carbon protonation of T_{OH}^- (k_2^{BH}[BH]); as shown below, general acid catalysis of the breakdown of T_{OH}^- to reactants (k_{-1}^{BH}[BH]) makes a negligible contribution. Hence k_{obsd} can be approximated by eq 7. For a given carboxylate buffer and pH,

$$k_{obsd} = \frac{K_a^{NOH}}{K_a^{NOH} + a_{H^+}}(k_{-1}^{H}a_{H^+} + k_2^{H}a_{H^+} + k_2^{BH}[BH]) \quad (7)$$

k_{obsd} was determined at four or five buffer concentrations. The intercepts and slopes of the buffer plots are summarized in Table 4, while the raw data are reported elsewhere.[22] Since it was more important to obtain accurate intercepts than slopes (see below), the rates were determined at rather low [BH] (≤0.05 M), which meant that in some cases no reliable slope could be determined

Table 4. Reaction of T_{OH}^- with Carboxylic Acids in 50% Me_2SO–50% Water at 20 °C[a,b]

Z	pH	BH	10^2 intercept, s^{-1} [c]	slope, M^{-1} s^{-1} [d]
4-Me	3.71	$ClCH_2COOH$	1.60	≈0.21
	4.26	$MeOCH_2COOH$	1.54	
	4.56		1.33	0.60
	4.91		1.06	1.20
	6.08	AcOH	0.254	
	6.35		0.099	0.98
H	3.71	$ClCH_2COOH$	2.17	≈0.31
	4.26	$MeOCH_2COOH$	2.01	0.50
	4.56		1.64	0.88
	4.91		1.33	1.37
	6.08	AcOH	0.182	
	6.21		0.115	0.99
	6.35		0.099	0.98
4-Br	3.71	$ClCH_2COOH$	3.47	≈0.68
	4.26	$MeOCH_2COOH$	3.22	0.96
	4.56		2.55	1.44
	5.78	AcOH	0.34	0.99
3-NO_2	3.71	$ClCH_2COOH$	9.30	≈2.8
	4.26	$MeOCH_2COOH$	4.35	2.25
	4.56		3.47	4.21
	5.78	AcOH	0.35	2.03
4-NO_2	3.71	$ClCH_2COOH$	4.73	≈2.80
	4.26	$MeOCH_2COOH$	3.13	2.40
	4.56	AcOH	2.49	1.17
	4.78		1.70	1.19

[a] Slopes and intercepts of buffer plots. [b] $\mu = 0.5$ M (KCl). [c] Estimated uncertainty ±10–20%. [d] Estimated uncertainty ±15–25%.

(Table 4). The intercepts are equal to k_{obsd} in the absence of buffer (eq 5) while the slopes are given by eq 8.

$$\text{slope} = \frac{K_a^{NOH}}{K_a^{NOH} + a_{H^+}} k_2^{BH} \qquad (8)$$

From inversion plots according to eq 9, $k_{-1}^H + k_2^H$ and $K_a^{NOH}(k_{-1}^H + k_2^H)$ can be determined, which then yield K_a^{NOH}.

$$\frac{1}{\text{intercept}} = \frac{1}{K_a^{NOH}(k_{-1}^H + k_2^H)} + \frac{1}{a_{H^+}(k_{-1}^H + k_2^H)} \qquad (9)$$

An alternative method of determining K_a^{NOH} is to use $K_a^{NOH}(k_{-1}^H + k_2^H)$ from the HCl experiments (eq 6). The pK_a^{NOH} values calculated by the two methods are quite comparable, but the set reported in Table 1 was obtained from the HCl experiments because $K_a^{NOH}(k_{-1}^H + k_2^H)$ determined from these experiments is subject to a smaller experimental error.

From $k_{-1}^H + k_2^H$ and eq 10 (Table 2), the individual k_{-1}^H and k_2^H values can now be calculated while k_2^{BH} is obtained from eq 8.

$$\frac{k_{-1}^H}{k_2^H} = \frac{[\text{NS–Z}]}{[T_{OH}^0]} \qquad (10)$$

Figure 2 shows a plot of k_{obsd} vs piperidinium ion concentration from pH-jump experiments into piperidine buffers at pH 11.02–12.02. Under these conditions, eq 8 simplifies to slope = k_2^{BH}.

3. Reaction of NS–Z with Water in Carboxylate Buffers. These experiments, aimed at determining $k_1^{H_2O}$, were conducted in chloroacetate, methoxyacetate, and acetate buffers at pH 3.71–5.78. The rates were very slow, and k_{obsd} was determined by the initial rate method (see the Experimental Section). Depending on the pH and buffer concentration, water addition to NS-Z ($k_1^{H_2O}$) or carbon protonation of T_{OH}^- ($k_2^H a_{H^+} + k_2^{BH}[BH]$) may be rate limiting; assuming T_{OH}^- is a steady state, k_{obsd} is given by eq 11. Since $k_{-1}^H \gg k_2^H$, rate-limiting water addition can only be achieved at relatively high pH and high buffer acid concentration, resulting in $k_2^{BH}[BH] \gg (k_{-1}^H + k_2^H)a_{H^+}$.

These results for a representative case (Z = 4-H) are reported in Table 5. With Z = H, fully rate limiting water addition is only achieved at pH 5.78 at relatively high acetic acid concentrations, while at lower pH, proton transfer is partially rate limiting. Similar behavior was observed for Z = 4-Me and 4-Br.[22] With Z = 4-NO_2 and 3-NO_2, the $k_1^{H_2O}$ step is rate limiting under all conditions used.[22] Our results also show that buffer catalysis of water addition $k_{-1}^B[B]$ is negligible. By virtue of the principle of microscopic reversibility, the $k_{-1}^{BH}[BH]$ term must then be negligible compared to $k_{-1}^H a_{H^+}$, an assumption made in deriving eq 7.

Table 5. Reaction of NS–Z (Z = H and 4-NO_2) with Carboxylic Acid Buffers in 50% Me_2SO–50% Water at 20 °C[a]

Z	pH	BH	[BH], M	$10^6 k_{obsd}$,[b] s^{-1}
H	3.71	$ClCH_2COOH$	0.25	0.300
	4.56	$MeOCH_2COOH$	0.25	0.401
	5.48	AcOH	0.50	0.552
	5.78		0.05	0.546
			0.10	0.564
			0.15	0.575
			0.20	0.584
			0.25	0.588

[a] $\mu = 0.5$ M (KCl). [b] Estimated error in k_{obsd} is ±6%.

