Proton-Transfer Reactions of Nitroalkanes: The Role of *aci*-Nitro Species

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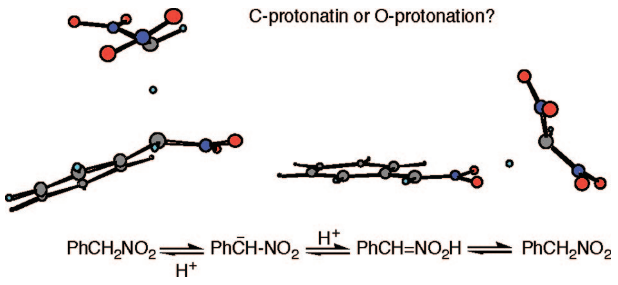

Proton-transfer reactions of two systems, ionization of a series of small carbon acids in water (the Pearson system) and reactions of substituted phenylnitromethanes, were examined in detail computationally. Comparison of experimental reactivity and pK_a with calculated relative activation barrier and reaction energy for the Pearson system suggested that the origin of the well-know nitroalkane anomaly does not reside in the reactivity but in the equilibrium. For the reactions of substituted phenylnitromethanes, proton transfers among three species, $PhCH_2NO_2$, $PhCHNO_2^-$, and $PhCH{=}NO_2H$, were examined, and the role of the *aci*-nitro species ($PhCH{=}NO_2H$) was evaluated on the basis of its stability and reactivity. Protonation of $PhCHNO_2^-$ by H_2O was suggested to occur kinetically on the oxygen site, but due to its instability $PhCH{=}NO_2H$ does not contribute to the overall reaction energetics. The protonation of $PhCHNO_2^-$ under acidic conditions occurs on the oxygen site to give $PhCH{=}NO_2H$ both kinetically and thermodynamically. The *aci*-nitro species thus formed appears to give $PhCH_2NO_2$ via intramolecular H_2O-mediated proton transfer, but a possibility of the route through $PhCHNO_2^-$—C-protonation would not be fully eliminated.

Introduction

The proton-transfer reactions of nitroalkanes are known to show abnormal reactivity, which is often called the nitroalkane anomaly. The nitroalkane anomaly has been observed in several ways.[1−4] Pearson and Dillon reported in 1953 that a logarithmic plot of deprotonation rate constants in water of 26 different small carbon acids against corresponding equilibrium constants gave linear Brønsted plots with the slope of 0.56 and that the points of CH_3NO_2 and $CH_3CH_2NO_2$ deviated downward by 2 to 3 logarithmic units from the correlation line.[1] Thus, the proton-transfer rates for nitroalkanes are slower than expected from their acidities. Similar anomalous behavior of nitro-substituted compounds in proton transfer and other reactions has been reported.[2] In a typical example, the pK_a value of RCH_2NO_2 decreases in the order $CH_3NO_2 > CH_3CH_2NO_2 > (CH_3)_2CHNO_2$ in water, whereas the rate of proton abstraction by hydroxide ion decreases in the same order. Here the reaction is slower for a more acidic substrate. An analogous system with an electron-withdrawing CN substituent, i.e., RR′CHCN, was reported to exhibit a normal rate−equilibrium relationship in water.[5]

Another well-known example is shown in eq 1, in which the Brønsted α values are larger than unity, indicating that the substituent effect is larger on the rate than on the equilibrium. For example, the α value is 1.54 for R = H, in H_2O,[3a,b] 1.37 for R = Me in 50% aq MeOH,[3c] and 1.18 for R = Me in 50%

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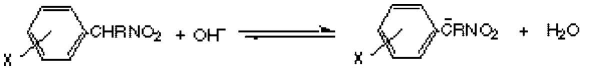
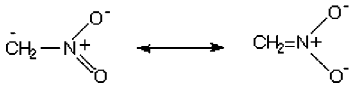
10.1021/jo8023939 CCC: $40.75

aq dioxane.[3d] Unusual behavior in the rate−equilibrium relationship of nitroalkanes has been reported not only for proton-transfer reactions but also for substitution reactions, in which nitronate anion acts as a nucleophile.[4]


(1)

The origin of the anomaly has been interpreted in terms of possible charge imbalance at the transition state (TS) and the product state.[2,6] Chart 1 shows the resonance structure of nitronate anion. In the product anion, the negative charge is largely localized on the NO_2 group, whereas a partial negative charge developed within the $RCHNO_2$ moiety at the TS is in part on the CH_2 subgroup due to electrostatic interaction between the negatively charged carbon and the positively charged proton in-flight. Thus, a larger fraction of negative charge is localized on the carbon at the TS than at the product state, which explains the larger-than-unity Brønsted α values observed for reaction 1. At the same time, since the ability of the resonatively stabilizing effect of the NO_2 group is not fully operating at the TS, the proton-transfer rates of RNO_2 are slower than expected from their pK_a values. The TS imbalance rationale has been developed by Bernasconi for proton-transfer reactions of various substrates.[6] The TS imbalance can be conveniently detected by looking at the charge on C_α and on NO_2 at both the TS and the product anion, and such TS charge imbalance for nitroalkanes has indeed been confirmed computationally by several authors.[7,8]

