JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2007; **20:** 484–490
Published online 9 May 2007 in Wiley InterScience
(www.interscience.wiley.com) DOI: 10.1002/poc.1182

Reactivities of acridine compounds in hydride transfer reactions

In-Sook Han Lee,* Hyun Joo Kil and Young Ran Ji

Department of Science Education, Kangwon National University, Chunchon 200-701, Korea

Received 1 February 2007; revised 8 March 2007; accepted 9 March 2007

ABSTRACT: Reactivities of acridine derivatives (10-benzylacridinium ion, **1a**$^+$, 10-methylacridinium ion, **1b**$^+$, and 10-methyl-9-phenylacridinium ion, **1c**$^+$) have been compared quantitatively for hydride transfer reactions with 1,3-dimethyl-2-substituted phenylbenzimidazoline compounds, **2Ha–h**. Reactions were monitored spectrophotometrically in a solvent consisting of four parts of 2-propanol to one part of water by volume at 25 ± 0.1 °C. Reduction potentials have been estimated for acridine derivatives by assuming that the equilibrium constants for the reductions of **1a**$^+$**–c**$^+$ by **2Hb** would be the same in aqueous solution and accepting −361 mV as the reduction potential of the 1-benzyl-3-carbamoylpyridinium ion. The resulting reduction potentials, E^o_{red}, are −47 mV for **1a**$^+$, −79 mV for **1b**$^+$, and −86 mV for **1c**$^+$. Each of acridine derivatives gives a linear Brønsted plot for hydride transfer reactions. The experimental slopes were compared with those obtained by Marcus theory. This comparison shows that the kinetic data are consistent with a one-step mechanism involving no high-energy intermediates. Copyright © 2007 John Wiley & Sons, Ltd.

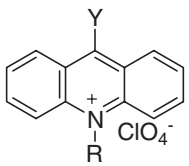
KEYWORDS: acridine derivatives; hydride transfer reaction; Brønsted α; Marcus theory

INTRODUCTION

Acridine derivatives, like most heterocyclic compounds, have been long-standing synthetic objectives due to their important biological activities.[1] Substituted acridines have been synthesized and reported to have antibacterial,[2] antimalarial,[3] anthelmintic,[4] analeptic,[5] and antineoplastic[6] activities. Acridine derivatives are also important in the study of reaction mechanisms because they have often been used as models of the coenzyme NAD$^+$ (nicotinamide adenine dinucleotide) for hydride transfer reactions.[7–10]

The oxidized forms of acridines, namely acridinium ions, undergo characteristic electrophilic addition reactions at the highly electron-deficient 9-position in the acridine ring and have served as hydride acceptors. On the other hand, the reduced forms, namely acridans, have served as hydride donors in model reactions for NAD$^+$–NADH interconversion.[11] Among them, 10-methylacridinium ion and the corresponding reduced form, 10-methylacridan, have frequently been used as convenient NAD$^+$ model compounds for kinetic and mechanistic studies for hydride transfer reactions[7,8] because they are easily prepared, stable in solution, and suitable for spectroscopic measurement due to their characteristic chromophores in the visible region. When 10-methylacridan is treated with hydride acceptors, it converts to 10-methylacridinium ion via a direct hydride transfer (one-step mechanism),[12a,13] by electron transfer followed by hydrogen transfer, or by sequential electron, proton, and electron transfer (stepwise mechanism),[7a–d] depending on the structures of acceptors and the reaction conditions.[7e,f]

For these reasons, further exploration of the reaction kinetics of acridine derivatives is of interest. We report here rate constants for the reactions of a series of 1,3-dimethyl-2-substituted phenylbenzimidazolines, **2Ha–h** with three kinds of hydride acceptors: 10-benzylacridium ion, **1a**$^+$, 10-methylacridinium ion, **1b**$^+$, and 10-methyl-9-phenylacridinium ion, **1c**$^+$. These acceptors differ in their substitution at N-1 and C-9. The hydride donors differ in their substitution on the phenyl ring.