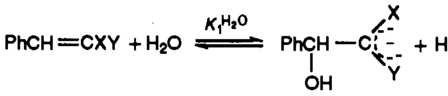
$$k_{obsd} = \frac{k_1^{H_2O}(k_2^H a_{H^+} + k_2^{BH}[BH])}{(k_{-1}^H + k_2^H)a_{H^+} + k_2^{BH}[BH]} \qquad (11)$$

4. Reaction of T_{OH}^0 with KOH and Amine Buffers. In strongly basic solution and in amine buffers, T_{OH}^0 is completely converted to products, as confirmed by HPLC analysis. Because of easier synthetic accessibility, Z = 4-Me and 4-Br were replaced by Z = 3-Cl and 3-CN in this study. The rates were inversely proportional to a_{H^+} and buffer independent; representative data are shown in Figure 3, while k_{obsd} values for the other substrates are reported elsewhere.[22] The results are consistent with eq 12.

$$k_{obsd} = \frac{K_a^{OH}}{a_{H^+}} k_4 \qquad (12)$$

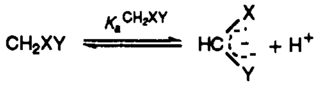
Discussion

Stability of T_{OH}^-. A major factor that determines the equilibrium constant for water (or OH^-) addition to an activated olefin (eq 13) is the capability of X and Y to stabilize the negative



$$\text{PhCH=CXY} + H_2O \overset{K_1^{H_2O}}{\rightleftharpoons} \text{PhCH(OH)–C}(X)(Y)^- + H^+ \qquad (13)$$

charge by inductive and resonance effects. Inasmuch as the acidity of the corresponding carbon acid (eq 14) depends on the same



$$CH_2XY \overset{K_a^{CH_2XY}}{\rightleftharpoons} HC(X)(Y)^- + H^+ \qquad (14)$$

factors, one expects a strong correlation between $K_1^{H_2O}$ and $K_a^{CH_2XY}$. Table 6 summarizes $pK_a^{CH_2XY}$ and $pK_1^{H_2O}$ values for five XY combinations, while Figure 4 shows a plot of $pK_1^{H_2O}$ vs $pK_a^{CH_2XY}$. The points for XY = (H, NO_2), $(CN)_2$, and $(COO)_2C(CH_2)_2$ show an excellent correlation with a slope of 0.76 ± 0.01; the points for benzylidene-1,3-indandione and α-nitrostilbene deviate positively by 1.2 and 1.7 log units, respectively. These deviations indicate that $K_1^{H_2O}$ is smaller than expected; the most likely reason for this deviation in $K_1^{H_2O}$ is that resonance stabilization of T_{OH}^- is diminished compared to that of $CHXY^-$, due to steric hindrance by the PhCH(OH) moiety of π-overlap.

Steric hindrance is also expected for T_{OH}^- derived from benzylidene Meldrum's acid. However, since resonance plays a

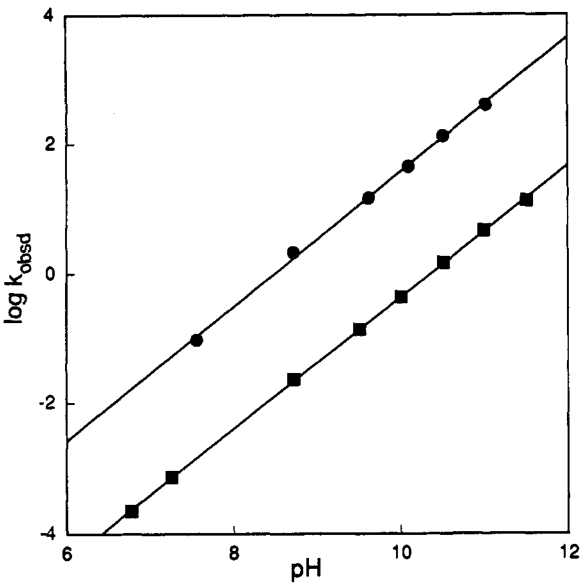


Figure 3. Pseudo-first-order rate constants as a function of pH (eq 12) for the conversion of T_{OH}^0 to benzaldehyde and PNM–Z⁻: ■, Z = H, ●, Z = 4-NO₂.

minor role in the stabilization of Meldrum's acid anions,[23] the steric effect has a minor impact on $K_1^{H_2O}$.

Rate of Formation of T_{OH}^-. Rate constants for OH⁻ and water additions (k_1^{OH} and $k_1^{H_2O}$) to five olefins of the type PhCH=CXY are summarized in Table 6. There is essentially no correlation between the rate and corresponding equilibrium constants, as is evident from Figure 5. This is because differences in *intrinsic* rate constants $(k_0)^2$ overshadow the expected correlation with the thermodynamics of the reaction. Using the dicyano derivative as a reference, a crude estimate of the *relative* intrinsic rate constants may be obtained by assuming that, if k_0 were independent of X and Y, the slope of the correlations of log $k_1^{H_2O}$ vs log $K_1^{H_2O}$ and log k_1^{OH} vs log K_1^{OH} would be 0.5.[24] The deviations from the lines of slope 0.5 through $(CN)_2$ thus give approximations for how much k_0 for nucleophilic addition to PhCH=CXY (log k_0^{XY}) is reduced compared to that for the reaction of PhCH=C(CN)₂ (log $k_0^{(CN)_2}$); these reduction are expressed as δ log k_0^{XY} = log k_0^{XY} – log $k_0^{(CN)_2}$ and reported in Table 7. Note that, if the slope of the lines were different from 0.5, δ log k_0^{XY} would change, especially for cases where log $K_1^{H_2O}$ and log K_1^{OH} for XY differ strongly from the corresponding parameters for $(CN)_2$. The error limits associated with the δ log k_0^{XY} values in Table 7 were calculated by assuming variations in the slope of the line between 0.3 and 0.7.

We first compare δ log k_0^{XY} for k_1^{OH} and $k_1^{H_2O}$. With XY = (H, NO₂) and (Ph, NO₂), they are roughly the same, but with XY = (COO)₂C(CH₃)₂ and (CO)₂C₆H₄, δ log k_0^{XY} for $k_1^{H_2O}$ is slightly positive while for k_1^{OH} it is substantially negative. This "anomaly" has been attributed to a transition-state stabilization by intramolecular hydrogen bonding involving one of the hydrogens of the attacking water molecule and one of the carbonyl oxygens of XY.[18]

For OH⁻ addition, the dependence of the intrinsic rate constants on XY may be compared with that for secondary alicyclic amine addition to the same substrates (k_1^A column in Table 7), eq 2, and also with that of the deprotonation of CH₂XY by secondary alicyclic amines, eq 1 (k_p column). The δ log k_0^{XY} values for k_1^A and k_p do not suffer from the same uncertainties as those for k_1^{OH} (and $k_1^{H_2O}$) because k_0^{XY} was obtained directly from Brønsted plots.[25]

Qualitatively, δ log k_0^{XY} shows the same dependence on XY for the three reaction types, i.e., the intrinsic rate constants decrease with increasing π-acceptor strength of X and Y. (Ph, NO₂) provides the strongest resonance stabilization for the respective carbanions, and δ log k_0^{Ph,NO_2} therefore shows the largest negative values in all reactions.

