ca. 10 eV and gave 80.2% α-d_3, 12.2% α-d_2, and 7.5% α-d_0 using the "preference factor" of 3.5 reported by Beynon et al.[22] in the calculation. *tert*-Butylbenzene was prepared by the method of Huston, Fox, and Bender[23] in 70% yield, bp 167.8-170.0°. This was distilled on the spinning-band column to afford a fraction in which no impurities could be detected by GLC. Commercial grade chlorobenzene was distilled in a jacketed Vigreux column and collected as a constant-boiling heart cut, bp 132°. Trichloroethylene was used as supplied as Baker Analyzed Reagent. *tert*-Butyl hypochlorite was prepared as previously described[13] with bp 79.0-80.0°.

Procedure. Relative reactivities were determined by competitive experiments using solutions of ca. 2 *M* in toluene or toluene-α-d_3, ca. 2 *M* in *tert*-butylbenzene, and 0.7 *M* in *tert*-butyl hypochlorite (plus 0.11 *M* in trichloroethylene in some runs) in chlorobenzene. The solution was placed in an ampoule, degassed by successive freezing in liquid nitrogen, evacuation, and thawing. The sealed ampoule was placed in an appropriate temperature bath and allowed to equilibrate. The solution was irradiated with a 275-W sunlamp, placed externally, and the temperature was followed with a thermocouple and maintained steady by addition of Dry Ice or ice as needed. Upon removal from the bath, completeness of reaction was checked by KI test. Analysis was carried out on an F & M Model 700 gas chromatograph using a 6 ft × ⅛ in. column packed with 5% XF-1150 and 5% Bentone 34 on Chromosorb W. Relative reactivities were obtained as previously described[13] using the chlorobenzene as an internal standard.

Acknowledgments. We thank Professor F. D. Greene of the Massachusetts Institute of Technology for valuable discussions and encouragement. We are indebted to the NSF-COSIP program and to the Southwestern Research and Creative Activities Committee for financial support.

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Kinetic Isotope Effects for Nitroalkanes and Their Relationship to Transition-State Structure in Proton-Transfer Reactions[1]

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Abstract: Primary isotope effects, k^H/k^D, have been determined for 1-phenylnitroethane and six of its meta substituted derivatives (pK_a's 6.0 to 7.5) with hydroxide ion, piperidine, diethylamine, and piperazine in water at 25°. A small increase in the ratio (from 7.2 to 9.6) was observed as ΔpK changed from −8.6 to −2.5. A secondary isotope effect of about 15% was observed for $PhCH_2NO_2$. A plot of log k^H/k^D vs. ΔpK using ten of these points and nine literature values gave a bell-shaped curve with gently sloping sides. Solvent isotope effects, k^{DO^-}/k^{HO^-}, were found to range around 1.35 for the parent, *m*-CH_3-, and *m*-ClArCHMeNO$_2$ compounds. Comparison of these values with those of other carbon acids showed that this ratio varied but little over wide ranges of ΔpK. In exoenergetic deprotonations, the k^H/k^D ratio and Brønsted coefficient are larger than expected for a reactant-like transition state while, for endoenergetic reactions, the effect of methyl substitution is generally to retard the deprotonation rate instead of accelerate it, as would be expected for a product-like transition state. These effects can be rationalized, however, by assuming a two-step mechanism, a rate-limiting deprotonation to form a pyramidal nitro carbanion followed by a rapid rehybridization to a planar nitronate ion. This mechanism also can accommodate inverse Brønsted correlations and Brønsted coefficients larger than one.

As part of a general study of the correlation of kinetic and equilibrium acidities of carbon acids, we have been examining various methods for assessing the transition-state structure in the deprotonation of nitroalkanes by bases.[1,3] Reactions of nitroalkanes with strong bases, such as hydroxide ion or methoxide ion, are strongly exoenergetic, which should lead to a "reactant-like" transition-state structure.[4] Evidence that the transition-state structure is not product-like in these instances comes from the finding of several examples of *negative* correlations between kinetic and equilibrium acidities.[3] For example, the increase in acidity (by 2.5 pK_a units in water) from CH_3NO_2 to Me_2CHNO_2 is no doubt caused primarily by the increased stability of the $Me_2C{=}NO_2^-$ ion, yet this stabilizing influence is not felt appreciably in the transition state for deprotonation by hydroxide ion, as may be judged by the 89-fold *slower* rate. Also, nitrocyclobutane is less acidic than nitrocyclopentane,[5] but this destabilizing influence is not felt appreciably in the deprotonation by lyate ion as may be judged by the *faster* rate for nitrocyclobutane.[5] (In 50% MeOH-H_2O, nitrocyclobutane has a 1.9 pK_a unit lower equilibrium acidity but reacts with lyate ion at a four-fold

