15 and 35 °C by monitoring the appearance of the OH peak in the solvent by NMR. For this purpose 100 mg of nitrocyclopropane was placed in an NMR tube and 0.5 mL of ~1 M NaOD/D_2O added. After making sure that in a 2-h trial run that the OH peak (δ 4.8) was not saturated at 60 Hz paper width and 200-s scan, fresh samples were used to scan the OH peak as a function of time. Peak areas were determined by cut-and-weigh, and the data analyzed as first-order kinetics.

Materials. Nitrocyclohexane was obtained as a gift from the Commercial Solvents Corp. and nitrocyclooctane was obtained as a gift from Professor J. G. Traynham. Other nitrocycloalkanes, except for nitrocyclopropane, were prepared by the oxidation of the keto oximes as described previously.[6] Nitrocyclopropane was prepared by the method of Lampman, Horne, and Hager[20] and purified by GLC using a ⅜ in. × 10 ft Carbowax on acid-washed Chromosorb W column at 110 °C and 160 mL/min flow rate to give a clear liquid: n^{23}_D 1.4380 [lit.[20] n^{20}_D 1.4395]; NMR ($CDCl_3$) δ 1.10 (m, 2 H), 1.60 (m, 2 H), 4.33 (m, 1 H); IR (film) 1540, 1370 cm^{-1}. 2-Methyl-1-nitrocyclopropane was prepared in a similar manner starting from 1,3-dibromobutane. GLC analysis indicated the presence of two isomers in a ratio of 10:1. Isolation of each was accomplished by preparative GLC using a ¼ in. × 20 ft 3% Carbowax on acid-washed Chromosorb W column at 80 °C and a flow rate of 80 mL/min. The products had similar, but slightly different NMR spectra: ($CDCl_3$) δ 1.2 (m, 6 H), 4.2 (m, 1 H). Upon treatment with aqueous 1 M NaOH for 0.5 h at 25 °C each was converted to the same 20:1 mixture of isomers (GLC analysis). The lesser product was therefore assigned the cis structure.

Acknowledgment. This research was supported by grants from the National Science Foundation and the National Institute of Health. We are indebted to Zafra Margolin for the pK measurements in Me_2SO solution.

Registry No.—*cis*-2-Methylnitrocyclopropane, 66303-44-4; *trans*-2-methylnitrocyclopropane, 15267-24-0; 1,3-dibromobutane, 107-80-2.

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Kinetic and Equilibrium Acidities of 3-Nitropropene and Some of Its Derivatives

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Rates of hydroxide ion deprotonation in water for 3-nitropropene and seven of its derivatives, $R_2R_3C{=}C(G)$-$CH(R_1)NO_2$, where R_1, R_2, and R_3 are either H or Me, and G is H, Me, Ph, or Br, have been measured and compared with their equilibrium acidities in water. These substitutions were found to cause a complex variation of kinetic and equilibrium acidities which was interpreted by assuming that the kinetic acidities were governed primarily by polar effects and steric inhibition of solvation in the transition state, whereas the equilibrium acidities were governed primarily by steric strains in the product nitronate ions. It was concluded that nitroalkane (and other carbon acids) deprotonations usually fail to conform to the Leffler–Grunwald rate–equilibrium relationship when the structural changes are made in the carbon acid. The rates of deprotonation in water for 3-nitropropene, 3-nitropropene-3,3-d_2, and 1-nitro-2-butene by pyridine and seven methyl-substituted pyridines were determined. The k_H/k_D isotope ratios were found to vary from 8.5 to 11.4. A Brønsted β of 0.59 was obtained. The significance of these data with respect to the mechanism of deprotonation of nitroalkanes is discussed.

In earlier papers in this series we have examined rates of deprotonation, equilibrium acidities, and isotope effects for a variety of nitroalkanes in an attempt to elucidate the mechanisms of deprotonation of carbon acids by bases.[2] It appeared to be of interest to extend the study of 3-nitropropene and some of its derivatives, since it was anticipated that these β,γ-unsaturated nitroalkanes, which are much more acidic than their saturated analogues, would provide useful information with regard to rate–equilibrium relationships and the variation in the size of k_H/k_D isotope effects with the strength of the base used in the deprotonation.

Results

Rates of proton removal from the β,γ-unsaturated nitroalkanes by hydroxide ion were measured spectrophotometrically in water at 25 °C under pseudo-first-order conditions. The kinetics were followed by stopped-flow except for 2-methyl-3-nitro-1-butene and 2-nitro-3-pentene, where the rates were measured on a Beckman Kintrac VII spectrophotometer. For 3-nitropropene, 1-nitro-2-butene, and 3-methyl-1-nitro-2-butene pK's were measured potentiometrically by a partial neutralization technique; other pK's were

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Table I. Kinetic and Equilibrium Acidities of Nitroalkenes, $R_2R_3C{=}C(G)CH(R_1)NO_2$, in Water at 25 °C.

R_1	R_2	R_3	G	registry no.	k_1,[a] $M^{-1}\ s^{-1}$	pK[b]	k_{-1}[c] (rel)
H	H	H	H	625-46-7	394	5.22[d]	(1.0)
H	Me	H	H	1809-69-4	128	5.44	0.52
H	Me	Me	H	1809-65-0	77	5.55	0.41
H	H	H	Me	1606-31-1	62	7.27	17
Me	Me	H	H	1806-28-6	5.9[e]	5.35	0.019
Me	H	H	Me	19031-81-3	2.5[e]	7.85	3.4
H	H	H	Ph	58502-68-4	185	7.26	50
H	H	H	Br	1809-71-8	3450	5.60	20

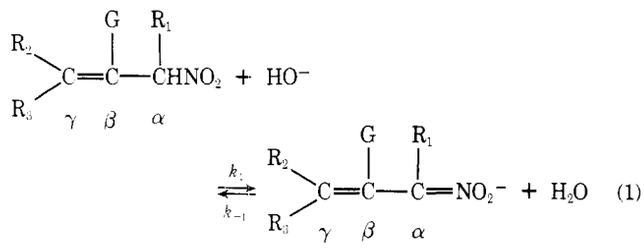
[a] Average from data on three photographs each comprising three superimposed runs on a Durrum–Gibson stopped-flow apparatus with hydroxide ion (SD < ±5%); not statistically corrected. [b] Average of two or more determinations (SD ± 0.03 pK units); activity coefficient corrections for differences in ionic strength have been applied. [c] Calculated from the equation $k'_{-2}/k_{-2} = K_{HA}k'_2/K'_{HA}k_2$. d_{pK} = 10.49 in MeOH. [e] Average of eight runs on a Beckman Kintrac VII spectrophotometer.