CHART 1

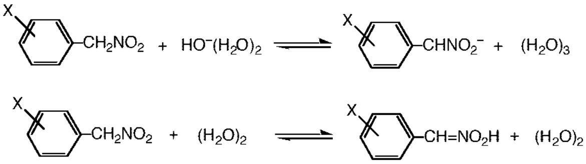


We have previously reported substituent effects on the proton-transfer reactions of $ArCH_2NO_2$ with CN^- and with $HO^-(H_2O)_2$.[8,9] In the latter calculations, $HO^-(H_2O)_2$ was used as a base because HO^- used in experiment was too strong a base in the gas phase and did not give TS in the calculations. Although only three substituents (*p*-OMe, H, *p*-NO_2) were used in these calculations, both calculations have clearly indicated the existence of the TS charge imbalance. However, they gave, at the same time, quite normal Brønsted α values of 0.51 and 0.38, respectively, and thus there was no anomaly in these gas-phase reactions. These results suggested that the TS charge imbalance might not be the sole origin of the nitroalkane anomaly. It has been shown experimentally that under acidic conditions, protonation to nitronate anion occurs not on the carbon but on the oxygen site to give *aci*-nitro species.[10−13] This apparently differs from the expectation for the protonation of nitronate anion with H_2O, which, based on the principle of microscopic reversibility, has implicitly been assumed to proceed via direct protonation to the carbon site of the anion to give nitro species and OH^-. Under these circumstances, examination of the whole process involved in the proton-transfer reaction of phenylnitromethanes was considered informative in understanding the proton-transfer chemistry of nitroalkane. In particular, the reaction energetics and substituent effect on the *aci*-nitro formation and decomposition processes need to be analyzed.

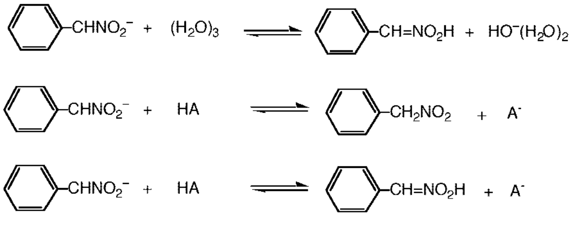
In the present study, the proton-transfer reactions of a series of small carbon acids with CN^-, eq 2, were first examined computationally. Second, the reaction processes involved in the proton-transfer reactions of phenylnitromethanes under basic and acidic conditions were studied in detail (eq 1−6). These calculations revealed that the protonation of the nitronate anion, by both H_2O and acids, occurs on the oxygen site, rather than the carbon site, leading to the *aci*-nitro intermediate, and thus the reaction could be more complex than usually thought.

$$R\text{-}H \quad CN^- \rightleftharpoons R^- + HCN \qquad (2)$$

R-H = CH_3NO_2, $C_2H_5NO_2$, $CH_2(NO_2)_2$, CH_3COCH_3, CH_3COCH_2Cl, $CH_3COCHCl_2$, $CH_3COCH_2COCH_3$, $CH_2(CHO)_2$, CH_3CN, $CH_2(CN)_2$, $CH_2(CO_2C_2H_5)_2$, CH_3CO_2H, $CH_2(CO_2H)_2$, CH_3CONH_2


(3)
(4)

X = *p*-NH_2, *p*-MeO, *p*-OH, *p*-Me, *m*-Me, H, *p*-Cl, *m*-Cl, *m*-F, *p*-CF_3, *p*-CN, *m*-CN, and *p*-NO_2, for reactions 3 and 4.


(5)
(6a)
(6b)

HA = $CH_2(NO_2)_2$, $CH_2(CHO)_2$. $CH_2(COCH_3)_2$

Computational Methods

Separated reactants, TSs, and products for reaction 2 were calculated for all acids at the B3LYP/6-31+G* level of theory, and were reoptimized at MP2/6-31+G* and G2(+) methods for selected acids.[14] Reactants, TSs, and products were also calculated for reactions 3−6 at B3LYP/6-31+G*. Reaction 3 is the proton-transfer reaction of phenylnitromethane with hydroxide ion, and reaction 4 is the water-mediated isomerization between the nitro vs *aci*-nitro forms. Reaction 5 is the protonation of the nitronate anion on the oxygen site by water. Reactions 6a and 6b are the protonation of the anion on the carbon and oxygen sites, respectively, by weak acids, $CH_2(NO_2)_2$, $CH_2(CHO)_2$, and $CH_2(COCH_3)_2$. Full-frequency analyses were carried out to confirm that the optimized structures were minima or saddle points on the potential energy surface. All activation and reaction energies reported are relative to separated reactants (in kcal mol^{-1}). We use enthalpies rather than free energies, since calculated entropies, and hence free energies as well, are known to be less reliable and not suitable for

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TABLE 1. Calculated Reaction and Activation Enthalpies for the Reactions of a Series of Carbon Acids with CN^- at Three Computational Methods

		B3LYP/6-31+G*		MP2/6-31+G*		G2(+)	
entry	carbon acid	ΔH	$\Delta H^{\ddagger}$	ΔH	$\Delta H^{\ddagger}$	ΔH	$\Delta H^{\ddagger}$
1	$CH_2(NO_2)_2$	−32.3	nd	−24.4	−22.9	−24.7	−23.3
2	$CH_2(CN)_2$	−18.1	−24.8	−12.8	−21.1	−14.9	−21.9
3	$CH_2(CHO)_2$	−13.8	−14.6	−10.9	−11.0	−9.9	−11.1
4	$CH_3COCH_2COCH_3$	−10.4	−14.1	−8.4	−11.8	−8.3	nd[a]
5	$CH_2(COOC_2H_5)_2$	−10.1	−15.1	nd	nd	nd	nd
6	$CH_2(COOH)_2$	−5.9	−12.8	nd	nd	nd	nd
7	$CH_3COCHCl_2$	−0.5	−15.5	1.9	−13.9	0.6	−14.3
8	$C_2H_5NO_2$	5.0	−8.8	8.1	−4.4	7.0	−4.8
9	CH_3NO_2	5.9	−9.0	7.9	−4.0	7.2	−4.9
10	CH_3COCH_2Cl	6.5	−8.7	nd	nd	nd	nd
11	CH_3COOH	15.6	−4.1	nd	nd	21.1	3.9
12	CH_3CHO	17.2	−0.73	17.9	3.5	17.0	2.3
13	CH_3COCH_3	21.1	2.8	21.3	5.9	19.3	3.9
14	CH_3CONH_2	29.2	9.0	28.4	10.1	26.8	8.4
15	CH_3CN	24.2	7.5	nd	nd	nd	nd
16	$CH_3CO_2CH_3$	19.3	−3.2	nd	nd	nd	nd
17	$CH_3CO_2C_2H_5$	15.8	−3.6	nd	nd	nd	nd
18	$CH_2(CONH_2)_2$	−5.9	−15.0	nd	nd	nd	nd

