Kinetics of Reversible Carbon Deprotonation of 2-Nitroethanol and 2-Nitro-1,3-propanediol by Hydroxide Ion, Water, Amines, and Carboxylate Ions. A Normal Brønsted α Despite an Imbalanced Transition State

Claude F. Bernasconi,* Markandeswar Panda, and Michael W. Stronach

Contribution from the Department of Chemistry and Biochemistry, University of California, Santa Cruz, California 95064

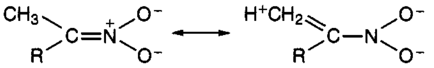
Received May 11, 1995®

Abstract: Rates of reversible carbon deprotonation of 2-nitroethanol (**2**) and 2-nitro-1,3-propanediol (**3**) by hydroxide ion, water, amines, and carboxylate ions and pK_a values for the ionization at carbon (pK_a^{CH}) and oxygen (pK_a^{OH}) and ionization of the aci-forms (pK_a^{NOH}) were determined in aqueous solution at 25 °C. The pK_a^{CH} values for **2** and **3** are 8.60 and 7.68, respectively, as compared to 10.22 for CH_3NO_2. The acidifying effect of the CH_2OH groups is attributed to a combination of inductive electron withdrawal and hyperconjugative stabilization of the respective nitronate ions, possibly coupled with intramolecular hydrogen bonding stabilization of this ion. The higher acidity of 2-nitroethanol compared to nitromethane is reflected in higher rates of proton transfer from 2-nitroethanol, implying a "normal" Brønsted α between 0 and 1. This contrasts with the negative α value based on the reaction of OH^- with nitromethane, nitroethane, and 2-nitropropane (Kresge, A. J. *Can. J. Chem.* **1974**, *52*, 1897). Reasons why a normal α value is observed in the current system are discussed.

Introduction

The kinetic investigation of proton transfers from nitroalkanes to a variety of bases[1-7] has played a central role in advancing our understanding of proton transfers from carbon acids in general, especially in systems that lead to charge delocalized, resonance stabilized carbanions. This is because the nitro group is one of the most powerful π-acceptors and hence the features that can be attributed to charge delocalization in the carbanion manifest themselves more clearly than in most other systems. These features are high intrinsic barriers (low intrinsic rate constants)[8] and imbalanced transition states[9] in the sense that charge delocalization into the π-acceptor lags behind proton transfer.[1-7,10] This latter feature manifests itself particularly dramatically in the "nitroalkane anomaly" which refers to the fact that the Brønsted α values for the deprotonation of substituted phenylnitromethanes by OH^- or amines are larger than unity.[2] The exalted α values are a direct consequence of the lag in charge delocalization; it causes the negative charge in the transition state to accumulate on the α-carbon rather than on the nitro group, thereby making the rate constant more sensitive than the pK_a to the electronic effect of the phenyl substituent.

Another type of "nitroalkane anomaly" was noted by Kresge[3] when comparing the deprotonation of nitromethane, nitroethane, and 2-nitropropane by OH^-. In this series the Brønsted α was found to be −0.5; the negative α reflects the fact that acidity increases in the order nitromethane < nitroethane < 2-nitropropane while the rate constant *decreases* in the order nitromethane > nitroethane > 2-nitropropane. The increase in acidity was attributed to hyperconjugative stabilization[3,11] of the C=N double bond by the methyl group(s) in the nitronate ions derived from nitroethane and 2-nitropropane (**1b**); this stabilization more than offsets the acidity lowering polar effect of the methyl group(s). The reason why the rate constants do not follow the same trend as the acidity constants can, in large measure, again be traced to the imbalanced nature of the transition state. The lag in charge delocalization into the nitro group creates a lag in the development of hyperconjugation and hence the transition state benefits little from this source of stabilization. On the other hand, the accumulation of negative charge on the α-carbon enhances the destabilization of the transition state by the inductive effect of the methyl group(s) due to their close proximity to this charge. An additional factor that destabilizes the transition state is the field effect of the methyl group(s) on the partially negative OH^-.



1a **1b**

The present paper reports kinetic data on the deprotonation of 2-nitroethanol (**2**) and 2-nitro-1,3-propanediol (**3**). The initial

---

® Abstract published in *Advance ACS Abstracts*, August 15, 1995.

(1) Fukyama, M.; Flanagan, P. W. K.; Williams, F. T., Jr.; Frainer, L.; Miller, S. A.; Schechter, H. *J. Am. Chem. Soc.* **1970**, *92*, 4689.

(2) (a) Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 3907; **1975**, *97*, 3447. (b) Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3107.

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

(4) (a) Keeffe, J. R.; Munderloh, N. H. *J. Chem. Soc., Chem. Commun.* **1974**, 17. (b) Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1295.

(5) Wilson, J. C.; Källsson, I.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 4780.

(6) Kurz, J. L. *J. Am. Chem. Soc.* **1989**, *111*, 8631.

(7) (a) Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J. X. *J. Org. Chem.* **1988**, *53*, 3342. (b) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1989**, *111*, 5893. (c) Gandler, J. R.; Bernasconi, C. F. *J. Am. Chem. Soc.* **1992**, *114*, 631. (d) Bernasconi, C. F.; Fassberg, J. *J. Am. Chem. Soc.* **1994**, *116*, 514.

(8) The intrinsic barrier (intrinsic rate constant) for a reaction with a forward rate constant k_1 and a reverse rate constant k_{-1} is defined as $\Delta G_0^\ddagger = \Delta G_1^\ddagger = \Delta G_{|\mathrm{Pv}|}^\ddagger$ when $\Delta G^\circ = 0$ ($k_0 = k_1 = k_{-1}$ when $K_1 = 1$). For proton transfers statistical factors are usually included, see below.

(9) (a) Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948. (b) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.

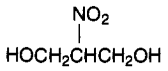
(10) (a) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301; **1992**, *25*, 9.

(11) Streitwieser, A., Jr.; Hammons, J. H. *Prog. Phys. Org. Chem.* **1965**, *3*, 43.