Table I. Primary Kinetic Isotope Effects on the Reaction of 1-Aryl-1-nitroethanes, $ArCH(D)NO_2CH_3$, with Hydroxide Ion in Water

Substituent	$k^{H},^{a}$ M^{-1} sec^{-1}	$k^{D},^{a}$ M^{-1} sec^{-1}	k^H/k^D
m-CH_3	5.42 ± 0.02	0.744 ± 0.022	7.3 ± 0.2
H	6.47 ± 0.06	0.911 ± 0.004	7.1 ± 0.1
m-CH_3O	8.46 ± 0.04	1.13 ± 0.01	7.5 ± 0.1
m-Cl	17.5 ± 0.1	2.21 ± 0.01	7.9 ± 0.1
m-NO_2	42.7 ± 0.2	6.10 ± 0.07	7.0 ± 0.1
p-NO_2	57.9 ± 1.5	8.94 ± 0.07	6.5 ± 0.3
m,m'-$(NO_2)_2$	302 ± 10	42.7 ± 0.6	7.1 ± 0.3
$k_0{}^{b}$	(6.18)[c]	(0.864)[d]	7.2

[a] In H_2O at 25°. [b] Log k_0 is the intercept of the Hammett plot at $\sigma = 0.0$. [c] $\rho = 1.18$ ($r = 0.9999$). [d] $\rho = 1.19$ ($r = 0.9999$).

Table II. Primary Kinetic Isotope Effects on the Reaction of 1-Aryl-1-nitroethanes, $ArCH(D)NO_2CH_3$, with Piperidine in Water

Substituent	$10^1 \times k^{H},^{a}$ M^{-1} sec^{-1}	$10^2 \times k^{D},^{a}$ M^{-1} sec^{-1}	k^H/k^D
m-CH_3	4.57 ± 0.29	4.85 ± 0.08	9.4 ± 0.8
H	5.21 ± 0.15	5.68 ± 0.05	9.2 ± 0.4
m-CH_3O	6.24 ± 0.05	6.81 ± 0.07	9.2 ± 0.2
m-Cl	11.4 ± 1.3	12.6 ± 0.3	9.0 ± 1.2
m-NO_2	23.8 ± 1.9	28.5 ± 0.8	8.4 ± 0.9
p-NO_2	36.9 ± 0.3	47.4 ± 1.4	7.8 ± 0.3
m,m'-$(NO_2)_2$	148 ± 26	144 ± 3	10.3 ± 2
$k_0{}^{b}$	(4.98)[c]	(5.51)[d]	9.0

[a] In H_2O at 25°, $\mu = 0.10$. [b] Log k_0 is the intercept of the Hammett plot at $\sigma = 0.0$. [c] $\rho = 1.02$ ($r = 0.9995$). [d] $\sigma = 1.00$ ($r = 0.9997$).

Table III. Primary Kinetic Isotope Effects on the Reaction of 1-Aryl-1-nitroethanes, $ArCH(D)NO_2CH_3$, with Diethylamine in Water

Substituent	$10^1 \times k^{H},^{a}$ M^{-1} sec^{-1}	$10^2 \times k^{D},^{a}$ M^{-1} sec^{-1}	k^H/k^D
m-CH_3	1.87 ± 0.03	1.94 ± 0.09	9.6 ± 0.7
H	2.20 ± 0.06	2.22 ± 0.09	9.9 ± 0.7
m-CH_3O	2.74 ± 0.18	2.71 ± 0.14	10.1 ± 1.2
m-Cl	5.18 ± 0.24	5.54 ± 0.18	9.4 ± 0.7
m-NO_2	11.6 ± 1.1	12.1 ± 0.4	9.6 ± 1.2
p-NO_2	18.5 ± 0.9	19.1 ± 0.5	9.7 ± 0.7
m,m'-$(NO_2)_2$	54.7 ± 4.4	79.0 ± 6.3	9.6 ± 1.2
$k_0{}^{b}$	(2.19)[c]	(2.21)[d]	9.9

[a] In H_2O at 25°, $\mu = 0.10$. [b] Log k_0 is the intercept of the Hammett plot at $\sigma = 0.0$. [c] $\rho = 0.99$ ($r = 0.9997$). [d] $\rho = 1.09$ ($r = 0.9993$).