Table II. Rate Constants for Deprotonation of 3-Nitropropene, 3-Nitropropene-*3,3*-d_2, and 1-Nitro-2-butene by Pyridine Bases in Water at 25 °C

base	pK_{BH^+}[a]	3-nitropropene 10^1k_H[b]	3-nitropropene 10^2k_D	3-nitropropene k_H/k_D	1-nitro-2-butene, 10^2k,[b] $M^{-1}\ s^{-1}$
pyridine	5.22	0.567	0.577	8.5	1.60
3-picoline	5.63	1.11	1.28	8.7	3.33
2-picoline	5.96	1.82	1.56	10.2	5.6
4-picoline	5.98	1.45	1.37	9.2	
3,4-lutidine	6.46	2.92	2.74	9.2	7.97
2,4-lutidine	6.63	4.27	4.07	9.1	12.5
2,6-lutidine	6.75	1.74	1.33	11.4	5.53
2,4,6-collidine	7.59	3.37	2.72	10.8	

[a] R. J. L. Andon, J. D. Cox, and E. F. G. Herington, *Trans. Faraday Soc.*, **50**, 923 (1958). [b] Determined by the buffer dilution method; standard deviations were all <5% (units are $M^{-1}\ s^{-1}$).

measured spectrophotometrically. The pK's of propene-3-nitronic acid and 2-butene-1-nitronic acid were also measured in order to determine whether or not the pK's of the corresponding nitroalkenes should be corrected for the presence of the aci form. Since the nitronic acids were found to be ~2 pK units more acidic than the nitroalkenes, the aci form is present in low concentration and the correction is within the experimental error of the measurements for the nitroalkenes. The results summarized in Table I refer to the reaction in eq 1.

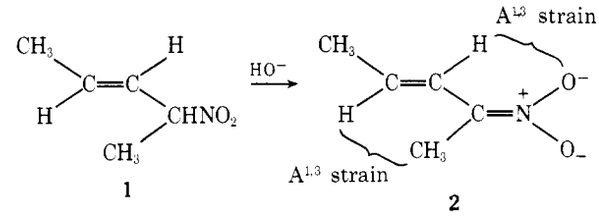


(1)

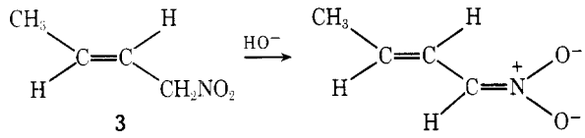
Rates of reaction of 3-nitropropene, 3-nitropropene-*3,3*-d_2, and 1-nitro-2-butene with a series of pyridine bases were determined in order to obtain Brønsted correlations and k_H/k_D isotope effects (Table II).

Discussion

Effects of Substitution on Kinetic and Equilibrium Acidities of 3-Nitropropenes. Substitution of methyl for a hydrogen atom α to the nitro group in $CH_3CH{=}CHCH_2NO_2$ (to give 1) causes an 11-fold retardation (statistically corrected) in rate. This result is comparable to the 10.5-fold retardation observed for substitution of an α-methyl group into nitroethane, a result that has been attributed to steric inhibition of solvation by methyl in the transition state for the deprotonation reaction.[2] On the other hand, this substitution causes an increase in equilibrium acidity of only 0.09 pK unit (Table I), whereas an increase of almost 1 pK unit is observed for the change from nitroethane to 2-nitropropane. For the saturated nitroalkanes, the substantial increase in acidity is believed to be caused by stabilization of the $MeCH{=}NO_2^-$ and $Me_2C{=}NO_2^-$ nitronate ions resulting from methyl substitution.[2] In the unsaturated compounds this effect is evidently either absent or offset by other factors. The latter seems to be the case, since examination of scalar models indicates that 1,3 steric interactions between methyl and hydrogen and between O^- and hydrogen nitronate ion (**2**) ($A^{1,3}$ strains[3]) are important in destabilizing this anion.

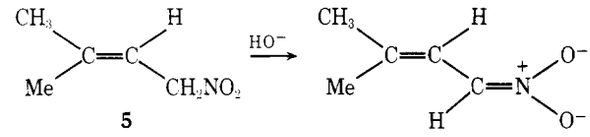


Substitution of methyl for a hydrogen atom γ to NO_2 in 3-nitropropene (to give **3**) causes a 3.1-fold decrease in kinetic acidity and a 0.2 pK unit decrease in equilibrium acidity (Table I). Methyl groups attached to sp^2 carbon atoms have electron-releasing effects, which could affect solvation in such a way as to raise the energy of the transition state in the deprotonation of **3**.[4] Since no change in hybridization at the carbon atom to which the methyl group is attached occurs when **3** is transformed to **4**, nitronate ion **4** is not stabilized, relative to **3**, by methyl substitution, as happens in the transformation of $MeCH_2NO_2$ to $MeCH{=}NO_2^-$.[2] Therefore, no appreciable change is expected in equilibrium acidities for $MeCH{=}CHCH_2NO_2$ vs. $HCH{=}CHCH_2NO_2$, and none is observed.



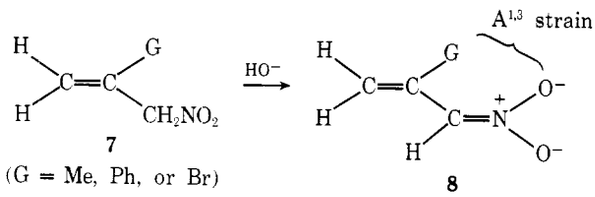
3 4

Substitution of methyl for the γ-hydrogen atom in **3** (to give **5**) introduces a cis interaction between Me and CH_2NO_2, which will destabilize **5**, relative to **3**. This interaction is also present in the nitronate ion (**6**) (comparable to $A^{1,3}$ strains in **2**). As a result, these effects balance one another, and the effect on acidity of introduction of the second methyl group differs but little from that observed for introduction of the first methyl group (Table I).



5 6

Substitution of methyl for a hydrogen atom β to NO_2 in $H_2C{=}CHCH_2NO_2$ (to give **7**, G = Me) causes a 6.4-fold decrease in kinetic acidity and a 2 pK unit decrease in equilibrium acidity (Table I). Here, the methyl effect on the kinetic acidity is similar to that for α substitution, but the methyl effect on equilibrium acidity differs markedly (2 pK unit decrease as compared to a 0.09 pK unit increase). This is understandable, since the $A^{1,3}$ steric interaction in **8** is between methyl and O^-, and is much more severe than that in **2**. This increased strain is responsible for the lowered equilibrium acidity of **7**.



7 (G = Me, Ph, or Br) 8 (G = Me, Ph, or Br)

Substitution of Ph for a β-hydrogen atom (**7**, G = Ph) causes a 2.2-fold decrease in kinetic acidity, which is accompanied by a 2 pK unit decrease in equilibrium acidity. The phenyl group in **8** must be tilted out of the plane of the C=CC=N bond system in order to relieve $A^{1,3}$ strain. Some delocalization of charge would be possible, even in this conformation, but this would be a cross-conjugation effect, and stabilization by Ph through this effect must be minimal. The sharp decrease in equilibrium acidity for β-Ph substitution is therefore understandable.

