(Me-4, s), 1.16 (Me-6, d, J = 6.6 Hz), 1.76 (Me-14, s), 2.18 (2 H, m), 2.32 (H-6, m), 2.55 (H-5, d, J = 9.5 Hz), 2.56 (H-8, dd, J = 17.5, 9.5), 2.76 (H-8, dd, J = 17.5 3 Hz), 3.14 (H-15, d, J = 12 Hz), 3.20 (OMe-10, s), 3.37 (NMe, s), 3.46 (H-15, d, J = 12 Hz), 3.62 (1 H, m), 3.88 (1 H, m), 3.98 (Ar OMe, s), 4.19 (H-10, d, J = 8 Hz), 5.42 (H-11, dd, J = 15, 8 Hz), 5.98 (H-13, d, J = 11 Hz), 5.60 (H-12, dd, J = 15, 11, 1 Hz), 6.81 (Ar, H, d, J = 2 Hz), 6.83 (Ar H, d, J = 2 Hz); IR ($CHCl_3$) ν 3400, 1724, 1644, 1576, 1095 cm^{-1}; mass spectrum m/z 521 (M^+), 503, 488, found 521.1105, calcd ($C_{27}H_{36}O_7N_1Cl_1$) 521.2178.

To a solution of the keto diol (−)-**29** [21.6 mg in CH_2Cl_2 (0.5 mL)] was added 0.5 M pyridine (0.3 mL) in CH_2Cl_2 with stirring at 0 °C. The stirring was continued for 15 min, and the reaction mixture was cooled down to −78 °C and mixed with excess ammoniacal MeOH (0.7 mL). After removal of the cooling bath, the resultant yellow solution was stirred for 20 min and then diluted with CH_2Cl_2. The organic layer was separated, washed with 5% $NaHCO_3$, water, and brine, dried over anhydrous Na_2SO_4, and then concentrated in vacuo affording the crude maytansinol **1**, which was purified by silica gel TLC with 5% MeOH–CH_2Cl_2 to give (−)-**1**, [13.6 mg in 58.1% yield, mp 190–192 °C, $[\alpha]_D$ −195° ($CHCl_3$, c 0.272)]. The racemic material (ca. 6.7 mg of ±**29**) was also converted into (±)-**1** in 67% yield (4.7 mg of white powder). ^1H NMR (400 MHz) δ 0.84 (Me-4, s), 1.29 (Me-6, d, J = 6.5 Hz), 1.54 (H-6, m), 1.69 (Me-14, s), ~1.25 (H-8, overlap), 2.15 (H-8, d, J = 14 Hz, s), 2.10 Hz (H-2, dd, J = 13.5, 2.0 Hz), 2.28 (H-2, dd, J = 13.5, 11.0 Hz), 2.57 (H-5, d, J = 9.5 Hz), 3.11 (H-15, d, J = 12.5 Hz), 3.47 (H-15, d, J = 12.5 Hz), 3.20 (OMe-10, s), 3.35 (NMe, s), 3.49 (H-10, d, J = 9.0 Hz), 3.54 (H-3, dd, J = 11.0, 2.0 Hz), 3.98 (Ar OMe, s), 4.34 (H-7, t, J = 11.0 Hz), 5.51 (H-11, dd, J = 15.0, 9.0 Hz), 6.14 (H-13, d, J = 11.0 Hz), 6.35 (NH, s), 6.43 (H-12, dd, J = 15.0, 11.0 Hz), 6.80 (Ar H, d, J = 2 Hz), 6.98 (Ar H, d, J = 2) (This signal appeared at δ 7.04 in a concentration of **1** being 15 mg/0.5 mL ($CDCl_3$), δ 6.98 (2.1 mg/0.5 mL), 6.94 (1 mg/0.5 mL), 6.91 (0.25 mg/0.5 mL), while the other aromatic H appeared at δ 6.80 in these concentrations.); IR ($CHCl_3$) ν 3420, 2920, 2850, 1703, 1650, 1575, 1455, 1341, 1095, 1080 cm^{-1}; mass spectra m/z 503 (M^+ − 61), 485 ,468, 450; found 503.2095, calcd ($C_{27}H_{34}O_6N_1Cl_1$) 503.2073 [M^+ − (H_2O + HNCO)].

Acknowledgment. Support of this work by Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Science and Culture, by Naito Science Foundation, by Yamada Science Foundation, and by Aichi Cancer Research Foundation are gratefully acknowledged. The authors are also indebted to Professors T. Masamune and H. Seto for the high-field ^1H NMR measurements. We thank Takeda Chem. Ind. for authentic maytansinol for comparison.

Supplementary Material Available: ^1H NMR and IR spectra of **1**, **17a**, **17b**, **28a**, **28b**, and **29** (14 pages). Ordering information is given on any current masthead page.

Nucleophilic Addition to Olefins. 10.[1] Kinetics of Cleavage of the Piperidine and Morpholine Adducts of α-Cyano-4-nitrostilbene and α-Cyano-2,4-dinitrostilbene

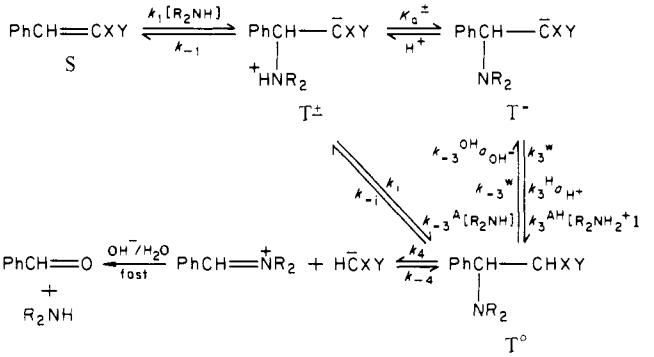
Claude F. Bernasconi* and Christopher J. Murray

Contribution from the Thimann Laboratories of the University of California, Santa Cruz, California 95064. *Received September 26, 1983. Revised Manuscript Received January 5, 1984*

Abstract: Rates of cleavage of the anionic piperidine and morpholine adducts (T^-) of α-cyano-4-nitrostilbene (**1-NO_2**) and α-cyano-2,4-dinitrostilbene (**1-$(NO_2)_2$**) into $PhCH{=}{}^+NR_2$ and 2-X-4-nitrophenylacetonitrile anion were determined. For the adducts of **1-$(NO_2)_2$** there is a change from rate-limiting carbon protonation (to form T^0) at low amine concentrations to rate-limiting cleavage of T^0 into products at high concentrations. For the adducts of **1-NO_2** cleavage is rate limiting throughout. Compared to the protonation of the anion of (2,4-dinitrophenyl)acetonitrile (**2-$(NO_2)_2^-$**), protonation of T^- derived from **1-$(NO_2)_2$** is slightly enhanced when the acid is water, strongly reduced when the acid is morpholinium or piperidinium ion ($R_2NH_2^+$), and strongly enhanced with H_3O^+. The slightly enhanced rate of the water reaction is attributed to an enhanced pK_a^0 of the adduct, the strongly depressed rate for the $R_2NH_2^+$ reactions to a steric effect. The enhanced rate with H_3O^+ is ascribed either to an intramolecular pathway via the nitrogen-protonated adduct ($T^\pm$) or to a stabilization, by the adjacent amine moiety, of the transition state for protonation by H_3O^+. Problems with either interpretation exist, though, and are discussed. Even after taking into account the different leaving group basicities, the cleavage of T^0 derived from **1-NO_2** is much slower than that of the previously studied T^0 derived from benzylidenemalononitrile, indicating a higher intrinsic barrier for the departure of the more delocalized (4-nitrophenyl)acetonitrile anion compared to $^-CH(CN)_2$. This is consistent with similar patterns observed with other carbanion-forming reactions such as deprotonations of C–H acids and nucleophilic additions to olefins. If one allows for a steric enhancement of the cleavage of T^0 derived from **1-$(NO_2)_2$**, it appears that the intrinsic barrier for departure of **2-$(NO_2)_2^-$** is also higher than that for the somewhat less delocalized (4-nitrophenyl)acetonitrile anion.