0002-7863/95/1517-9206$09.00/0

$HOCH_2CH_2NO_2$

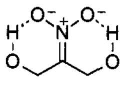
2



$HOCH_2CH(NO_2)CH_2OH$

3

motivation for this study was to examine the potential effect of intramolecular hydrogen bonding in the nitronate ion on the acidity of **2** and **3** and their rates of deprotonation by various bases. According to a report by Herman and ApSimon,[12] the synthesis of 2-nitro-1,3-propanediol leads to the aci-form believed to be stabilized by two intramolecular hydrogen bonds from the OH group to the nitro group. This implies that intramolecular hydrogen bonding in the nitronate ion, **4**, might



4

be very strong and have a substantial effect on the pK_a and proton transfer rate of **3** and perhaps of **2** as well. Our results suggest that such hydrogen bonding may indeed be present even in aqueous solution, although the effect is not dramatic and our data are equally consistent with hyperconjugative stabilization of the nitronate ion by the CH_2OH group, or a combination of the two. However, the interplay between this hydrogen bonding and/or hyperconjugation on the one hand and the inductive effect of the CH_2OH group on the other will be shown to lead to interesting structure–reactivity relationships that are relevant to both types of "nitroalkane anomalies" mentioned above. Our study also deals with a question that has remained unexplored, namely whether the decrease in the rate constants in the order nitromethane > nitroethane > 2-nitropropane may, at least in part, reflect a steric effect.

Results

Synthesis of 2-Nitro-1,3-propanediol (3). The title compound was synthesized both by the method of Herman and ApSimon[12] and that of Seebach and Knochel.[13] The major difference between the two procedures is that in the former paraformaldehyde is condensed with nitromethane in the presence of catalytic amounts of KF and n-Bu_4NCl under neutral conditions, whereas in the latter the sodium salt is first generated in NaOMe/MeOH and then acidified. The product obtained by the method of Herman and ApSimon had spectral characteristics similar to those reported by these authors and interpreted as indicative of the aci-form of 2-nitro-1,3-propanediol. In particular, the ^1H NMR showed only two signals, a doublet at 3.73 ppm for the CH_2 protons and a triplet at 4.95 ppm for the OH protons, but no signal for a CH proton. In contrast, the ^1H NMR for the product obtained by the method of Seebach and Knochel showed a triplet at 3.62 ppm for the CH_2 protons,[14] a quintuplet at 4.56 ppm for the CH proton, and a triplet at 5.09 ppm for the OH protons, consistent with the nitro-form of **3**.

When dissolved in basic aqueous solution samples of **3** synthesized by the two methods yielded the same UV spectra. Most kinetic measurements were performed with the sample synthesized by the method of Seebach and Knochel; in the cases where determinations were made with both samples the results were the same within experimental error.

Kinetics of Proton Transfer. All measurements were made in aqueous solution at 25 °C and an ionic strength of 0.5 M maintained by KCl. Rates were determined in KOH, amine buffers, carboxylate buffers, and HCl solutions. Pseudo-first-order conditions with the nitro compound as the minor component were used throughout. In KOH solution the reactions can be described by eq 1, while the pseudo-first-order rate constant is given by eq 2.

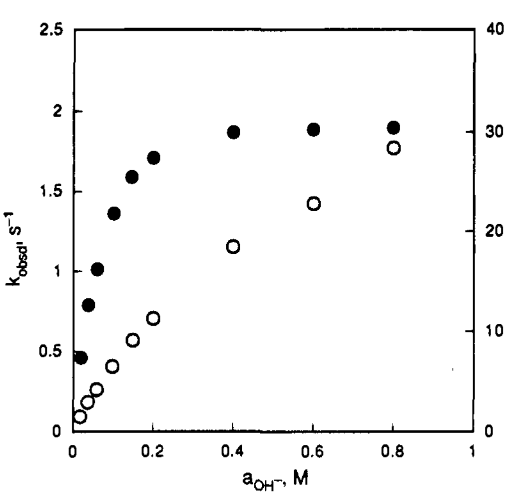


Figure 1. Plots according to eq 2 for the reactions of OH^- with 2-nitroethanol (○, right Y axis) and 2-nitro-1,3-propanediol (●, left Y axis).

$$^{-}OCH_2CH(R)NO_2 \underset{K_{OH}a_{OH^-}}{\rightleftharpoons} HOCH_2CH(R)NO_2 \xrightarrow{k_1^{OH}a_{OH^-}} HOCH_2C(R){=}NO_2^- \qquad (1)$$

$$R = H \text{ or } HOCH_2$$

$$k_{obsd} = \frac{k_1^{OH}a_{OH^-}}{1 + K_{OH}a_{OH^-}} \qquad (2)$$

Figure 1 shows plots of k_{obsd} vs a_{OH^-} obtained in KOH solutions for **2** and **3**, respectively. The curvature in these plots clearly indicates that, at high pH, ionization of the hydroxyl group is significant and, for **3**, the K_{OH} equilibrium is almost completely shifted to the alkoxide ion form when $a_{OH^-} > 0.2$ M. The k_1^{OH} and K_{OH} values determined from inversion plots of $1/k_{obsd}$ vs $1/a_{OH^-}$ are summarized in Table 1.

In principle, one would expect that the alkoxide ion also undergoes deprotonation, to form $^{-}OCH_2C(R){=}NO_2^-$. If this were a significant reaction, k_{obsd} for **3** would not reach a plateau ($k_{obsd} = k_1^{OH}/K_{OH}$ for $K_{OH}a_{OH^-} \gg 1$) but would continue to increase with increasing a_{OH^-}, with a slope of k_2^{OH}, the rate constant for deprotonation of $^{-}OCH_2CH(NO_2)CH_2OH$ by OH^-. No such increase is apparent, though. If one assumes an error of 3% in the individual k_{obsd} values, a slope in the high concentration region of the plot of ≥ 0.3 M^{-1} s^{-1} should have been detectable. Hence, the absence of such a slope implies that $k_2^{OH} \leq 0.3$ M^{-1} s^{-1}, i.e., less than 1% of k_1^{OH} (30.7 M^{-1} s^{-1}).