Table IV. Primary Kinetic Isotope Effects on the Reaction of 1-Aryl-1-nitroethanes, $ArCH(D)NO_2CH_3$, with Piperazine in Water

Substituent	$10^1 \times k^{H},^{a}$ M^{-1} sec^{-1}	$10^2 \times k^{D},^{a}$ M^{-1} sec^{-1}	k^H/k^D
m-CH_3	1.35 ± 0.01	1.41 ± 0.06	9.6 ± 0.5
H	1.54 ± 0.01	1.62 ± 0.03	9.5 ± 0.2
m-CH_3O	1.81 ± 0.01	1.90 ± 0.05	9.5 ± 0.4
m-Cl	3.33 ± 0.04	3.41 ± 0.19	9.8 ± 0.7
m-NO_2	6.98 ± 0.07	7.50 ± 0.23	9.3 ± 0.4
p-NO_2	11.6 ± 0.3	13.2 ± 0.2	8.8 ± 0.3
$k_0{}^{b}$	(1.51)[c]	(1.58)[d]	9.6

[a] In H_2O at 25°, $\mu = 0.10$. [b] Log k_0 is the intercept of the Hammett plot at $\sigma = 0.0$. [c] $\rho = 0.93$ ($r = 0.9984$). [d] $\rho = 0.94$ ($r = 0.9979$).

faster rate.[5b]) There are also several pieces of data that point to a nonreactant-like transition state, however. These include: (a) the close correspondence of $\Delta S^{\ddagger}$ with $\Delta S°$ in the deprotonation of nitroethane by hydroxide ion;[6] (b) the magnitude of the solvent isotope effect in the deprotonation of nitromethane by hydroxide ion;[7] and (c) the size of the Brφnsted β found in the deprotonation of various nitroalkanes by amines (β = 0.5 to 0.65).[3d] We now present results of a study of k^H/k^D isotope effects on nitroalkane deprotonations, which provide an additional probe relative to transition-state structures.

Westheimer has presented theoretical arguments to show that, for a series of related proton transfers, the isotope effect, k^H/k^D, will be a maximum when the transition state is symmetrical.[8] Although Westheimer's treatment ignores bending frequencies and makes other simplifying assumptions,[8] its overall conclusion has been generally accepted,[9] and the magnitude of the primary isotope effect has been frequently used as a guide to the structure of the transition state in reactions where proton transfer is rate limiting.[10]

$$B^- + H{-}A \longrightarrow B{-}H + A^-$$

Bell and Goodall[11] have suggested for a simple proton transfer that the most symmetrical transition state should occur when B^- and A^- are of approximately equal basicity, i.e., when

$$\Delta pK = pK_{HA} - pK_{HB} = 0$$

They have presented a plot of log (k^H/k^D) vs. ΔpK for a number of different carbon acids with different bases (20 points in all) and demonstrated what appeared to be a general trend of increasing log (k^H/k^D) with decreasing absolute ΔpK. In our preliminary communication, we supplemented their plot with many additional points near ΔpK = 0 and showed that the maximum was real, although the slope of ascending and descending lines was small.

Longridge and Long have found an apparent maximum in base-catalyzed exchange of protonated aromatic hydrocarbons in acidic solution for a plot of k^H/k^D vs. ΔpK.[12] Kresge, Sagatys, and Chen have observed an apparent similar maximum for proton transfer to C=C but have pointed out that the relationship breaks down when proton transfers to other types of substrates are included.[13]

Bell and Cox have also found an apparent maximum in a plot of k^H/k^D vs. ΔpK for the racemization of (−)menthone catalyzed by hydroxide ion to which DMSO was added to change the H_- function.[14] The pK_a of menthone was estimated at 21 and the H_- function used as a measure of the pK of the base. Although the ratio does rise and fall around ΔpK = 0, total variation in k^H/k^D was small (<15%) over the 6.3 unit range of ΔpK studied. Barnes and Bell obtained data for three additional ketonic substrates and for ethyl nitroacetate. The latter provided a number of points near ΔpK zero, and a maximum near this point was clearly evident.[15a] Recently Keefe and Munderloh found a maximum near ΔpK = 0 for $PhCH_2NO_2$ reacting with a variety of bases over a 17.5 ΔpK range.[15b]

In the present paper, we report the details of the results described in our preliminary communication.[1]

Results

Preparation of Deuterated Samples. Seven 1-aryl-1-deuterionitroethanes were prepared from the corresponding nitroalkane[3d] via their sodium salts.[16] The dried salt was dissolved in a buffer prepared from acetic acid-d_1, sodium acetate, and D_2O. The deuterated nitroalkane was extracted into ether and purified as before;[3d] the isotopic purity was typically >98% deuterium at the 1 position (NMR). Phenylnitromethane-1-d_1 (>97% deuterium at C-1) was prepared by the same method. By repeating the procedure on this product twice more, phenylnitromethane-1-d_2 with >98% deuterium at the 1 position was obtained.