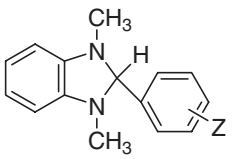


1$^+$

1a$^+$, Y = H, R = $C_6H_5CH_2$

1b$^+$, Y = H, R = CH_3

1c$^+$, Y = C_6H_5, R=CH_3



2H

Z = **a**, *p*-CH_3
b, H
c, *p*-F
d, *p*-Cl
e, *m*-F
f, *m*-Cl
g, *m*-CF_3
h, *m,m'*-Cl_2

*Correspondence to: I.-S. Lee, Department of Science Education, Kangwon National University, Chunchon 200-701, Korea.
E-mail: ishl@kangwon.ac.kr

1,3-Dimethyl-2-phenylbenzimidazoline, **2Hb**, has been reported previously as a powerful reducing agent whose corresponding oxidant, 1,3-dimethyl-2-phenylbenzimidazolinium ion, $\mathbf{2b}^+$ has a reduction potential of −471 mV.[14] Benzimidazoline derivatives can be also regarded as NADH analogs,[15] and, depending on the structures of acceptors, can undergo hydride transfer to hydride acceptors by a one-step mechanism,[14,16] or by a mechanism involving successive single electron transfer (SET) and hydrogen-atom transfer (HAT), which will be called an SET–HAT mechanism.[15]

We estimated the reduction potentials for the oxidants $\mathbf{1a}^+$–$\mathbf{c}^+$ in order to compare their reactivity for hydride transfer reactions. We analyze the kinetic results by using Marcus theory, which is based on a one-step mechanism.[17] The Marcus equation provides a relationship between the free energy of activation, the intrinsic barrier, and the overall Gibbs free energy of reaction, and it provides insight into the two-dimensional characterization of the transition structure as well as the reaction mechanism.

THEORY

Semiempirical Marcus theory[18] has been applied with considerable success to hydride transfer between NAD^+ analogs, and this analysis demonstrates that such transfers form a single, large family of reactions.[12,13] In semiempirical calculations of rate constants for hydride transfer by Marcus theory, the rate constants for the related symmetrical (or degenerate) reactions play a key role.[12,13]

A reaction series is defined by Eqn (1), where i and j indicate the hydride acceptor and donor, respectively.

$$A_i^+ + D_jH \rightarrow A_iH + D_j^+ \tag{1}$$

If the reactants and products are structurally related and of the same charge type, it is assumed that the free energy required for forming an encounter complex or a precursor structure [19,20] from the separated reactants, W^r, is the same as the free energy for forming a successor structure from the separated products, W^p. In that case, the Marcus relations[10,18] predict that the free energy of activation is given by[13,18]

$$\Delta G^* = W^r + (1 + \Delta G^\circ/\lambda)^2 \cdot \lambda/4 \tag{2}$$

where ΔG° is the Gibbs free energy of reaction, and λ is the intrinsic barrier given by

$$\lambda = (\lambda_i + \lambda_j)/2 \tag{3}$$

where λ_i and λ_j are free energies of activation for the related symmetrical reactions shown as Eqns (4, 5).

$$A_i^{*+} + A_iH \quad \rightarrow \quad A_i^*H + A_i^+ \tag{4}$$

$$D_j^{*+} + D_jH \quad \rightarrow \quad D_j^*H + D_j^+ \tag{5}$$

The overall free energy is related to the equilibrium constant by

$$K = \exp(-\Delta G^\circ/RT) \tag{6}$$

where R is the gas constant and T is the temperature. The free energy of activation is related to the rate constant by

$$k = \frac{k_B T}{h} \exp\left(\frac{-\Delta G^*}{RT}\right) \tag{7}$$

where k_B is Boltzmann's constant and h is Planck's constant.

As shown in Eqn (2), ΔG^* is assumed to be the sum of two parts. The work term W^r is that part of ΔG^* that is insensitive to the value of ΔG°. It has been found[10] that nonzero values of W^r are required even when the potential energy surfaces from which they were calculated had no metastable intermediates. For reactions of the type studied here, it has been found[12–14] that W^r is about −8 kJ/mol,[12–14] and we will use that value. The full explanation of why part of the free energy of activation should ultimately be sought in valence bond theory,[21] but that is beyond the scope of the present paper. However, the value of −8 kJ/mol may be considered reasonable in light of the charge-transfer interaction between the reactants.[13] The final conclusions of Marcus theory analysis are not overly sensitive to W^r, as long as it is not too far from zero.[13]