The cleavage of activated olefins in the presence of an amine proceeds by a complex, multistep mechanism. This mechanism is shown in Scheme I for a benzylidene-type substrate PhCH= CXY where X and/or Y are electron-withdrawing groups. The reaction $T^\pm \rightleftharpoons T^-$ is shown as a rapid equilibrium even though in some cases the k_{-1} step is of comparable magnitude to the rate of deprotonation of $T^\pm$.[1-4] $k_i - k_{-i}$ refer to an intramolecular proton switch which might occur in competition with the $T^\pm \rightleftharpoons T^- \rightleftharpoons T^0$ pathway.[5]

Scheme I



Detailed kinetic studies have recently been reported for the $Ph_2C{=}C(NO_2)_2$/morpholine,[2] $PhCH{=}C(COO)_2C(CH_3)_2$/

(1) Part 9: Bernasconi, C. F.; Zitomer, J. L.; Fox, J. P.; Howard, K. A. *J. Org. Chem.* **1984**, *49*, 482.
(2) Bernasconi, C. F.; Carrê, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 2698.
(3) Bernasconi, C. F.; Fox, J. P.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 2810.
(4) Bernasconi, C. F.; Murray, C. J.; Fox, J. P.; Carrê, D. J. *J. Am. Chem. Soc.* **1983**, *105*, 4349.
(5) Bernascni, C. F.; Hibdon, S. A.; McMurry, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3459.

0002-7863/84/1506-3257$01.50/0

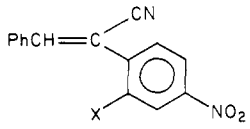
Table I. Rate and Equilibrium Constants for Nucleophilic Addition (Steps S ⇌ $T^{\pm}$ ⇌ T^- in Scheme I) in 50% Me_2SO–50% Water at 20 °C[a]

	morpholine (pK_a^{AH} = 8.72)	piperidine (pK_a^{AH} = 11.02)
	1-$(NO_2)_2$	
k_1, M^{-1} s^{-1}	6.36	61.4
k_{-1}, s^{-1}	6.66×10^4	4.74×10^3
K_1, M^{-1}	0.95×10^{-4}	1.29×10^{-2}
$pK_a^{\pm}$	5.83	8.13
$K_1K_a^{\pm}$	1.40×10^{-10}	0.96×10^{-10}
	1-NO_2	
k_1, M^{-1} s^{-1}	1.48[b]	26.0
k_{-1}, s^{-1}	≈6.36×10^5[b]	≈7.87×10^4
K_1, M^{-1}	≈2.33×10^{-6}[b]	≈3.57×10^{-4}
$pK_a^{\pm}$	≈6.37	≈8.67
$K_1K_a^{\pm}$	9.93×10^{-13}[b]	7.63×10^{-13}

[a] Reference 4. [b] See ref 9.

morpholine,[6] and PhCH=C$(CN)_2$/piperidine[3] systems. The mechanistic scheme is the same in each case (Scheme I), but experimental observations vary considerably from one system to another, because differences in the relative rates of the various steps lead to different rate-limiting steps.

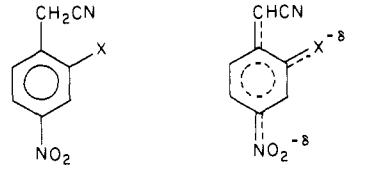
In this paper we report our results for the reactions of piperidine and morpholine with α-cyano-4-nitrostilbene (**1-NO_2**) and α-cyano-2,4-dinitrostilbene (**1-$(NO_2)_2$**). These reactions are



1-NO_2 (X = H)
1-$(NO_2)_2$ (X = NO_2)

characterized by two well-separated kinetic processes.[7] The first (rapid) process is on the stopped-flow time scale and refers to the first two steps of Scheme I (S ⇌ $T^{\pm}$ ⇌ T^-). A detailed kinetic analysis of these two steps has already been reported.[4] It allowed a determination of k_1, k_{-1}, $K_1 = k_1/k_{-1}$, and $pK_a^{\pm}$.[8] The values of these rate and equilibrium constants which will be referred to frequently in this paper are summarized in Table I.[9]

The second (slow) process is the subject of this paper. It refers to the formation of benzaldehyde and (4-nitrophenyl)acetonitrile (**2-NO_2**) or (2,4-dinitrophenyl)acetonitrile **2-$(NO_2)_2$**, respectively.



2-NO_2 (X = H) 2-NO_2^- (X = H)
2-$(NO_2)_2$ (X = NO_2) 2-$(NO_2)_2^-$ (X = NO_2)

Depending on the pH these latter products may of course be present in their anionic forms (**2-NO_2^-** and **2-$(NO_2)_2^-$**). Since this second process is much slower than the first it is safe to treat the first two steps of Scheme I as rapid preequilibria. This will simplify the kinetic analysis which is dealt with in the Results section.

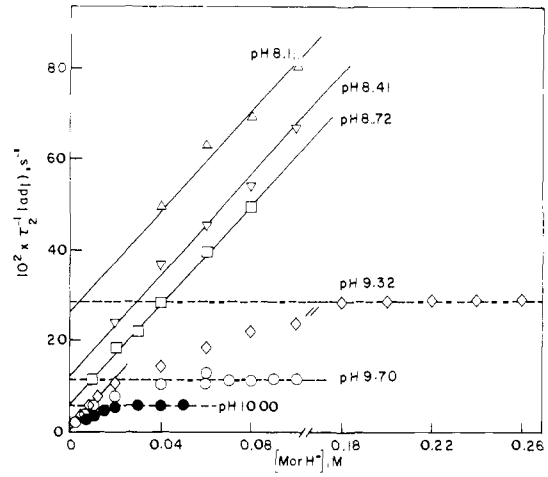


Figure 1. τ_2^{-1}(adj) for the morpholine adduct of α-cyano-2,4-dinitrostilbene (**2-$(NO_2)_2$**).

In the Discussion section we will address the following questions: (1) Is carbon protonation of T^- by H_3O^+ faster than in analogous systems (**2-NO_2^-**, **2-$(NO_2)_2^-$**) without the adjacent $PhCHNR_2$ group? (2) Since the evidence shows that there is such an acceleration, does that necessarily imply an intramolecular proton switch (k_i in Scheme I) or are there alternative interpretations? (3) Does the breakdown of T^0 into $PhCH{=}^+NR_2$ and **2-NO_2^-** (**2-$(NO_2)_2^-$**) follow the same structure–reactivity patterns as observed in the deprotonation of **2-NO_2** and **2-$(NO_2)_2$**,[11] and in the amine addition to **1-NO_2** and **1-$(NO_2)_2$**?[7] Specifically, is the intrinsic barrier for the departure of the more strongly delocalized **2-$(NO_2)_2^-$** higher than that for **2-NO_2^-**?

Results

General Features. It was established by UV/vis spectroscopy that the reaction products are benzaldehyde and **2-NO_2^-** or **2-$(NO_2)_2^-$**, respectively. All kinetic determinations were made in 50% Me_2SO–50% water (v/v) at 20 °C, and at an ionic strength of 0.5 M maintained with KCl. Pseudo-first-order conditions with the amine in large excess were used throughout. The rates were measured spectrophotometrically, usually by monitoring the loss of substrate or, in some cases, by monitoring the formation of benzaldehyde, or the loss of the adduct T^-.[12]

Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine. The reaction was monitored at 480 or 420 nm. The latter wavelength was preferred at high pH because T^-, which is present at significant concentrations in strongly basic solution, also has a strong absorption at 480 nm.[12]

The reciprocal relaxation time, τ_2^{-1}, was measured as a function of amine concentration at eight different pH values between pH 8.11 and 10.05. The data are summarized in Table II. They show a greater than first order dependence on amine concentration at low pH which reflects the fact that one amine molecule is used to form T^- (rapid preequilibrium) while a second molecule acts as a proton-transfer catalyst in the k_3^{AH} step (Scheme I).