Substitution of Br for a β-hydrogen atom (**7**, G = Br) causes a ninefold *increase* in kinetic acidity, which is accompanied by a 0.4 pK unit decrease in equilibrium acidity. Apparently the much greater polar effect of Br, as compared to Me or Ph, is sufficient to override steric inhibition of solvation in the transition state for the hydroxide ion deprotonation. (A plot of σ_m vs. log k_1 for the β-Me, β-Ph, and β-Br compounds gave a linear correlation, r = 0.9999, slope = 3.8, suggesting that polar effects are influential in controlling these deprotonation rates.) The slight decrease in equilibrium acidity for $H_2C{=}C(Br)CH_2NO_2$, relative to $H_2C{=}CHCH_2NO_2$, can be explained as the result of a balance between the sizable polar effect of Br, which is acid strengthening, and the sizable steric effect of Br, which is acid weakening.

We have seen that substitution of various groups for a hydrogen atom at the α, β, and γ positions of 3-nitropropene causes a complex variation of kinetic and equilibrium acidities, including substantial decreases in kinetic acidities accompanied by little change in equilibrium acidity [$MeCH{=}CHCH(Me)NO_2$ vs. $MeCH{=}CHCH_2NO_2$], substantial increases in kinetic acidities accompanied by little change in equilibrium acidity [$CH_2{=}C(Br)CH_2NO_2$ vs. $CH_2{=}CHCH_2NO_2$], and substantial decreases in both kinetic and equilibrium acidities [$CH_2{=}C(Me)CH(Me)NO_2$ vs. $CH_2{=}CHCH_2NO_2$]. These results have been interpreted by assuming that the kinetic acidities are governed primarily by two factors, steric inhibition of solvation in the transition state and a polar factor, which are probably interrelated, and that equilibrium acidities are governed primarily by steric strains ($A^{1,3}$ strains) in the nitronate ions. These steric strains are evidently not operative in the transition state for deprotonation of these nitroalkenes by hydroxide ion.

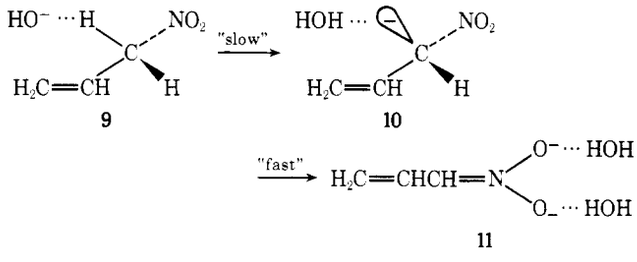
The lack of correlation between the kinetic and equilibrium acidities of alkyl-substituted 3-nitropropenes is comparable to the lack of such correlations with saturated alkyl-substituted nitroalkanes and nitrocycloalkanes.[2] These failures of the Brønsted relationship represent failures of the Leffler–Grunwald rate–equilibrium relationship (eq 2), wherein α was assumed to be confined to the limits of 0 and 1.0.[5]

$$\delta\Delta G^{\ddagger} = \alpha\delta\Delta G^{\circ} \qquad (2)$$

Failures of eq 2 are common for nitroalkanes. They are observed not only when structural changes occur near to the reactive site and are largely steric in nature, as in the examples just mentioned, but also when the substituents are remote and are largely polar in nature, as in the electronic effects of substituents, G, in $G(CH_2)_3NO_2$ and $GC_6H_4CH_2NO_2$ systems.[2] In all of these examples eq 2 fails because the substituent changes do not cause changes on the transition state energy that are *intermediate* between those caused on the reactants and products, but instead are *greater* in the transition state (either more stabilizing or more destabilizing) than in the reactants and/or products. The complex variation in kinetic and equilibrium acidities for the $R_2R_3C{=}C(G)CHR_1NO_2$ system, as R_1, R_2, R_3, and G are changed, therefore fits the general pattern of behavior observed previously for nitroalkanes. It can be accommodated by the mechanism for deprotonation discussed in the earlier papers in this series wherein formation of an essentially pyramidal, singly H-bonded intermediate is assumed (**10** in Scheme I).[2]

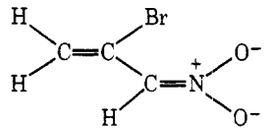
Examining the substituent changes (Table I) in light of this mechanism we see that the rate retardations observed for α-Me or β-Me substitution and the rate acceleration observed for β-Br substitution can be attributed to polar effects on the (essentially pyramidal) transition state leading to intermediate **10**, whereas the effects of these substituents on the equilibria include important contributions from steric effects, which are felt primarily in the (planar) nitronate ion product and not in the transition state. The interplay between these substituent effects on transition state and product can best be seen with the more polar substituents, Br and Ph. Substitution of a β-H atom by Br produces a nearly ninefold acceleration in the deprotonation rate, attributable to a substantial

Scheme I

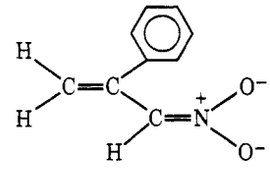


9 10 11

electron-withdrawing polar effect on the transition state leading to the intermediate. This is accompanied by a 0.4 pK unit *decrease* in equilibrium acidity, attributable to larger steric destabilization than polar stabilization of the product nitronate ion (**12**). The polar Ph group, when substituted for a β-H atom, causes a twofold retardation in the deprotonation rate accompanied by a 2 pK unit decrease in equilibrium acidity. The substantial decrease in equilibrium acidity suggests that not only is the Ph group unable to stabilize the nitronate ion **13** by a conjugative interaction, but also that it interferes with the ability of the CH_2=CH group to do so.



12



13

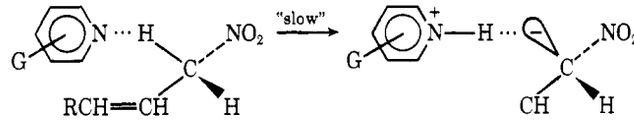
The polar effect of a β-Ph group should accelerate deprotonation of H_2C=C(Ph)CH_2NO_2 by HO^-. The observation of a twofold rate *retardation* (Table I) indicates that the large steric effect in **13** must be felt to some degree in the transition state for the intermediate believed to precede **13** along the reaction profile (Scheme I). In describing this intermediate as being "essentially pyramidal" we do not wish to imply that *no* rehybridization has occurred, but merely that rehybridization, and the accompanying solvent reorganization, is incomplete. For highly endoenergetic deprotonations, such as that of nitrocyclopropane, the evidence points to substantial rehybridization in the transition state (see the preceding paper in this issue) and, when conjugation between the developing charge on the α carbon and an α substituent can occur, rehybridization in the transition state would be expected to increase to take advantage of this stabilizing influence. On this basis we expect a greater degree of rehybridization in intermediate **10** than in comparable intermediates where an alkyl group has replaced the vinyl group at the α-carbon atom. The extent of this rehybridization in the transition state leading to **10** does not seem to be large, however, judging from the small rate retarding β-Ph effect. Also, the point for α-Ph fits reasonably well on a Taft plot constructed for deprotonation rates in 50% MeOH–H_2O for nitroalkanes of the type $G(CH_2)_nNO_2$, where n = 1, 2, or 3 (see Figure 1 in paper 3 in this series). The present data, when corrected for the change in solvent, indicate that the α-vinyl point will also fit this plot reasonably well.