Primary Isotope Effect. Rates of reaction of the deuterated nitroalkanes with hydroxide ion in water at 25° were determined spectrophotometrically, as previously described.[3d] Rates with amine bases were obtained in water by the buffer dilution method.[3d] Because of the importance of the reverse reaction, which is not retarded by an isotope effect,

Table V. Rate Constants for Reactions of Phenylnitromethane-d_0, -d_1, and -d_2 with Bases in Water

Nitroalkane	k_2, M^{-1} sec^{-1} HO$^-$ (12.6°)	HO$^-$ (26°)	Morpholine (25°)
$PhCH_2NO_2$	$5.47 \pm 0.22 \times 10^1$	$1.59 \pm 0.03 \times 10^2$	$9.82 \pm 0.14 \times 10^{-1}$
$PhCHDNO_2$	$2.72 \pm 0.09 \times 10^1$	$8.48 \pm 0.20 \times 10^1$	$4.98 \pm 0.06 \times 10^{-1}$
$PhCD_2NO_2$	6.68 ± 0.16	$2.60 \pm 0.02 \times 10^1$	$1.064 \pm 0.008 \times 10^{-1}$

Table VI. Solvent Isotope Effect on the Neutralization of 1-Aryl-1-nitroethanes with Lyate Ion in Water and Heavy Water at 25°

Substituent	$k_2^{\mathrm{HO}^-}$, M^{-1} sec^{-1}	$k_2^{\mathrm{DO}^-}$, M^{-1} sec^{-1}	$k^{\mathrm{DO}^-}/k^{\mathrm{HO}^-}$
m-CH_3	5.42 ± 0.02	7.44 ± 0.30	1.37 ± 0.06
H	6.47 ± 0.06	9.18 ± 0.24	1.42 ± 0.05
m-Cl	17.5 ± 0.1	23.4 ± 1.2	1.34 ± 0.07

the rates with morpholine, the weakest base used, were determined only for the *m*-chloro and *m*-nitro derivatives. The results are summarized in Tables I-IV.

Secondary Isotope Effect. In order to determine the secondary isotope effect for phenylnitromethane, the rates of base-initiated nitronate ion formation from the three species $PhCH_2NO_2$, $PhCHDNO_2$, and $PhCD_2NO_2$ were determined spectrophotometrically with hydroxide ion at 12.6° and with morpholine in water at 25.0° using a Beckman Kintrac VII. The rate constants with hydroxide ion were also measured at 26° using a Durrum-Gibson stopped-flow spectrophotometer (Table V).[17]

The secondary isotope effects were calculated from these data by the method of Bell and Goodall,[11] which requires the assumption that the secondary isotope effect on proton abstraction from $PhCHDNO_2$ is the same as that on deuteron abstraction from $PhCD_2NO_2$. The values obtained were 1.18 ± 0.18 for HO$^-$ at 12.6°, 1.14 ± 0.10 for HO$^-$ at 26°, and 1.12 ± 0.06 for morpholine at 25°.

Solvent Isotope Effect. A solution of sodium deuterioxide in D_2O was prepared by dissolving clean metallic sodium in ice-cold deuterium oxide (99.90 mol %). The base was standardized by titration with standard acid. The rates of neutralization of three nitroalkanes were measured at 25°; two of the rates were determined at different base concentrations, 5.1×10^{-3} and 1.2×10^{-2} *M*. The results are shown in Table VI along with the rates in H_2O and the resulting isotope effect. As always with the ratios of two experimentally determined numbers, the anticipated errors are substantial.

Discussion

Examination of Tables I-IV shows that, for reaction of a given base with a series of 1-arylnitroethanes differing in pK_a by 1.5 units, there is no obvious trend in the k^H/k^D values. Trends do become apparent, however, when values with different bases reacting with a given 1-arylnitroalkane are compared. Thus the ratios are significantly higher for the reactions of diethylamine ($k^H/k^D = 9.9$ for the intercept of the Hammett plot) than for the reaction of piperidine ($k^H/k^D = 9.0$ for the intercept of the Hammett plot), despite the equal basicity of these amines. Higher values are common for interactions between more hindered substrates.[18] Comparison of the values for hydroxide ion and three amines expected to have common steric interactions are made in Table VII.

The trend toward higher k^H/k^D values as Δp*K* approaches zero appears to be real but is obscured somewhat by the scattering in the values. This is a consequence of the uncertainty in the individual values of k^H/k^D. Rate constants for reactions weaker than hydroxide ion in water must be determined in buffered media and usually require a buffer dilution plot, that is, the rate constant must be measured at constant buffer ratio (pH), but at varying buffer concentration. Since each point has an error associated with it, and since the desired rate constant is obtained from the slope of k_{obsd} vs. buffer concentration, the error associated with the specific rate constant is increased. Although, in general, the standard deviation of the slope in our buffer dilution plots is less than 5%, an uncertainty of 5% in the rate constants for both the hydrogen and deuterium compounds leads to an uncertainty of about 10% in the ratio k^H/k^D. Thus, in the region of the maximum, where $k^H/k^D \simeq 10$, an error of 5% in each number leads to an uncertainty of ±1 in the ratio. In view of the small changes in observed k^H/k^D near $\Delta pK = 0$, this uncertainty is disturbingly large. The errors due to uncertainties in the data were minimized in the present instance by using the k^H/k^D value for the parent compound obtained from the intercept of the Hammett plot. Since the correlation coefficients in these plots were all high ($r > 0.99$), and the agreement between ρ determined for the protium and deuterium compounds was excellent, considerable confidence can be placed in these values.