An expression for τ_2^{-1} can be derived by treating the first two steps in Scheme I as rapid preequilibria (see introduction), by applying the steady-state approximation to T^0, and by assuming that the hydrolysis of $PhCH{=}^+NR_2$ is much faster than its reversion to T^0 (k_{-4}). This latter assumption is certainly valid for the initial phases of the reaction ([H^-CXY] ≈ 0) and appears to hold thoughout the reaction. If it did not, it would lead to curvature in the log ΔOD vs. time plots under conditions where the

(6) Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329.
(7) Not counting the competing direct hydrolysis of the olefin.
(8) For the morpholine reactions proton transfer is (partially) rate limiting and thus rate constants for proton transfer could also be determined.[4]
(9) As pointed out in our previous report,[4] the kinetic and equilibrium parameters for the reaction of **1-NO_2** with morpholine have a larger uncertainty than for the other reactions, mainly because k_1 and $k_{-1}/K_a^{\pm}$ were difficult to evaluate. The numbers given in Table I for this reaction reflect slight adjustment in these parameters which give a $K_1K_a^{\pm}$ value that is in better agreement with the results in the present paper and also with the frequent finding that $K_1K_a^{\pm}$ for the morpholine reaction is somewhat larger than for the corresponding piperidine reaction.[3,4,10] These slight changes in k_1, k_{-1}, and K_1 do not alter any of the conclusions drawn in the previous report.
(10) Bernasconi, C. F.; Carrè, D. J.; Fox, J. P. In "Techniques and Applications of Fast Reactions in Solution"; Gettins, W. J., Wyn-Jones, E., Eds.; Reidel: Dordrecht, Holland, 1979; p 453.
(11) Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 4343.
(12) Spectra are shown in ref 4.

Table II. Kinetic Data for the Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine in 50% Me_2SO–50% Water (v/v), at 20 °C, μ = 0.5 M

pH	$[R_2NH]$, M	$[R_2NH_2^+]$, M	$10^3\tau_2^{-1}$, s^{-1}	$(1 + K_1K_a^{\pm}[R_2NH]/a_{H^+})/(K_1K_a^{\pm}[R_2NH]/a_{H^+})$	$10^2\tau_2^{-1}$(adj),[a] s^{-1}
8.11	0.010	0.040	0.089	5540	49.3
	0.012	0.061	0.142	4440	63.0
	0.020	0.080	0.249	2770	69.0
	0.025	0.100	0.360	2210	79.9
8.41	0.010	0.020	0.086	2780	23.9
	0.020	0.040	0.265	1390	36.8
	0.030	0.060	0.492	927	45.6
	0.040	0.080	0.779	695	54.2
	0.050	0.100	1.19	557	66.5
8.72	0.010	0.010	0.083	1360	11.3
	0.020	0.020	0.272	681	18.5
	0.030	0.030	0.479	455	21.8
	0.040	0.040	0.825	341	28.1
	0.060	0.060	1.74	228	39.6
	0.080	0.080	2.89	171	49.4
9.32	0.016	0.004	0.161	215	3.46
	0.032	0.008	0.498	108	5.38
	0.048	0.012	1.01	72.3	7.30
	0.080	0.020	2.30	43.8	10.1
	0.160	0.040	6.06	22.4	13.6
	0.240	0.060	11.6	15.3	17.8
	0.320	0.080	18.8	11.7	22.0
	0.400	0.100	24.4	9.56	23.3
	0.72	0.18	49.6	5.76	28.6
	0.80	0.20	53.8	5.27	28.4
	0.88	0.22	58.7	4.89	28.7
	0.96	0.24	63.8	4.56	28.8
	1.04	0.26	66.9	4.29	28.7
9.67	0.0297	0.003	0.452	52.5	2.37
	0.045	0.005	1.11	35.0	3.88
	0.090	0.010	3.06	18.0	5.50
	0.180	0.020	8.08	9.49	7.67
	0.360	0.040	19.7	5.25	10.3
	0.540	0.060	33.9	3.83	13.0
9.72	0.60	0.06	32.1	3.27	10.5
	0.70	0.07	37.9	2.95	11.2
	0.80	0.08	41.4	2.70	11.2
	0.90	0.09	44.8	2.52	11.3
	1.00	0.10	49.0	2.36	11.6
10.05	0.095	0.005	3.14	7.70	2.42
	0.143	0.007	4.92	5.45	2.68
	0.190	0.010	7.69	4.35	3.35
	0.238	0.012	9.98	3.68	3.67
	0.285	0.015	12.8	3.23	4.14
10.00	0.380	0.020	19.5	2.88	5.62
	0.570	0.030	24.3	2.25	5.48
	0.760	0.040	28.9	1.94	5.61
	0.950	0.050	34.1	1.75	5.97

[a] Based on $K_1K_a^{\pm} = 1.40 \times 10^{-10}$, ref 4.

k_4 step is rate limiting (see below). Such curvature was not observed. With these assumptions τ_2^{-1} is given by eq 1 in which

$$\tau_2^{-1} = \frac{K_1K_a^{\pm}[R_2NH]/a_{H^+}}{1 + (K_1 + K_1K_a^{\pm}/a_{H^+})[R_2NH]} \times \frac{\{k_3^{w} + k_3^{AH}[R_2NH_2^+] + (k_3^{H} + k_i/K_a^{\pm})a_{H^+}\}k_4}{k_{-3}^{OH}a_{OH^-} + k_{-3}^{A}[R_2NH] + k_{-3}^{w} + k_{-i} + k_4} \quad (1)$$

$K_1 = k_1/k_{-1}$. By rearranging eq 1 we can define an "adjusted" τ_2^{-1} as

$$\tau_2^{-1}(\text{adj}) = \tau_2^{-1}\frac{1 + K_1K_a^{\pm}[R_2NH]/a_{H^+}}{K_1K_a^{\pm}[R_2NH]/a_{H^+}} = \frac{\{k_3^{w} + k_3^{AH}[R_2NH_2^+] + (k_3^{H} + k_i/K_a^{\pm})a_{H^+}\}k_4}{k_{-3}^{OH}a_{OH^-} + k_{-3}^{A}[R_2NH] + k_{-3}^{w} + k_{-i} + k_4} \quad (2)$$

Table II lists τ_2^{-1}(adj) values which were calculated by using $K_1K_a^{\pm} = 1.40 \times 10^{-10}$ (Table I), and Figure 1 shows plots of τ_2^{-1}(adj) vs. $[R_2NH_2^+]$ at various pH values. At pH 8.11, 8.41, and 8.72 τ_2^{-1}(adj) is seen to depend linearly on $[R_2NH_2^+]$, with slopes that are pH independent. The linearity indicates that $k_{-3}^{A}[R_2NH] \ll k_{-3}^{OH}a_{OH^-} + k_{-3}^{w} + k_{-i} + k_4$ while the pH independence of the slopes shows that $k_{-3}^{OH}a_{OH^-} \ll k_{-3}^{w} + k_{-i} + k_4$. Thus, eq 2 simplifies to

$$\tau_2^{-1}(\text{adj}) = \frac{\{k_3^{w} + k_3^{AH}[R_2NH_2^+] + (k_3^{H} + k_i/K_a^{\pm})a_{H^+}\}k_4}{k_{-3}^{w} + k_{-i} + k_4} \quad (3)$$

Inspection of Figure 1 further reveals that at the highest $[R_2NH_2^+]$ used the k_3^{AH} pathway dominates, i.e., $k_3^{AH}[R_2NH_2^+] \gg k_3^{w} + (k_3^{H} + k_i/K_a^{\pm})a_{H^+}$. This implies, by virtue of the principle of microscopic reversibility, that the k_{-3}^{A} pathway is also

Table III. Experimental Rate Constants for **1-$(NO_2)_2$**

R_2NH	k_3^{AH}, M^{-1} s^{-1}	k_3^W, s^{-1}	$k_3^H + k_i/K_a^{\pm}$, M^{-1} s^{-1}	k_4/K_a^0,[a] M^{-1} s^{-1}
morpholine	5.11 ± 0.25		$3.76 \pm 0.15 \times 10^7$	$5.70 \pm 1.00 \times 10^8$
piperidine	0.40 ± 0.03	$9.24 \pm 1.00 \times 10^{-3}$	$\leq 5.37 \times 10^7$	$5.96 \pm 0.90 \times 10^9$

[a] K_a^0 is the C–H acidity constant of T^0.

the dominant one in the reverse direction, i.e., $k_{-3}^A[R_2NH] \gg k_{-3}^{OH}a_{OH^-} + k_{-3}^w + k_{-i}$. Hence, the inequality $k_{-3}^A[R_2NH] \ll k_{-3}^w + k_{-i} + k_4$ deduced earlier must be due entirely to a large k_4 value ($k_4 \gg k_{-3}^w + k_{-i}$). Thus, eq 3 is further reduced to

$$\tau_2^{-1}(\text{adj}) = k_3^w + (k_3^H + k_i/K_a^{\pm})a_{H^+} + k_3^{AH}[R_2NH_2^+] \quad (4)$$

At pH 9.32, 9.67, and 10.00 (10.05) the plots of τ_2^{-1}(adj) vs. $[R_2NH_2^+]$ are curved and reach a plateau. This appears to be mainly a consequence of the *free* amine concentration becoming higher at high pH (Table II) which enhances the $k_{-3}^A[R_2NH]$ term in the denominator of eq 2 and leads to $k_{-3}^A[R_2NH] \gg k_4$. There might also be a small contribution from the enhanced $k_{-3}^{OH}a_{OH^-}$ although further analysis (see below) suggests that this is insignificant. At the plateau eq 3 simplifies to

$$\tau_2^{-1}(\text{adj}) = k_4a_{H^+}/K_a^0 \quad (5)$$

because the proton-transfer step $T^- \rightleftharpoons T^0$ is now at equilibrium; K_a^0 is the C–H acid dissociation constant of T^0.