In basic amine buffers the reactions conform to eq 3 with k_{obsd} being given by eq 4. Plots of k_{obsd} vs free amine concentration ([B]), typically consisting of 6 to 10 points, gave

$$HOCH_2CH(R)NO_2 \underset{k_{-1}^{H_2O} + k_{-1}^{BH}[BH]}{\overset{k_1^{OH}a_{OH^-} + k_1[B]}{\rightleftharpoons}} HOCH_2C(R){=}NO_2^- \qquad (3)$$

$$k_{obsd} = k_1^{OH}a_{OH^-} + k_{-1}^{H_2O} + k_1^{B}[B] + k_{-1}^{BH}[BH] \qquad (4)$$

---

(12) Herman, L. W.; ApSimon, J. W. *Tetrahedron Lett.* **1985**, *26*, 1423.

(13) Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1982**, *67*, 261.

(14) The triplet for the CH_2 protons arises from the fact that the coupling constants for CH–CH_2 and HO–CH_2 coupling are apparently about the same (≈10 Hz).

Table 1. Summary of Rate and Equilibrium Constants of Proton Transfers from 2-Nitroethanol and 2-Nitro-1,3-propandiol in Water at 25 °C[a]

	pK_a^{BH}	$HOCH_2CH_2NO_2$ (**2**)	$HOCH_2CH(NO_2)$-CH_2OH (**3**)
pK_a^{CH}		9.40	9.07
K_{OH} (pK_a^{OH})[b]		2.52 (13.33)	13.5 (12.60)
pK_a^{NOH}		≈3.29	≈3.27
k_1^{OH}, $M^{-1}\,s^{-1}$	15.46	87.0	30.7
$k_{-1}^{H_2O}$, s^{-1}	15.46	4.09×10^{-3}	6.75×10^{-4}
k_1^{Pip}, $M^{-1}\,s^{-1}$	11.40	7.07	2.19
$k_{-1}^{PipH^+}$, $M^{-1}\,s^{-1}$	11.40	7.07×10^{-2}	1.02×10^{-2}
k_1^{Mor}, $M^{-1}\,s^{-1}$	8.78	0.163	7.29×10^{-2}
$k_{-1}^{MorH^+}$, $M^{-1}\,s^{-1}$	8.78	0.679	0.142
$k_1^{BuNH_2}$, $M^{-1}\,s^{-1}$	10.84	0.711	0.25
$k_{-1}^{BuNH_3^+}$, $M^{-1}\,s^{-1}$	10.84	2.58×10^{-2}	4.25×10^{-3}
k_1^{ME},[c] $M^{-1}\,s^{-1}$	9.63		4.67×10^{-2}
$k_{-1}^{MEH^+}$,[c] $M^{-1}\,s^{-1}$	9.63		1.29×10^{-2}
k_1^{GLA},[d] $M^{-1}\,s^{-1}$	8.18	1.54×10^{-2}	8.73×10^{-3}
$k_{-1}^{GLAH^+}$,[d] $M^{-1}\,s^{-1}$	8.18	2.49×10^{-1}	6.78×10^{-2}
k_1^{GLE},[e] $M^{-1}\,s^{-1}$	7.67	8.09×10^{-3}	3.98×10^{-3}
$k_{-1}^{GLEH^+}$,[d] $M^{-1}\,s^{-1}$	7.67	4.24×10^{-1}	9.99×10^{-2}
$k_1^{HONH_2}$, $M^{-1}\,s^{-1}$	6.12	2.15×10^{-3}	1.09×10^{-3}
$k_{-1}^{HONH_3^+}$, $M^{-1}\,s^{-1}$	6.12	4.01	9.40×10^{-1}
k_1^{CMA},[f] $M^{-1}\,s^{-1}$	5.52	4.38×10^{-4}	2.32×10^{-4}
$k_{-1}^{CMAH^+}$,[f] $M^{-1}\,s^{-1}$	5.52	3.32	8.23×10^{-1}
$k_1^{AcO^-}$, $M^{-1}\,s^{-1}$	4.61	1.74×10^{-4}	7.25×10^{-5}
k_{-1}^{AcOH}, $M^{-1}\,s^{-1}$	4.61	10.5	2.09
$k_1^{MeOAcO^-}$, $M^{-1}\,s^{-1}$	3.40	2.44×10^{-5}	1.02×10^{-5}
$k_1^{MeOAcOH}$, $M^{-1}\,s^{-1}$	3.40	23.7	4.73
$k_1^{ClAcO^-}$, $M^{-1}\,s^{-1}$	2.66	9.13×10^{-6}	1.96×10^{-6}
k_{-1}^{ClAcOH}, $M^{-1}\,s^{-1}$	2.66	47.9	5.05
$k_1^{H_2O}$, s^{-1}	−1.74	2.11×10^{-7}	9.70×10^{-7}
$k_{-1}^{H^+}$, $M^{-1}\,s^{-1}$	−1.74	5.32×10^{2}	1.14×10^{3}

[a] $\mu = 0.5$ M (KCl). [b] Based on $K_w = 1.87 \times 10^{-14}$ M^2: Harned, H. S.; Owen, B. B. *The Physical Chemistry of Electrolytic Solutions*; Reinhold: New York, 1950; p 488. [c] ME = 2-methoxyethylamine. [d] GLA = glycinamide. [e] GLE = glycine ethyl ester. [f] CMA = cyanomethylamine.

excellent straight lines whose slopes are given by eq 5,[15] with

$$\text{slope} = k_1^B\left(1 + \frac{a_{H^+}}{K_a^{CH}}\right) \tag{5}$$

K_a^{CH} referring to the carbon pK_a of the nitro compound. Based on the pK_a^{CH} values (see Experimental Section), k_1^B could then be obtained from eq 5. The k_1^B and $k_{-1}^{BH} = k_1^B K_a^B / K_a^{CH}$ values, with K_a^{BH} being the acid dissociation constant of BH, are reported in Table 1.