The Brønsted α parameter, which equals $d(\ln k)/d(\ln K)$, can be obtained from Eqns (1–7), which yields

$$\alpha = \chi \pm 0.5(\tau - 1) \mp 0.5\left(\frac{RT \ln K}{\lambda}\right)^2 (\tau - 1) \tag{8}$$

where

$$\chi = 0.5\left(1 - \frac{(RT \ln K)}{\lambda}\right) \tag{9}$$

and

$$\tau - 1 = \frac{d(\ln k_i)}{d(\ln K^\circ)} \tag{10}$$

where K° is the equilibrium constant of the reaction of A_i^+ with a standard hydride donor. We can write

$$K^\circ = \exp\left(\frac{-\Delta G^{\circ\circ}}{RT}\right) \tag{11}$$

where $\Delta G_i^{\circ\circ}$ is the overall Gibbs free energy of reaction for the reaction of A_i^+ with a standard hydride donor. The upper signs are used in Eqn (8) if the structural variation is in the acceptor, and the lower signs are used if the structural variation is in the donor.[12] For the present work, each system has the structural variation in the hydride donor so we used the lower signs consistently.

The parameter χ is called the resemblance parameter and it accounts for the parallel effect, also called the Leffler–Hammond effect.[22] The parameter τ is called the tightness parameter and it accounts for the perpendicular effect, also called the Thornton effect.[23]

For consistency with previous work,[12a] 10-methylacridan, **1Hb**, has been used as the standard donor. Using

DOI: 10.1002/poc

Eqn (10), the variation in rate constants of symmetrical reactions with K^o can be used to evaluate the parameter τ. Or, conversely, the effect of changes in hydride affinity of A_i^+ on the value of λ_i can be evaluated from the change in $\Delta G_i^{\circ\circ}$, which is measurable. For hydride transfer between NAD^+ analogs, τ was found to be reasonably constant with an average value of 0.81[13] and this value is used in the present work. The third term in Eqn (8) is negligible in most cases because $(RT/\lambda)^2$ will usually be very small. It has been shown, however, that both of the first two terms in Eqn (8) are required for a satisfactory estimate of α.[12–14]

Note that τ was originally defined as the sum of the bond orders of the in-flight hydrogen at the critical configuration,[12a] but, more generally, it is a phenomenological parameter related to the distance between the end groups as well as the partial charge on the in-flight atom or group.[10] Theoretical work suggests[18] that it is approximately constant over a long range of K values, as long as the end atoms are unchanged.

In this paper we consider three reaction series: when the structural variation for hydride transfer reaction is in the hydride donor as shown by Eqns (12–14),

$$\mathbf{1a}^+ + \mathbf{2H} \rightarrow \mathbf{1Ha} + \mathbf{2}^+ \quad (12)$$

$$\mathbf{1b}^+ + \mathbf{2H} \rightarrow \mathbf{1Hb} + \mathbf{2}^+ \quad (13)$$

$$\mathbf{1c}^+ + \mathbf{2H} \rightarrow \mathbf{1Hc} + \mathbf{2}^+ \quad (14)$$

the Brønsted α parameter can be obtained by using Eqn (8) with the lower signs. Using the same donors for all three systems makes the comparison possible in terms of the Brønsted α, χ, and τ. The perpendicular effect, τ, on α is the same for all three systems and the magnitude of the variation of α depends entirely on χ. Ratios of α values are given by

$$\frac{\alpha_{1a+}}{\alpha_{1b+}} = \frac{[\mathrm{d}(\ln k_{1a+})/d(\ln k_{1b+})]}{[\mathrm{d}(\ln K_{1a+})/\mathrm{d}(\ln K_{1b+})]} \quad (15)$$

The numerator in Eqn (15), the derivative involving rate constants, is accessible experimentally by measuring the rate constants, k, for the three reaction systems, and the denominator, the derivative involving equilibrium constants, is unity for the present system because the same hydride donors, **2Ha–h**, are used with each of the three acceptors. These ratios demonstrate the Leffler–Hammond or parallel effect. They are much less dependent on the accuracy of the K values than the individual values. Therefore, these ratios are very useful in comparing the experimental results with Marcus theory.

SYNTHESIS

Compounds $\mathbf{1a}^+$ and $\mathbf{1b}^+$ were prepared by benzylation and methylation of acridine using benzyl bromide and methyl iodide, respectively,[9] and followed by an ion exchange reaction with $NaClO_4$. Compound $\mathbf{1c}^+$ was prepared by addition of Grignard reagent to $\mathbf{1b}^+$ followed by oxidation reaction with *p*-chloranil and perchloric acid.[12b] All the acridine compounds were identified by their physical and spectroscopic properties. Compounds **2Ha–h** were prepared by the method of Craig *et al*.[24] with a small modification.