Before proceeding further some comments on two points are called for. (1) In principle, the curvature in the plots at high pH could have a different origin. For example, in view of the relatively high free amine concentrations which prevail in the curved regions, complexation between the free amine and its conjugate acid ($R_2NH_2^+\cdots NHR_2$) could possibly lead to curvature. Such complexation is known to significantly affect proton-transfer rates involving phenol buffers.[13] In the present situation, however, this seems quite unlikely. If curvature and the plateau at pH 10.00 in Figure 1 were due to complexation, one would have to assume that the complex has no catalytic activity at all and that the equilibrium constant for association has a value of about 10 M^{-1}. Such a complex would presumably also reduce nucleophilic reactivity of the amine. Such reduction has not been found under conditions similar to those used in this present study.[2,6,10]

(2) Equation 5, which is equivalent to

$$\tau_2^{-1} = \frac{K_1K_a^{\pm}[R_2NH]}{1 + \frac{K_1K_a^{\pm}}{a_{H^+}}[R_2NH]}\frac{k_4}{K_a^0} \quad (6)$$

is only valid as long as T^0 does not accumulate to levels comparable to, or higher than, T^-, i.e., as long as $a_{H^+} < K_a^0$ ($pH > pK_a^0$). If $pH \leq pK_a^0$ eq 6 must be expanded to

$$\tau_2^{-1} = \frac{K_1K_a^{\pm}[R_2NH]}{1 + K_1K_a^{\pm}[R_2NH]\left\{\frac{1}{a_{H^+}} + \frac{1}{K_a^0}\right\}}\frac{k_4}{K_a^0} \quad (7)$$

Since eq 7 could provide a means to evaluate K_a^0 we tested for the significance of the K_a^0 term by rearranging eq 7 into

$$\frac{K_1K_a^{\pm}[R_2NH]}{\tau_2^{-1}} = \left(1 + K_1K_a^{\pm}[R_2NH]\left\{\frac{1}{a_{H^+}} + \frac{1}{K_a^0}\right\}\right)\frac{K_a^0}{k_4} \quad (8)$$

and plotting the left-hand side of eq 8 vs. $[R_2NH]$. Such plots (not shown) for the plateau values at pH 9.32, 9.72, and 10.00 afford slopes which are, within experimental error, proportional to $1/a_{H^+}$, indicating $pH > pK_a^0$. Thus, eq 6 *is* valid and K_a^0 cannot be determined experimentally. Nevertheless, the lowest pH value used permits an upper limit $pK_a^0 < (\ll)$ 9.32 to be estimated.

(13) Hibbert, F.; Robbins, H. J. *J. Am. Chem. Soc.* **1978**, *100*, 8239.

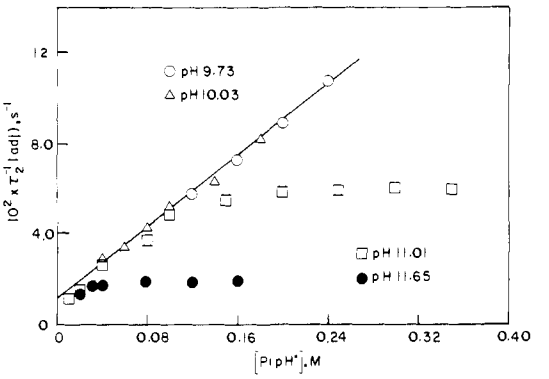


Figure 2. τ_2^{-1}(adj) for the piperidine adduct of α-cyano-2,4-dinitrostilbene (**2-$(NO_2)_2$**).

Rate constants, summarized in Table III, were calculated as follows:

(1) The slopes at pH 8.41 and 8.72 and the initial slope at pH 9.32 in Figure 1 are 5.13, 5.41, and 4.80 M^{-1} s^{-1}, respectively, for an average $k_3^{AH} = 5.11 \pm 0.25$ M^{-1} s^{-1}.

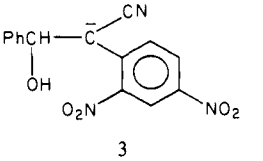
A plot (not shown) of the intercepts vs. a_{H^+} yields, according to eq 4, $k_3^H + k_i/K_a^{\pm} = 3.76 \pm 0.15 \times 10^7$ M^{-1} s^{-1} and $k_3^w \approx 0$. The fact that k_3^w is indistinguishable from zero indicates that protonation by water is an insignificant pathway in the pH range studied. By virtue of the principle of microscopic reversibility we conclude, as mentioned earlier, that the k_{-3}^{OH} pathway is also insignificant.

(3) From the plateau values in Figure 1 we obtain $k_4/K_a^0 = 5.7 \pm 1.0 \times 10^8$ M^{-1} s^{-1} (eq 5); the dashed lines in the figure were calculated on the basis of this value.

Reaction of α-Cyano-2,4-dinitrostilbene with Piperidine. The methodology in studying this reaction was essentially the same as that for the morpholine reaction. Measurements were carried out at pH 10.03, 10.41, 11.00, 11.02, 11.62, and 11.66. Values for τ_2^{-1} and τ_2^{-1}(adj) are summarized in Table S1[14] while Figure 2 shows plots of τ_2^{-1}(adj) vs. $[R_2NH_2^+]$. These plots show the same change from rate-limiting proton transfer at low pH to rate-limiting breakdown of T^0 at high pH as are seen with the morpholine reaction. The various rate constants are summarized in Table III.

As can be seen by comparing Figures 1 and 2 there is one important difference between the results for the morpholine and those for the piperidine reaction. In the latter the intercepts show no pH dependence, indicating that $(k_3^H + k_i/K_a^{\pm})a_{H^+} \ll k_3^w$. The main reason for this result is that the pH range investigated with piperidine (9.73–11.66) was higher than that for morpholine (8.11–10.05).

An evaluation of the $(k_3^H + k_i/K_a^{\pm})$ term from experiments at lower pH would have been desirable but was impractical. At lower pH the concentration of free piperidine becomes so low that not enough T^- is formed for favorable competition with hydrolysis of the olefin via **3**. Nevertheless, an upper limit, $(k_3^H + k_i/K_a^{\pm})$



3

$\leq 5.37 \times 10^7$ M^{-1} s^{-1}, can be estimated from our data by dividing

(14) See paragraph concerning supplementary material at the end of this paper.

Table IV. Experimental Rate and Equilibrium Constants for **1**-NO_2

R_2NH	k_4/K_a^0,[a] M^{-1} s^{-1}	$K_1K_a^{\pm}$	k_4,[a] s^{-1}	$K_a^0(pK_a^0)$,[a,b] M
morpholine	$1.33 \pm 0.10 \times 10^8$	$9.3 \pm 2.0 \times 10^{-13}$	$2.9 \pm 1.0 \times 10^{-4}$	$2.2 \pm 0.5 \times 10^{-12}$ (11.65 ± 0.10)
piperidine	$30.3 \pm 1.0 \times 10^8$	$10 \pm 2 \times 10^{-13}$	$4.5 \pm 1.2 \times 10^{-3}$	$1.5 \pm 0.3 \times 10^{-12}$ (11.82 ± 0.10)

[a] $K_a^0(pK_a^0)$ is the C–H acidity constant of T^0. [b] Based on $K_1K_a^{\pm}$ determined directly (see Table I).