Brønsted Correlations for Deprotonation with Pyridine Bases. Brønsted plots using the data in Table II for the first six bases and two nitroalkenes gave linear correlations (r = 0.990 and 0.986). The points for 2,6-lutidine and 2,4,6-collidine fell well below the lines and the k_H/k_D isotope effects were enhanced, which is usual for these sterically hindered bases.[8] The large k_H/k_D isotope ratios observed (near 9) are indicative of a transition state where H–C bond breaking is substantial and $\Delta G°$ is somewhere near zero. The broad maximum observed in k_H/k_D vs. ΔpK plots where the nature of the carbon acid and base are both changed makes it difficult to use the size of the k_H/k_D ratio as a guide to the position of the transition state along the reaction coordinate.[11a] The overall reaction, **14** → **16**, has a $\Delta G°$ near zero, but, if formation of an intermediate (**15**) is postulated, the rate-limiting step would probably be on the endoenergetic side. There is no apparent trend in the k_H/k_D ratio as ΔpK is changed, which supports the view that transition-state structures vary but little with small changes in $\Delta G°$.[11] The Brønsted β is in each instance 0.59, which is slightly smaller than that observed for the reaction of pyridine bases in water with nitroethane (β = 0.65[8a]). It is possible, as has frequently been postulated,[5,9,10] that the size of β gives a measure of the extent of proton transfer in the transition state for deprotonation reactions, but when one considers that in comparing the reactions of amine bases with such diverse carbon acid substrates as 3-nitropropene, nitroethane,[13] cyclohexanone,[12] and 3-cyclohexenone[14] β falls in the narrow range of 0.5–0.6 despite changes in $\Delta G°$ that are probably greater than 10 kcal/mol, it is clear that β cannot be a very sensitive guide to transition-state structure.

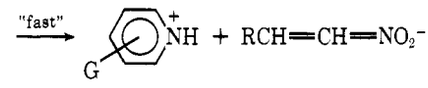
Table III. Effects on Equilibrium and Kinetic Acidities of Introducing β,γ Unsaturation into Various Carbon Acids

type of parent carbon acid	pK (Me_2SO)[a]	ΔpK (Me_2SO)[c]	log ($k_{\beta\gamma}/K$(^{E}
nitroalkane	~18	~5	~2
ketone	~27	~7	~3[f]
sulfone	~32	~7.5	~4[g]
alkene	~42[b]	~10[d]	~6[h]

[a] Average values for simple compounds in this class (see ref 17). [b] Taken as equal to the lowest of the values extrapolated for toluene (ref 18). [c] ΔpK = pK(RCH_2G) − pK($PhCH_2G$) unless otherwise noted. [d] Estimate based on pK($PhCH_3$) − pK($PhCH_2Ph$). [e] Rate ratio for deprotonation by HO^- (or RO^-) in H_2O (or ROH) unless otherwise noted. [f] From rate data at 0 °C for cyclohexanone (ref 20) and at 25 °C for cyclohexenone (ref 14). [g] Rate for $PrCH_2SO_2CH_3$ vs. $PrCH$=$CHCH_2SO_2CH_3$ (ref 21). [h] Rate for CH_2=$CHCH_2CH$=CH_2 vs. CH_2=$CHCH_2Me$ (ref 22).



14 (R = H or Me) **15** (R = H or Me)



(G = Me or diMe) **16** (R = H or Me)

Correlation of Equilibrium and Kinetic Acidities for Structural Changes in Various Weak Carbon Acids. From the data in this and the two preceding papers in this series we have concluded that deprotonations of nitroalkanes usually fail to conform to the rate–equilibrium relationships (eq 2) when structural changes in the nitroalkanes cause effects that are either primarily polar or steric in nature. This is believed to be a consequence of the extensive rehybridization and solvent reorganization in the carbon acid that accompany these deprotonations. It seems likely that most other carbon acids will behave similarly, although the lack of correlation may be less extreme and therefore less obvious. Experimental data to test this point are meager, since nitroalkanes are the only monofunctional substrates acidic enough to permit equilibrium acidities, as well as kinetic acidities, to be determined in protic media. The lower acidity of other monofunctional carbon acids means that, with a given base, deprotonations will be more endoenergetic, and the transition state will be more product-like (Leffler–Hammond postulate[15,16]). Therefore, we would expect a greater degree of rehybridization in the transition state leading to intermediates comparable to **10** or to **15**. An estimate of the relative extent of such rehybridization in weaker carbon acids can be obtained by comparing the effect on kinetic and equilibrium acidities

of introducing β,γ unsaturation into various types of carbon acids of decreasing strengths (Table III).

