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Direct and Remote Substituent Effects in Radical Cation–Nucleophile Combination Reactions. Substituent Effects on Rate Constants and Oxidation Potentials

Vernon D. Parker,* Monica Pedersen, and Björn Reitstöen

Department of Chemistry and Biochemistry, Utah State University, Logan, Utah 84322-0300, USA

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Remote substituent effects on oxidation potentials and second-order rate constants have been determined for several series of reactions involving radical cations of 9-arylanthracenes (**1**) with pyridine derivatives in acetonitrile. The substituent effects were compared with those observed with 9-substituted anthracene (**2**) radical cations. Correlation of $\log k$ vs. Hammett σ^+ resulted in ρ equal to 0.47(5) for reactions of $\mathbf{1}^{+\bullet}$ and 2.4(3) for those of $\mathbf{2}^{+\bullet}$, respectively, with various pyridines. Hammett ρ values for correlation of $(F/2.303RT)E_{ox}$ vs. σ^+ were observed to be equal to 1.50 and 7.83 for **1** and **2**, respectively. Free energies of activation ($\Delta G^{\ddagger}$) for the radical cation–nucleophile combination reactions correlated linearly with substrate oxidation potentials with slopes equal to −0.43(5) for the 9-arylanthracene reactions series and −0.41(6) for the 9-substituted anthracene radical cation reaction series. The attenuation of the Hammett ρ values on going from the directly 9-substituted anthracene radical cations to similarly substituted 9-arylanthracene electrophiles was attributed to decreased conjugation between the substituent and the anthracene nucleus due to non-coplanarity of the phenyl and anthracene ring systems. It was concluded that the activation barriers for the reactions of both series of radical cations with pyridine nucleophiles are related, to very nearly the same degree, to the corresponding reversible electrode potentials for substrate oxidation.

The reactions of radical cations with nucleophiles have been actively studied over the past thirty-five years.[1–19] Mechanistic questions which have occupied workers in this area have changed with time and include:

(a) does the primary electrode reaction involve 1 or 2 e^- (1957–1969)?

(b) what is the primary reactant, radical cation or dication (1969–1984)?

(c) are radical cation–nucleophile combinations slow (1978–1992)?

(d) what determines radical cation reaction barriers (1986–1992)?

A rotating disk electrode study definitively answered question (a) in 1969.[2] Limiting currents at high rotation rates for the oxidation of 9,10-diphenylanthracene in the presence of pyridine nucleophiles were observed to correspond to the transfer of a single electron while at lower rotation rates the reaction between radical cation and nucleophile gave rise to an overall two-electron oxidation.

Question (b) is somewhat more difficult to answer definitively. Dications are very much more reactive than radical cations. If the disproportionation of the radical cation to the dication and the neutral substrate is thermodynamically favorable, the dication is clearly expected to be the reacting species. However, this is generally not the case, and direct interaction between nucleophile and radical cation appears to be the most likely reaction pathway in most cases. Various mechanisms for radical cation–nucleophile reactions have been considered and reviewed in 1984.[8]

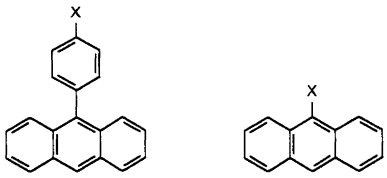
In 1978 Eberson compared the data available for radical cation–nucleophile reactions with that of appropriate carbenium ion–nucleophile reactions and concluded that the radical cation reactions are slow.[7] Later, Pross rationalized the apparent sluggishness of the radical cation–nucleophile reactions in terms of the configuration mixing (CM) model.[9] The conclusions of this study were quickly challenged and it was shown that reaction barriers are low for the reactions of 9-phenylanthracene radical cation with pyridine nucleophiles.[12] This was followed by a study of the reactions of radical cations of anthracene derivatives with anionic nucleophiles, some of which were observed to have unusually low reaction barriers.[14]

* To whom correspondence should be addressed.

Question (d) remains largely unanswered and is currently an active area of research. The CM model approach to radical cation–nucleophile reactivity has been amplified and guidelines for the semi-quantitative prediction of reaction barriers from gas-phase energetics of ionization have been proposed.[16] This treatment[16] was based upon the reactivity of the radical cation/nucleophile association complex and this was compared to that of cation/nucleophile complexes. This approach has recently been re-examined[19, 20] and it was found that some modification is necessary in order to analyze reactions of association complexes. Thölmann and Grützmacher have discussed the reactions of aryl halides with ammonia in terms of the CM model for reactions of the association complexes in the gas phase.[17] In this paper we contribute to the understanding of question (d) by making a comparison of direct and remote substituent effects on the reactions of radical cations of anthracene derivatives with pyridine nucleophiles. Little work has been reported on substituent effects for this type of reaction.