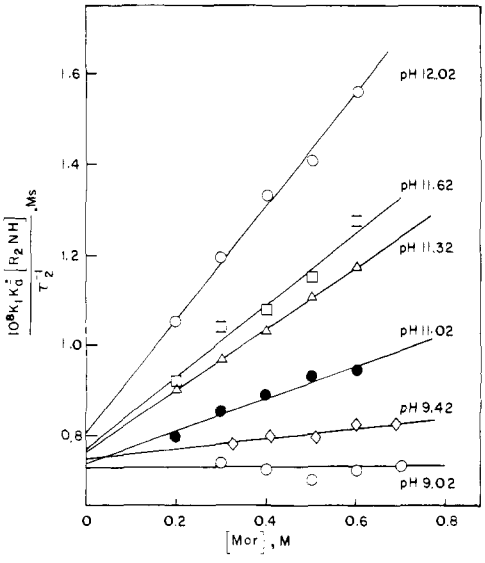


Figure 3. Plots according to eq 8 for the morpholine adduct of α-cyano-4-nitrostilbene (**1**-NO_2).

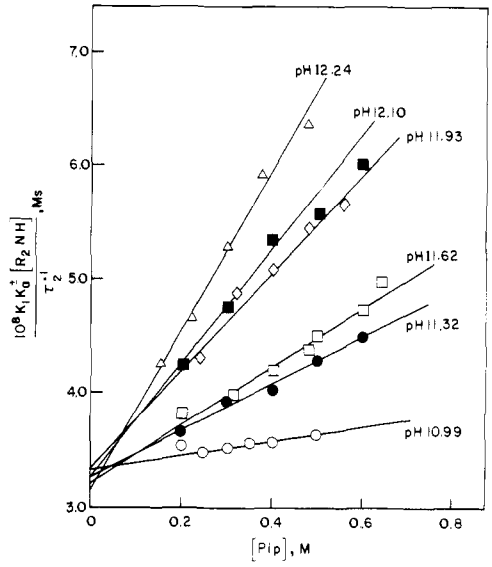


Figure 4. Plots according to eq 8 for the piperidine adduct of α-cyano-4-nitrostilbene (**1**-NO_2).

the uncertainty of the intercepts in Figure 2 ($\approx 10^{-2}$ s^{-1}) by a_{H^+} prevailing at the lowest pH (9.73) used.

Reactions of α-Cyano-4-nitrostilbene with Morpholine and Piperidine. These reactions were monitored at 340 nm which corresponds to the loss of substrate. At this wavelength excellent first-order kinetic plots were obtained for $[R_2NH] \geq 0.05$ M. At lower concentrations biphasic kinetics was observed, most likely because of interference with hydrolysis (see Discussion). Biphasic plots were also observed when monitoring the reaction at $\lambda > 400$ nm (formation of **2**-NO_2^-), even at $[R_2NH] \geq 0.05$ M. This can be traced to a decomposition reaction of **2**-NO_2^-.[15]

The morpholine reaction was investigated at pH 9.02, 9.42, 11.02, 11.62, 11.81, and 12.02, using five different amine concentrations at each pH. The results are summarized in Table S2.[14] At the lowest two pH values used morpholine acted as its own buffer, while at the highest four pH values a dilute piperidine buffer (0.005 to 0.01 M total concentration) was added to maintain the pH. At these low concentrations competing nucleophilic addition by piperidine is negligible.

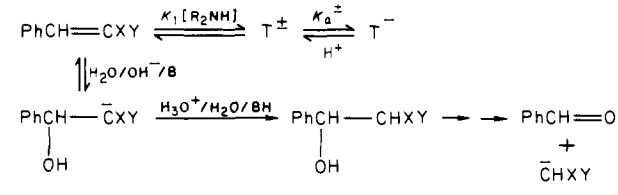
The piperidine reaction was studied in a similar way at pH 10.99, 11.32, 11.62, 11.93, 12.10, and 12.23 with the results in Table S3.[14]

For both amines the data obey eq 5 fairly well, i.e., τ_2^{-1}(adj) does not increase with $[R_2NH_2^+]$ at any pH, indicating that the k_4 step is rate limiting throughout. However, τ_2^{-1}(adj) has a tendency to decrease at high concentrations, suggesting that eq 5 and 6 begin to break down because of accumulation of T^0 at high amine concentrations. We therefore analyzed our results via eq 8. Figures 3 and 4 show plots according to eq 8. As required by the equation, the intercepts are pH independent and yield k_4/K_a^0, while the ratio slope/intercept is given by

$$\frac{\text{slope}}{\text{intercept}} = \frac{K_1K_a^{\pm}}{a_{H^+}} + \frac{K_1K_a}{K_a^0} \qquad (9)$$

Analysis of the data affords the parameters summarized in Table IV. The good agreement between the $K_1K_a^{\pm}$ values obtained via eq 9 and those obtained more directly[4] (Table I) shows that our analysis is sound.

Scheme II



Discussion

Mechanism. In aqueous or partially aqueous solution, hydrolysis of the olefin via water or OH^- attack[16-18] always competes with aminolysis. Thus one needs to ask whether our results might possibly be consistent with an alternative mechanism in which the amine simply acts as a catalyst of hydrolysis. This is illustrated by Scheme II.

One possibility is that the amine could act as a general-base catalyst for rate-limiting water adition to the olefin, or, perhaps more likely, the protonated amine could act as a proton-transfer catalyst for rate-limiting carbon protonation of the hydroxy adduct. Preliminary measurements of the formation of the OH adduct of **1**-$(NO_2)_2$ show that this reaction is much slower than the τ_2^{-1} process under the reported experimental conditions, thus excluding these possibilities. The observed rate late is also inconsistent with such alternative interpretations. For example, under conditions where $K_1K_a^{\pm}[R_2NH]/a_{H^+}$ is small, at best a first-order dependence on amine concentration should be observed for Scheme II, which is inconsistent with the nearly second-order dependence observed. Similar considerations apply under other experimental conditions.

There must of course be a point at which hydrolysis takes over. In the benzylidene-substituted Meldrum's acid system[6] this situation is reached when the free amine concentration drops below ≈0.05 M. At this point the formation of the hydroxide adduct

(15) Minch, M. J.; Giaccio, M.; Wolff, R. *J. Am. Chem. Soc.* **1975**, *97*, 3766.

(16) 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.

(17) Bernasconi, C. F.; Carrē, D. J.; Kanavarioti, A. *J. Am. Chem. Soc.* **1981**, *103*, 4850.

(18) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5133, 5143.

Table V. Rate Constants for Carbon Protonation of T^-(1-$(NO_2)_2$) and of 2-$(NO_2)_2^-$

catalyst	nucleophile	$k_3^{cat}(T^-)$, M^{-1} s^{-1}	k_3^{cat}(2-$(NO_2)_2^-$), M^{-1} s^{-1}	$k_3^{cat}(T^-)/k_3^{cat}$(2-$(NO_2)_2^-$)
H_2O	piperidine	$9.24 \times 10^{-3}/27.6$	$5.39 \times 10^{-3}/27.6$	1.71
$pipH^+$	piperidine	0.40 (0.32)[a]	27.2	0.0147
$morH^+$	morpholine	5.11	3.40×10^2	0.0150
H_3O^+	morpholine	3.76×10^7 [b] ($k_i = 55.6$ s^{-1})[c]	4.39×10^5	85.6
H_3O^+	piperidine	$\leq 5.37 \times 10^7$ [b] ($k_i \leq 0.40$ s^{-1})[c]		

[a] Corrected for pK_a^0, see footnote 19. [b] $k_3^H + k_i/K_a^{\pm}$. [c] Based on the assumption that $k_i/K_a^{\pm} \gg k_3^H$, see text.

as a non-steady-state intermediate becomes important, which manifests itself by the onset of biphasic kinetics. In the 1-NO_2 system we observed a similar phenomenon at about the same amine concentrations, which probably has the same origin as in the benzylidene-substituted Meldrum's acid. A confirmation of this conclusion must of course await the detailed kinetic study of the reaction of 1-NO_2 with OH^-.

In the 1-$(NO_2)_2$ systems competition by the formation of the OH^- adduct does not occur at amine concentrations ≥ 0.005 M.

C–H **Acidity of T^0 (pK_a^0).** The pK_a^0 values of the adducts derived from 1-NO_2 are 11.65 ± 0.10 for the morpholine and 11.82 ± 0.10 for the piperidine derivative (Table IV). With the pK_a of 2-NO_2 being 12.62,[11] this represents an acidifying effect of ≈0.8 to ≈1.0 unit by the $PhCHNR_2$ moieties.