The estimates summarized in Table III are necessarily rough, since the data available are limited and are taken from a variety of sources in different types of solvents. (Data in solvents of the same type are not available.) The equilibrium acidities are measured or extrapolated from data in Me_2SO solvent,[17,23] while the rate data are for deprotonation rates using hydroxide or alkoxide ion as the base in protic solvents. Since substitution of either a Ph or CH_2=CH group for R in RCH_2NO_2 has an effect of the same order of magnitude on equilibrium and kinetic acidities, we have assumed that this will also be true for other carbon acids. (Substitution of Ph for Et in $EtCH_2NO_2$ increases the acidity by 4.8 pK units and a 5.8 pK unit is observed for vinyl substitution; the rate accelerations for deprotonation by RO^- in protic solvents are ~30-fold and 85-fold, respectively.[2]) Examination of Table III shows that there is a progressive decrease in the size of ΔpK from the weakest carbon acid (the alkene) to the strongest carbon acid (the nitroalkane). This corresponds to a progressive decrease in the negative charge density at the carbon atom of the acidic site in the parent acid as it becomes stronger (resonance saturation effect[19]). A similar, but smaller, effect is observed on the rates. Here the negative charge density at the carbon atom of the acidic site apparently becomes progressively greater in the transition state for the deprotonation as the acid becomes progressively weaker, in agreement with the expectation of a more product-like transition state[15,16] and a progressively greater ability of the α-Ph (or α-C=C) substituent to stabilize the charge by delocalization. Although the comparisons are crude, it would appear that rehybridization in the transition state becomes progressively greater as the acid gets weaker, and that the effect on the rate begins to approach that on the equilibrium. In other words, the Brønsted α increases in size, as anticipated by the Leffler–Grunwald rate–equilibrium equation (eq 2). The data in Table III suggests, therefore, that for deprotonation reactions that span large $\Delta G°$ ranges, variation in transition-state structures may be large enough to conform approximately to eq 2. On the other hand, for small $\Delta G°$ ranges, such as those encountered in this series of papers, where substituent effects on a single type of carbon acid are considered, the variation in transition-state structure is slight and eq 2 does not hold, even approximately. In such instances the size of α will change depending on the details of the mechanism for deprotonation, which is likely to be complex.[2] For carbon acids where deprotonation is accompanied by extensive structural and solvent reorganization, such as $ArCH_2NO_2$ or $R_1R_2CHNO_2$, we have seen that substituent effects on the transition state for deprotonation may be larger or in an opposite direction to those on the product anions, leading to Brønsted α's larger than 1.0 or negative in sign. These data have been rationalized by assuming that rehybridization of the carbon atom at the acidic site has progressed but little in the transition state. For weaker carbon acids the data in Table III suggest that rehybridization in the transition state for deprotonation becomes progressively greater as the acid becomes weaker. At the same time the extent of delocalization of the negative charge in the product anion becomes progressively less as the acid becomes weaker. We can anticipate, therefore, that for very weak carbon acids rehybridization of the carbon atom at the acidic site in the transition state for deprotonation will differ but little from that in the product anion,[15,16] and that substituent effects on the kinetic and equilibrium acidities will correspond more closely to that predicted by eq 2. This does not mean, however, that we can expect substituent effects to be intermediate to those on reactants and products or that the Brønsted α can provide more than a rough guide to the transition-state structure.

Experimental Section[24]

Instruments and Analyses. Infrared spectra were taken on either a Baird Model AB-2 or a Beckman IR 5 spectrophotometer with the polystyrene 6.243-μm band as a standard. Nuclear magnetic resonance spectra were taken on either a Varian Model A60 or Varian Model T60 instrument with tetramethylsilane as an internal standard. Analytical and preparative gas–liquid chromatography were performed on an F & M Model 5750 research chromatograph equipped with a thermal conductivity detector and a disc integrator, using helium carrier gas, an injection port temperature of 250 °C, and a detector temperature of 290 °C. The column employed for purification and analysis of the nitroalkenes was QF-1 on specially acid washed Chromosorb W.[25]

pK Determinations. 1. Potentiometric. The pK's of 3-nitropropene, 1-nitro-2-butene, and 3-methyl-1-nitro-2-butene were measured in water at 25 °C by the partial neutralization technique described previously.[2] The pH measurements were performed on a Sargent Model DR digital readout pH meter equipped with a Corning semimicro combination electrode. Equilibrium was attained in ~10 min and measurements were taken every 10 min for 1 h. After 1 h, the solutions began to decompose.

2. Spectrophotometric. The pK's of the remaining nitroalkenes were measured spectrophotometrically in water at 25 °C using a Cary Model 15 recording spectrophotometer with a brass cell block thermally controlled by an Aminco circulating water bath.

Constant ionic strength buffer solutions were prepared using reagent grade materials which were not further purified. The pH's were measured immediately prior to use and never differed by more than 0.04 units from that calculated.

In a typical experiment with nitroalkenes which do not isomerize in buffer, 3.0 mL of the appropriate solvent (water, 0.1 M sodium hydroxide or buffer) was pipetted into a cuvette. After thermal equlibration 10–40 μL of ~0.01 M nitroalkene solution in methanol (prepared as described for the potentiometric pK measurements) was injected using a 50-μL Hamilton 710N syringe. The syringe always contained 5–10 μL of methanol behind the nitroalkene solution in order to ensure complete delivery. The resulting concentration of nitroalkene in the cuvette was in the range of 5×10^{-5} to 2×10^{-4} M. The ultraviolet spectra were recorded from 350 to 220 nm.

The spectrum of nitroalkene in water (slightly acidified) was assumed to be that of the protonated species, and the spectrum in 0.1 M sodium hydroxide to be of the nitronate anion. The extinction coefficients at various wavelengths were then calculated for both forms. These extinction coefficients, rather than literature values, were used in order to eliminate errors resulting from possible differences between the actual concentration of nitroalkene and that calculated.

The spectrum of nitroalkene in buffer (the pH of which was in the region of the expected nitroalkene pK) was scanned at appropriate intervals until equilibrium was established (1–24 h) and continued for several additional hours. The pK was calculated from the equations

$$C_{HA} = T - C_{A^-} \tag{3}$$

$$A_{obsd} = C_A - \epsilon_{A^-} + (T - C_{A^-})\epsilon_{HA}$$

$$C_{A^-} = (A_{obsd} - T\epsilon_{HA})/(\epsilon_{A^-} - \epsilon_{HA}) \tag{4}$$

$$pK = pH + \log(C_{HA}/C_{A^-}) - \log \gamma_{\pm} \tag{5}$$

A_{obsd} is the equilibrium absorbance value of the nitroalkene in buffer at a specified wavelength, ϵ_{HA} and ϵ_{A^-} are the extinction coefficients of the nitroalkene and its anion at that wavelength, C_{HA} and C_{A^-} are the molar concentrations of nitroalkene and anion, T is the total calculated molar concentration of substrate, $-\log \gamma_{\pm}$ is an activity coefficient correction factor which was taken to be equal to the activity coefficient of aqueous potassium chloride at the ionic strength of the buffer, and the pH is that measured for the buffer prior to the experiment. The pK was calculated in this manner at three different wavelengths, usually the λ_{max} for the nitronate anion and 15–20 nm above and below this value. The entire procedure was repeated at least twice for every pK value reported. The standard deviation was generally 0.01–0.02 pK units and never exceeded 0.05 unit.

For those nonconjugated (β,γ-unsaturated) nitroalkenes which isomerize readily in buffer solution to the conjugated (α,β-unsaturated) form a more complicated treatment was necessary. The conjugated nitroalkene (α,β isomer) was synthesized independently, and its spectrum in the buffer employed was recorded in the manner described previously. The extinction coefficients at the wavelengths used for the pK measurement were calculated from this spectrum. The spectrum in buffer was found to be identical with that in slightly

Table IV. Ultraviolet Spectra of Conjugated Nitronate Ions in Water at 25 °C[a]

nitronate ion	registry no.	μ_{max}, nm	ϵ_{max}
$CH_2{=}CHCH{=}NO_2^-$	60211-46-3	275	20 700
$MeCH{=}CHCH{=}NO_2^-$	66291-29-0	274	23 500
$CH_2{=}C(Me)CH{=}NO_2^-$	66291-28-9	276	14 570
$CH_2{=}C(Br)CH{=}NO_2^-$	66291-27-8	276	13 100
$CH_2{=}C(Ph)CH{=}NO_2^-$	66291-26-7	288	10 990

[a] Spectra of the nitroalkenes in 0.1 M NaOH; anion concentration 2–4 × 10^{-5} M.

acidified water, although it decreased over long time periods and after ~24 h no observable absorbance remained. No spectral change which indicated nitronate ion formation was observed, in accordance with the expected low acidity of the conjugated nitroalkene.