[a] nd: not determined.

linear free energy analyses. Hammett plots were made by using relative activation or reaction enthalpy at 298 K.

Results and Discussion

Rate−Equilibrium Correlation of Simple Carbon Acids. The proton-transfer reactions of a series of small carbon acids with CN^- were examined computationally. Acids used are listed in Table 1. Pearson and Dillon have reported the proton-transfer rates of a variety of carbon acids with H_2O in water and demonstrated that the Brønsted plot gave a good correlation with the α value of 0.56 and that the points of CH_3NO_2 and $C_2H_5NO_2$ deviate downward from the correlation line.[1] We used in the present calculation CN^- as a base, since H_2O is too week a base and we could not obtain TS for reactions with strong acids. A gas-phase reaction commonly proceeds via a double-well potential with weak reactant and product complexes. The present reactions indeed show such reaction potentials in all cases examined. However, since the present study aims at modeling reactions in solution and interpreting the effect of structural perturbation such as substituent on the reactivity, we do not focus on these weak complexes and discuss the relative stabilities of separated reactants, products, and TSs, and substituent effects on them. Table 1 lists the activation and reaction enthalpies calculated at three different methods. Correlations of the activation enthalpies and the reaction enthalpies for different theories are shown in Figure 1. It can be seen that the three different methods gave similar relative energies without any particular trend, suggesting that the results with more accessible B3LYP theory allow reliable discussion.

In Figure 2 are shown the Brønsted plot for the proton-transfer reaction calculated at B3LYP/6-31+G* and G2(+). As is seen in Figure 2, the plots gave some scattering, but it should be noted that the points for $MeNO_2$ and $EtNO_2$ fit exactly on the correlation lines with slopes of ca. 0.51 (B3LYP/6-31+G*) and 0.63 (G2(+)), indicating that the nitroalkane anomaly does not exist in the gas phase. Thus the well-know anomaly occurs only in solution chemistry. With this result in mind, the calculated and experimental activation and reaction energies for the Pearson system are compared. Figure 3A illustrates the correlation of the calculated activation enthalpy against the experimental reactivity (log *k*) in water taken from the literature.[1] There exists a very nice linear relationship including the points of $MeNO_2$ and $EtNO_2$, indicating that there is no anomaly in the reactivity. By contrast, the plot of the calculated reaction enthalpy against the experimental pK_a values[1] in Figure 3B revealed that the points of $MeNO_2$ and $EtNO_2$ largely deviate upward from the correlation line. Thus, the present calculations suggested that the well-known nitroalkane anomaly does not arise from abnormal reactivity as usually assumed but comes from the equilibrium process in solution. The possibility may be that (1) the equilibrium process is more complex than normally believed or (2) a stronger solvation effect exists on the equilibrium process than on the rate process.

Proton-Transfer Reactions of Substituted Phenylnitromethanes: Deprotonation Reactions under Basic Conditions. The proton-transfer reaction of 13-substituted phenylnitromethanes (*p*-NH_2, *p*-CH_3O, *p*-OH, *p*-CH_3, *m*-CH_3, H, *p*-Cl, *m*-Cl, *m*-F, *p*-CF_3, *m*-CN, *p*-CN, *p*-NO_2) with solvated hydroxide anion $OH^-(H_2O)_2$ was calculated at B3LYP/6-31+G*. The optimized TS structure for the parent compound is shown in Figure 4A. In Table 2 are listed the calculated reaction and activation enthalpies for the proton-transfer reaction of substituted phenylnitromethanes with $OH^-(H_2O)_2$.

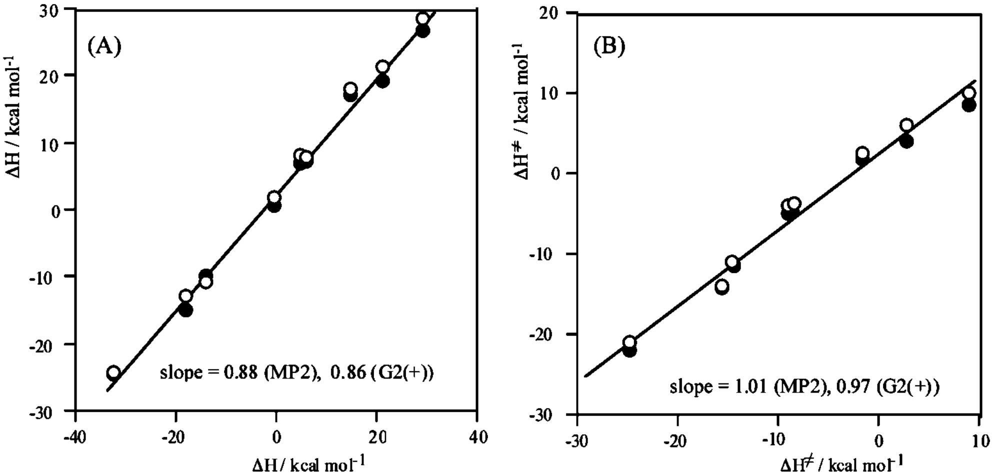

FIGURE 1. Comparison of (A) reaction enthalpies and (B) activation enthalpies calculated at MP2/6-31+G* (open circle) and G2(+) (closed circle) with those calculated at B3LYP/6-31+G*.