The finding that pK_a^0 for the piperidine adduct is somewhat higher than that for the morpholine adduct is reasonable in view of the weaker electron-withdrawing effect of the piperidino group. However, not too much significance can be attached to the numerical pK_a^0 difference (0.17 unit) because the combined experimental errors in the two pK_a^0 values are about as large as this difference.

For the derivatives of 1-$(NO_2)_2$ only an upper limit, $pK_a^0 < 9.32$, for the morpholine adduct could be estimated from our data (see Results). A lower limit, $pK_a^0 \geq 8.36$, can be set for the piperidine adduct, based on the fact that carbon protonation of T^- by water is almost twice as fast as protonation of 2-$(NO_2)_2^-$ (Table V), as discussed in more detail below.

Carbon Protonation of T^- by Water and by $R_2NH_2^+$. Rate constants for carbon protonation of T^- derived from 1-$(NO_2)_2$ are summarized in Table V; the table also includes the corresponding rate constants referring to the protonation of 2-$(NO_2)_2^-$ and the ratios $k_3^{cat}(T^-)/k_3^{cat}$(2-$(NO_2)_2^-$) for the catalysts water, $R_2NH_2^+$, and H_3O^+. The following points are noteworthy.

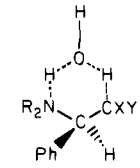
(1) Protonation of the piperidine adduct by water occurs 1.7 times faster than protonation of 2-$(NO_2)_2^-$. This requires the pK_a^0 of the adduct (T^0) to be higher than the pK_a of 2-$(NO_2)_2^-$. If one assumes a $\beta = 0.75$ (dependence on carbon pK_a) as for the protonation of 2-NO_2^- vs. 2-$(NO_2)_2^-$,[11] the 1.7-fold higher rate constant implies that pK_a^0 is about 0.3 unit higher than the pK_a of 2-$(NO_2)_2$, i.e., 8.36. It is possible that k_3^w is subject to a small steric retardation; in this case 8.36 is a lower limit for pK_a^0.

(2) Protonation of T^- by $pipH^+$ and $morH^+$ is much slower than protonation of 2-$(NO_2)_2^-$ by the same acids. These rate reductions must be caused by a steric effect, due to the bulkiness of $R_2NH_2^+$; they amount to at least a factor of 100 if the protonation by water is not subject to a steric effect and to a greater factor if water protonation is also sterically hindered. The fact that the ratio $k_3^{AH}(T^-)/k_3^{AH}$(2-$(NO_2)_2^-$) is virtually the same for both amines indicates that the Brønsted α for protonation of T^- by $R_2NH_2^+$ ($\alpha = 0.52$)[19] is virtually the same as for the protonation of 2-$(NO_2)_2^-$ by the same two $R_2NH_2^+$ ($\alpha = 0.50$).[11]

Carbon Protonation of T^- by H_3O^+. The ratio $k_3^H(T^-)/k_3^H$-(2-$(NO_2)_2^-$) = 85.6 is much larger than the ratio $k_3^w(T^-)/k_3^w$-(2-$(NO_2)_2^-$) = 1.71. The fact that the former ratio refers to the morpholine adduct, the latter to the piperidine adduct, even slightly underestimates the difference between the rate ratios, because of the slightly lower pK_a^0 of the morpholine adduct.

Since steric effects, if they exist at all, should be about the same for water and H_3O^+, the enhanced ratio for H_3O^+ indicates that the presence of the $PhCHNR_2$ moiety either provides a special stabilization to the transition state of the k_3^H step or that there is a new reaction pathway in the form of an intramolecular proton switch ($k_i/K_a^{\pm}$) as shown in Scheme I.

Similar, or even larger, rate enhancements have been observed with the morpholine adducts of 1,1-dinitro-2,2-diphenylethylene,[2] benzylidene-substituted Meldrum's acid,[6] and β-nitrostyrene.[20] They have been interpreted in terms of an intramolecular proton switch whose transition state most likely includes a water bridge[5] (**5**).



5

Table V includes k_i values, calculated under the assumption that $k_i/K_a^{\pm} \gg k_3^H$. Effective molarities,[21] EM's, are estimated to be ≈0.34 M for the morpholine adduct and ≤0.031 for the piperidine adduct.[22] They are calculated as $EM = k_i/k_3^{AH}(corr)$ where $k_3^{AH}(corr)$ is the rate constant for protonation of T^- by a $R_2NH_2^+$ whose $pK_a = pK_a^{\pm}$ (Table I); $k_3^{AH}(corr)$ is estimated from $\log k_3^{AH}(corr) = \log k_3^{AH} + 0.52\ (pK_a^{AH} - pK_a^{\pm})$ with 0.52 being the α value determined above from the $k_3^{morH^+}/k_3^{pipH^+}$ ratio. Our EM values are rather low which is typical for proton transfers.[22]

Tapuhi and Jencks[23] have also reported an exalted rate constant for carbon protonation of the acetone enolate ion by H_3O^+. However, they attributed the rate enhancement to a stabilization of the transition state by hydrogen bonding of the solvated proton to the oxygen anion of the enolate. They prefer this interpretation to a fully concerted intramolecular proton switch from the hydroxyl group to carbon in the enol.

One can estimate the extent of the rate enhancement which might occur by hydrogen bonding in our system by applying the Hine[24] equation. This equation expresses the association constant of a hydrogen-bonded complex AH·B as

$$\log K_{AH\cdot B} = \tau(pK_{H_3O^+} - pK_{BH})(pK_{AH} - pK_{H_2O}) - \log [H_2O] \quad (10)$$

If one uses Jencks' value of 0.013 for τ in water[25] one obtains $K_{AH\cdot B} = 9.33$ for the piperidine adduct and 2.14 for the morpholine adduct.[27] These values are, respectively, 257 and 59 times larger

(19) This α value is obtained after correction of $k_3^{pipH^+}$ for the slightly higher pK_a^0 of the piperidine adduct (value in parentheses in Table V); a $\beta = 0.65$[11] was used for this correction.

(20) Bernasconi, C. F.; Tia, P. R.; Renfrow, R. A., unpublished observations.

(21) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.

(22) For a discussion of potential problems in defining effective molarities of intramolecular proton transfer where the donor and acceptor atoms are separated by only one carbon, see ref 5.

(23) Tapuhi, E.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 5758.

(24) Hine, J. *J. Am. Chem. Soc.* **1972**, *94*, 5766.

(25) (a) Funderburk, L. H.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 6708. (b) This value has now also been confirmed experimentally.[26]

than $K_{AH\cdot B} = [H_2O]^{-1}$ in the absence of hydrogen bonding. The factors 257 and 59 are essentially a measure of the advantage of having the hydronium ion in close proximity to the carbon which is being protonated over having to take it from dilute solution ("induced intramolecularity"[26]); these factors are large enough to account for the observed accelerations.

Experimental support in favor of either the concerted intramolecular proton transfer or the hydrogen-bonding mechanism could possibly come from structure–reactivity relationships, such as the dependence of the rate constants on $pK_a^{\pm}$. Our data are not very extensive in this respect, but they allow at least a discussion of the problem.

If one interprets our results in terms of an intramolecular reaction, one obtains

$$\alpha = \partial \log k_i / \partial \log K_a^{\pm} \geq 0.933 \qquad (11)$$

from k_i^{mor} and the estimated upper limit of k_i^{pip}. A more rigorous treatment, which takes into account the small change in pK_a^0 from the morpholine to the piperidine adduct, leads to

$$\alpha = (\partial \log k_i / \log K_a^{\pm})_{pK_a^0} = \partial \log k_i / \partial \log K_a^{\pm} + \left(\frac{\partial \log k_i}{\partial pK_a^0}\right)_{pK_a^{\pm}} \frac{\partial pK_a^0}{\partial pK_a^{\pm}} \qquad (12)$$

Since the second term on the right-hand side of eq 12 is a small positive number, eq 12 implies that the true α is larger than $\partial \log k_i / \partial \log K_a^{\pm}$, i.e., $\alpha > 0.933$ and probably very close to 1.0.