Table VII. Effect of Base Strength on k^H/k^D for 1-Arylnitroethanes in Water at 25°

Base	1-*m*-Nitrophenylnitroethane k^H/k^D	ΔpK^a	1-*m*-Chlorophenylnitroethane k^H/k^D	ΔpK^a
Hydroxide ion	7.0 ± 0.1	−9.4	7.9 ± 0.1	−9.0
Piperidine	8.4 ± 0.9	−4.8	9.0 ± 1.2	−4.5
Piperazine	9.3 ± 0.4	−3.3	9.8 ± 0.7	−2.9
Morpholine	8.6 ± 0.5	−2.1	10.2 ± 0.2	−1.9

[a] $\Delta pK = pK(\mathrm{HA}) - pK(\mathrm{HB}) + \log(p_{\mathrm{HA}}q_{\mathrm{B}}/p_{\mathrm{HB}}q_{\mathrm{A}})$.

Secondary Isotope Effects. Before correlating the data just described with other data in the literature, it will be advantageous to consider corrections due to secondary isotope effects.

Previous workers have chosen not to make corrections for secondary deuterium isotope effects because of the uncertainty of the size of the correction to apply.[11-13] In part, this rationale was dictated by the belief that the size of the correction would vary considerably with the nature of the interacting species (e.g., as determined by Δp*K*). It will become apparent later in this discussion, however, that primary isotope effects are not very sensitive to changes in Δp*K*. It might be anticipated from this that secondary isotope effects also would not be very sensitive to changes in Δp*K*, and the limited amount of data available supports this view. Streitwieser and Van Sickle obtained a value of 1.15 for the α-secondary isotope effect in the reaction of toluene with cyclohexylamide in cyclohexylamine ($\Delta pK \simeq +3$).[19] Bell and Goodall[11] reported a value of 1.18 for the secondary isotope effect in the reaction of nitroethane with hydroxide ion ($\Delta pK = -7.1$), but doubted its accuracy. In view of the good agreement of this value with those reported herein, these doubts appear unjustified. Furthermore, in view of the close agreement of the secondary isotope effects

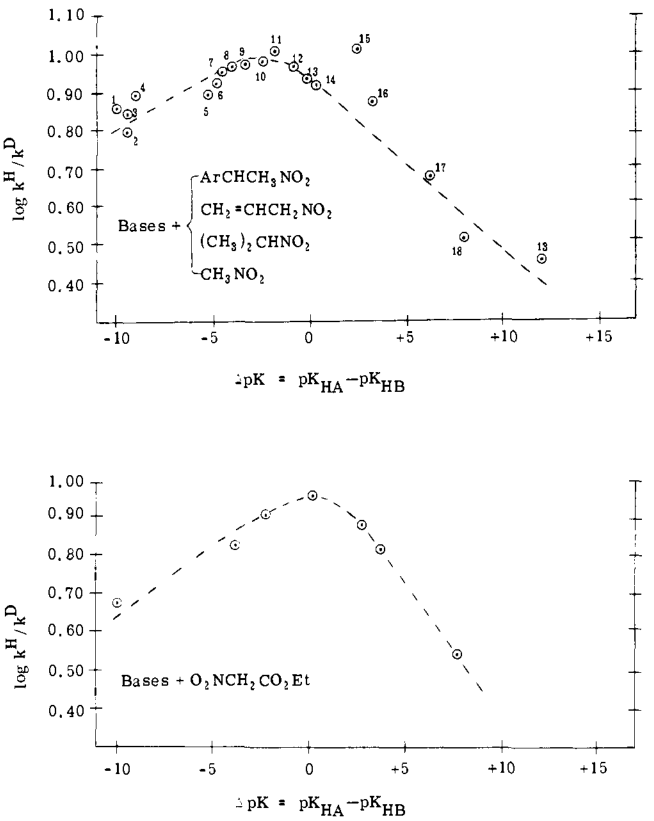


Figure 1.[21] Variation of k^H/k^D isotope effects with ΔpK. The data for $NO_2CH_2CO_2Et$ are taken from the paper by Barnes and Bell (ref 15). The data for the plot shown at the top of the figure are from Table IX, the numbers corresponding to those in the table.

for a span of ca. 12 ΔpK units, it appears that a correction should be applied, regardless of ΔpK. We have chosen the average value of 1.15 for compounds with two acidic protons, which coincides with the value of Streitwieser and Van Sickle, and a value of $(1.15)^2 = 1.32$ for compounds with three acidic protons.