In acidic amine and carboxylate buffers and in HCl solutions the reactions were conducted in the reverse direction, i.e., by reacting the nitronate ion with the acidic buffer. In this situation rapid protonation of the nitro group acts as a pre-equilibrium as shown in eq 6. Here k_{obsd} is given by eq 7. Data obtained in HCl solutions, plotted according to eq 8, are shown in Figure 1S (supporting information).[16] Included in the figure are

$$HOCH_2CH(R)NO_2 \xleftarrow{k_{-1}^{H}a_{H^+} + k_{-1}^{BH}[BH]}$$
$$HOCH_2C(R){=}NO_2^- \underset{K_a^{NOH}}{\overset{H^+}{\rightleftharpoons}} HOCH_2C(R){=}NO_2H \tag{6}$$

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

$$\frac{1}{k_{obsd}} = \frac{1}{k_{-1}^{H}K_a^{NOH}} + \frac{1}{k_{-1}^{H}a_{H^+}} \tag{8}$$

intercepts of plots (not shown) of k_{obsd} *vs* methoxyacetic acid concentration at three different pH values. Analysis according to eq 8 yields $pK_a^{NOH} = 3.44 \pm 0.02$ for **2** and 3.60 ± 0.02 for **3**, and $k_{-1}^{H} = 532 \pm 15$ $M^{-1}\,s^{-1}$ for **2** and 1140 ± 22 $M^{-1}\,s^{-1}$ for **3**. The low standard deviations for the k_{-1}^{H} and pK_a^{NOH} values are probably not a reliable indicator of the accuracy of these parameters because of the relatively limited pH range from which the data were obtained. Extension of this range toward higher pH values was impractical because the intercepts of buffer plots at higher pH become too small for a reliable determination. In fact even the intercepts from the methoxyacetic buffer data are quite small and have an uncertainty of 10 to 20%; their relatively good fit with the HCl data in Figure 1S[16] might therefore be fortuitous.

The slopes of the methoxyacetic acid buffer plots provided a second method for the determination of pK_a^{NOH}. A plot (not shown) of the inverse slopes *vs* a_{H^+} according to eq 9 at pH

$$\frac{1}{\text{slope}} = \frac{1}{k_{-1}^{BH}} + \frac{a_{H^+}}{K_a^{NOH}k_{-1}^{BH}} \tag{9}$$

3.09, 3.40, and 3.69 yields $pK_a^{NOH} = 3.29 \pm 0.05$ for **2** and 3.27 ± 0.04 for **3**, while $k_{-1}^{BH} = 23.7 \pm 1.3$ $M^{-1}\,s^{-1}$ for **2** and 4.73 ± 0.24 $M^{-1}\,s^{-1}$ for **3**. The pK_a^{NOH} values obtained via eq 9 are somewhat lower than those obtained via eq 8 although the differences are not very large and the similarity of the pK_a^{NOH} values determined by the two methods indicates that our data are internally consistent. Since the pK_a^{NOH} values calculated via eq 8 are based on a larger data set which spans a wider pH range than those determined via eq 9, they will be adopted as the actual pK_a^{NOH} values.

A number of experiments were performed with acetic acid and chloroacetic acid buffers. The k_{-1}^{BH} values were obtained from the slopes of plots according to eq 7, in which k_{-1}^{BH} is the only unknown.

Reaction of Nitromethane with Piperidine, Morpholine, and Acetate Ion. Rate constants for reversible deprotonation of nitromethane by piperidine, morpholine, and acetate ion have been obtained previously at 20 °C.[7a] For purposes of comparison with **2** and **3**, the rate constants for the nitromethane reactions were redetermined at 25 °C by the same methodology described earlier.[7a] They are $k_1^B = 5.68$ $M^{-1}\,s^{-1}$ and $k_{-1}^{BH} = 0.338$ $M^{-1}\,s^{-1}$ for piperidine, $k_1^B = 0.119$ $M^{-1}\,s^{-1}$ and $k_{-1}^{BH} = 2.99$ $M^{-1}\,s^{-1}$ for morpholine, and $k_1^B = 8.94 \times 10^{-5}$ $M^{-1}\,s^{-1}$ and $k_{-1}^{BH} = 36.4$ $M^{-1}\,s^{-1}$ for acetate ion.

Discussion

Brønsted β-Values and Intrinsic Rate Constants. All rate and equilibrium constants for the reactions of **2** and **3** are summarized in Table 1. Brønsted plots are shown in Figure 2 for **2** and Figure 3 for **3**, with the parameters determined from the Brønsted plots, β, and the intrinsic rate constant reported as log k_0, given in Table 2. The Brønsted plots were obtained

---

[15] The $k_1^B a_{H^+}/K_a^{CH}$ term in eq 5 comes from $k_{-1}^{BH}[BH] = k_{-1}^{BH}[B]a_{H^+}/K_a^{BH}$ and $k_{-1}^{BH}/K_a^{BH} = k_1^B/K_a^{CH}$.

[16] See paragraph concerning supporting information at the end of this paper.

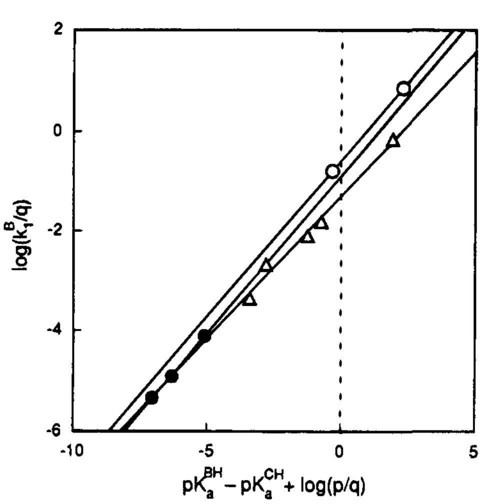


Figure 2. Brønsted plots for the reaction of 2-nitroethanol with amines and carboxylate ions: (○) piperidine/morpholine; (△) 1°RNH_2; (●) $RCOO^-$. The points where the Brønsted lines intersect with the dashed vertical line correspond to log k_0.

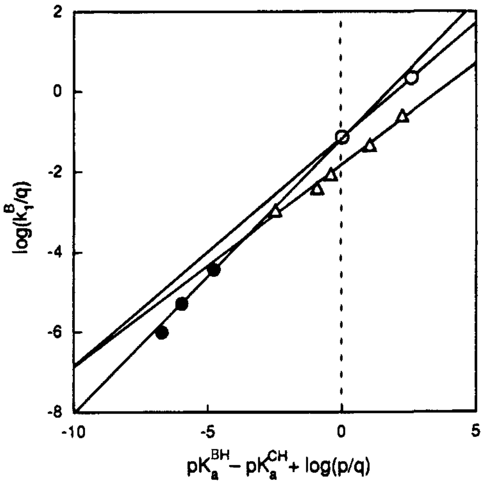


Figure 3. Brønsted plots for the reaction of 2-nitro-1,3-propandiol with amines and carboxylate ions: (○) piperidine/morpholine; (△) 1°RNH_2; (●) $RCOO^-$. The points where the Brønsted lines intersect with the dashed vertical line correspond to log k_0.