The experimental procedure was identical with that described for the nonisomerizing nitroalkenes. The pK was calculated from the equations

$$A_{obsd}^{\lambda_1} = C_A - \epsilon_{A^-}^{\lambda_1} + C_{\beta\gamma}\epsilon_{\beta\gamma}^{\lambda_1} + C_{\alpha\beta}\epsilon_{\alpha\beta}^{\lambda_1} \quad (6)$$

$$A_{obsd}^{\lambda_2} = C_{A^-}\epsilon_{A^-}^{\lambda_2} + C_{\beta\gamma}\epsilon_{\beta\gamma}^{\lambda_2} + C_{\alpha\beta}\epsilon_{\alpha\beta}^{\lambda_2} \quad (7)$$

$$T = C_{A^-} + C_{\beta\gamma} + C_{\alpha\beta} \quad (8)$$

$$pK = pH + \log (C_{\beta\gamma}/C_{A^-}) - \log \gamma_{\pm} \quad (9)$$

with the aid of a Control Data 6400 computer. The terms λ_1 and λ_2 refer to two wavelengths, generally the λ_{max} of the nitronate anion and that of the α,β isomer; $A_{obsd}^{\lambda_1}$ and $A_{obsd}^{\lambda_2}$ are the absorbance values at these wavelengths of the β,γ isomer in buffer solution; $\epsilon_{A^-}^{\lambda_1}$, $\epsilon_{\beta\gamma}^{\lambda_1}$, $\epsilon_{\alpha\beta}^{\lambda_1}$, $\epsilon_{A^-}^{\lambda_2}$, $\epsilon_{\beta\gamma}^{\lambda_2}$, and $\epsilon_{\alpha\beta}^{\lambda_2}$ are the extinction coefficients of the nitronate anion, the $\beta\gamma$ isomer, and the α,β isomer at each wavelength; C_{A^-}, $C_{\beta\gamma}$, and $C_{\alpha\beta}$ are the molar concentrations of the three species; T is the total substrate concentration; pH and $-\log \gamma_{\pm}$ are the same as defined above.

The concentrations of the three species and the pK were calculated at several time intervals prior to and after attainment of equilibrium. At the outset the concentration of nitronate anion increases at the expense of the β,γ isomer, and a concentration of the α,β isomer slowly appears. After equilibrium is established, the concentration of the conjugated isomer continues to increase, while both the nitronate anion and the nonconjugated isomer decrease, but the ratio of the latter concentrations remains constant. Each pK value reported is the average of at least two determinations, with standard deviations of ~0.03 pK units (Table IV).

pK in Methanol. The pK of 3-nitropropene in methanol was measured by the spectrophotometric technique described above. An acetic acid/sodium acetate buffer in methanol was prepared as described by Belikov[26] using standardized 1.0 M acetic acid in methanol and 1.0 M sodium methoxide in methanol.

pK of Nitronic Acids. The pK values for propene-3-nitronic acid and 2-butene-1-nitronic acid were determined potentiometrically as described above except that partial neutralization was accomplished by adding increments of standard hydrochloric acid to a solution of the aci anion.

In a typical experiment, a standard solution of the aci anion (~0.01 M) in water was prepared from the sodium salt of the nitroalkane.[27] Increments (25-mL) of this solution were pipetted into wide-mouthed glass bottles with ground-glass stoppers. An increment of standard hydrochloric acid was added to effect a percentage neutralization in the range of 30–60%. Immediately after addition of the acid, the electrodes were immersed in the solution and pH readings were begun. Due to the isomerization of the liberated acid, the pH was observed to increase with time. However, since this increase with time was linear within experimental error, pH readings taken at various time intervals after addition of the acid could be extrapolated back to zero time in order to obtain the initial pH. This extrapolated pH value was used in the Henderson–Hasselbach equation to calculate the pK_{aci}. The above procedure was repeated four times for each nitronic acid using a different volume of hydrochloric acid in order to effect a different percentage neutralization. The pK_{aci} values calculated agreed within 0.03 pK units.

Kinetic Procedure. The rates of deprotonation by hydroxide ion in water at 25 °C were determined spectrophotometrically by following the appearance of the nitronate ion absorption in the ultraviolet region (λ_{max} 275–290 nm, ϵ_{max} 10 000–25 000) as previously described. The measurements for nitroalkenes were performed on a Durrum–Gibson stopped-flow spectrophotometer or on the Beckman Kintrac VII spectrophotometer.

The rates of deprotonation and dedeuteration by pyridine bases in water at 25 °C were measured spectrophotometrically by the buffer dilution method previously described.[2] The buffer pH was in all cases sufficiently high to ensure that the nitroalkene deprotonation was complete.

Preparations and Purifications. A sample of 2-methyl-3-nitrobutene prepared by Dr. E. W. Garbisch from the reaction of acetyl nitrate with 2-methyl-2-butene was redistilled and purified by vapor-phase chromatography. All other β,γ-unsaturated nitroalkanes were prepared by treatment of the allylic bromides or chlorides with silver nitrite according to the method of Kornblum and Ungnade.[28] A typical procedure is given below for 3-nitropropene. The purity of all nitroalkenes employed was at least 98% as evidenced by vapor-phase chromatography. The boiling points, refractive indices, and NMR spectral data are presented in Table V.

3-Nitropropene. The reaction was performed in a dark room equipped with a red safelight until the silver salts and nitrite esters were removed. Silver nitrite was prepared by adding a solution of 85 g of silver nitrate in 250 mL of water in several small portions with vigorous mixing to a solution of 35 g of sodium nitrite in 125 mL of water. The suspension was allowed to stand in the dark for 1 h. The yellow silver nitrite solid was separated by suction filtration, washed three times with 125 mL of water and twice with 100 mL of absolute methanol, and dried to constant weight in a vacuum desiccator over phosphorus pentoxide (36–48 h).

Eastman 3-bromopropene (34 g, 0.28 mol) was added dropwise over 1 h to a vigorously stirred suspension of 64.8 g (0.422 mol) of silver nitrite in 100 mL of anhydrous ether contained in a 500-mL three-neck flask equipped with a Teflon sleeve mechanical stirrer and a condenser protected with a drying tube. The flask was immersed in a large Dewar filled with ice–water to maintain a temperature of 0–5 °C throughout the reaction. Following the bromide addition, the solution was vigorously stirred for 12 h, at which time the supernatnat liquid gave a negative halide test (alcoholic silver nitrate).