The importance of applying secondary isotope corrections is illustrated by their application to the data for nitromethane, nitroethane, and 2-nitropropane (Table VIII). Whereas without this correction the k^H/k^D ratio appears to rise rather steeply with diminishing ΔpK, the corrected values show no obvious trend.

Correlation of Corrected k^H/k^D Values with ΔpK. In the previous paper, a plot of log k^H/k^D vs. ΔpK was made from 21 points chosen from the 29 available in Tables I-IV so as to cover the broadest range of ΔpK as evenly as possible, together with (corrected) values for nitroalkanes and ketonic substances selected from the literature.[1] The reasons for the wide scatter in this plot, as commented on earlier, are: (a) experimental error; (b) secondary isotope effects; (c) changes in the degree of substitution for a given type of substrate; (d) changes in the type of substrate; and (e) internal return.[20] Steric and tunneling effects, which appear to be closely allied,[18] are important in c and d. When a single nitroalkane or a limited number of nitroalkanes are selected, these effects are minimized, and the scatter is sharply reduced (Figure 1).

Solvent Isotope Effects. Another experimental probe that has been suggested for determining the extent of proton transfer in the transition state is the solvent isotope effect (k^{H_2O}/k^{D_2O}). This effect can take several forms depending on the reaction involved. Acid-catalyzed reactions can exhibit isotope effects due to the action of either the lyonium ion or the solvent acting as an acid, and base-catalyzed reactions can similarly involve either solvent or lyate ion. Reactions involving more than one step as, for example, the acid-catalyzed halogenation of ketones, frequently involve nonnegligible isotope effects on each step. Superimposed on all these possible isotope effects is a genuine solvent effect on all the reactions and on the individual steps of each reaction. The complexity of the solvent isotope effect on rates of reactions and on equilibria has been reviewed recently by Laughton and Robertson.[22]

Table VIII. Magnitude of the Secondary Isotope Correction for the Reaction of Simple Nitroalkanes with Hydroxide Ion

Nitroalkane	k^H/k^D, obsd^a	$(k^H/k^D)/1.15^{(n-1)}$	n
CH_3NO_2	10.2	7.7	3
$CH_3CH_2NO_2$	9.3	8.1	2
$(CH_3)_2CHNO_2$	7.4	7.4	1

^{a} Data of Bell and Goodall in water at 25°.

Despite the many complicating factors, Swain and his coworkers have suggested that the position of the proton in the transition state can be determined from the solvent isotope effects in light and heavy water.[7,23] For example, the degree of proton transfer in a proton-abstraction reaction by lyate ion can be calculated from the observed isotope effect for the reaction and the isotope effect on the equilibrium

$$DO^- + HO \overset{K_n'}{\rightleftarrows} DO + HO^-$$

Solution of the equation

$$(K_n')^\alpha = k^{DO^-}/k^{HO^-}$$

gives α, the fractional degree of proton transfer in the transition state.[23] Conversely, if α is known from some other source, the isotope effect can be calculated and factored out of a more complex expression involving, perhaps, a solvent isotope effect on a preceding or subsequent step.[24,25] The data accumulated to date for base-initiated deprotonations of carbon acids, including our data on 1-arylnitroethanes, is summarized in Table X.

The size of α depends on the value of K_n'. Of the various values available, 1.79,[7] 2.0,[24] 2.1,[30] and 2.47,[31] the value of 2.1 was chosen (Table X) as perhaps being more reliable. If the larger value of 2.47 is used, the α values shown in Table X will be even more compressed. The data presented in Table X once again emphasize the gradual nature of the changes in reaction parameters over wide ranges of ΔpK.

Structure-Reactivity Relationships and Transition-State Structures for Nitroalkanes. When a series of reactions involves only a single reaction mechanism, there is often a parallelism between rate and equilibrium constants, which can be expressed in the form of a *rate-equilibrium relationship*:[32]

$$\delta\Delta G^{\ddagger} = \alpha\delta\Delta G^\circ \qquad (1)$$

Equation 1 predicts that the extent of H-C bond breaking will be slight for an exoenergetic reaction and extensive for an endoenergetic reaction. The principal probes that have been used in connection with the rate-equilibrium relationship to determine the extent of proton transfer in the transition state are the Brφnsted relationship and kinetic isotope effects.