In *quantitative* terms, the δ log k_0^{XY} values are quite comparable for OH⁻ and amine addition, especially with β-nitrostyrene (H, NO₂) and α-nitrostilbene (Ph, NO₂), but only about half or less than half of those for the proton transfer. This smaller sensitivity of log k_0^{XY} to the resonance effect in the carbanion of T_{OH}^- and $T_A^{\pm}$ (eq 2) compared to that in CHXY⁻ has been attributed to a combination of several factors.[4a,b] One is that steric hindrance of coplanarity of XY with the carbanionic carbon in T_{OH}^- or $T_A^{\pm}$ reduces the resonance effect of XY.

A second factor is that there is a smaller lag in the resonance development. This is believed to be a consequence of the change from sp³ hybridization of the CXY carbon in CH₂XY to sp² hybridization in PhCH=CXY, which facilitates charge delocalization into X and/or Y at the transition state. Evidence for the smaller lag is that the imbalances in the nucleophilic addition of amines (α_{nuc}^n – β_{nuc}^n)[15] are much smaller than in the corresponding proton transfers (α_{CH} – β_B).[12] In the reaction of OH⁻ or water with PhCH=CXY, no β_{nuc}^n and hence no imbalance can be measured but α_{nuc}^n alone can give a qualitative assessment of the imbalance. α_{nuc}^n for the reaction of NS-Z with OH⁻ and water was determined as the slope of plots of log $k_1^{H_2O}$ and log k_1^{OH} vs log K_1^{OH} as function of Z (Figure 6). The α_{nuc}^n values are reported in Table 8, along with α_{nuc}^n for piperidine addition to NS–Z and α_{CH} for deprotonation of PNM–Z by OH⁻ and piperidine. The α_{nuc}^n values for water and OH⁻ addition are seen to be quite high, even higher than for amine addition. Unless C–O bond formation is ~80 to ~90% complete, which is unlikely in view of much evidence that β_{nuc}^n for nucleophilic addition to olefins is generally quite log (≤ 0.5),[1c] the high α_{nuc}^n values suggest a significant imbalance. On the other hand, α_{nuc}^n is not nearly as high as α_{CH} for the proton transfer, indicating that the imbalance for nucleophilic addition to α-nitrostilbene is smaller than that for deprotonation of phenylnitromethane.[29]

A third factor that has been suggested to contribute to the discrepancy between δ log k_0^{XY} for nucleophilic additions and δ log k_0^{XY} for proton transfers is hydrogen bonding in the transition state for proton transfer. Since the hydrogen bond should be stronger in a reaction where the negative charge is more localized on the carbon,[12f,30] the reaction where X and Y are weak π-acceptors will benefit the most from this hydrogen bonding stabilization and this will increase k_0.[31] As has been shown recently,[12f] with strong π-acceptors in X and Y, this effect becomes small or disappears altogether, i.e., k_0^{XY} is only subject to the depressing effect of the delayed resonance development. Hydrogen bonding thus leads to a wider spread in k_0^{XY} values between the carbon acids with strong π-acceptors and those with weak π-acceptors.

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(23) (a) Arnett, E. M.; Maroldo, S. G.; Schilling, S. L.; Harrelson, J. A. *J. Am. Chem. Soc.* **1984**, *106*, 6759. (b) Wang, X.; Houk, K. N. *Ibid.* **1988**, *110*, 1870. (c) Wiberg, K. B.; Laidig, K. E. *Ibid.* **1988**, *110*, 1872.

(24) This is equivalent to applying the simplest version of the Marcus equation, $\Delta G^{\ddagger} = \Delta G_0^{\ddagger} + 0.5\Delta G^{\circ} + (\Delta G^{\circ})^2/16\Delta G_0^{\ddagger}$, and neglecting the third term: Marcus, R. A. *J. Chem. Phys.* **1965**, *43*, 679.

(25) Plots of log k_1^A or log k_p vs p$K_a^{R_2NH_2^+}$.

(26) It should be noted that we are subscribing to the traditional interpretation of β_B and β_{nuc}^n as approximate measures of charge transfer or bond formation at the transition state.[8,27] This interpretation is not universally accepted.[28]

(27) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; p 156. (b) Jencks, W. P., *Chem. Rev.* **1985**, *85*, 511. (c) Jencks, W. P. *Bull. Soc. Chim. Fr.* **1988**, 218.

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

(29) The fact that α_{CH} for the deprotonation of ArCH₂NO₂ was obtained in water instead of 50% Me₂SO contributes to the large difference between α_{CH} and α_{nuc}^n because α_{CH} tends to become smaller upon addition of Me₂SO, e.g., α_{CH} = 0.92 in 100% Me₂SO with PhCOO⁻ as the base.[12b]

(30) Bednar, R. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1985**, *107*, 7117.

(31) Even though charge delocalization into strong π-acceptors is not well advanced at the transition state, this does not mean that delocalization is absent, i.e., there should be more charge on the carbon with weak π-acceptors than with strong π-acceptors. This point has been discussed in more detail in ref 12f.

Table 6. Equilibrium and Rate Constants for Water ($K_1^{H_2O}$, $k_1^{H_2O}$) and OH⁻ (K_1^{OH}, k_1^{OH}) Addition to PhCH═CXY, Rate Constants for Collapse to T_O^- (k_4), and pK_a Values of CH_2XY in 50% Me_2SO–50% Water at 20 °C

PhCH═CXY	p$K_a^{CH_2XY}$	p$K_1^{H_2O}$	log K_1^{OH}	$k_1^{H_2O}$, s⁻¹	k_1^{OH}, M⁻¹ s⁻¹	k_4, s⁻¹
PhCH═C(COO)$_2$C(CH$_3$)$_2$[a,b]	4.83	5.43	8.30	0.55	7.44×10^2	1.88×10^{10}
PhCH═C(CO)$_2$C$_6$H$_4$[c]	6.35	7.79	8.11	8.30×10^{-3}	1.01×10^2	3.22×10^6
PhCH═C(Ph)NO$_2$[d]	7.93	9.53	6.37	5.88×10^{-7}	0.22	1.03×10^4
PhCH═C(CN)$_2$[e]	10.21	9.50	6.40	1.05×10^{-3}	1.00×10^3	5.9×10^5
PhCH═CHNO$_2$[f]	11.32[g]	10.37	5.53	2.20×10^{-6}	1.31	1.59×10^2

[a] In water at 25 °C. [b] Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1980**, *102*, 1361; **1982**, *104*, 5143. [c] Reference 18. [d] This work. [e] Reference 19. [f] Reference 20. [g] Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J.-X. *J. Org. Chem.* **1988**, *53*, 3342.