If, on the other hand, the results are attributed to protonation by H_3O^+ (k_3^H) with transition-state stabilization by the adjacent amine nitrogen, one obtains a β value for transition-state stabilization,

$$\beta_s = \partial \log k_3^H / \partial pK_a^{\pm} \leq 0.067 \qquad (13)$$

or, again taking into account the slight change in pK_a^0, $\beta_s \approx 0.0$.

It appears that neither mechanism accounts very satisfactorily for the α or β_s value. An $\alpha \approx 1.0$, which contrasts with $\alpha = 0.52$ for *inter*molecular protonation by $R_2NH_2^+$, implies that the nitrogen has completely lost the proton in the transition state. This suggests a mechanism that might be stepwise, with the first step being an equilibrium proton transfer from $T^{\pm}$ to water, followed by rate-limiting carbon protonation by H_3O^+. If the H_3O^+ formed in the first step is at equilibrium with the solvent, this mechanism becomes indistinguishable from a direct carbon protonation by a H_3O^+ which comes from the bulk solution, i.e., the term "intramolecular" proton transfer becomes meaningless. This would be consistent with Jencks'[23] view that the most likely immediate protonating agent is H_3O^+.

However, there is a problem with the Jencks mechanism, too. The rate accelerations suggested by the Hine equation (257- and 59-fold for the piperidine and morpholine adduct, respectively) imply a $\beta_s = 0.28$ instead of the observed $\beta_s \approx 0$. In fact the observed β_s value suggests that there is essentially no hydrogen-bonding interaction. If there is no interaction, one wonders what the source of transition-state stabilization would be which can lead to the exalted k_3^H values.

We have currently no firm answers to these questions but wish to make the following points:

(1) Our $\alpha(\beta_s)$ values do not appear to be an artifact caused by possible errors in estimating K_1 and $K_a^{\pm}$.[4] The adjustment factor used to calculate τ_2^{-1}(adj) (eq 2) does *not* depend on K_1 and $K_a^{\pm}$ separately, but rather on the product $K_1K_a^{\pm}$ which *is* experimentally determined.[4] Similarly, even though the absolute values of k_i depend on the estimated values of $K_a^{\pm}$, $\alpha(\beta_s)$ does not since only ratios come into play.

(2) A seemingly attractive way out of our difficulties is to assume that the $k_3^H(T^-)$ values only *appear* exalted because they are being compared with $k_3^H(\mathbf{2}\text{-}(NO_2)_2^-)$ for protonation of $\mathbf{2}\text{-}(NO_2)_2^-$ but that such a comparison is inappropriate. Specifically, one could imagine that the $PhCHNR_2$ moiety somehow changes the characteristics of T^- beyond the effects discussed earlier, and in such a way as to alter its Brønsted behavior. A higher k_3^H/k_3^w ratio might be the consequence. However, such an enhanced k_3^H/k_3^w ratio would most likely imply a higher Brønsted α for protonation by other acids. Since α for protonation of T^- by $morH^+$ and $pipH^+$ is virtually the same (0.52) as for protonation of $\mathbf{2}\text{-}(NO_2)_2^-$ (0.50), this becomes an unattractive interpretation, too. Also, if the non-coplanarity of the *o*-nitro group were to make T^- ($\mathbf{1}\text{-}(NO_2)_2$) resemble $\mathbf{2}\text{-}NO_2^-$ more than $\mathbf{2}\text{-}(NO_2)_2^-$ in its Brønsted behavior, a *smaller* rather than larger α value would result.[11]

(3) An α value near unity is *suggestive* of a stepwise mechanism but does not require it. It only indicates that the amine nitrogen has essentially completely lost its positive charge in the transition state. It does not tell whether there is an intermediate or not.

Intrinsic Barrier to the Breakdown of T^0. Values for k_4, pK_a^0, and pK_a^{lg} are summarized in Table VI. For comparison purposes the corresponding values of the T^0 adduct of benzylidenemalononitrile[6] are also included.

The less basic $\mathbf{2}\text{-}(NO_2)_2^-$ is a better leaving group than $\mathbf{2}\text{-}NO_2^-$, as one might have expected, but if $^-CH(CN)_2$ is included in this comparison (Table VI) there is no correlation between k_4 and pK_a^{lg}. In fact, $^-CH(CN)_2$ departs 3.5 times faster than $\mathbf{2}\text{-}(NO_2)_2^-$, even though it is 2.15 pK units more basic than $\mathbf{2}\text{-}(NO_2)_2^-$, and k_4 for departure of $\mathbf{2}\text{-}(NO_2)_2^-$ is probably strongly enhanced by a steric effect, as discussed below. Or, compared to $\mathbf{2}\text{-}NO_2^-$, $^-CH(CN)_2$ leaves 7.33×10^3 times faster even though the pK_a of $CH_2(CN)_2$ is only 2.41 units lower than that of $\mathbf{2}\text{-}NO_2$.

By correcting for the different pK_a^{lg} one can estimate an approximate ratio of the intrinsic rate constants,[28] $k_0^{(CN)_2}/k_0^{(CN)C_6H_4\text{-}4\text{-}NO_2}$. Using an estimated $\beta_{lg} = \partial \log k_4/\partial pK_a^{lg} = -0.5$ (-0.3, -0.7) leads to $k_0^{(CN)_2}/k_0^{(CN)C_6H_4\text{-}4\text{-}NO_2} = 4.57 \times 10^2$ (1.39×10^3, 1.51×10^2).

These considerations show that the intrinsic rates (intrinsic barriers) for $\mathbf{2}\text{-}NO_2^-$ or $\mathbf{2}\text{-}(NO_2^-)_2$ departure are much lower (higher) than for $^-CH(CN)_2$ departure. This is the same qualitative pattern which was observed with the deprotonation of malononitriles compared to that of $\mathbf{2}\text{-}NO_2$ and $\mathbf{2}\text{-}(NO_2)_2$,[11] and with amine addition to benzylidenemalononitrile compared to addition to $\mathbf{1}\text{-}NO_2$ and $\mathbf{1}\text{-}(NO_2)_2$.[4] The reasons for these patterns have been discussed in detail elsewhere.[29] Briefly, they are related to the difference in the amount of resonance stabilization in the carbanion—strong resonance stabilization leads to high intrinsic barriers because of a larger degree of structural and solvational reorganization during the reaction.

A less dramatic, but nevertheless significant, increase in the intrinsic barrier for proton transfer and olefin addition was also

Table VI. pK_a^0, pK_a^{lg}, and k_4 for the Reactions of $\mathbf{1}\text{-}(NO_2)_2$, $\mathbf{1}\text{-}NO_2$, and Benzylidenemalononitrile

	pK_a^0	pK_a^{lg}	k_4, s^{-1}
		$\mathbf{1}\text{-}(NO_2)_2$	
morpholine	≈8.65[a]	8.06[b]	≈1.3 (3.25×10^{-2})[c]
piperidine	≈8.80[a]	8.06[b]	≈9.4 (0.17)[c]
		$\mathbf{1}\text{-}NO_2$	
morpholine	11.65	12.62[b]	2.9×10^{-4}
piperidine	11.82	12.62[b]	4.5×10^{-3}
		$PhCH{=}C(CN)_2$[d]	
piperidine	8.73[e]	10.21[f]	33[e]

[a] Estimated, see text. [b] Reference 11. [c] Estimated value in the absence of steric acceleration, see text. [d] Reference 3. [e] These values differ slightly from those given in ref 3, because no correction for the slightly higher pK_a^0 of the piperidine adduct was made. [f] Reference 1.

(26) Jencks, W. P., personal communication.

(27) In 50% Me_2SO–50% water at 20 °C, $pK_{H_3O^+} = -1.44$, $pK_{H_2O} = 17.34$, $pK_{AH} = pK_{H_3O^+}$, $pK_{BH} = 8.13$ for the piperidine adduct and 5.83 for the morpholine adduct (Table I).

(28) $k_0 = k_4 = k_{-4}$ when $K_4 = 1$.

(29) For a recent review, see: Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.