A typical synthetic procedure is as follows: A mixture of substituted benzoic acid (1.2 eq), *o*-phenylendiamine (1 eq), and polyphosphoric acid (three times of weight of acid) was heated with stirring at 175 °C for 1.5 h and then cooled to room temperature. An aqueous solution of NH_4OH (7%) was added to neutralize unreacted acids (benzoic acid and polyphosphoric acid). The solid was filtered and thoroughly rinsed with the NH_4OH solution to give 2-substituted phenylbenzimidazole. The yields were generally over 90%. Without further purification, the product was treated with methyl iodide (3 eq) in methanol containing NaOH (1 eq). The reaction mixture was heated at 110 °C overnight in a pressure tube. The crude product was recrystallized from absolute ethanol to give $\mathbf{2}^+$ (yields, over 80%). To a solution of $\mathbf{2}^+$ (1 eq) in methanol (25 ml/g), $NaBH_4$ (3 eq) was slowly added . The reaction mixture was stirred vigorously for 1 h under N_2. After removal of the solvent under reduced pressure the solid was recrystallized from EtOH–H_2O (2:1, v/v) to give a colorless crystalline product, **2H** (yields, over 70%).

KINETICS MEASUREMENTS

All kinetic measurements were conducted in a solvent containing four parts of 2-propanol to one part of water by volume at 25 ± 0.1 °C to facilitate comparison with a large body of analogous results already available in this solvent system.[13] 2-Propanol and water were distilled before use. Reactions of $\mathbf{1a}^+$ and $\mathbf{1b}^+$ with **2H** had half-lives less than 1 s. The reaction rate constants were determined with a stopped-flow apparatus (Hi-Tech Scientific, SFA-20) attached to the spectrophotometer (Beckmann DU-7500) by monitoring the decay of the absorption of $\mathbf{1a}^+$ and $\mathbf{1b}^+$ at 420 nm. Reactions of $\mathbf{1c}^+$ with **2H** were slow enough to monitor the decay of its absorption at 420 nm. These reactions went to completion in the presence of excess of **2H** ($>2.5 \times 10^{-3}$ M). All kinetic experiments were carried out with at least 25-fold excess of the spectroscopically inactive constituent, **2H**. Therefore, k_{obs} was obtained from the first-order rate law:[26]

$$k_{obs} = t^{-1} \ln\left(\frac{A_o - A_\infty}{A_t - A_\infty}\right) \quad (16)$$

and the second-order rate constants, k, were given by k_{obs}/C, where C is the concentration of the substance in excess.

All kinetic experiments were performed at least four times, in separate experiments. More than 20 experiments were performed for fast reactions of $\mathbf{1a}^+$ and $\mathbf{2b}^+$,

DOI: 10.1002/poc

Table 1. Rate constants and equilibrium constant for hydride transfer reactions

Reductant	Oxidant, k ($M^{-1}\,s^{-1}$)			
2H	$\mathbf{1a}^+$	$\mathbf{1b}^+$	$\mathbf{1c}^+$	K[a]
a	1.37×10^3	4.11×10^2	2.91×10^{-1}	6.58×10
b	9.80×10^2	2.94×10^2	1.92×10^{-1}	3.60×10
c	7.17×10^2	1.61×10^2	8.35×10^{-2}	1.72×10
d	5.35×10^2	1.12×10^2	7.17×10^{-2}	4.46
e	3.21×10^2	6.71×10	5.80×10^{-2}	2.52
f	2.15×10^2	5.47×10	4.87×10^{-2}	1.65
g	1.55×10^2	4.05×10	2.15×10^{-2}	1.17[b]
h	5.90×10	1.60×10	9.53×10^{-3}	1.12×10^{-1}

[a] The equilibrium constant for the reaction of 1-benzyl-3-carbamoylpyridinium ion with **2H** in Ref. 14.
[b] This value was obtained by extrapolation of a plot of ln$K$ as a function of σ in Ref. 14.

because the stopped-flow apparatus required small volumes, which give rise to greater-than-usual uncertainties in the concentrations. The average deviations from mean values of k_{obs} were about 5–8% for compounds $\mathbf{1a}^+$ and $\mathbf{1b}^+$ and 5% for compound $\mathbf{1c}^+$.