Table 2. Brønsted β Values and Intrinsic Rate Constants

parameter	$HOCH_2CH_2NO_2$ (**2**)	$HOCH_2CH(NO_2)CH_2OH$ (**3**)
β(pip/mor)	0.62^a	0.56
log k_0(pip/mor)	-0.59^a $(-0.70)^{a,b}$	-1.14
β(1°RNH_2)	0.57 ± 0.04	0.54 ± 0.03
log k_0(1°RNH_2)	-1.30 ± 0.09 $(-1.43)^b$	-1.84 ± 0.06
β($RCOO^-$)	0.64 ± 0.03	$0.70^{a,c}$
log k_0($RCOO^-$)	-0.90 ± 0.14 $(-1.01)^b$	$-1.09^{a,c}$

[a] No standard deviation can be calculated but error may be assumed to be similar to that for the other corresponding parameters. [b] Statistically corrected for the fact that **2** has two equivalent protons while **3** has only one. [c] Based on AcO^- and $MeOCH_2COO^-$ only.

by applying the usual statistical factors to the buffer, i.e., p = number of equivalent protons on BH and q = number of equivalent basic sites on B. For better comparison between **2**, **3**, and other nitroalkanes such as nitromethane (see below), log k_0 values were also determined by applying an additional statistical correction that takes into account the different number of equivalent acidic protons in the various nitroalkanes.[17] The values in parentheses in Table 2 reflect this additional correction.

The β values for both **2** and **3** are well within the range usually observed for the deprotonation of nitroalkanes[2,4a,7a,c,18-20] as well as for many other carbon acids activated by strong π-acceptors.[20] In particular, the fact that the β-values for primary and secondary alicyclic amines are comparable and that β for the carboxylate ions is somewhat higher than for amines is quite generally observed. We also note that log k_0(pip/mor) is about 0.7 log units higher than log k_0(1 °RNH_2). This reflects a well-known phenomenon[20] that has been explained by the stronger solvation of the conjugate acid of primary amines compared to that of secondary amines, coupled with late development of this solvation along the reaction coordinate.[17,21]

A difference between log k_0(pip/mor) and log k_0(1°RNH_2) on the order of 0.7 to 1.0 log units is generally taken as evidence that the proton transfer to these amines is not severely affected by steric crowding in the transition state.[20,22] On the other hand, differences in log k_0 of substantially less than that are interpreted as arising from significant steric hindrance which reduces log k_0 for the sterically bulkier secondary amines more strongly than log k_0 for the primary amines.[23,24] Based on this criterion, the difference of about 0.7 log units between log k_0(pip/mor) and log k_0(1°RNH_2) in the deprotonation of **2** and **3** suggests that, if steric effects are present, they cannot be very severe. Another indication that steric effects cannot be dramatic is the fact that the difference between log k_0(pip/mor) and log k_0(1°RNH_2) is almost the same for **2** and **3**, even though **3** is significantly bulkier than **2**. However, below it will be shown that in the deprotonation of **3** steric effects are not completely negligible.

Comparison of the Effects of the CH_2OH and CH_3 Groups on Reactivity. The most interesting conclusions from this study relate to the large differences in how the CH_2OH and CH_3 groups affect pK_a^{CH}, pK_a^{NOH}, and the rates of proton transfer. The relevant parameters are summarized in Table 3.

Substitution of one or two hydrogens in nitromethane by a methyl group lowers pK_a^{CH} substantially, from 10.22 to 8.60 to 7.68. The effect is even more dramatic when the statistically corrected pK_a^{CH} values are used (10.70, 8.90, and 7.68, respectively). As mentioned in the Introduction, this increase in acidity has been attributed to hyperconjugation (**1a** ↔ **1b**) which more than offsets any polar effect from the methyl groups.

Replacement of the hydrogens with a CH_2OH group also lowers pK_a^{CH}, but less than with a CH_3 group. There are three factors that may contribute to the increased acidity of **2** and **3**. One is the inductive effect of the CH_2OH group. It is doubtful, though, that this factor can account for the bulk of the acidifying effect, since by most measures the inductive effect of the CH_2OH group is quite weak. This is reflected, for example, in the small values of the Hammett σ_m, the σ_I, and Swain–Lupton F

---

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

(18) (a) Gregory, M. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1967**, *89*, 2327. (b) Bruice, P. Y. *J. Am. Chem. Soc.* **1984**, *106*, 5959.

(19) Bernasconi, C. F.; Wiersema, D.; Stronach, M. W. *J. Org. Chem.* **1993**, *58*, 217.

(20) For a recent review, see refs 10a and 10b.

(21) Jencks, W. P. *Catalysis in Chemistry and Enzymology*: McGraw-Hill: New York, 1969; p 178.

(22) (a) Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 4343. (b) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (c) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969. (d) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1987**, *109*, 7115. (e) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1990**, *112*, 8448. (f) Bernasconi, C. F.; Ohlberg, D. A. A.; Stronach, M. W. *J. Org. Chem.* **1991**, *56*, 3016.

(23) (a) Bernasconi, C. F.; Bunnell, R. D.; Terrier, F. *J. Am. Chem. Soc.* **1988**, *110*, 6514. (b) Bernasconi, C. F.; Fairchild, D. E. *J. Phys. Org. Chem.* **1992**, *5*, 409. (c) Bernasconi, C. F.; Sun, W. *J. Am. Chem. Soc.* **1993**, *115*, 12526.

(24) Farrell, P. G.; Terrier, F.; Xie, H.-Q.; Boubaker, T. *J. Org. Chem.* **1990**, *55*, 2546.