Table VII. β_N Values

	1-NO_2	1-$(NO_2)_2$
β_N	0.52	0.36
$\beta_N^n = \beta_N/\beta_N^{eq}$ [a]	≥0.43	≥0.30

[a] Based on an estimated $\beta_N^{eq} \leq 1.2$, see text.

found when changing from the less delocalizing $(CN)C_6H_4$-4-NO_2 to the more delocalizing $(CN)C_6H_4$-2,4-$(NO_2)_2$ systems (**2-NO_2** vs. 2-$(NO_2)_2$ and **1-NO_2** vs. **1-$(NO_2)_2$**).[4,11] One would, therefore, expect to see a similar behavior in the breakdown of T^0. This should manifest itself by k_4(**1-$(NO_2)_2$**)/k_4(**1-NO_2**) ratios which are relatively small.

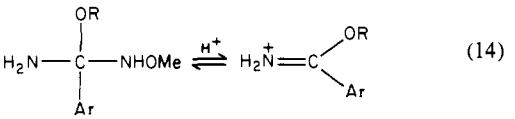
The actual ratios are $\approx 4.48 \times 10^3$ for the morpholine adducts and $\approx 2.09 \times 10^3$ for the piperidine adducts. Since the pK_a^{lg} difference is only 4.56 units, these ratios appear to be very large and at variance with our prediction. There are, in principle, two ways to explain this variance.

(1) It could simply be the result of an authentic exception to the pattern observed in other reactions. In view of the many examples found so far, which obey the pattern without exception,[4,11,29,30] and in particular in view of the "normal" behavior of the **2-NO_2**/**2-$(NO_2)_2$** pair with respect to proton transfer and of the **1-NO_2**/**1-$(NO_2)_2$** pair with respect to nucleophilic addition, this explanation seems highly unsatisfactory.

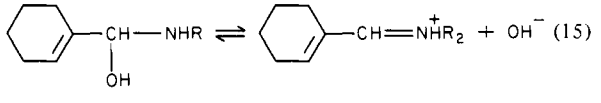
(2) A more appealing explanation is that there is another factor which affects the k_4(**1-$(NO_2)_2$**)/k_4(**1-NO_2**) ratio. This other factor is most likely the release of steric strain in T^0 caused by the *o*-nitro group. One may estimate the magnitude of this steric acceleration by assuming that the ratio of the intrinsic rate constants $k_0^{(CN)C_6H_4\text{-}4\text{-}NO_2}/k_0^{(CN)C_6H_3\text{-}2,4\text{-}(NO_2)_2}$ is ≈5, just slightly lower than the corresponding ratio (11) for proton transfer.[11] Using again $\beta_{lg} \approx -0.5$ for the piperidine adduct, one estimates that, in the absence of a steric acceleration, $k_4 \approx 0.17\ s^{-1}$ (value in parentheses in Table VI). This implies a 55-fold steric acceleration.

Structure–Reactivity Coefficients. We note that the breakdown of the piperidine adducts is significantly faster than that of the morpholine adducts (Table VI). This indicates that there is a considerable "push" by the lone pair on the amine nitrogen, i.e., there is substantial positive charge development on the amine nitrogen in the transition state. A Brønsted coefficient for this push can be defined as $\beta_N = \partial \log k_4/\partial pK_a^{\pm}$. β_N values are summarized in Table VII. It should be noted that these β_N values must be quite reliable because they depend on few assumptions. Specifically, they do not depend on the assumptions made in estimating $pK_a^{\pm}$ [4] and pK_a^0 of the **1-$(NO_2)_2$** adducts, except for our estimate that pK_a^0 of the piperidine adduct is 0.15 unit higher than that for the morpholine adduct. An error of 0.1 unit in this estimate would change β_N by less than 0.04.

β_N for the equilibrium reaction is not available, and thus we cannot calculate a normalized β_N ($\beta_N^n = \beta_N/\beta_N^{eq}$) which could provide an estimate of the amount of positive charge development on nitrogen in the transition state. A study by Gilbert and



(14)



(15)

Jencks[31] of a related reaction (eq 14) suggests that β_N^{eq} might possibly be >1. Also, based on data by Kayser and Pollack[32] a $\beta_N^{eq} = 1.4$ can be estimated for reaction 15. However, β_N^{eq} for our k_4 step is likely to be smaller than that for reaction 20, because the phenyl group can help stabilize the positive charge by resonance ($^+C_6H_5$=CH—NR_2), thereby lessening the demand for stabilization by the R groups.

We conclude that if β_N^{eq} is larger than unity at all it cannot be very much larger, probably not larger than 1.2. This would make $\beta_N^n \geq 0.30$ for **1-$(NO_2)_2$** and ≥0.43 for **1-NO_2**, suggesting about 30–40% positive charge development in the transition state.

Because of the steric acceleration of the breakdown of T^0 derived from **1-$(NO_2)_2$** meaningful β_{lg} values cannot be estimated, and the more interesting $\beta_{lg}^n = \beta_{lg}/\beta_{lg}^{eq}$ is also inaccessible. However, we would predict that $\beta_{lg}^n < \beta_N^n$, for the same reason which causes $\alpha_{CH} < \beta_\beta$ in the deprotonation of **2-NO_2** and **2-$(NO_2)_2$**[11] and $\alpha_{nuc}^n < \beta_{nuc}^n$ in the addition of piperidine and morpholine to **1-NO_2** and **1-$(NO_2)_2$**.[4]

Conclusions

To the best of our knowledge, our study represents one of the first attempts at measuring a Brønsted α value for an intramolecular proton transfer from nitrogen to carbon.[33] The fact that α approaches unity is puzzling, though, and casts some doubts as to whether the reaction is truly intramolecular in the sense of a concerted double proton transfer (**5**). We have shown that the alternative interpretation, according to which the reaction simply represents a carbon protonation by H_3O^+, with a transition state stabilized by hydrogen bonding, is not very satisfactory either. Work in progress will hopefully clarify the situation.

The comparison between the breakdown rates of T^0 derived from **1-NO_2** and from benzylidenemalononitrile shows the now familiar pattern that carbanions which are strongly resonance stabilized are formed at rates which are intrinsically slower than those which are subject to less resonance stabilization.

Experimental Section

Materials. α-Cyano-4-nitrostilbene (**1-NO_2**) and α-cyano-2,4-dinitrostilbene (**1-$(NO_2)_2$**) were available from a previous study.[4] Piperidine and morpholine were purified as described before.[2] Reagent grade Me_2SO was stored over 4A molecular sieves prior to use. All other chemicals were reagent grade and were used without further purification.

Reaction Solutions, pH Measurements. The procedures used were essentially those described earlier.[2]

Kinetics. Rates of aminolysis ($1/\tau_2$) were measured spectrophotometrically on a Gilford 2000 or Perkin-Elmer 559A spectrophotometer. The reactions of **1-$(NO_2)_2$** were monitored at 420 nm (formation of **2-$(NO_2)_2$**$^-$) or 480 nm (loss of T^-). The reactions of **1-NO_2** were monitored at 255 nm (formation of benzaldehyde) or at 340 nm (loss of **1-NO_2**). Pseudo-first-order rate constants were obtained from the slopes of semilog plots of OD − OD_∞ vs. time which were linear over three or more half-lives. Rate constants for reactions with half-lives greater than 3 h were obtained by following the reaction for 2–4 half-lives and estimating the OD_∞ by using a computer program based upon the Guggenheim method.

Acknowledgment. This research was supported by Grant CHE80-24261 from the National Science Foundation. We thank Professor William P. Jencks for comments on this manuscript.

Supplementary Material Available: Tables S1–S3 containing kinetic data for the reaction of piperidine with α-cyano-2,4-dinitrostilbene (S1) and for the reaction of morpholine and piperidine with α-cyano-4-nitrostilbene (S2 and S3) (6 pages). Ordering information is given on any current masthead page.

(30) Gilbert, H. F. *J. Am. Chem. Soc.* **1980**, *102*, 7059.
(31) Gilbert, H. F.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 6769.
(32) Kayser, R. H.; Pollack, R. M. *J. Am. Chem. Soc.* **1977**, *99*, 3379.

(33) Okuyama et al.[34] report data for an intramolecular proton transfer from carbon to the nitrogen of a morpholino and a piperidino group in a hemithioacetal, from which one can estimate an $\alpha = 0.21$ in the direction ^+NH–C^- → N–CH, much lower than our $\alpha \approx 1.0$. However, since the transition state is a six-membered ring without including a mediating water molecule and hence probably does not involve such a water molecule, this system is hardly comparable to ours.
(34) Okuyama, T.; Komoguchi, S.; Fueno, T. *J. Am. Chem. Soc.* **1982**, *104*, 2582.