RESULTS

Rate constants for hydride transfer reactions are listed in Table 1. We also list the equilibrium constants for the reaction of 1-benzyl-3-carbamoylpyridinium ion with **2H** in Table 1. Equilibrium constants, Brønsted α parameters, and Hammett ρ parameters for hydride transfer reactions are listed in Table 2 along with the values of λ (kJ/mol), E^o_{red} (−mV), and pK_R. The parameters required for analyzing the parallel effect for hydride transfer reaction are listed in Table 3. The correlation of ln$k$ with ln$K$ for the reactions shown in Eqns (12–14) is shown in Fig. 1.

Table 2. Equilbrium constants, Brønsted αs, and Hammett ρs for hydride transfer reactions

Parameter	$\mathbf{1a}^+$	$\mathbf{1b}^+$	$\mathbf{1c}^+$
K[a]	1.45×10^{12}[b]	1.23×10^{11}[c]	7.81×10^{10}[c]
χ	0.41	0.42	0.43
λ (kJ/mol)	383	385	456
α (expt.)	0.50 ± 0.03[d]	0.51 ± 0.02[d]	0.52 ± 0.05[d]
α (calc.)[e]	0.51	0.52	0.53
ρ	-1.57 ± 0.11[d]	-1.62 ± 0.08[d]	-1.63 ± 0.15[d]
E^o_{red} (−mV)	47	79[f]	85
pK_R	6.66[g] (8.92)[h]	7.60[i] (10.00)[h]	8.57[j] (11.03)[k]

[a] Equilibrium constants for reactions of each oxidant with **2Hb**.
[b] Determined by the ladder procedure.
[c] Values obtained from Ref 25.
[d] The uncertainty is a probable error.
[e] Values obtained from Eqn (8).
[f] This value was obtained from Ref. 12d.
[g] An estimated value from extrapolation of a plot of pK_R in our solvent system (2-propanol: H_2O, 4:1 v/v) against pK_R in H_2O.
[h] Values obtained in H_2O from Ref. 9.
[i] This value was obtained from Ref. 31 (This value was reported as 7.74 due to a systematic computational error in the literature.)
[j] The value was obtained from Ref. 12c.
[k] The value was obtained from Ref. 27.

The parallel effects for the reactions between NAD^+ analogs are shown in Fig. 2. The correlation of ln$k$ with σ for the reactions in Eqns (12–14) is shown in Fig. 3.

DISCUSSION

As shown in Table 1, the order of reactivity of the oxidants is $\mathbf{1a}^+ > \mathbf{1b}^+ > \mathbf{1c}^+$. The oxidant $\mathbf{1a}^+$ is more reactive than $\mathbf{1b}^+$ due to the greater inductive effect of benzyl as compared to methyl; σ_I for phenyl, which distinguishes the two substitutes, is 0.1.[28] However, the introduction of a phenyl group at the 9-position of the acridine ring, which is the reactive site, decreases the reaction rate by more than a factor of 10^3, resulting in $\mathbf{1c}^+$ being much less reactive than $\mathbf{1b}^+$. These trends are consistent with those observed for the reactions of 1-benzyl-1,4-dihydronicotinamide with $\mathbf{1b}^+$ and $\mathbf{1c}^+$ in acetonitrile at 20 °C, where $\mathbf{1b}^+$ reacts 31 times faster than $\mathbf{1c}^+$ as a hydride acceptor.[29] It is believed that the steric effect of the phenyl group predominates the inductive effect for $\mathbf{1c}^+$. This reactivity trend is also consistent with the values of pK_R listed in Table 2 because log$k$ may be linearly correlated with pK_R.[9]

Another way to compare the reactivity of the oxidant is to measure the magnitude of reduction potential. By using a ladder procedure with the value of K for the reaction of $\mathbf{1b}^+$ with **2Hb** and previously reported values of K (the equilibrium constants for the reactions of $\mathbf{1a}^+$ and $\mathbf{1b}^+$ with 3-methyl-2-phenylbenzothiazoline, respectively),[12d]

Table 3. Demonstration of the parallel effect

oxidant	Slope[a,b]	Ratio of ρs	Calculated ratio of αs
$\mathbf{1a}^+$–$\mathbf{1b}^+$	0.97 ± 0.05	0.97	0.98
$\mathbf{1b}^+$–$\mathbf{1c}^+$	0.96 ± 0.07	0.99	0.98
$\mathbf{1a}^+$–$\mathbf{1c}^+$	0.93 ± 0.08	0.96	0.96

[a] The slopes of the plots of ln$k$ in one series as a function of ln$k$ in another series for the same hydride donors, **2Ha–h**, with a different hydride acceptor, $\mathbf{1}^+$.
[b] The uncertainty is a probable error.