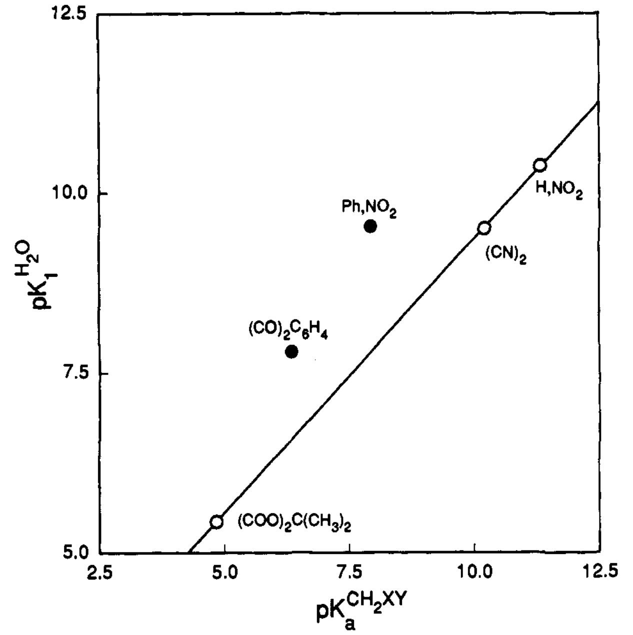
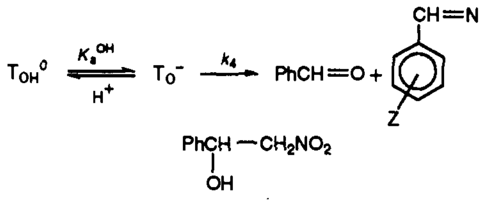


Figure 4. Correlation of p$K_1^{H_2O}$ for water addition to PhCH═CXY with the acidity of CH_2XY (p$K_a^{CH_2XY}$).

Collapse of T_O^- into Benzaldehyde and PNM–Z⁻. The $K_a^{OH}k_4$ values for reaction 15 allow us to estimate k_4 as follows. The



(15)

1

pK_a^{OH} for **1** is 14.80.[20] The acidifying effect of the extra phenyl group in T_{OH}^0 is estimated to lower the pK_a^{OH} to about 14.4, on the basis of the pK_a difference between CH_3CH_2OH and $PhCH_2CH_2OH$.[32] This yields $k_4 \approx 1.03 \times 10^4$ s⁻¹ for NS–H; k_4 values for the other systems are reported in Table 6, while Figure 7 shows a plot of log k_4 vs p$K_a^{CH_2XY}$.[33] As in the plot of log k_1^{OH} vs log K_1^{OH}, the correlation is very poor, which again is mainly a consequence of vastly different intrinsic rate constants of the k_4 process. Inasmuch as the k_4 process also leads to the formation of a carbanion, one expects a similar qualitative dependence of k_0 on X and Y as found for nucleophilic addition to PhCH═CXY and deprotonation of CH_2XY.

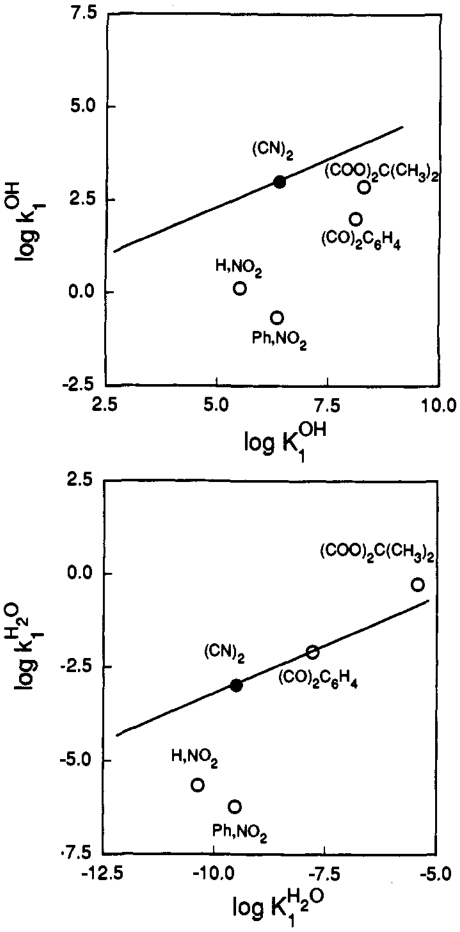


Figure 5. Correlation between rate constants for OH⁻ and H_2O addition to PhCH═CXY with the respective equilibrium constants. The lines through the points for (CN)$_2$ have a slope = 0.5, see text.

A *quantitative* assessment of this dependence, expressed in terms of δ log k_0^{XY} = log k_0^{XY} – log $k_0^{(CN)_2}$ as for the k_1^{OH} process, is more difficult in this case for two reasons. (1) There is not much information available that would allow one to obtain a reliable estimate of the slope of the correlation in the absence of changes in k_0^{XY}. (2) Steric effects which enhance k_4 are likely to play an important role in some cases, notably for XY = (COO)$_2$C(CH$_3$)$_2$, (CO)$_2$C$_6$H$_4$, and (Ph, NO$_2$). Nevertheless, it is clear from Figure 7 that, for the k_4 step, $|\delta$ log $k_0^{XY}|$ for XY = (Ph, NO$_2$) and (H, NO$_2$) must be quite large and probably of a magnitude similar to that for the k_1^{OH} process.

Further insights are obtained from the substituent dependence of $K_a^{OH}k_4$. The Hammett plot shown in Figure 8 affords $\rho(K_a^{OH}k_4) = 2.56 \pm 0.08$. On the basis of the substituent dependence of the pK_a of $T_A^\pm$ derived from piperidine and NS–Z,[34] a $\rho(K_a^{OH}) \approx 1.02$ may be estimated which leads to a $\rho(k_4) = \rho(K_a^{OH}k_4) - \rho(K_a^{OH}) \approx 1.54$. With $\rho(K_a^{PNH-Z}) = 1.43$ for the acidity constant of the substituted phenylnitromethanes in 50% Me_2SO–50% water,[35] this yields $\alpha_{elim} = \rho(k_4)/\rho(K_a^{PNH-Z}) \approx 1.08$; α_{elim} is equivalent to the slope of a plot of log k_4 vs log K_a^{PNH-Z}.[36] α_{elim} is an approximate measure of α^n_{elim} = d log k_4/d log K_4, the counterpart to α_{CH} in the deprotonation of CH_2XY and α^n_{nuc} in the nucleophilic addition to PhCH═CXY.

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(32) Takahashi, S.; Cohen, L. A.; Miller, H. K.; Peake, E. G. *J. Org. Chem.* **1971**, *36*, 1205.

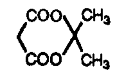
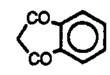
(33) A plot of log k_4 vs log K_4 would be more desirable, but K_4 was experimentally inaccessible in this system.[17]

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

(35) Bernasconi, C. F.; Kittredge, K. W. Unpublished results.

(36) The symbol α_{elim} is used in keeping with α_{CH} and α^n_{nuc}, which refer to changes in rates caused by changes in the substituents of the substrates. In different contexts, the symbol β_{lg} might be preferred ($\beta_{lg} = -\alpha_{elim}$).