Table 3. Comparison of Rate and Equilibrium Constants of Proton Transfers from Various Nitroalkanes in Water at 25 °C

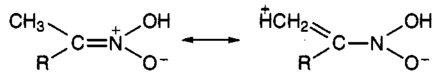
	CH_3NO_2	$HOCH_2CH_2NO_2$ (**2**)	$HOCH_2CH(NO_2)CH_2OH$ (**3**)	$CH_3CH_2NO_2$	$CH_3CH(NO_2)CH_3$
pK_a^{CH}	10.22[b]	9.40	9.07	8.60[b]	7.68[c]
pK_a^{CH}(corr)[a]	10.70	9.70	9.07	8.90	7.68
pK_a^{NOH}	3.25[c]	3.44	3.60	4.40[c]	5.10[c]
k_1^{OH}, $M^{-1}\ s^{-1}$	27.6[d]	87.0	30.7	5.19[d]	0.316[d]
k_1^{OH}(corr),[a] $M^{-1}\ s^{-1}$	9.2	43.5	30.7	2.60	0.316
$k_1^{AcO^-}$, $M^{-1}\ s^{-1}$	8.94×10^{-5}	1.55×10^{-4}	7.25×10^{-5}	3.24×10^{-5} [e]	2.69×10^{-6} [e]
$k_1^{AcO^-}$(corr),[a] $M^{-1}\ s^{-1}$	2.98×10^{-5}	8.68×10^{-5}	7.25×10^{-5}	1.62×10^{-5}	2.69×10^{-6}
k_1^{Mor}, $M^{-1}\ s^{-1}$	0.119	0.163	7.29×10^{-2}		
k_1^{Mor}(corr),[a] $M^{-1}\ s^{-1}$	0.040	0.082	7.29×10^{-2}		
k_1^{Pip}, $M^{-1}\ s^{-1}$	5.68	7.07	2.19	<0.653[f]	
k_1^{Pip}(corr),[a] $M^{-1}\ s^{-1}$	1.89	3.53	2.19	<0.326	

[a] Statistically corrected, see text. [b] Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439. [c] Nielsen, A. J. In *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Wiley-Interscience: New York, 1969; Vol. 1, p 349. [d] Bell, R. P.; Goodall, D. M. *Proc. R. Soc. London (A)* **1966**, *294*, 273. [e] Cox, B. G.; Gibson, A. *Faraday Symp. Chem. Soc.* **1975**, *10*, 107. [f] Reference 18a, value given is at 30 °C.

constants of the CH_2OH group.[25] It is also evident from the fact that the statistically corrected pK_a of ethylene glycol (15.1)[27] is only 0.4 unit lower than that of methanol (15.5),[27] even though the negative charge in the anion of ethylene glycol is one atom closer.

A second factor that may contribute to the enhanced acidity of **2** and **3** is intramolecular hydrogen bonding in the nitronate ion, as shown, e.g., in **4**. It is plausible that this factor would mainly affect pK_a^{CH} while the effect on pK_a^{NOH} should be small because the aci-form can also be stabilized by intramolecular hydrogen bonding. Support for the hydrogen bonding hypothesis comes from two observations. One is that the aci-form of **3** is stable enough to be isolated. The other is that in 90% Me_2SO–10% water even *inter*molecular hydrogen bonding complexes between protonated amines and nitronate ions such as $CH_2{=}NO_2^-$ and $PhCH{=}NO_2^-$ are readily formed.[7a]

Even though suggestive, the above observations do not prove intramolecular hydrogen bonding is a dominant factor in affecting pK_a^{CH} and pK_a^{NOH}. If it were, one would expect that the aci-form of CH_3NO_2 should have the highest pK_a^{NOH} because there is no hydrogen bonding, while that of **3** should have the lowest pK_a^{NOH} because the anion has two intramolecular bonds whereas the aci-form has only one. This contrasts with the fact that, even though the pK_a^{NOH} values differ very little, the trend is in the direction CH_3NO_2 < **2** < **3**. Hence, another factor must play a more important role. This factor is best appreciated by changing the point of reference, i.e., instead of focusing on the fact that **2** and **3** have lower pK_a^{CH}-values than CH_3NO_2, we note that **2** is 0.8 pK unit less acidic than nitro*ethane* and **3** is 1.4 pK unit less acidic than 2-nitropropane.[28] This suggests that conversion of a methyl into a CH_2OH group reduces the hyperconjugative stabilization of the nitronate ion but does not annihilate it, i.e., the third factor is residual hyperconjugation by the CH_2OH group. This interpretation can also account for the trend in the pK_a^{NOH} values of CH_3NO_2, **2**, and **3**, and also for the fact that there is a further increase in pK_a^{NOH} for nitroethane and 2-nitropropane. Indeed, this trend finds a natural explanation if one assumes that hyperconjugative stabilization of the aci-form is greater than that of the nitronate ion. This assumption is not unreasonable if one compares **1b** with **5b**: **1b** is likely to be destabilized by the repulsive interaction of the two negative charges, a feature that does not affect **5b**.



5a **5b**

In conclusion, inductive electron withdrawal by the CH_2OH group cannot account for its entire acidifying effect on **2** and **3**; stabilization of the nitronate ion by hyperconjugation and possibly by intramolecular hydrogen bonding must contribute significantly. Further support for this conclusion comes from the *rate constants* of proton transfer. The factors expected to affect these rate constants include not only the inductive effect, hyperconjugation, and intramolecular hydrogen bonding but also interactions present only at the transition state such as steric crowding and a field effect interaction between the charge on the proton acceptor and the CH_2OH group. In assessing the relative importance of these factors a basic premise is that charge delocalization into the nitro group invariably lags behind proton transfer at the transition state.

(1) The inductive effect of a group attached to the α-carbon should be relatively strong since the negative charge at the transition state is substantially localized on the α-carbon. According to Kresge's[3] estimates, the change in rate resulting from this inductive effect may be as large or larger than the change in pK_a^{CH} arising from the same effect. Thus, if the entire pK_a^{CH}(corr) difference of one unit between **2** and nitromethane were due to an inductive effect, this should lead to 10-fold or even larger rate enhancement.