DOI: 10.1002/poc

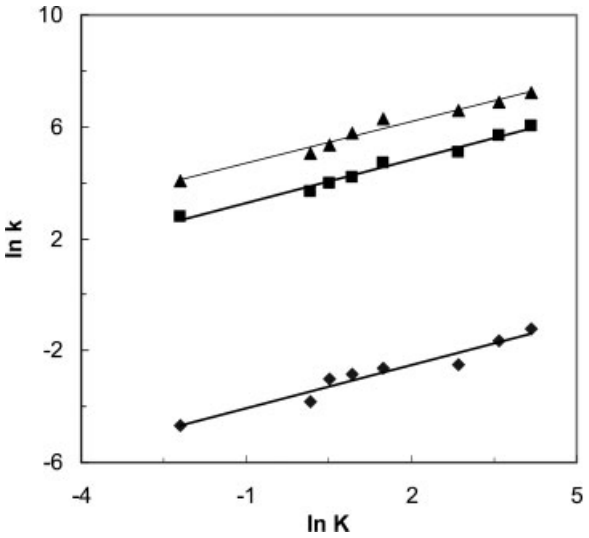


Figure 1. The correlation of ln*k* with ln*K* for the reactions shown in Eqns (12–14). The slopes of plots (the Brønsted α) are 0.50 ($r = 0.974$) for $\mathbf{1a}^+$ (▲), 0.51 ($r = 0.987$) for $\mathbf{1b}^+$ (■), and 0.52 ($r = 0.945$) for $\mathbf{1c}^+$ (◆), respectively

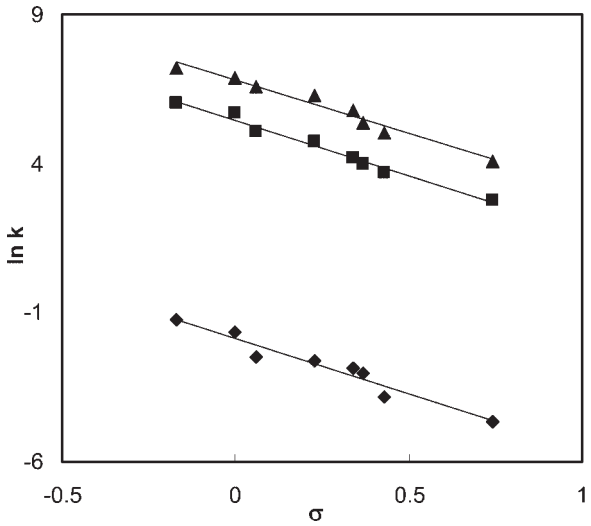


Figure 3. The correlation of ln*k* with σ for the reactions in Eqns (12–14). The slopes of plots, which are the values of ρ, are -1.57 ($r = 0.970$) for $\mathbf{1a}^+$ (▲), -1.62 ($r = 0.984$) for $\mathbf{1b}^+$ (■), and -1.63 ($r = 0.944$) for $\mathbf{1c}^+$ (◆), respectively. The slopes are divided by 2.3 to convert them to ρ values

we can calculate that the equilibrium constant for the reaction of $\mathbf{1a}^+$ with **2Hb** is 1.45×10^{12}. The equilibrium constants for the reactions of **1Ha** with $\mathbf{1b}^+$ and **1Hc** with $\mathbf{1b}^+$ in the same solvent system can be also obtained by another ladder, which yields 8.48×10^{-2} for $\mathbf{1a}^+$ and 6.35×10^{-1} for $\mathbf{1c}^+$.[25] With these values of K, reduction potentials, E^{o}_{red}, of -47 mV for $\mathbf{1a}^+$ and -85 mV for $\mathbf{1c}^+$, are obtained by

$$RT \ln K = nF\Delta E^{\circ} \quad (17)$$

where F is the Faraday constant and n is the number of electrons transferred (two in this case).[31]