Leffler and Grunwald have pointed out that, in a seemingly simple deprotonation reaction, such as the deprotonation of a nitroalkane or ketone, the α in eq 1 can be equated with the Brφnsted coefficient. Support for this conclusion comes from studies of the deprotonation of a series of ketone-type substrates by alkanecarboxylate ions where Bell

Table IX. Primary Isotope Effects in the Deprotonation of Selected Nitroalkanes by Bases in Water at 25°

Carbon acid (AH)	p*K*(AH)	Base	p*K*(BH)	Δp*K*[a]	k_H/k_D[d]
1. m,m'-$(O_2N)_2C_6H_3CHNO_2CH_3$	5.95	OH^-	15.75	−10.1	7.1
2. p-$O_2NC_6H_4CHNO_2CH_3$	6.51	OH^-	15.75	−9.5	6.5
3. m-$O_2NC_6H_4CHNO_2CH_3$	6.67	OH^-	15.75	−9.4	7.0
4. m-$ClC_6H_4CHNO_2CH_3$	7.05	OH^-	15.75	−9.0	7.9
5. CH_3NO_2[b]	10.22	OH^-	15.75	−5.3	7.8
6. m-$O_2NC_6H_4CHNO_2CH_3$	6.67	Piperidine	11.21	−4.8	8.4
7. m-$ClC_6H_4CHNO_2CH_3$	7.05	Piperidine	11.21	−4.5	9.0
8. $C_6H_5CHNO_2CH_3$	7.39	Piperidine	11.21	−4.1	9.2
9. m-$O_2NC_6H_4CHNO_2CH_3$	6.67	Piperazine	9.93	−3.3	9.3
10. $C_6H_5CHNO_2CH_3$	7.39	Piperazine	9.93	−2.5	9.5
11. m-$ClC_6H_4CHNO_2CH_3$	7.05	Morpholine	8.68	−1.9	10.2
12. $CH_2{=}CHCH_2NO_2$[c]	5.22	3,4-Lutidine	6.45	−0.9	9.2
13. $CH_2{=}CHCH_2NO_2$[c]	5.22	3-Picoline	5.63	−0.1	8.7
14. $CH_2{=}CHCH_2NO_2$[c]	5.22	Pyridine	5.20	+0.3	8.5
15. $(CH_3)_2CHNO_2$[b]	7.74	Pyridine	5.20	2.5	10.3
16. $(CH_3)_2CHNO_2$[b]	7.74	$CH_3CO_2^-$	4.75	3.3	7.6
17. CH_3NO_2[b]	10.22	$CH_3CO_2^-$	4.75	6.2	4.7
18. CH_3NO_2[b]	10.22	$CH_2ClCO_2^-$	2.87	8.1	3.3
19. CH_3NO_2[b]	10.22	H_2O	−1.75	12.0	2.9

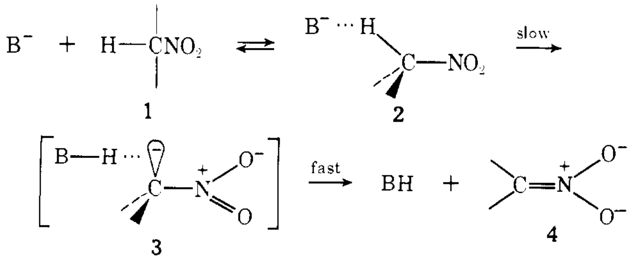
[a] $\Delta pK = pK(AH) - pK(BH) + \log(p_{AH}q_B/p_{BH}q_A)$. [b] Reference 11. [c] Reference 5b. [d] Corrected for α-secondary isotope effects.

Table X. Solvent Isotope Effects in the Deprotonation of Carbon Acids by Lyate Ion in Water and Heavy Water

Substrate	k^{DO^-}/k^{HO^-}	α[a]	Δp*K*[b]	*T*, °C	Ref
m-$ClC_6H_4CHNO_2CH_3$	1.34 ± 0.07	0.39 ± 0.07	−9.0	25	Table VI
$C_6H_5CHNO_2CH_3$	1.42 ± 0.05	0.47 ± 0.05	−8.7	25	Table VI
m-$CH_3C_6H_4CHNO_2CH_3$	1.37 ± 0.06	0.42 ± 0.06	−8.6	25	Table VI
$(CH_3)_2CHNO_2$	1.36 ± 0.01	0.41	−8.3	5	26
$CH_3CH_2NO_2$	1.39 ± 0.02	0.44	−7.1	5	26
CH_3COCH_3	1.46	0.50	(+4.7)	25	27
$C_6H_5C{\equiv}CH$	1.34	0.39	(+3.9)	25	28
$C_6H_5CH(OH)CO_2^-$	1.40	0.52[c]	>15	100	29

[a] Calculated from $(K_n')^\alpha = k^{DO^-}/k^{HO^-}$ with $K_n' = 2.1$.[33] [b] Calculated as in Table IX. [c] Calculated using $K_n' = 1.9$, estimated from data of L. Steffa, U.S. Atomic Energy Commission NYO-3041-1 (1965), p 1, at 80.5°.