(2) In contrast to the inductive effect, both hyperconjugation and intramolecular hydrogen bonding should be weakly developed at the transition state. Using Kresge's[3] figures, the transition state stabilization energy from hyperconjugation may be from about one-third to as little as one-sixth of the stabilization enjoyed by the nitronate ion. The situation is likely to be similar for hydrogen bonding.[10a,30] Hence, the rate enhancement that would arise from these effects is expected to be relatively small, perhaps a factor of 2 or less for a pK_a^{CH} decrease of 1 unit.

---

(25) $\sigma_m = 0.0$,[26] $\sigma_I = 0.11$,[26] $F = 0.03$.[26]

(26) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(27) Ballinger, P.; Long, F. A. *J. Am. Chem. Soc.* **1960**, *82*, 795.

(28) We are indebted to a reviewer for pointing out that Hine's double bond stabilization parameter is 0.6 kcal/mol smaller for a $MeOCH_2$ group than for an n-alkyl group.[29] Our results indicate a somewhat larger difference (0.95 to 1.1 kcal/mol) between a $HOCH_2$ and a methyl group.

(29) Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley-Interscience: New York, 1975; p 273.

(30) (a) Bernasconi, C. F.; Kanavarioti, A. *J. Am. Chem. Soc.* **1986**, *108*, 7744. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.

(31) Charton, M. The Quantitative Description of Steric Effects. *Stud. Org. Chem. (Amsterdam)* **1991**, *42*, 629.

(3) The field effect interaction between the CH_2OH group and the charge on the proton acceptor will destabilize the transition state in the reactions with amines because of the incipient positive charge on the proton acceptor but stabilize it in reactions with negatively charged bases (OH^-). The magnitude of this effect can be significant even for an α-group with a modest inductive effect. Kresge[3] has estimated a transition state destabilization of about 0.6 kcal/mol for the interaction of an α-methyl group with OH^-. In the case of a carboxylate ion as proton acceptor the effect should be smaller because of greater dispersion of the negative charge.

(4) Steric crowding in the transition state should lower the rate constants.

On the basis of the above predictions the following conclusions may be drawn from the observed trends in the rate constants.

(a) Substitution of one hydrogen in nitromethane by a CH_2OH group increases k_1^{OH}(corr) 4.7-fold while the acidity increases 10-fold. On a Brønsted plot of log k_1^{OH}(corr) vs log K_a^{CH}(corr) (more on this below) this corresponds to $\alpha = 0.67$. If all or most of the increase in acidity were due to an inductive effect, the increase in k_1^{OH}(corr) should be substantially larger than 4.7-fold, or α larger than 0.67, not only for the reasons stated under (1) but also because a strong inductive effect would imply a strong transition state stabilization by interaction of the CH_2OH group with OH^-, as described under (3). A case in point is the reaction of substituted phenylnitromethanes with OH^-, where all changes in pK_a^{CH} are due to inductive effects and $\alpha = 1.54$.[2a]

Incidentally, the importance of the field effect interaction between the CH_2OH group and OH^- in the transition state can be seen from the fact that k_1^{AcO}(corr) for **2** is only about 3-fold and k_1^{Pip}(corr) and k_1^{Mor}(corr) only about 2-fold higher than for nitromethane, respectively. These lower reactivity ratios compared to the reactions with OH^- may be attributed to the reduced transition state stabilization by the field effect interaction with the more dispersed negative charge of the acetate ion and to a transition state *de*stabilization in the reactions with amines, respectively. In the deprotonation of substituted phenylnitromethanes by morpholine the same kind of transition state destabilization manifests itself in a lowering of the Brønsted α value from 1.54 in the reaction with OH^- to 1.29 for the morpholine reaction.[2a]

The above analysis, according to which the increase in k_1^{OH}(corr) for **2** compared to nitromethane is smaller than one would expect if most of the enhanced acidity of **2** were due to an inductive effect of the CH_2OH group, corroborates our earlier conclusion that hyperconjugation and perhaps intramolecular hydrogen bonding must play a significant role in the higher acidity of **2**. On the other hand, the increase in k_1^{OH}(corr) in going from nitromethane to **2** seems too large to be *solely* accounted for by hyperconjugation and intramolecular hydrogen bonding, i.e., there must be contributions by the inductive effect and the field effect interaction of the CH_2OH group with OH^- in the transition state.

(b) The substitution of a second hydrogen by a CH_2OH group leads to small *de*creases in k_a^{OH}(corr), k_1^{AcO}(corr), and k_1^{Pip}(corr), even though the acidity increases by 0.63 p*K* unit. This indicates the operation of a steric effect. The fact that the decreases are quite similar for the three bases (1.42-fold for OH^-, 1.20-fold for AcO^-, and 1.61-fold for piperidine) is perhaps somewhat surprising but may be a consequence of small differences in transition state geometry.[31] These could significantly affect the magnitude of the steric effect, thereby masking expected differences in other effects such as the field effect interactions between the CH_2OH groups and the charge on the proton acceptor. The magnitude of the steric effect on the reaction with OH^- may be estimated from a Brønsted plot of log k_1^{OH}(corr) vs log K_a^{CH}(corr) for nitromethane, **2**, and **3** shown in Figure 4. Assuming that in the absence of a steric effect the point for **3** would lie on the line defined by nitroethane and **2**, the steric rate reduction amounts to a factor of 3.7.

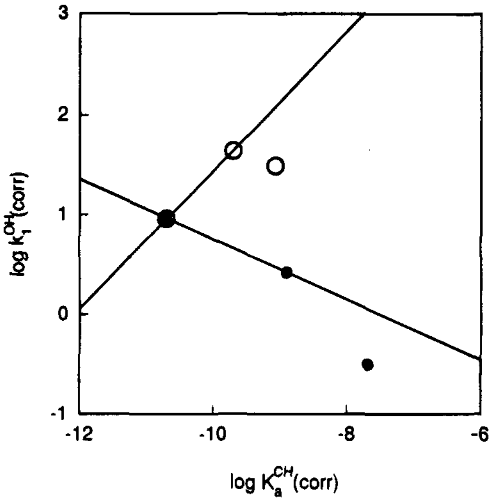


Figure 4. Brønsted plots for the deprotonation of nitroalkanes by OH^-: (○) nitromethane, 2-nitroethanol, and 2-nitro-1,3-propandiol; (●) nitromethane, nitroethane, and 2-nitropropane.