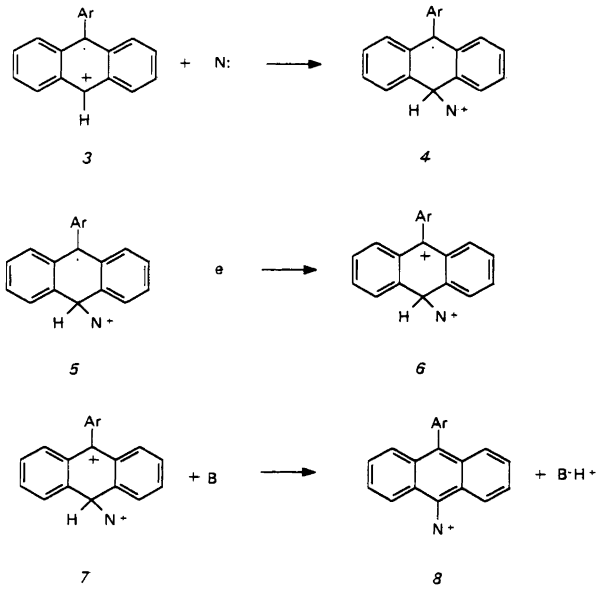
Results and discussion

The radical cations of 9-arylanthracene (**1**) provide a series of reactants for combination with nucleophiles to study the effect of *para*-substituents in the aryl group on reaction rates. The substituents are remote to the reactive site, i.e., the 10-position of the anthracene ring. Owing to steric interactions between the 1,8-hydrogens of the anthracene nucleus and the 2,6-hydrogens of the aryl group, the benzene ring of the aryl group is rotated out of the plane of the anthracene nucleus.[21] The latter gives rise to decreased conjugation and can be expected to affect the magnitude of the substituent effects on the properties of **1** and $\mathbf{1}^{+\bullet}$. These can then be compared with the relevant substituent effects observed for the directly substituted anthracene derivatives **2** and $\mathbf{2}^{+\bullet}$.



1 2

The overall reaction (Scheme 1) between pyridine nucleophiles and $\mathbf{1}^{+\bullet}$ (X = H) in acetonitrile has been studied in detail and has been observed to result in the pyridinium salts **8**.[23] In contrast with the reactions of 9,10-diphenylanthracene radical cation, for which complex kinetics are observed during nucleophilic attack by pyridines,[8] nucleophilic attack at the unsubstituted position of $\mathbf{1}^{+\bullet}$ is accompanied by the observation of simple second-order kinetics.[12, 19] Thus, substituent effects observed on the rates of the reactions correspond to nucleophilic attack of the pyridine to give the initial adduct.



Scheme 1.

Reversible oxidation potentials of the anthracene substrates in acetonitrile/Bu_4NBF_4 (0.1 M) vs. the ferrocene/ferrocenium couple ($Fc/Fc^{+\bullet}$) are summarized in Table 1. Second-order rate constants for the reactions with pyridine nucleophiles (pyridine, 4-cyanopyridine, 2-ethylpyridine and 2,6-lutidine) measured using the prepeak method[12, 24] in acetonitrile/Bu_4NBF_4 (0.1 M) at 298 K are summarized in Table 2. The decrease in the rate constants for the reactions of $\mathbf{1}^{+\bullet}$ with 4-cyanopyridine as compared with pyridine is due to the electronic effect of the 4-cyano group which decreases the nucleophilic character of the nitrogen lone pair of the pyridine ring. On the other hand the attenuation of the second-order rate constants for the reactions of 2-ethylpyridine and 2,6-lutidine is the result of increased steric congestion around the nucleophilic nitrogen.[19]

Correlation parameters for the reactions of $\mathbf{1}^{+\bullet}$ and $\mathbf{2}^{+\bullet}$ with pyridine nucleophiles in acetonitrile/Bu_4NBF_4 (0.1 M) as well as those for substrate oxidation potentials are compared in Table 3. The first two lines of data show the differences in ρ values for $\mathbf{1}^{+\bullet}$ and $\mathbf{2}^{+\bullet}$ observed for Hammett correlations of $(F/2.303RT)E_{rev}$ as well as log k vs. σ^+. Two observations can be made from the data. First, ρ values for the correlation of electrode potentials

Table 1. Reversible potentials for the oxidation of 9-arylanthracenes in acetonitrile/Bu_4NPF_6 (0.1 M) at 298 K.

para-Substituent[a]	E_{rev}/V vs. $Fc/Fc^{+\bullet}$
NO_2	0.926
Cl	0.874
H	0.850
CH_3	0.828
OCH_3	0.788

[a] The *para*-substituent in structure **1**.