Table 7. Relative Intrinsic Rate Constants, δ log k_0^{XY} = log k_0^{XY} − log $k_0^{(CN)_2}$, for the Deprotonation of CH_2XY by Secondary Alicyclic Amines (k_p) and the Nucleophilic Addition of OH^- (k_1^{OH}), Water ($k_1^{H_2O}$), and Secondary Alicyclic Amines (k_1^A) to PhCH=CXY in 50% Me_2SO–50% Water at 25 °C

X Y	k_p[a]	k_1^{OH}	$k_1^{H_2O}$	k_1^A
CN CN	0	0	0	0
	−3.10[b]	−1.08 ± 0.38[c]	0.69 ± 0.81[c]	−0.84[c]
	−3.87	−1.86 ± 0.34	0.05 ± 0.34	−0.74
NO_2 H	−6.27	−2.44 ± 0.17	−2.55 ± 0.17	−2.39
NO_2 Ph	−7.25	−3.66 ± 0.01	−3.25 ± 0.01	−3.52

[a] Reference 4b. [b] In 50% Me_2SO–50% water at 20 °C. [c] In water at 25 °C.

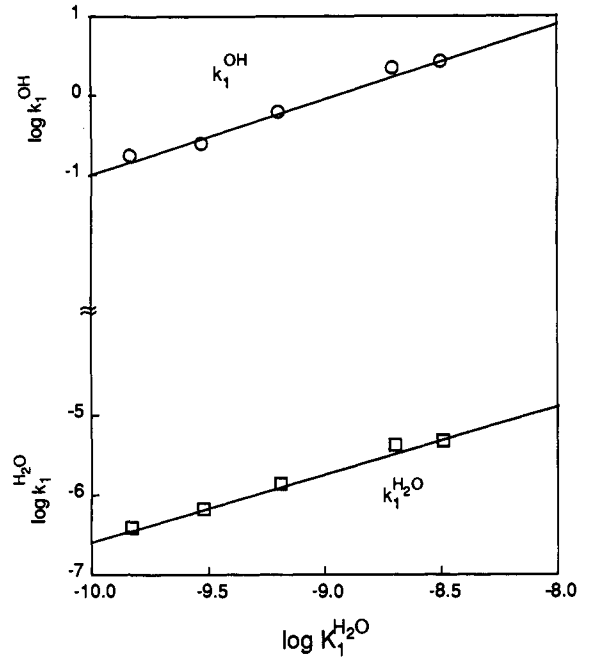
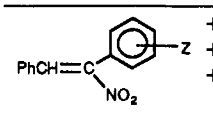
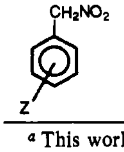


Figure 6. Brøsted-type plots for log $k_1^{H_2O}$ and log k_1^{OH} for water and OH^- addition, respectively, to NS–Z.

Table 8. Brønsted Coefficients for the Reactions of α-Nitrostilbenes with Water, OH^-, and Piperidine and of the Deprotonation of Phenylnitromethanes by OH^- and Piperidine

reaction		α	β	α − β
	$+H_2O$[b]	α^n_{nuc} = 0.86 ± 0.05[a]		
	$+OH^-$[b]	α^n_{nuc} = 0.95 ± 0.08[a]		
	$+R_2NH$[b]	α^n_{nuc} = 0.67[c]	0.37[c]	0.30[c]
	$+OH^-$[d]	α_{CH} = 1.54		
	$+R_2NH$[d]	α_{CH} = 1.29	0.55	0.74

[a] This work. [b] In 50% Me_2SO–50% water at 20 °C. [c] Reference 34. [d] In water at 25 °C, ref 12a.

Because of the various approximations ($\rho(K_a^{OH})$, $\alpha_{elim} \approx \alpha^n_{elim}$), it cannot be established that α^n_{elim} is definitely larger than unity but it is clearly close to 1.0 and thus probably somewhat larger than α^n_{nuc} for water, OH^-, and amine addition (Table 8).

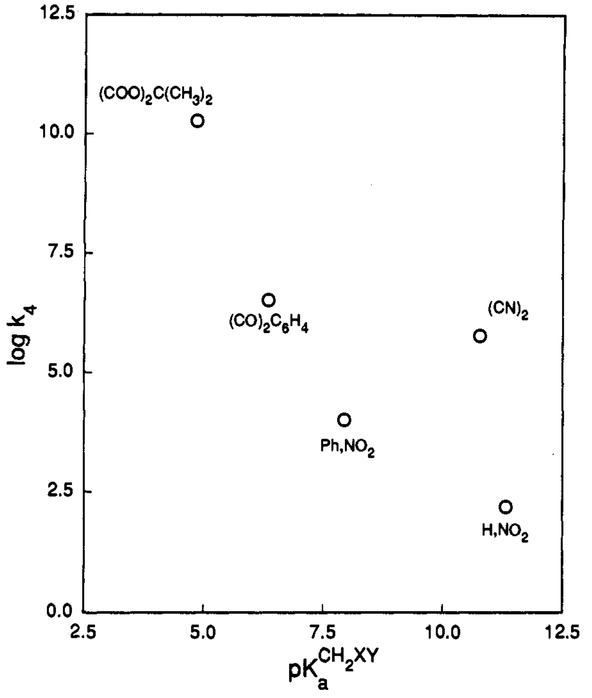


Figure 7. Correlation of log k_4 for collapse of T_O^- derived from PhCH=CXY with $pK_a^{CH_2XY}$.

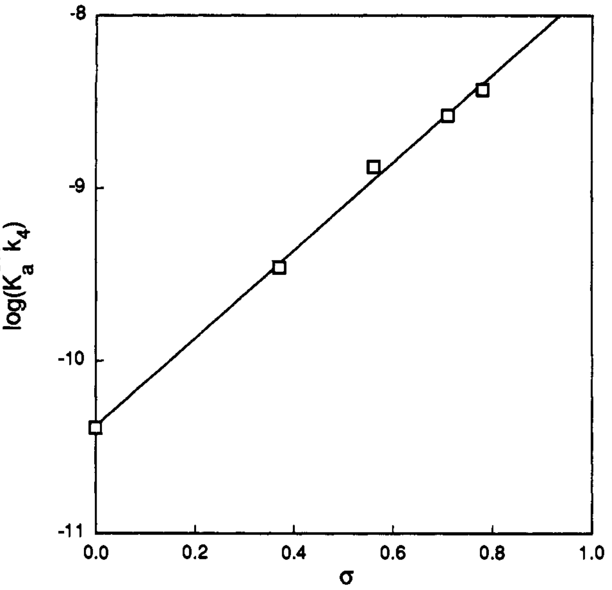


Figure 8. Hammett plot for $K_a^{OH}k_4$ (Z = H, 3-Cl, 3-CN, 3-NO_2, and 4-NO_2).