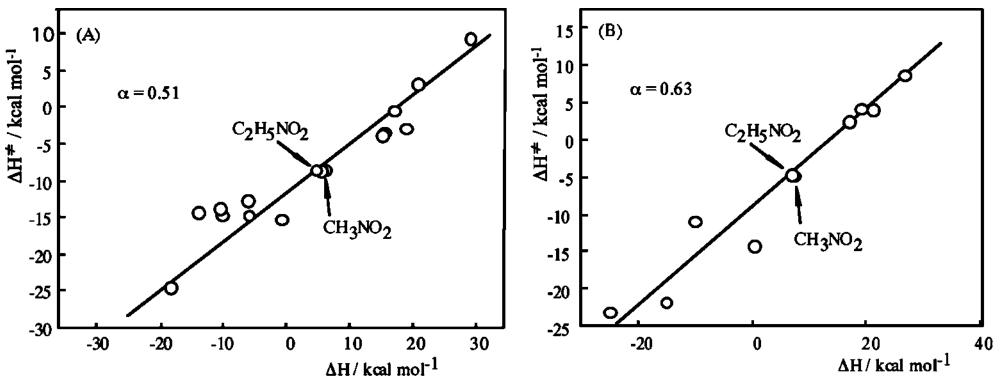

FIGURE 2. Brønsted plot for proton transfer of a series of small carbon acids with CN^- calculated at (A) B3LYP/6-31+G* and (B) G2+.

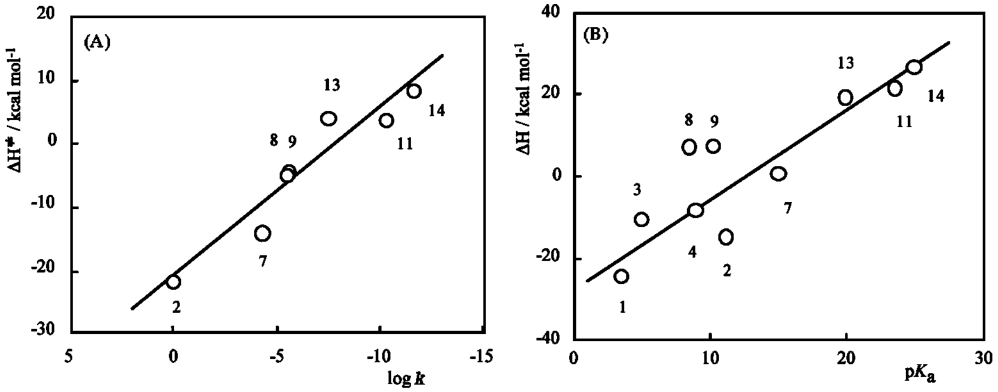

FIGURE 3. Correlation of the (A) calculated activation enthalpy at G2(+) with experimental reactivity and (B) calculated reaction enthalpy at G2(+) with experimental pK_a.

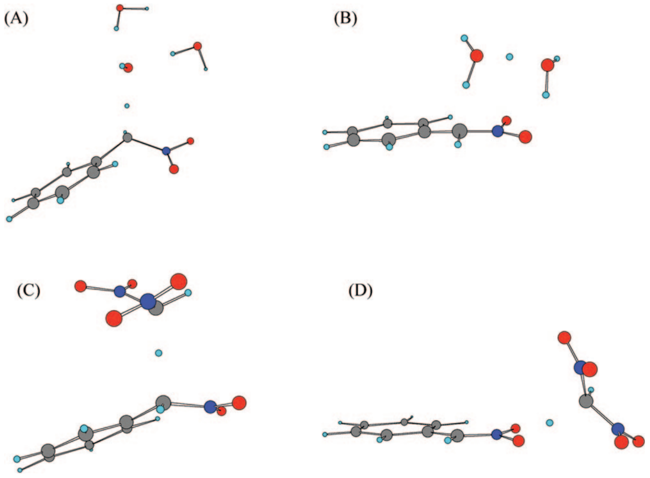

FIGURE 4. B3LYP/6-31+G* optimized TS structures for (A) the proton abstraction reaction of $PhCH_2NO_2$ with $OH^-(H_2O)_2$; (B) the two-water mediated isomerization of $PhCH_2NO_2$ to $PhCH{=}NO_2H$, (C) C-protonation, and (D) O-protonation of $PhCHNO_2^-$ with $CH_2(NO_2)_2$.

The calculations gave linear Hammett plots for both the rate and equilibrium processes of deprotonation of substituted phenylnitromethanes with $OH^-(H_2O)_2$, with ρ values of 6.90 (Figure 5A) and 12.6 (figure not shown), respectively. Figure 5B shows the Brønsted plot for this process, which gave an excellent linear correlation with a normal α value of 0.55 (R^2 = 0.991). Thus, no anomaly was detected in the gas-phase reactions of phenylnitromethanes.