The silver salts were removed by suction filtration and slurried three times with 75 mL of anhydrous ether. The combined ether filtrates were allowed to stand overnight in the dark with 8 mL of absolute methanol to hydrolyze the nitrite esters to the methyl ether of allyl alcohol.

The solvent was removed at atmospheric pressure using an 8 in. Vigreux column. The residue was distilled to yield 10 g (41%) of 3-nitropropene. *CAUTION:* The distillation residue must be cooled to room temperature before exposure to the atmosphere and due caution exercised in disposal, which should be done immediately following air exposure. Final purification employed gas–liquid chromatography.

3-Nitropropene-d_2. The nitroalkene dideuterated in the 3 position was prepared by the method described previously[2] using a deuterated succinic acid/sodium succinate buffer. Dideuterated succinic acid was prepared by refluxing succinic anhydride in deuterium oxide for 1 h. The isotopic purity of the nitroalkene in the 3 position was 98% (NMR).

Substituted 3-Nitropropene Derivatives. The substituted derivatives were prepared as described for 3-nitropropene above. The starting halide employed and any deviation in reaction conditions (i.e., temperature or reaction time) are given below (nitroalkene, starting halide, reaction conditions): 1-nitro-2-butene, 3-chloro-1-butene (Aldrich),[29] 12 h at 0–5 °C; 3-methyl-1-nitro-2-butene, 3-methyl-1-nitro-2-butene, 3-methyl-1-bromo-2-butene,[30] 24 h at 0–5 °C; 2-methyl-3-nitropropene, 2-methyl-3-chloropropene (Aldrich), 8 h at 0–5 °C, 24 h at 25 °C, and 36 h at reflux; 2-phenyl-3-nitropropene, 2-phenyl-3-bromopropene (prepared from α-methylstyrene by the method of Reed[31]), 48 h at 0–5 °C; 2-bromo-3-nitropropene, 2,3-dibromopropene (Aldrich), 12 h at 0–5 °C; 2-nitro-3-pentene, 2-bromo-3-pentene (prepared from Chemical Samples 3-penten-2-ol by the method of Hwa and Sims[32]), 24 h at 0–5 °C.

2-Methyl-1-nitropropene (17). The α,β-unsaturated nitroalkene was prepared from 2-methyl-3-nitropropene (**7**, G = Me) by triethylamine-catalyzed isomerization in hexane according to the method of Hesse et al.[33] An equilibrium mixture of 82% **17** and 18% **7** was obtained. Pure **17** was isolated by vapor-phase chromatography: UV max (C_2H_5OH) 250 nm (ϵ 8600), (H_2O) 262 nm (ϵ 8900), (*n*-hexane) 240 nm (ϵ 9000) [lit.[34] UV max (C_2H_5OH) 251 nm (ϵ 8600), (*n*-hexane) 235 nm (ϵ 10 000)]; NMR ($CDCl_3$) δ 1.98 (s, 3, methyl cis to hydrogen), 2.26 (s, 3, methyl cis to nitro), and 6.98 (s, 1 =C**H**NO_2).

2-Methyl-3-nitro-2-butene (18). The α,β-unsaturated nitroalkane was prepared from 3-nitro-2-methyl-2-butyl acetate according to the

Table V. Physical Properties of 3-Nitropropene and Its Derivatives

nitroalkene	bp, °C (mmHg)	n_D (temp, °C)	lit. n_D (temp, °C)	NMR $\delta_{Me_4Si}(CDCl_3)$, ppm
3-nitropropene	44 (27)	1.4258 (21)	1.4260 (20)[a]	4.98 (d, 2, J = 7 Hz, CH_2NO_2), 5.3–5.5 (m, 2, H_2C=), 6.1 (m, 1, =CH–)[2]
1-nitro-2-butene	60 (25)	1.4387 (21)	1.4391 (20)[b]	1.78 (d, 3, J = 5 Hz, CH_3CH=), 4.85 (d, 2, J = 6 Hz, CH_2NO_2), 5.8 (m, 2, –CH=CH)
3-methyl-1-nitro-2-butene	55 (8)	1.4490 (21)	1.4489 (20)[b]	1.75 (m, 6, $(CH_3)_2C$=), 4.90 (d, 2, J = 8 Hz, CH_2NO_2), 5.5 (t, 1, J = 8 Hz, =CH–)
2-methyl-3-nitropropene	38 (12)	1.4323 (21)	1.4331 (20)[b]	1.82 (s, 3, =C(CH_3)–), 4.92 (s, 2, CH_2NO_2), 5.2 (bs, 2, H_2C=
2-phenyl-3-nitropropene	84 (0.3)	1.5831 (20)		5.20 (s, 2, CH_2NO_2), 5.35, 5.65 (2s, 2, H_2C=), 7.25 (bs,5, C_6H_5
2-bromo-3-nitropropene	34 (0.3)	1.4963 (21)	1.4970 (20)[b]	5.26 (s, 2, CH_2NO_2), 5.9–6.2 (m, 2, H_2C=)
2-nitro-3-pentene	61 (30)	1.4348 (21)	1.4356 (20)[b]	1.60 (d, 3, J = 6.6 Hz, CH_3CHNO_2), 1.75 (d, 3, J = 5 Hz, CH_3CH=), 5.00 (q, 1, J = 6.5 Hz, $CHNO_2$), 5.7 (m, 2, –CH=CH–)
2-methyl-3-nitrobutene	50 (15)	1.4365 (21)	1.4352 (20)[c]	1.67 (d, 3, J = 7 Hz, CH_3CHNO_2), 1.82 (s, 3, =C(CH_3)–), 5.07 (q, 1, J = 7 Hz, $CHNO_2$), 5.17 (s, 2, H_2C=)

[a] N. Kornblum and D. C. Iffland, unpublished work reported in *Org. React.*, **12**, 131 (1962). [b] Yu. V. Baskov and V. V. Perekalin, *Zh. Org. Khim.*, **1**, 236 (1965). [c] Reference 37.

Table VI. NMR Spectra of 3-Nitropropene and the Sodium Salt of Its Anion in D_2O and in MeOD

substrate	δ CH_2=, ppm	δ =CH–, ppm	δ CH_2NO_2, ppm
CH_2=$CHCH_2NO_2$[a]	5.45	6.15	4.97
CH_2=$CHCH$=$NO_2^-Na^+$[b]	5.45	6.75	6.85
CH_2=$CHCH_2NO_2$[c]	5.45	6.15	5.00
CH_2=$CHCH$=$NO_2^-Na^+$[d]	5.0	6.7	6.7

[a] Neat. [b] 5% solution in D_2O. [c] 40% solution in MeOD. [d] 5% solution in MeOD.

method of Hesse et al.[33] Final purification was by vapor-phase chromatography: bp 60 °C (15 mm); $n^{21}D$ 1.4605 [lit.[35] bp 69.2 °C (20 mm); $n^{20}D$ 1.4618]; UV max (*n*-hexane) 251 nm (ε 3500) [lit.[35] UV max (*n*-heptane) 250 nm (ε 3900)]; NMR ($CDCl_3$) δ ~1.8 (m, 6, cis methyl groups) and ~2.2 (m, 3, methyl cis to nitro).