The fact that the reaction of **3** is subject to steric retardation suggests that deprotonation of 2-nitropropane may also suffer from such an effect. The negative deviation of 2-nitropropane from the Brønsted line defined by nitromethane and nitroethane (Figure 4) suggests a rate reduction of 3.5-fold, almost the same as for **3**. This steric effect was not taken into account by Kresge[3] in calculating a Brønsted α value of about −0.5. When it is taken into account, α becomes −0.3, still a substantially negative value, and hence Kresge's qualitative conclusions are not affected.

Acidity of the OH Groups. The pK_a^{OH} values of the alcoholic hydroxyl groups in **2** and **3** are 13.33 and 12.60, respectively, or, after statistical correction, 12.90 for **3**. These pK_a values mainly reflect the electron withdrawing inductive effect of the nitro group and, in the case of **3**, an additional small electron withdrawing effect by the CH_2OH group. They fit quite well on Ballinger and Long's[27] correlation of RCH_2OH acidities with σ^*.[33]

Deprotonation of $^-OCH_2CH(NO_2)CH_2OH$. The absence of any measurable contribution by the k_2^{OH} pathway, i.e., the deprotonation of $^-OCH_2CH(NO_2)CH_2OH$, to k_{obsd} at high pH (Figure 1) suggests $k_2^{OH} \leq 0.3\ M^{-1}\ s^{-1}$ or $k_2^{OH}/k_1^{OH} \leq 10^{-2}$. This ratio might seem unusually low but it is just another consequence of the imbalanced transition. In other words, due to the strong localization of the negative charge on the α-carbon, the electron donating inductive effect of the CH_2O^- group leads to destabilization of the transition state and the same is true for the field effect interaction between the CH_2O^- group and OH^-; in addition, there is a destabilizing electrostatic repulsion between the negative charge on the α-carbon and OH^-. Furthermore, intramolecular hydrogen bonding and hyperconjugative stabi-

---

[32] σ^* for CH_2NO_2 is assumed to be 1.60 based on the relationship $\sigma^*(CH_2NO_2) = \sigma_I(NO_2)/0.45^{33}$ and $\sigma_I(NO_2) = 0.72$.[33]

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

lization of $^{-}OCH_2C(=NO_2^{-})CH_2OH$ is expected to be smaller than in the reaction of **3**. All these factors decrease the k_2^{OH}/k_1^{OH} ratio.

Conclusions

The increase in the rate of proton transfer induced by substitution of one hydrogen in CH_3NO_2 by a CH_2OH group is tantamount to a "normal" Brønsted α value (α = 0.67 with OH^- and 0.31 with morpholine). This contrasts with the anomalous α values in the deprotonation of arylnitromethanes by OH^- (α = 1.54) or morpholine (α = 1.29) and α = −0.30 in the deprotonation of $CH_3CH_2NO_2$ vs CH_3NO_2 by OH^-. The normal α values for the nitromethane/2-nitroethanol pair do *not* mean that the reactions have balanced transition states. Rather they derive from the fact that the extent to which the three acidifying factors of the CH_2OH group, i.e., inductive effect, hyperconjugation, and intramolecular hydrogen bonding, are expressed at the transition state is quite different *because* of the imbalanced nature of the transition state.

Experimental Section

Materials. Nitromethane (Aldrich) was used as received. 2-Nitroethanol (Aldrich) was purified by vacuum distillation. 2-Nitro-1,3-propanediol was synthesized by the methods of Herman and ApSimon[12] and of Seebach and Knochel.[13] The product obtained by the first method is consistent with the aci-form, as reported by Herman and ApSimon: mp 163−165 °C (lit.[12] mp 63.2 °C). ^1H NMR (DMSO-d_6) δ 3.73 (4H, d, CH_2), 4.95 (2H, t, OH); after addition of one drop of CF_3COOH, δ 3.73 (s, CH_2), 9.80 (s, OH + COOH). MS, *m/e* (rel abundance, assignment): 121 (2.5, M), 104 (2.0, M−OH), 87 (6.7, M−2OH), 86 (7.0, M−OH−H_2O), 73 (22.1, M−OH−CH_2OH), 58 (18.0, M−OH−NO_2), 57 (100, M−H_2O−NO_2). The product obtained by the second method is consistent with the nitro-form: mp 52−53 °C (lit.[13] mp 53−55 °C). ^1H NMR (DMSO-d_6) δ 3.62 (4H, t, CH_2),[14] 4.56 (1H, q, CH), 5.09 (2H, t, OH). Note that the ^1H NMR spectrum in DMSO-d_6 was much cleaner than in acetone-d_6, the solvent used by Seebach and Knochel.[13]

Piperidine, morpholine, and *n*-butylamine were distilled over CaH_2 under nitrogen and stored in the cold and dark. Analytical grade acetic acid, methoxyacetic acid, chloroacetic acid, and 2-methoxyethylamine were used as received. Hydroxylamine hydrochloride, glycine methyl ester, and glycinamide were recrystallized from ethanol. Cyanomethylamine hydrochloride was recrystallized from boiling ethanol using activated charcoal as decolorizing agent. The hot filtered solution gave pure white crystals upon cooling.

pK_a Values. The pK_a values of 2-nitroethanol (**2**) and 2-nitro-1,3-propanediol (**3**) were determined spectrophotometrically at 240 (**2**) and 242 nm (**3**), respectively; at these wavelengths only the nitronate ion absorbs. This method yielded pK_a = 9.41 ± 0.01 for **2** and 9.07 ± 0.02 for **3**. For **2** a potentiometric determination afforded pK_a = 9.37 ± 0.01; the average, 9.39, has been adopted as the actual pK_a for **2**. The pK_a values of the various buffers at 0.5 M ionic strength were determined potentiometrically.

Kinetic Experiments. The kinetic experiments were performed as described previously;[7a] the reactions were monitored at 242 or 246 nm.

Acknowledgment. This research was supported by Grant Nos. CHE-8617370 and CHE-9307659 from the National Science Foundation.

Supporting Information Available: Figure S1, inversion plots according to eq 8 (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA951534G