This suggests that the imbalance for the k_4 step is at least as large as, and possibly larger than, for the k_1^{OH} and k_1^A processes.

Protonation of T_{OH}^-. The rate constants for carbon protonation of T_{OH}^- by water ($k_2^{H_2O}$), hydronium ion (k_2^H), and chloroacetic, methoxyacetic, and acetic acid (k_2^{BH}) as well as pK_a^{NOH} values for $T_{OH,aci}^0$ are summarized in Table 1. A comparison of these parameters for T_{OH}^- (Z = H) with the corresponding values for the protonation of PhCH=NO_2^- reveals them to be quite similar (Table 9). This is consistent with the similarity of the two nitronate ions although the PhCH(OH) moiety in T_{OH}^- probably affects pK_a^{CH}, pK_a^{NOH}, and the protonation rates by a number factors that partially compensate each other. For example, there must be an acidifying inductive effect which, however, is counteracted by the steric hindrance of resonance in T_{OH}^-. With respect to pK_a^{NOH}, these effects appear to virtually completely offset each other although this is not necessarily true with respect to pK_a^{CH}. The rates of protonation should be enhanced by both

Table 9. Rate Constants for Carbon Protonation and pK_a^{NOH} Values for Nitro Group Protonation of T_{OH}^- (Z = H) and PhCH═NO_2^- in 50% Me_2SO–50% Water at 20 °C

	T_{OH}^- (Z = H)	PhCH═NO_2^- [a]
$k_2^{H_2O}$, s^{-1}	2.05×10^{-5}	1.8×10^{-5}
k_2^{H}, M^{-1} s^{-1}	0.85×10^{2}	2.09×10^{2}
$k_2^{ClCH_2COOH}$, M^{-1} s^{-1}	4.56	
$k_2^{MeOCH_2COOH}$, M^{-1} s^{-1}	2.53	7.98
k_2^{AcOH}, M^{-1} s^{-1}	1.02	
k_2^{PipH}, M^{-1} s^{-1}	9.20×10^{-3} [b]	2.85×10^{-2}
pK_a^{NOH}	4.85	4.75

[a] Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J.-X. *J. Org. Chem.* **1988**, *53*, 3342. [b] Z = 4-NO_2.

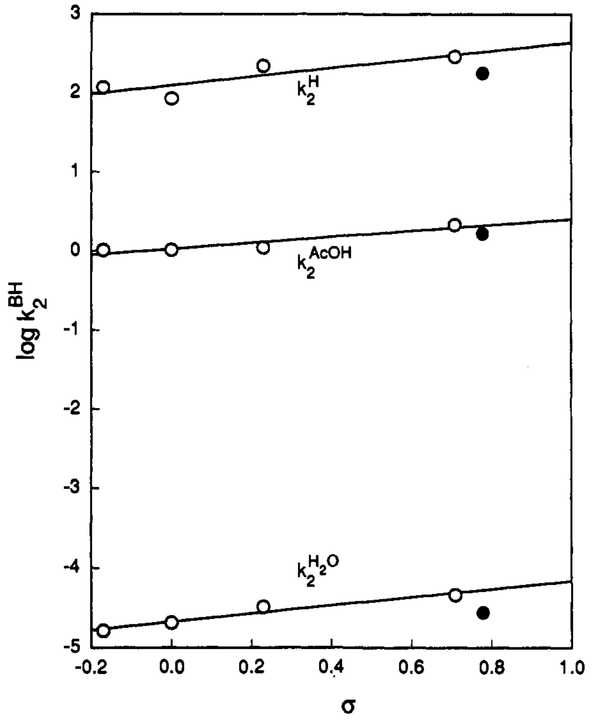


Figure 9. Hammett plots for the rate constants of carbon protonation of T_{OH}^- (Z = H, 4-Me, 4-Br, 3-NO_2, and 4-NO_2) by water, acetic acid, and H_3O^+.

the inductive effect[37] and the reduced resonance, but steric hindrance by the PhCH(OH) moiety to the approach of the proton donor will reduce the rates.

The effect of the Z substituent on the various protonation rate constants is also revealing. Figure 9 shows Hammett plots for $k_2^{H_2O}$, k_2^{H}, and k_2^{AcOH}; plots for $k_2^{MeOAcOH}$ and k_2^{ClAcOH} (not shown) are quite similar. Because of the rather large experimental uncertainty in the rate constants, the plots suffer from considerable scatter. Nevertheless, it is clear that the dependence on Z is quite small and in the direction of a slight increase in the rates with increasing electron-withdrawing strength of Z, implying negative Brønsted β_C values. This result is reminiscent of Bordwell's findings with substituted phenylnitromethanes where protonation of ArCH═NO_2^- by water yielded $\beta_C = -0.54$.[12a] Figure 9 also shows a negative deviation for the 4-nitro derivative (filled circle), again in analogy to the protonation of PNM-4-NO_2^-.[38,39] This negative deviation reflects a decrease in the intrinsic rate constant caused by the resonance effect of the 4-nitro group.

Conclusions. Deprotonation of CH_2XY, nucleophilic addition to PhCH═CXY, and collapse of PhCH(O^-)CHXY into PhCH═O + $CHXY^-$ represent three different carbanion-forming reactions. Their intrinsic rate constants display a qualitatively similar dependence on the π-acceptor strength of X and Y, i.e., k_0 decreases with increasing resonance stabilization of the respective carbanion. With XY = (Ph, NO_2), the resonance stabilization is the greatest of those of all systems studied to date and this is reflected in the largest $|\delta \log k_0|$ values for all three carbanion-forming processes studied in this work. The lowering of k_0 is attributed to the lag in the resonance development behind charge transfer or bond formation at the transition state. Again, with XY = (Ph, NO_2), the high α_{CH}, α_{nuc}^n, and α_{elim} values indicate that the imbalances are the largest among the systems investigated thus far.

Experimental Section

Materials. *N*-methylmorpholine, morpholine, piperidine, and methylamine were refluxed over calcium hydride and stored at 4 °C in the dark. Chloroacetic acid was recrystallized from petroleum ether. Reagent grade methoxyacetic acid, acetic acid, KCl, and dimethyl sulfoxide were used without further purification. Concentrated KOH and HCl solutions ("Dilut it", Baker) were diluted appropriately with deionized water. The substituted α-nitrostilbenes (NS–Z) were available from a previous study.[34]

Synthesis of the T_{OH}^0 Intermediates. General. The method by Bordwell and Garbish[40] was used. It entails the preparation of the *threo-β*-nitroacetate from the corresponding *trans*-stilbene by reaction with acetyl nitrate followed by acid-catalyzed ester exchange in methanol to form the *threo-β*-nitro alcohol. More details can be found in ref 22. The assignment of the β-nitroacetate and alcohol as the threo isomer was based on the melting points of the parent and 4-nitro derivatives which matched those of the known threo isomers;[40,41] it was presumed that the threo isomer is the predominant species for the other T_{OH}^0 intermediates as well. *trans*-Stilbene (Z = H) was available from Aldrich; the substituted *trans*-stilbenes were prepared from the corresponding benzaldehydes and benzyltriphenylphosphonium chloride in a Wittig reaction.[42] Benzyltriphenylphosphonium chloride was prepared from triphenylphosphine and benzyl chloride.[42]

1,2-Diphenyl-2-nitro-1-ethanol (T_{OH}^0, Z = H). The nitroacetate of *trans*-stilbene was obtained in 60% yield, mp 135–136 °C (lit.[40] 134–135 °C). Conversion to the alcohol gave T_{OH}^0 with mp 98–100 °C (lit.[40] 100–101 °C).