Role of *aci*-Nitro Species. It has been reported that the *aci*-nitro species, in addition to nitroalkane and nitronate anion, plays an important role in proton-transfer reactions of nitroalkanes.[10−13] Therefore, in order to understand the whole process of protonation−deprotonation reactions of $PhCH_2NO_2$, it is important to clarify the stability and reactivity of *aci*-nitro species ($PhCH{=}NO_2H$).

a. Nitronate vs *aci*-Nitro Equilibrium. The stability of *aci*-nitro species has been measured experimentally, and extensive kinetic study has been carried out for the proton-transfer reaction of $PhCHNO_2^-$. It has been shown that the protonation of $PhCHNO_2^-$, which was formed by the treatment of $PhCH_2NO_2$ with HO^-, with acid gave $PhCH{=}NO_2H$ upon O-protonation in equilibrium with $PhCHNO_2^-$. The rate of protonation leading to $PhCH_2NO_2$ with a small excess of acid conditions could be measured by monitoring the λ_{max} of $PhCHNO_2^-$, whereas under low pH conditions, in which all $PhCHNO_2^-$ was converted to $PhCH{=}NO_2H$, the λ_{max} of $PhCH{=}NO_2H$ was used to follow the reaction. By assuming the reaction scheme shown in eq 7, the equilibrium constant (pK_a^{NOH}) and the C-protonation rate with acid (k_{-1}) were estimated as 3.64 and 5.71 L mol^{-1} s^{-1}, respectively. Together with a pK_a (6.77) of $PhCH_2NO_2$, the concentration ratio $[PhCH{=}NO_2H]/[PhCH_2NO_2]$ in water was estimated as 7.41 × 10^{-4}.[10]

$$PhCH_2NO_2 \xleftarrow[k_{-1}]{} PhCHNO_2^- + H^+ \underset{K_a^{NOH}}{\rightleftharpoons} PhCH{=}NO_2H \qquad (7)$$

Previous computational studies have demonstrated that the *aci*-nitro form is less stable than the nitro form by 14.1 (G2MP2), 22.9 (MP2/6-31G*), and 20.0 (MP2/6-31G**) kcal

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TABLE 2. Calculated Reaction and Activation Enthalpies for the Proton-Transfer Reaction of Substituted Phenylnitromethanes with $OH^-(H_2O)_2$ at B3LYP/6-31+G*

	eq 3 (nitro → nitronate)		eq 4 (nitro → *aci*-nitro)		eq 5 (nitronate → *aci*-nitro)
substituent	$\Delta H^\ddagger$	ΔH	$\Delta H^\ddagger$	ΔH	ΔH
p-NH$_2$	−14.53	−8.45	23.29	8.20	16.66
p-CH$_3$O	−16.11	−10.68	23.07	8.41	19.08
p-OH	−16.67	−11.28	22.97	8.39	19.66
p-CH$_3$	−16.60	−12.88	22.59	8.36	21.24
m-CH$_3$	−16.80	−12.93	22.43	8.45	21.38
H	−17.38	−13.67	22.21	8.32	21.99
p-Cl	−20.10	−18.69	21.58	7.86	26.54
m-Cl	−20.30	−19.46	21.29	8.01	27.47
m-F	−19.77	−18.43	21.38	8.01	26.44
p-CF$_3$	*nd*[a]	−24.57	20.37	7.52	32.09
m-CN	−23.97	−24.97	20.41	7.49	32.45
p-CN	−26.52	−28.55	19.71	7.06	35.61
p-NO$_2$	−28.19	−33.96	18.96	6.76	40.72

[a] nd: not determined.

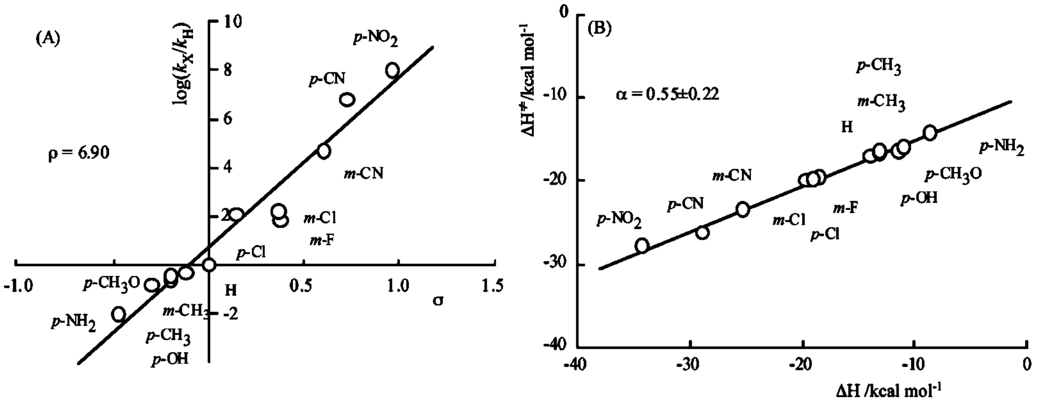


FIGURE 5. (A) The Hammett and (B) the Brønsted plot for the reactions of phenylnitromethanes with $OH^-(H_2O)_2$.

mol^{-1} for CH_3NO_2.[7a,15] The present study agrees qualitatively with these previous results in that PhCH═NO$_2$H was calculated to be unstable relative to PhCH$_2$NO$_2$ by 8.3 kcal/mol at B3LYP/6-31+G* (Table 2). The substituent effect on the nitro vs *aci*-nitro equilibrium (eq 4) was calculated for a series of substituted phenylnitromethanes, and the results are compiled in Table 2. The Hammett plot is illustrated in Figure 6B. The observed small ρ value (0.83) indicates that the substituent effect on the relative stability of these two neutral species (PhCH$_2$NO$_2$ vs PhCH═NO$_2$H) is small, which in turn means that the substituent effect on the protonation equilibrium between $PhCHNO_2^-$ and PhCH═NO$_2$H (K_a^{NOH}) gives a quite large negative ρ value ($-11.8 = 0.8 - 12.6$).