2-Phenyl-1-nitropropene (19). The α,β-unsaturated nitroalkane was prepared by treating 2-phenyl-1-nitro-2-propyl acetate[36] (2.0 g, 0.009 mol) with 10 mL of triethylamine in 20 mL of chloroform. The solution was stirred at room temperature for 1 h and then poured into 50 mL of 3 N hydrochloric acid. The layers were separated and the aqueous layer was extracted with three 60-mL portions of chloroform. The combined chloroform layers were washed with two 50-mL portions of water and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to yield 1.3 g (88%) of a mixture of 77% **19** and 23% **7** (G = Ph). The mixture was chromatographed on silica gel with dichloromethane eluent, but the highest purity obtainable was 80% **19** and 20% 2-phenyl-3-nitropropene. However, the ultraviolet spectrum of pure **19** could be obtained from this mixture, since the spectrum of pure 2-phenyl-3-nitropropene is known.

NMR Spectra. NMR data for 3-nitropropene and the sodium salt of its anion in D_2O and in MeOD are summarized in Table VI. The absence of an upfield shift of the H_2C= protons on the conversion to the nitronate ion contrasts sharply with the marked upfield shift for the H_2C= protons in allyllithium relative to allyl alcohol.[37,38] The negative charge in nitronate ions is known to be concentrated on oxygen,[27] and must remain primarily there, at least in protic solvents, even when delocalization in the carbon moiety becomes possible. The downfield shift observed for the α protons (and also the slight downfield shift for the β proton) is expected because of the change in hybridization of the α-carbon atom.

Acknowledgment. We are grateful to the National Science Foundation and the National Institutes of Health for support of this research.

Registry No.—3-Nitropropene-*3,3-d*$_2$, 66291-25-6; 3-bromopropene, 106-95-6; 2-methyl-1-nitropropene, 1606-30-0; 2-methyl-3-nitro-2-butene, 19031-80-2; 2-phenyl-1-nitropropene, 15795-70-7; 3-nitro-2-methyl-2-butyl acetate, 66291-24-5; 2-phenyl-1-nitro-2-propyl acetate, 66291-23-4.

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(2) See the preceding papers in this issue, and references cited therein.
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Comparison of the Acidities and Basicities of Amino-Substituted Nitrogen Heterocycles

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Seventeen amino-substituted heterocycles, including pyridines, pyrimidines, cytosines, isocytosines, and adenines, have been compared with respect to acidity (pK_{HA}, deprotonation at amino) and basicity (pK_{BH^+}, protonation at ring nitrogen). Unlike the analogous deaza compounds, in which protonation and deprotonation occur at the same site, there is no correlation between pK_{HA} and pK_{BH^+}. The pK_{BH^+} for amino protonation of some of these compounds can be calculated, however, and in these cases the points fall very near the line for the deaza compounds. The displacement from this line can be regarded as a measure of the difference in basicity of the amino nitrogen atom and an aza nitrogen atom in the heterocycle in question.

The basic nature of organic amines is well known (eq 1), their acidic character much less so (eq 2).

$$RNH_3^+ \rightleftharpoons H^+ + RNH_2 \quad (1)$$

$$K_{BH^+} = [H^+][RNH_2]/[RNH_3^+]$$

$$RNH_2 \rightleftharpoons H^+ + RNH^- \quad (2)$$

$$K_{HA} = [H^+][RNH^-]/[RNH_2]$$

Recent studies of the ionization of aminoarenes[1] and aminoheterocycles[2] in basic aqueous dimethyl sulfoxide have provided us with a considerable number of pK_{HA} values (standard state, water) and we herein examine the relationship between proton gain (pK_{BH^+}) and proton loss (pK_{HA}) in such compounds.

Listed in Tables I and II are the available data for those aminoheterocycles in which a primary amino substituent NH_2 is the *acidic* center and for which both pK_{BH^+} and pK_{HA} are known. In most amino substituted nitrogen heterocycles the most *basic* center in the molecule is not the amino group but rather a ring nitrogen atom,[3] and this is so for all the heterocyclic compounds listed in the tables.

Previous work had shown that for most anilines and diphenylamines there is a linear relation between pK_{BH^+} and pK_{HA}, with the acidity, as represented by pK_{HA}, being more sensitive to substitution than basicity, as represented by pK_{BH^+}.[4] (The slope of a plot of pK_{HA} against pK_{BH^+} is 1.3.) The exceptions to this generality are those anilines and diphenylamines containing nitro groups at the ortho or para positions. The presence of one such group causes a large increase in acidity with the effect of additional nitro groups being much less. The change in *basicity*, however, is quite regular as successive nitro groups are introduced to the ortho and para positions. The net result is that a plot of pK_{HA} against pK_{BH^+} for anilines and diphenylamines has a discontinuity and a change of slope near the place where ortho and para nitroamines appear. There are two other commonly encountered -R groups in organic chemistry, cyano and carbonyl. The former does not appear to behave like nitro in the above respect, whereas there is some indication that the latter does. (Compare the effects of multiple substitution of these groups on methane acidity.[5])

We have plotted in Figure 1 the most recently published values of pK, many of which have been obtained by extrapolative techniques.[1a] It can be seen that for compounds in which the locus of protonation and deprotonation is the amino group (anilines, filled circles) there is a fairly regular, though nonlinear, relationship.

The most acidic and least basic compound in Figure 1 is 2,4,6-trinitroaniline, whose pK_{BH^+} and pK_{HA} values are in some doubt. It is half-protonated in 96% H_2SO_4[6] and earlier literature values are more negative than that[7] used here. Its response to base, likewise, is ambiguous, since there is evidence that it forms Meisenheimer complexes by addition of base, which accompanies or precedes proton loss.[8] Any attempt to accommodate these uncertainties by displacing the point in Figure 1 would have the effect of *increasing* the degree of curvature of the line.

The amino-substituted heterocycles (open triangles) all fall well off the line in Figure 1, and in the expected direction. That is, if the amino group is not the favored site of protonation then another location (invariably a ring nitrogen atom in conjugation with the amino group) must have a more positive pK_{BH^+} and such compounds will deviate in the direction shown. Furthermore, for several of these compounds, the aminopyridines and aminopyrimidines, the pK_{BH^+} for amino protonation can be calculated using the Hammett equation.[9] When this is done and the points included in the figure (filled triangles) it is found that these compounds now fall near the line determined by the anilines. The shifts in position of these

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