and his students have shown that the Brφnsted β coefficient increases from 0.42 for 3-bromo-2,4-pentanedione to 0.88 for acetone, a change from $\Delta G° = +6$ to $+22$ kcal/mol.[33] On the other hand, from a survey of Brφnsted β coefficients for reactions including deprotonations of nitroalkane and ketone-type substrates with a variety of bases covering a range of $\Delta G°$ from −10.5 to about +20, little variation and no consistent trend were observed.[3d] Furthermore, when substituent changes were made in the nitroalkane substrate, rather than in the attacking base,[34] Brφnsted coefficients, constants greater than 1.0 or less than zero, were encountered.[3] These are "anomalous" according to eq 1.[32] For the past several years, we have been rationalizing the appearance of such anomalous Brφnsted coefficients by assuming that the deprotonations of nitroalkanes, and like substrates, are not simple one-step reactions but instead involve the formation of an anion intermediate (**3**).



According to this scheme, the first step in the reaction is formation of a hydrogen-bonded complex (**2**) between the base, B⁻, and the nitroalkane substrate (**1**). This is comparable to the first step in the Eigen mechanism for the deprotonation of oxygen acids[35] but differs in that the hydrogen bond in **2** is very weak. In the second, rate-limiting step, the H-C bond is broken, and a "singly-solvated" essentially pyramidal nitro carbanion (**3**) is formed. By "singly-solvated" we mean that a strong hydrogen bond is formed between the conjugate acid of the attacking base and a localized (or incompletely delocalized) carbanion. Solvation involving other BH solvent molecules and the anion is certainly present, particularly at the oxygen sites, but we consider this as secondary. Anion **3** may be partially rehybridized, with some of the negative charge appearing on oxygen, but we look on **3** as differing markedly from **4** with respect to geometry and solvation and therefore refer to it as an "essentially pyramidal nitro carbanion". In the final, rapid step, rehybridization of **3** is completed to give **4**; this step is believed to be accompanied by extensive solvent reorganization.[36] In this two-anion mechanism, the changes in rates brought about by substituent changes ($\delta\Delta G^{\ddagger}$) relate to the step where **2** is converted to **3**, whereas the changes in equilibrium brought about by substituent changes ($\delta\Delta G°$) refer to the equilibrium between **1** and **4**. We see that, for this mechanism, eq 1 does not apply, and that substituent changes can affect rates and equilibria quite differently. Whereas rate changes depend on how substituent changes affect the energy of the transition state for conversion of **2** to **3**, equilibrium changes will depend on how substituent changes affect the total equilibrium between **1** and **4**. (Usually the equilibrium position will depend primarily on how substituent changes affect the energy of nitronate ion **4**.) Since eq 1 does not apply, Brφnsted coefficients cannot be equated to α in this equation, and Brφnsted coefficients larger than one and less than zero can be accommodated.[37] In subsequent papers, we will show how the two-anion mechanism can be used to rationalize substituent effects on rate and equilibrium constants in (a) arylnitromethanes, (b) 3-substituted 1-nitropropanes, (c) alkyl-substituted nitroalkanes, (d) α-, β-, and γ-substituted 3-nitropropenes, and (e) nitrocycloalkanes.

According to the two-anion mechanism, kinetic isotope effects involving deprotonations of nitroalkanes, or the like, by bases refer to the transition state of the reaction wherein **2** is deprotonated to give **3**. Plots of $k^{\mathrm{H}}/k^{\mathrm{D}}$, such as those shown in Figure 1, are not applicable since ΔpK in Figure 1 refers to the difference in pK between BH and the nitroalkane substrate (equilibrium between **1** and **4**), which does not give a measure of $\Delta G°$ for the conversion of **2** to **3**. It seems likely that the change in $\Delta G°$ with a change in substituents ($\delta\Delta G°$) for the conversion of **2** to **3** will be considerably smaller than $\delta\Delta G°$ for the conversion of **1** to **4**. This makes the very gradual changes observed in $k^{\mathrm{H}}/k^{\mathrm{D}}$ seem reasonable. Furthermore, the large values of $k^{\mathrm{H}}/k^{\mathrm{D}}$ for deprotonations of nitroalkanes appear to be in better accord with the largest isotope effect occurring at a symmetrical transition state[8] since $\Delta G°$ for these reactions might be near zero instead of rather strongly negative, as it is when $\Delta G°$ is considered to be deprotonation of the nitroalkane to form the nitronate ion. We see then, that the two-anion mechanism for deprotonation of nitroalkanes can account for the kinetic isotope effects observed at least as well, and perhaps better, than does the one-step mechanism.

Acknowledgment. This work was supported by the National Science Foundation (GP-29539X). We benefited from discussions with Professors Maurice Kreevoy and James Keeffe.

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