The TS for the isomerization from PhCH$_2$NO$_2$ to PhCH═NO$_2$H could not be optimized when no intervening H_2O molecule was included. However, if one or two water molecules were included, TSs with barrier heights of 33.0 and 22.2 kcal mol^{-1}, respectively, were obtained. The TS structure with $(H_2O)_2$ bridging the NO_2 oxygen and the α-carbon is shown in Figure 4B. The activation enthalpies calculated for the isomerization TS with $(H_2O)_2$ were summarized in Table 2, and the Hammett plots on the water-mediated proton transfer are shown in Figure 6A. The substituent effect on rates gave a medium-sized ρ value of 2.29, which is larger than the small ρ value (0.83) observed on the equilibrium. Thus, the apparent Brønsted α coefficient is much larger than unity. This means that the TS receives more stabilization with an electron-withdrawing substituent than the product. Such stabilization at the isomerization TS can be explained by the TS structure in Figure 4B, which shows that the isomerization is basically proton transfer within the protonated water dimer that is interacting with the nitronate anion. Indeed the calculated group NPA charge on H_2O--H--H_2O is 0.74, meaning that a more negative charge (−0.26) resides on the PhCHNO$_2$ moiety at the TS than at the nitro and *aci*-nitro forms, which are neutral species.

b. Protonation on the Nitronate Anion. The question arises here whether the protonation to nitronate anion occurs at the carbon site or the oxygen site. The protonation to $PHCHNO_2^-$ with H_2O under neutral conditions, which is the reverse reaction of PhCH$_2$NO$_2$ with OH^-, is considered to proceed via C-protonation according to the principle of microscopic reversibility, although no direct kinetic study has been reported for this process. On the other hand, protonation under acidic conditions has been studied experimentally and considered to occur at the oxygen site.[10−13,16−18] Thus, it is often assumed that the site of protonation varies depending on the acidity of the proton source. To obtain a better understanding of the different protonation site under different reaction conditions, calculations were carried out for protonations of $PhCHNO_2^-$ with three carbon acids with different acidities (eq 6).

We chose $CH_2(NO_2)_2$, $CH_2(CHO)_2$, and $CH_2(COCH_3)_2$ as acids, because they have moderate acidity, which is higher or lower than that of PhCH$_2$NO$_2$ itself. In Table 3 are listed calculated activation and reaction enthalpies for the C- and O-protonation processes of $PhCHNO_2^-$ with three acids, together with the proton affinities (PAs) of the conjugate bases of the acids. Table 3 shows that the C-protonation is exothermic for $CH_2(NO_2)_2$ and $CH_2(CHO)_2$, whereas it is endothermic for

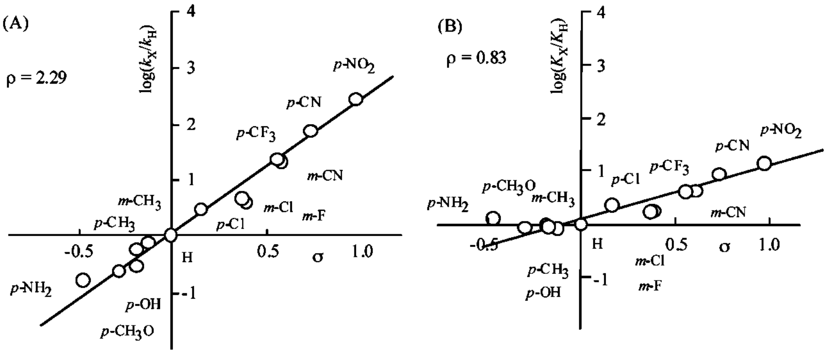
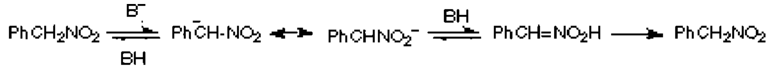


FIGURE 6. The Hammett plots for (A) the rate and (B) equilibrium of nitro → *aci*-nitro isomerization of phenylnitromethanes with $(H_2O)_2$.

CHART 2



$$PhCH_2NO_2 \underset{BH}{\overset{B^-}{\rightleftharpoons}} Ph\bar{C}H\text{-}NO_2 \longleftrightarrow PhCHNO_2^- \overset{BH}{\rightleftharpoons} PhCH{=}NO_2H \longrightarrow PhCH_2NO_2$$

					calcd ΔH (kcal mol^{-1})	exp K
$PhCH{=}N(O)OH$		$\rightleftharpoons$	$PhCH_2NO_2$		-8.3 ($\Delta H^{\ddagger}$ = 13.9)	1.3 x 10^3
$PhCHNO_2^-$ +	$(H_2O)_3$	$\rightleftharpoons$	$PhCH_2NO_2$	+ $OH(H_2O)_2^-$	13.7	
$PhCHNO_2^-$ +	H_2O	$\rightleftharpoons$	$PhCH_2NO_2$	+ OH^-		1.5 x 10^{-9}
$PhCHNO_2^-$ +	$(H_2O)_3$	$\rightleftharpoons$	$PhCH{=}NO_2H$	+ $OH(H_2O)_2^-$	22.0	
$PhCHNO_2^-$ +	H_2O	$\rightleftharpoons$	$PhCH{=}NO_2H$	OH^-		1.1 x 10^{-12}
$PhCHNO_2^-$ +	$CH_2(NO_2)_2$	$\rightleftharpoons$	$PhCH_2NO_2$	+ $CH(NO_2)_2^-$	-20.5	
$PhCHNO_2^-$ +	H_3O^+	$\rightleftharpoons$	$PhCH_2NO_2$	+ H_2O		5.9 x 10^6
$PhCHNO_2^-$ +	$CH_2(NO_2)_2$	$\rightleftharpoons$	$PhCH{=}NO_2H$	+ $CH(NO_2)_2^-$	-12.2	
$PhCHNO_2^-$ +	H_3O^+	$\rightleftharpoons$	$PhCH{=}NO_2H$	+ H_2O		4.4 x 10^3