Table 2. Second-order rate constants for the reactions of 9-arylanthracenes radical cations with pyridine nucleophiles in acetonitrile/Bu_4NPF_6 (0.1 M) at 298 K.

Nucleophile	*para*-Substituent	$\log(k/M^{-1}\,s^{-1})$
Pyridine	NO_2	7.81
	Cl	7.42
	H	7.26
	CH_3	7.11
	OCH_3	6.99
4-Cyanopyridine	NO_2	6.06
	Cl	5.80
	H	5.64
	CH_3	5.46
	OCH_3	5.47
2-Ethylpyridine	NO_2	5.96
	Cl	5.68
	H	5.56
	CH_3	5.38
	OCH_3	5.26
2,6-Lutidine	NO_2	2.81
	Cl	2.61
	H	2.22
	CH_3	2.48
	OCH_3	2.03

are about three times greater than those for correlation of log k. Second, ρ values for correlation of data for $\mathbf{2}^{+\bullet}$ are of the order of five times as great as those involving data for $\mathbf{1}^{+\bullet}$.

The last line in Table 3 compares correlations of the free energies of activation ($\Delta G^{\ddagger}$) for the reactions of $\mathbf{1}^{+\bullet}$ and $\mathbf{2}^{+\bullet}$ with pyridine nucleophiles vs. $(F/2.303RT)E_{rev}$ for substrate oxidation. The point of interest here is that the average slopes observed for the reactions of the two radical cations are the same within the variance of slopes observed for different nucleophiles with the same radical cation.

The data indicate that substituent effects on the thermodynamic electrode potentials are of the order of three times as great as those on the rate constants for the radical cation–nucleophile combination reactions. From this we can conclude that the substituents have a greater effect on the thermodynamic stabilities of the radical cations than on their reactivity toward nucleophiles. The fivefold increase in Hammett ρ values on comparing reactions of $\mathbf{1}^{+\bullet}$ with those of $\mathbf{2}^{+\bullet}$ can be attributed to attenuation of the substituent effect at the remote position ($\mathbf{1}^{+\bullet}$) as compared with the case where the substituent is attached directly to the anthracene nucleus ($\mathbf{2}^{+\bullet}$).

The fact that the correlations of $\Delta G^{\ddagger}$ vs. $(F/2.303RT)E_{rev}$ gave slopes in the same range for both radical cation reaction series is intriguing. As explained below this is the expected qualitative effect according to the CM model.[16] However, correlations of electrophile/nucleophile reactivity with electrode potentials have previously been explained in terms of the relationship between nucleophile oxidation potentials and reactivity.[25, 26]

According to the CM model, the barrier for a radical cation–nucleophile combination reaction can be estimated using eqns. (1) and (2).[16] In eqn. (1) I is the vertical ionization potential of the nucleophile, A is the vertical electron affinity of the radical cation in solution and $\Delta E_{ST}(\pi\pi^*)$ is the singlet–triplet energy of substrate. In eqn. (2) f is a number with a magnitude of the order of 0.2 and β is the avoided crossing parameter equal to about 10 kcal mol^{-1}. Eqn. (1) is applicable for the infinitely separated reactants. The terms f and β are only expected to be constants for closely related reaction families. The families of radical cations, $\mathbf{1}^{+\bullet}$ and $\mathbf{2}^{+\bullet}$, are expected to fit into this category.

$$\text{Gap} = I_{N:}^*(s) - A_E^*(s) + \Delta E_{ST}(\pi\pi^*) \quad (1)$$

$$\Delta G^{\ddagger} = f\text{Gap} - \beta \quad (2)$$

It has recently been shown[20] that eqn. (1) is incomplete for analysis of reactions of the association complexes[16] and must be modified with appropriate association constants for ground- and excited-state reactants. While it is unnecessary to go into the details it suffices to say that the pertinent association constants that must be included in eqn. (1) are generally unknown and this adds an uncertainty as great as about 23 kcal mol^{-1} to the initial gap (Gap). It was therefore concluded[19] that application of the CM model should be limited to qualitative discussions of radical cation–nucleophile combination reactions.