1-Phenyl-2-(3-chlorophenyl)-2-nitro-1-ethanol (T_{OH}^0, Z = 3-Cl). *trans*-3-Chlorostilbene was prepared by dissolving 25 g (0.178 mole) of 3-chlorobenzaldehyde in 400 mL of ethanol containing 5.48 g (0.233 mole) of dissolved sodium metal. After addition of 73 g (0.178 mole) of benzyltriphenylphosphonium chloride in 440 mL of ethanol, white crystals formed immediately. The crystals were collected by vacuum filtration and washed with water. Recrystallization from 100% ethanol yielded 10.1 g of *trans*-3-chlorostilbene, mp 73–73.5 °C (lit.[43] 71–72 °C).

A 3.52-g (0.0163 mol) sample of *trans*-3-chlorostilbene was dissolved in a solution of 4.5 g (0.0174 mol) of nitric acid, 45 mL of acetic anhydride, and 2 drops of sulfuric acid. After adding 30 mL of water, the mixture was allowed to sit overnight. 3-Chloronitroacetate (1.03 g) was recovered from recrystallization with 95% ethanol, mp 104–104.5 °C. ^1H NMR (60 MHz, $CDCl_3$): δ 2.01 (3H, s, $CH_3C{=}O$), 5.5–5.7 (1H, dd, *J* = 12 Hz, C*H* threo of CHOAc), 6.25–6.45 (1H, dd, *J* = 12 Hz, C*H* threo of $CHNO_2$), 7.0–7.1 (9H, Ar*H*, 3-ClAr*H*).

A 0.325-g (0.001 mole) sample of the 3-chloronitroacetate was dissolved in 5 mL of methanol at 50 °C. A 1-mL portion of a 70% sulfuric acid–methanol solution was added to the warm solution, stirred at room temperature for 2 h, and poured over 50 mL of ice water. Purification of the pale yellow oil from benzene–hexanes and ethanol–hexanes followed by drying under vacuum (12 mm) with $CaCl_2$ for 2 days yielded 0.25 g of T_{OH}^0 (Z = 3-Cl) as pale yellow oil. ^1H NMR (60 MHz, $(CD_3)_2SO$): δ 5.15–5.23, 5.32–5.40 (1H, dd, *J* = 4.8 Hz, C*H* threo of CHOH), 5.75–5.92 (1H, dd, *J* = 10.2 Hz, C*H* threo of $CHNO_2$), 6.0–6.08 (1H, dd, *J* = 4.8 Hz, O-*H*, exchangeable with D_2O), 6.9–7.3 (9H, m, Ar*H*, 3-ClAr*H*). Analysis by HPLC showed a single peak with a retention time of 4.40 min using a reverse-phase ODS Hypersil, 4.6- × 10.0-mm column, 52%

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(37) Nitronate ions display the unusual characteristic that remote electron-withdrawing substituents enhance the rate of protonation even though the basicity decreases.[12a] There is more on this below.

(38) Data from ref 12a as discussed in ref 4b.

(39) A larger negative deviation was observed in pure Me_2SO.[12b]

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acetonitrile, 48% water (pH = 2.5, buffered by phosphoric acid), 1 mL/min, 40 °C, monitoring at $\lambda = 230$ nm.

1-Phenyl-2-(3-cyanophenyl)-2-nitro-1-ethanol (T_{OH}^0, Z = 3-CN). *trans*-3-Cyanostilbene was prepared by dissolving 10 g (0.076 mol) of 3-cyanobenzaldehyde in 100 mL of ethanol containing 2.34 g (0.099 mol) of sodium metal. After addition of 31.2 g (0.076 mol) of benzyltriphenylphosphonium chloride dissolved in 190 mL of ethanol and 100 mL of water, the cloudy solution was allowed to sit for 24 h. A silver precipitate was collected by vacuum filtration which, after recrystallization from ethanol–water, yielded 2.58 g of product, mp 61 °C (lit.[43] 61 °C).

A 2.65-g (0.014 mol) sample of *trans*-3-cyanostilbene was dissolved in a solution of 1.5 mL of nitric acid, 25 mL of acetic anhydride, and 2 drops of sulfuric acid. Water (150 mL) was added, and the mixture was allowed to sit overnight, producing a yellow oil product. Purification of the product from 95% ethanol along with extraction of the product with methylene chloride and drying over calcium chloride resulted in 0.5 g of the β-nitroacetate of 3-cyanostilbene in the form of a yellow oil. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.01 (3H, s, $CH_3C{=}O$), 5.65–5.70 (1H, dd, $J = 9$ Hz, C*H* threo of C*H*OAc), 6.25–6.40 (1H, dd, $J = 9$ Hz, C*H* threo of C*H*NO_2), 6.9–7.3 (9 H, m, Ar*H*, 3-CNAr*H*).

A 0.5-g (.0016 mole) sample of the β-nitroacetate of 3-cyanostilbene was dissolved in 6 mL of methanol at 45 °C. A 1.5-mL 70% sulfuric acid–methanol solution was added. The solution was stirred at room temperature for 5 h and poured into 50 mL of ice water. A yellow oil formed. Extraction of the oil with methylene chloride and drying over calcium chloride gave 0.3 g of a nearly pure sample of T_{OH}^0 (3-CN) (yellow oil). ^{1}H NMR (360 NHz, $(CD_3)_2SO$): δ 5.470–5.504 (1H, dd, $J = 10.2$ Hz, C*H* threo of CHOH), 5.974–6.007 (1H, dd, $J = 10.2$ Hz, C*H* threo of $CHNO_2$), 7.059–7.893 (9H, m, Ar*H*, 3-CNAr*H*).

This sample was purified by preparative HPLC (Beckman, model 334) using a reverse-phase ODS Hypersil 10- × 250-mm column, 40% acetonitrile, 60% water (pH = 2.5, buffered by phosphoric acid), 1 mL/min, 40 °C, monitoring at $\lambda = 230$ nm. After purification, analysis by HPLC showed a pure compound with a retention time of 3.99 min using a reverse-phase ODS Hypersil, 4.6- × 100-mm column under the same conditions.