For all the systems, Brønsted plots were made by plotting the values of ln*k* against the values of ln*K* for the reactions shown in Eqns (12–14). The equilibrium constants are obtained from the reactions of 1-benzyl-3-carbamoylpyridinium ion with **2H**.[14] It is assumed that since the structural variations are in the donors (**2H**), the equilibrium constants for the present system are proportional to those for the reactions of

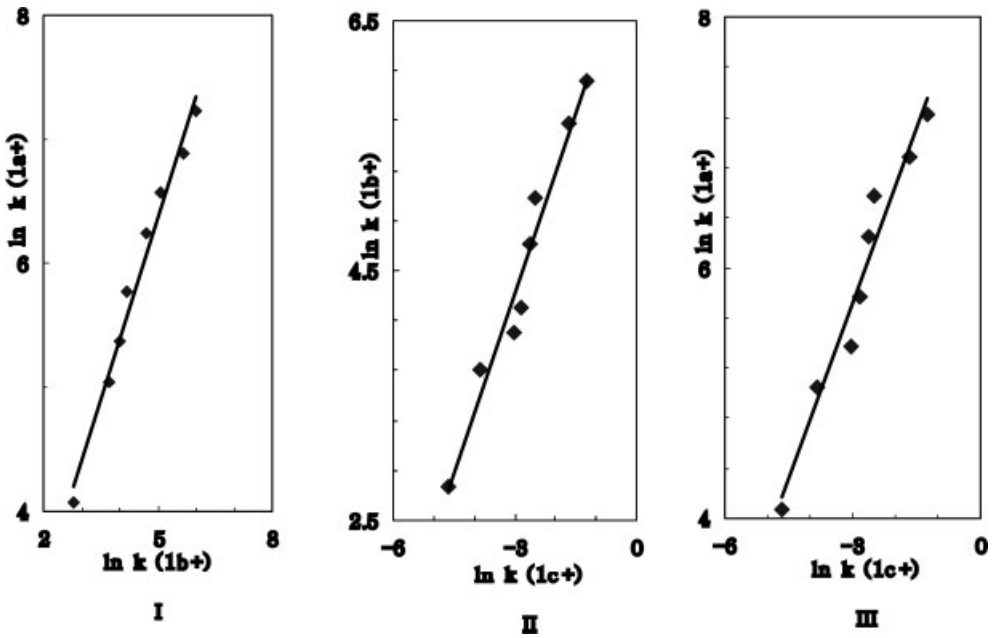


Figure 2. The parallel effects for hydride transfer reactions between NAD^+ analogs. The slopes are 0.97 ($r = 0.982$), 0.96 ($r = 0.967$), and 0.93 ($r = 0.954$) for I, II, and III, respectively. They are in good agreement with the ratios of calculated α values, as shown in Table 3

DOI: 10.1002/poc

1-benzyl-3-carbamoylpyridinium ion with **2H**.[14] All three plots are quite reasonably linear, as shown in Fig. 1. According to Eqn (8), their slopes are the Brønsted α values; these are given in Table 2, along with the probable errors of the slopes. The values of slopes are 0.50 ± 0.03 for $\mathbf{1a}^+$, 0.51 ± 0.02 for $\mathbf{1b}^+$, and 0.52 ± 0.05 for $\mathbf{1c}^+$, respectively. Since the same values of K were used for all three plots, errors in α values due to errors in K values (about 10%)[14] are completely compensated when ratios of α values are taken. In other words, differences in α are almost unaffected by errors in the K values and such ratios are much more reliable than would be suggested by the probable errors of the values of α themselves.

The calculated values of α in Table 2 can be obtained from the Marcus theory in Eqns (8, 9) if the values of W^r, τ, λ, are available (the values of W^r (-8 kJ/mol) and τ (0.81) were described above). With the values of ΔG^*, ΔG°, and W^r in hand, λ and χ were evaluated from Eqns (8, 9). They are listed in Table 2. The intrinsic barrier of **2Hb**, $\lambda_{\mathbf{2Hb}}$, has been reported as 413 kJ/mol.[14] With this value we can estimate the individual values of λ by applying to Eqn (3), giving 353 (kJ/mol) for $\lambda_{\mathbf{1a}+}$, 357 (kJ/mol) for $\lambda_{\mathbf{1b}+}$, and 502 (kJ/mol) for $\lambda_{\mathbf{1c}+}$, respectively. The compound $\mathbf{1c}^+$ has the highest reaction barrier among them, leading to the lowest reactivity. The introduction of phenyl group at C-9 on the acridine ring for $\mathbf{1c}^+$ gives a significant steric effect which overcomes the electronic effect, resulting in the reduction of the reactivity. This provides additional support for the order of reactivity.