Nevertheless, the fact that the $\Delta G^{\ddagger}$ vs. E_{rev} correlations are linear, suggests that eqn. (2) can be applied to the data and the magnitudes of f and β required can be evaluated. For this purpose, we can assume that solvation energies of $\mathbf{1}^{+\bullet}$ and $\Delta E_{ST}(\pi\pi^*)$ will be very nearly the same for the entire series since the remote substituents are expected to have a minimal effect on these quantities. Making this assumption, it follows that for a particular $\mathbf{1}^{+\bullet}$–nucleophile combination, relative E_{rev} observed as X is varied should be inversely related to the initial energy

Table 3. Correlation parameters for the reactions of the radical cations of 9-arylanthracenes and 9-substituted anthracenes with pyridine nucleophiles in acetonitrile/Bu_4NPF_6 (0.1 M) at 298 K.

	Radical Cations from	
Correlation parameters	9-Arylanthracenes[a]	9-Substituted anthracenes[b]
$\rho(16.9\,E_{rev}$ vs. $\sigma^+)$	1.50 ($r = 0.995$)	7.83 ($r = 0.99$)
$\rho(\log k$ vs. $\sigma^+)$	0.47(5)	2.4(3)
Slope($\Delta G^{\ddagger}$ vs. $16.9\,E_{rev}$)[c]	−0.43(5)	−0.41(6)

[a] This study. [b] Data taken from Ref. 19. [c] Rate constants were converted into $\Delta G^{\ddagger}$ from the relationship $\Delta G^{\ddagger} = 17.45 - 1.364 \log k$, from the absolute rate equation at 298.15 K.

gap. This term has been proposed to be equal to 112 kcal mol^{-1} when X is H and the nucleophile is pyridine.[16] The initial energy gap for reactions of the other $\mathbf{1}^{+\bullet}$ could then be approximated from the relative values of E_{rev}. Considering once again the data in Table 1 we see that the values of E_{rev} span only a total of 138 mV. This corresponds to a span of only 3.2 kcal mol^{-1} in the initial gap making the assumptions outlined above. To be consistent with the CM model treatment, for these series of reactions f is equal to 0.43(5) and β is 41 kcal mol^{-1}. A similar treatment of the published[19] data for $\mathbf{2}^{+\bullet}$ results in f equal to 0.41(6) and a β value of 38.5 kcal mol^{-1}.

The β values for the $\mathbf{1}^{+\bullet}$ and $\mathbf{2}^{+\bullet}$ reactions with nucleophiles could conceivably be reduced by as much as 20 kcal mol^{-1} by incorporating the pertinent association constants[20] into the initial gap. Since there is no way of evaluating these constants we are therefore forced to neglect them. Our conclusion at this point with regard to the use of the CM model to analyze these reactions is that both f and β are greater than expected but our data is qualitatively consistent with the prediction of the model.

Experimental

Materials. Reagent-grade acetonitrile was distilled from P_2O_5 before being passed through a column of active neutral alumina to remove water and protic impurities. Dichloromethane, after being passed through active neutral alumina, was used without further purification. Tetrabutylammonium hexafluorophosphate (Aldrich) was recrystallized from dichloromethane–ether before use. 9-Arylanthracenes were prepared according to published procedures.[27] All pyridines were purified the same day prior to use using standard techniques.

Instrumentation and data handling procedures. Cyclic and linear sweep voltammetry were performed using a JAS Instrument Systems, J-1600-B potentiostat driven by a Hewlett Packard 3314A function generator. After being passed through a Stanford Research Systems, Inc. Model SR640 dual channel low pass filter the data were recorded on a Nicolet Model 310 digital oscilloscope with 12-bit resolution. The oscilloscope and function generator were controlled by an IBM AT compatible personal computer via an IEEE interface. The current–potential curves were collected at selected trigger intervals to reduce periodic noise[28] and 20 curves were averaged before being treated with a frequency domain low pass digital filter and numerical differentiation.

Cyclic voltammetry measurements. A standard three-electrode one-compartment cell was used for all kinetic measurements. Positive feedback IR compensation was used to minimize the effects of uncompensated solution resistance. Reference electrodes were $Ag/AgNO_3$ (0.01 M) in acetonitrile constructed in the manner described by Moe.[29] The working electrodes, 0.2–0.8 mm Pt, were prepared by sealing wire in glass and polishing to a planar surface as described previously.[30] The working electrodes were cleaned before each series of measurements with a fine polishing powder (Struers, OP-Alumina Suspension) and wiped with a soft cloth. The cell was immersed in a water bath controlled to 25 ± 0.2 °C.

Kinetic measurements. Rate constants were obtained by comparing derivative cyclic voltammetry[31] data with theoretical data obtained by digital simulation.[32] The reactions were studied under second-order conditions using solutions containing **1** (1.0 mM) and pyridine nucleophile (0.25–2.0 mM).

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