1-Phenyl-2-(3-nitrophenyl)-2-nitro-1-ethanol (T_{OH}^0, Z = 3-NO_2). *trans*-3-Nitrostilbene was synthesized by the same procedure as *trans*-3-chlorostilbene, mp 109–110 °C (lit.[43] 112 °C). The 3-nitronitroacetate was obtained as described for the 3-cyanonitroacetate, mp 91–92 °C (pale yellow crystals). ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.06 (3H, s, $CH_3C{=}O$), 5.70–5.85 (1H, dd, $J = 9$ Hz, C*H* from threo CHOAc), 6.35–6.50 (1H, dd, $J = 9$ Hz, C*H* from threo $CHNO_2$), 6.90–8.05 (9H, Ar*H*, 3-NO_2-Ar*H*).

A 0.667-g (.002 mol) sample of the 3-nitro-β-nitroacetate in 9 mL of methanol was heated to 70 °C. A 2.5-mL 60% sulfuric acid–methanol solution was added. The solution was stirred for 4 h, poured into 50 mL of ice water, and stirred for 5 min. A pale yellow oil formed. Crystallization of the oil from benzene–hexanes yielded 0.083 g of T_{OH}^0 (Z = 3-NO_2) (white crystals), mp 85–87 °C. ^{1}H NMR (300 MHz, $(CD_3)_2SO$): δ 5.554–5.568, 5.587–5.601 (1H, ddd, $J = 4.2$ Hz, C*H* from threo CHOH), 6.269–6.297 (1H, dd, $J = 9.9$ Hz, CH from threo $CHNO_2$), 6.447–6.461 (1H, dd, $J = 4.2$ Hz, O*H*, exchangeable with D_2O), 7.157–8.386 (9H, m, Ar*H*, 3-NO_2Ar*H*). Analysis by HPLC showed a pure compound with a retention time of 5.134 min using a reverse-phase ODS Hypersil, 4.6- × 100-mm column, 40% acetonitrile, 60% water (pH 2.5, buffered by phosphoric acid), 1 mL/min, 40 °C, monitoring at $\lambda = 230$ nm.

1-Phenyl-2-(4-nitrophenyl)-2-nitro-1-ethanol (T_{OH}^0, Z = 4-NO_2). *trans*-4-Nitrostilbene was prepared by the same method as *trans*-3-nitrostilbene, mp 152.5–154 °C (lit.[44] 155 °C). The 4-nitronitroacetate was obtained as described for the 3-cyanonitroacetate, mp 154–155 °C (lit.[41] 156–157 °C).

A 0.272-g (0.0008 mol) sample of the 4-nitro-β-nitroacetate was refluxed in 13.6 mL of methanol. A 0.76-g sample of sulfuric acid was added to the hot solution. The solution was stirred for 8 h at room temperature and then poured over 50 mL of ice water. The cloudy solution was placed in an ice bath for 1 h. A pale yellow oil formed. Extraction of the oil with methylene chloride followed by purification of the oil from benzene–hexanes gave 0.100 g of the desired T_{OH}^0 (Z = 4-NO_2) in the form of a pale yellow oil. ^{1}H NMR (300 MHz, $(CD_3)_2SO$): δ 5.537–5.552, 5.571–5.585 (1H, ddd, $J = 4.5$ Hz, C*H* threo of CHOH), 6.247–6.214 (1H, dd, $J = 9.9$ Hz, C*H* threo of $CHNO_2$), 6.450–6.465 (1H, dd, $J = 4.5$ Hz, O*H*, exchangeable with D_2O), 7.121–7.350 (5H, Ar*H*), 7.804–7.883, 8.099–8.128 (4H, dd, 4-NO_2Ar*H*). Analysis by HPLC showed a pure compound with a retention time of 6.546 min using a reverse-phase ODS Hypersil, 4.6- × 100-mm column, 40% acetonitrile, 60% water (pH = 2.5, buffered by phosphoric acid), 1 mL/min, 40 °C, monitoring at $\lambda = 230$ nm.

Reaction Solutions. Solutions in 50% Me_2SO–50% water (v/v) were prepared by adding appropriate amounts of aqueous stock solutions to a volumetric flask containing 50% Me_2SO, and then diluting to the correct volume with water. All pH measurements were performed on an Orion Research 611 digital pH meter with a Corning No. 476022 glass electrode and a Beckman No. 39400 calomel reference electrode. The pH meter was calibrated for Me_2SO–water solutions with standard buffer solutions described by Hallé et al.[45]

Rate Measurements. The reactions were monitored spectrophotometrically in a Perkin-Elmer 559A UV-vis spectrophotometer and a Durrum Gibson stopped-flow spectrophotometer with computerized data acquisition and analysis. For reactions followed in the Perkin-Elmer spectrophotometer, microliter amounts of a stock substrate solution in Me_2SO or acetonitrile were added to a cuvette containing buffer solution (2–3 mL) preequilibrated at 20 °C. For the stopped-flow experiments, a dilute solution of the substrate (10^{-4}–10^{-5} M) in 50% Me_2SO–50% H_2O was mixed with a buffer solution in a 1:1 ratio. For pH-jump experiments, a solution of the T_{OH}^- adduct was generated *in situ* by diluting a stock solution of α-NS–Z into 0.01 M KOH solution. This solution was mixed with various concentrations of acidic buffers. pH-jump experiments were generally performed within 2 h after forming the T_{OH}^- adduct. Stock solutions of T_{OH}^0 in acetonitrile were diluted to concentrations ca. 10^{-4}–10^{-5} M in solutions containing HCl (0.01 M) in 50% Me_2SO–50% water before mixing with buffers in the stopped-flow. For reactions which could be followed to completely ($k_{obsd} > 10^{-4}$ s^{-1}), rates were measured by observing linear plots of log(OD – OD_∞) vs time for at least three half-lives (with $\Delta OD \geq 0.1$). For $k_{obsd} < 10^{-5}$ s^{-1}, the initial rate method was used for calculating rate constants.

Product Analysis. Reaction products were analyzed by HPLC using reverse-phase ODS Hypersil, 4.6- × 100-mm column, and a Hewlett-Packard 1090 Model instrument with a diode-array detector. The components of the product mixture were identified by comparison of retention times and spectra with a known compound under identical conditions. Hence, chromatograms were obtained for product mixtures and compared to those obtained for substituted α-nitrostilbenes, phenylnitromethanes, T_{OH}^0 adducts, and substituted benzaldehydes. Both the isolated components and the product mixtures were observed in an acetonitrile–water solvent system maintaining the aqueous solution at pH = 2.5 with phosphoric acid (0.025 M H_3PO_4/0.025 M $H_2PO_4^-$) with a flow rate of 1 mL/min, a temperature of 40 °C, and a wavelength of 230 nm. (Hydrolysis and deprotonation of the components were minimized by keeping the column acidic.) The reaction products were quenched with HCl if the pH of the solution was basic, converting PNM–Z$^-$ and the T_{OH}^- into T_{OH}^0.

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