TABLE 3. Calculated Activation and Reaction Enthalpies for the C- and O-Protonation Processes of $PhCHNO_2^-$ with Carbon Acids, and the Proton Affinities of Their Conjugate Bases[a]

	eq 6a (C-protonation)		eq 6b (O-protonation)		PA
acid	$\Delta H^{\ddagger}$	ΔH	$\Delta H^{\ddagger}$	ΔH	ΔH
$CH_2(NO_2)_2$	−10.9	−20.5	−18.5	−12.2	313.8
$CH_2(CHO)_2$	−5.1	−7.8	−11.1	0.5	326.5
$CH_2(COCH_3)_2$	1.8	1.3	−4.2	9.6	336.7

[a] Numbers are in kcal mol^{-1}. PA of $PhCHNO_2^-$ is 334.3.

$CH_2(COCH_3)_2$. The structures of two TSs for the reactions of $CH_2(NO_2)_2$ are shown in Figure 4C,D. The plot of calculated activation enthalpies with respect to the separated reactants vs PAs is shown in Figure 7. An important finding is that the O-protonation TSs are lower in energy than the corresponding C-protonation TSs for all acids by 6−8 kcal mol^{-1}, despite the C-protonated product being more stable than the O-protonated one by 8.3 kcal mol^{-1}. The slopes of the Brønsted-type plots in Figure 7 for the two processes are not very much different from each other, which implies that O-protonation is kinetically favorable for acids with a wide range of acidities. Unfortunately, an unrealistic hydrogen bond interfered with the attempted optimization of the O-protonation TS for the reaction of $PhCHNO_2^-$ with $(H_2O)_3$, and therefore direct comparison between C- vs O-protonation with neutral water could not be made. However, it appears quite safe to conclude on the basis of the results in Figure 7 that protonation by water on $PhCHNO_2^-$ occurs on the oxygen site to give $PhCH{=}NO_2H$. The kinetic preference for O-protonation is understandable in view of the fact that proton transfer between oxygen or nitrogen bases is much faster than that between carbon bases, due to lower intrinsic barriers for the former.[19]

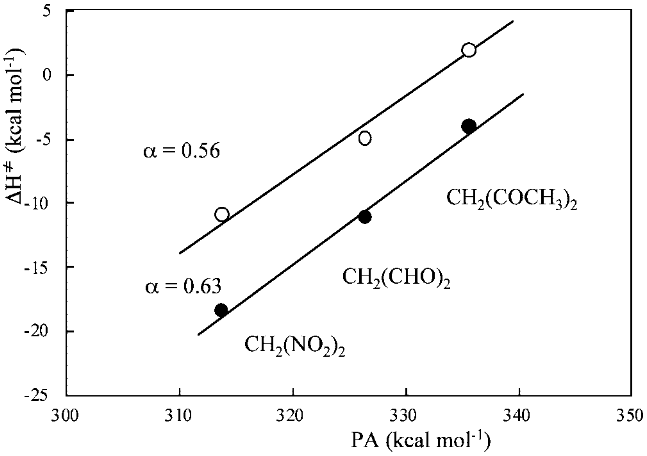


FIGURE 7. Correlation between activation enthalpies for C-protonation (open circle) and O-protonation (filled circle) with three carbon acids vs proton affinities.

It is now clear that the nitronate anion gives kinetically *aci*-nitro species by O-protonation. The mechanism of the conver-

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(16) Sun, S. F.; Folliard, J. T. *Tetrahedron* **1971**, *27*, 323.

(17) Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1950**, *72*, 3574.

(18) Edward, J. T.; Tremaine, P. H. *Can. J. Chem.* **1971**, *49*, 3483.

(19) See among others: Jones, J. R. *The Ionization of Carbon Acids*; Academic Press: New York, 1973.

sion of thus formed *aci*-nitro species to the nitro form is the next question to answer. There are two possibilities. First, $PhCH{=}NO_2H$ regenerates $PhCHNO_2^-$, and $PhCH_2NO_2$ is formed through kinetically unfavorable C-protonation on $PhCHNO_2^-$ (eq 6). Alternatively, $PhCH{=}NO_2H$ isomerizes to $PhCH_2NO_2$ in an intramolecular manner via a proton-transfer relay through solvent water (eq 4). Previous experimental studies have indicated that the protonation of the nitronate anion under the acidic conditions is accelerated by acid and that the observed rate shows saturation kinetics with acid concentration.[10,11] However, the reported experimental results did not allow the two mechanistic schemes mentioned above to be distinguished, since both schemes are consistent with the kinetic observations.

Summary of Reaction Energetics. To answer the question whether protonation of $PhCHNO_2^-$ directly gives $PhCH_2NO_2$ by C-protonation or via the O-protonation−isomerization route, the calculated reaction energies in the gas phase are summarized, together with experimental equilibrium constants in water, in Chart 2. Experimental equilibrium constants were derived from pK_a values of H_2O, $PhCH_2NO_2$, and $PhCH{=}NO_2H$. Here, $PhCHNO_2^- + (H_2O)_3$ and $PhCHNO_2^- + CH_2(NO_2)_2$ are taken as model reactions of protonation with neutral water and acid, respectively. The C-protonation reaction of $PhCHNO_2^-$ with water to give $PhCH_2NO_2$ is an uphill process by 13.7 kcal mol^{-1}, and it is even more uphill for the O-protonation (22.0 kcal mol^{-1}). However, as mentioned above, the O-protonation is kinetically favored by 6−8 kcal mol^{-1}, and therefore $PhCH{=}NO_2H$ should be involved in the overall process as a transient component.