The equilibrium constants are much larger than unity for the present system, giving χ values of 0.41, 0.42, and 0.43 for $\mathbf{1a}^+$, $\mathbf{1b}^+$, and $\mathbf{1c}^+$, respectively. But the calculated values of α are 0.51, 0.52, and 0.53 for $\mathbf{1a}^+$, $\mathbf{1b}^+$, and $\mathbf{1c}^+$, respectively, as shown in Table 2. The experimental and calculated α values are in fairly good agreement. The calculated values reproduce the trend in the experimental values almost exactly. This trend is an expression of the Leffler–Hammond or parallel effect. It shows the gradual change in transition state structures as the reactions become more spontaneous even though the difference is not large. It should be pointed out that most α values for the present system are greater than 0.5 even though the values of K are much greater than unity, although conventionally one would expect them to be less than 0.5.[22] This is explained by the perpendicular effect, that is, by the second term in Eqn (8).[30] The structural variation is in the hydride donor in the present system and the perpendicular effect ($0.5(\tau - 1)$) should be subtracted from χ in Eqn (8). As mentioned in the Section 'Theory', τ is 0.81, leading to the contribution of the perpendicular effect of $-0.5(0.81 - 1) = +0.1$ on the Brønsted α in the present case. This leads to the value of α greater than χ by itself.

Plotting of ln$k$ values for reduction of one oxidant as a function of ln$k$ for reduction of another oxidant by the same donors, **2Ha–h**, can demonstrate the parallel effect as described in the Section 'Theory'. This method can avoid the use of the series of K values by cancellation of the ratio of K in denominator in Eqn (15). The plots are shown in Fig. 2. The slopes of these plots slightly differ from unity because of the parallel effect. This effect for the present system may not be as significant as the earlier observation[14] due to a narrow range of K values compared to the previous system which had a much wide range of K values (10^{12}), but it is still appreciable as shown in Table 3. They should be given by ratios of calculated α values according to Eqn (15). They are also in good agreement.

The Hammett parameter[32] can be also used for mechanistic study by comparing ρ values in a similar way. The correlations of ln$k$ with Hammett parameter, σ, show a good linearity for all three series as shown in Fig. 3, giving ρ values of -1.57, -1.62, and -1.63 for $\mathbf{1a}^+$, $\mathbf{1b}^+$, and $\mathbf{1c}^+$, respectively, after dividing by 2.3 to put them on the usual scale. As expected, the values of ρ are negative because the reacting site at C-2 on the benzimidazole ring of **2H** develops a positive charge in the transition state. The ratios of ρ are very similar to the slopes shown in Fig. 2 as well as the ratios of the calculated α values. All the selectivity parameters indicate that the reactivity-selectivity principle (RSP) holds, so that rates of the hydride transfer are more dependent on basicities rather than on intrinsic barriers.

The foregoing results are consistent with the mechanism that the present system undergoes direct hydride transfer from **2H** to $\mathbf{1a}^+$-$\mathbf{c}^+$ without high-energy intermediate.

CONCLUSIONS

The introduction of phenyl group on the acridine ring affects the reactivity and the reactivity depends on its location. The order of reactivity for the acridine compounds is $\mathbf{1a}^+ > \mathbf{1b}^+$ and $> \mathbf{1c}^+$ and their reduction potentials, E^o_{red}, are -47 mV for $\mathbf{1a}^+$, -79 mV for $\mathbf{1b}^+$, and -85 mV for $\mathbf{1c}^+$, respectively. The Brønsted α for the present system can be calculated with the aid of Marcus theory which is based on a one-step mechanism and the calculated and experimental α values are in good agreement. Within Marcus formalism the present system can also demonstrate the Leffler–Hammond or parallel effect by introducing the same structural variation in the hydride donor, **2H**.

Acknowledgements

This work was supported by Korea Science and Engineering Foundation (R01-2004-10279). The authors thank Professors D. G. Truhlar and M. M. Kreevoy in the

DOI: 10.1002/poc

University of Minnesota for valuable comments and discussion as well as for proofreading the manuscript.

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DOI: 10.1002/poc