The barrier for the C-protonation on $PhCHNO_2^-$ leading to $PhCH_2NO_2$ can be estimated as the sum of 13.7 kcal mol^{-1} (reaction energy) and the activation barrier for deprotonation of $PhCH_2NO_2$ with OH^-, which is no more than 10 kcal mol^{-1}.[3b] The barrier for the O-protonation−isomerization route, on the other hand, would be 22.0 kcal mol^{-1} (reaction energy) + 13.9 kcal mol^{-1} (isomerization barrier). Thus, it is concluded that the overall protonation reaction of $PhCHNO_2^-$ with water proceeds via direct C-protonation of the anion, with $PhCH{=}NO_2H$ as a minor equilibrium component. This, in turn, means that the deprotonation of $PhCH_2NO_2$ with OH^- proceeds as direct proton transfer, rather than via the $PhCH{=}NO_2H$ intermediate. It should be noted, however, that the difference of the overall barrier heights for the two routes is not larger than 6.3 kcal mol^{-1} (13.9 − 7.6 kcal mol^{-1}), if we assume that the energy difference (7.6 kcal mol^{-1}) of the C-protonation and O-protonation TSs calculated for $CH_2(NO_2)_2$ is applicable for protonation with other acids. If there is any isomerization process ($PhCH{=}NO_2H \rightarrow PhCH_2NO_2$) whose barrier is lower than 13.9 kcal mol^{-1}, the barrier difference, 6.3 kcal mol^{-1}, becomes even smaller.

Protonation of $PhCHNO_2^-$ with an acid preferentially occurs on oxygen to give $PhCH{=}NO_2H$ as a major component in equilibrium with $PhCHNO_2^-$. The *aci*-nitro species thus formed may give $PhCH_2NO_2$ via the isomerization or the deprotonation−C-protonation route. When $CH_2(NO_2)_2$ is used as an acid, the barrier from $PhCH{=}NO_2H$ to $PhCH_2NO_2$ via $PhCHNO_2^-$ is the sum of 12.2 kcal mol^{-1} ($PhCH{=}NO_2H \rightarrow PhCHNO_2^-$) and the barrier for the C-protonation on $PhCHNO_2^-$. The latter value is estimated as the sum of the C- vs O-protonation barrier difference (7.6 kcal mol^{-1}) and the barrier for the O-protonation, which could be small. Thus, the overall barrier for $PhCH{=}NO_2H \rightarrow PhCHNO_2^- \rightarrow PhCH_2NO_2$ would be a little higher than 19.8 kcal mol^{-1}. On the other hand, the barrier for the isomerization step ($PhCH{=}NO_2H \rightarrow PhCH_2NO_2$) was calculated to be 13.9 kcal mol^{-1} as a water-mediated process. The argument with energetics appears to indicate that the conversion of $PhCHNO_2^-$ to $PhCH_2NO_2$ under acidic conditions, the reverse process of deprotonation with H_2O, proceeds via the $PhCHNO_2^- \rightarrow PhCH{=}NO_2H \rightarrow PhCH_2NO_2$ route. This, in turn, implies that the deprotonation of $PhCH_2NO_2$ with neutral water proceeds via the *aci*-nitro intermediate.

The comparison of activation energies for the two routes under acidic conditions, however, is not straightforward, since the reaction energy of the proton transfer depends on the strength, concentration, and possibly the identity of the acid used. Although the above argument appears suggestive, it is not certain that the analysis based on energetics of the reactions with $CH_2(NO_2)_2$ is applicable to the reaction with aq HCl. In view of the fact that the calculated substituent effect on the *aci*-nitro to nitro isomerization is much smaller ($\rho = 2.29$) than the estimated ρ value for the $PhCH{=}NO_2H \rightarrow PhCHNO_2^- \rightarrow PhCH_2NO_2$ route (6.02 = 6.9 − 0.8), we hope that the comparison of experimental substituent effects on the rates of the protonation of $PhCHNO_2^-$ under neutral and acidic conditions would solve this problem, and such a study would be warranted.

Conclusions

Calculations on the rate and equilibrium processes of a series of carbon acids did not show an anomaly. Comparison of the calculated results in the gas phase with experimental results in water suggested that the nitroalkane anomaly arises from the equilibrium process rather than the rate process as is widely assumed.

The energetics consideration of model proton-transfer reactions indicated that the protonation process of $PhCHNO_2^-$ with H_2O, formed by deprotonation of $PhCH_2NO_2$ with OH^-, occurs kinetically on the oxygen site, but due to its instability the *aci*-nitro does not contribute to the overall reaction energetics. Thus, $PhCH_2NO_2$ is formed by direct C-attack on $PhCHNO_2^-$ by H_2O. It may be concluded that the so-called nitroalkane anomaly does not arise from the complexity of the equilibrium process, but may be partly due to TS imbalance and also due in part to the solvation effect on the nitronate anion product, which could be much stronger than that on the proton-transfer TS.

The protonation of nitronate anion under acidic conditions occurs on the oxygen site to give *aci*-nitro species both kinetically and thermodynamically. The *aci*-nitro species thus formed appears to give the nitro species via intramolecular H_2O-mediated proton transfer, but a possibility of the route through nitronate anion−C-protonation would not be eliminated on the basis of an energetic argument alone. Experimental study on the substituent effect for the *aci*-nitro to nitro conversion under both acidic and neutral conditions may help solve this problem.

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Supporting Information Available: Table S1−S3, structural parameters and energies of compounds treated in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

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