

Electrochemistry of Electron Transfer Probes. Observation of the Transition from Activation to Counterdiffusion Control in the Fragmentation of α -Aryloxyacetophenone Radical Anions^{1a}

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Abstract: The cleavage of radical anions of substituted α -phenoxyacetophenones, X-C₆H₄COCH₂OPh, **IIa–k**, has been studied in DMF by voltammetric and coulometric techniques. The standard potentials (E°) for formation of and rate constants, k , for the cleavage of the radical anions were determined using linear sweep voltammetry, LSV, together with digital simulation and previously reported laser flash photolysis data. The rate constants cover a range of almost eight orders of magnitude (0.4 s⁻¹ for X = *p*-MeCO- to 1.3·10⁷ s⁻¹ for X = *p*-MeO-). The relative driving forces, $\Delta\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$, for the heterolytic cleavage of the radical anions (to give R[•] + X⁻) were estimated from thermochemical cycles. A combined plot of log(k) versus $\Delta\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ for the radical anions of **IIa–k** and of α -aryloxyacetophenones gave a curve with $\alpha = 0.5$ at high driving forces and $\alpha = 1$ at low driving forces, where $\alpha = \partial\Delta G^\circ_{\text{het}}/\partial\Delta G^\circ$. The plot was analyzed using a model in which reversible cleavage of the radical anions takes place inside the solvent cage followed by (counter)diffusion of the fragments out of the solvent cage. The change in the value of α is interpreted as a change in the rate limiting process from chemical activation (i.e., fragmentation) to counterdiffusion. The model allowed the determination of the absolute values of $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ and the intrinsic barrier, ΔG°_0 , for the fragmentation of the radical anions (8 ± 1 kcal mol⁻¹, 0.35 eV). This leads to an estimate of the homolytic bond dissociation free energy of the C–OPh bond in the unsubstituted α -phenoxyacetophenone.

Introduction

The unimolecular cleavage of radical anions has been suggested as suitable clock-reactions to distinguish hydride transfer from electron transfer/radical pathways in the reduction of carbonyls with different hydride donors.^{2–9} The idea follows from the well established free radical clocks¹⁰ that led to the development of a number of useful chemical probes to report the existence of short lived free radical intermediates. Free radical clocks are now available that cover a range in radical lifetime from milliseconds down to subpicoseconds.¹¹ When used as chemical probes the main consideration is to ensure that the “clock reaction” is much faster than the other competing processes. This is in contrast to the use of clock reactions as a kinetic tool in which the kinetics of the competing processes must be of the same order of magnitude.

In order to make use of electron transfer probes the rate constants for the reactions of the intermediate radical ions must either be known or simple to estimate. Tanner and his

co-workers attempted to determine the rate constant for cleavage of the α -phenoxyacetophenone radical anion from competition by assuming the rates of cleavage of α - and ring-substituents were independent.² Unlike the reactions of neutral free radicals, one might expect substitution in either the phenoxy or acetophenone ring to have a significant influence on the thermodynamics of both the formation and the reaction of the radical anion. While the relationship between the kinetics and thermodynamics of reactions of organic radical ions is reasonably well understood,^{12–18} the magnitude of the substituent effects on the α -phenoxyacetophenone radical anion fragmentation is difficult to predict. This is because direct measurement of the relevant thermochemical and/or kinetic properties of the radical anions is made difficult by their short lifetimes. The lack of directly measured thermochemical properties have in a few cases been circumvented by constructing thermochemical cycles in which most of the terms are thermochemical properties of closed shell compounds.¹⁹ Examples include the estimation of pK_a values of radical cations,^{20–23} basicity of radical anions,²⁴ and cleavage of radical anions^{13,25,26} and radical cations.^{26,27}

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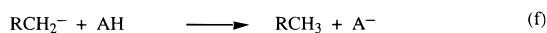
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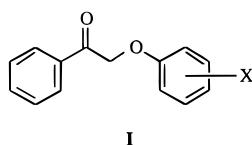
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Scheme 1



α -Aryloxyacetophenones are ideal substrates for a systematic study of the cleavage of radical anions. The cathodic cleavage of the ether bond which follows an ECE/DISP type mechanism, Scheme 1, results in the formation of an acetophenone and a phenol.¹³ We previously reported the effect of the leaving group on the cleavage of radical anions of α -aryloxyacetophenones, **I**, and showed that the free energy of the cleavage of the radical



anion in that case can be calculated conveniently from eq 1, where $\Delta G^\circ_{\text{exch}}$ is the difference in the bond dissociation free energies, BDFE, of the compounds RX and HX (eq 2).

$$\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-}) = 2.303RT \text{p}K_a(\text{HX}) + FE^\circ(\text{RX}) - FE^\circ(\text{H}^+) + \Delta G^\circ_{\text{exch}} \quad (1)$$

$$\Delta G^\circ_{\text{exch}} = \text{BDFE}(\text{RX}) - \text{BDFE}(\text{HX}) \quad (2)$$

In this paper we describe a systematic study of the influence of substitution in the acetophenone ring on the rate of radical anion fragmentation of the α -phenoxyacetophenones, **IIa–k**. This substitution leads primarily to variations in the E° value in eq 1, while keeping the other terms constant since the leaving group (phenolate) is the same for all these α -phenoxyacetophenones and since BDFE(RX) may be considered to be independent of the substituent (*vide infra*).²⁸ These data, when combined with data from our previous study,¹³ now cover a range in driving force of ca. 20 kcal mol⁻¹ and in rate constants of ca. 9 orders of magnitude. They are analyzed in the context of a simple kinetic model that leads directly to the bond dissociation free energies of the radical anions and the intrinsic

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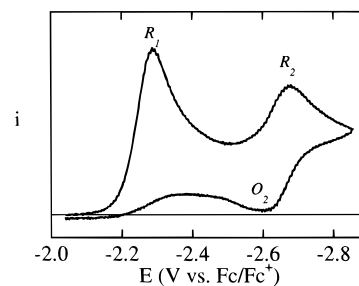


Figure 1. Cyclic voltammogram of **IIa** in DMF containing 0.1 M TEAP. HMDE, scan rate = 1 V·s⁻¹, T = 25 °C.

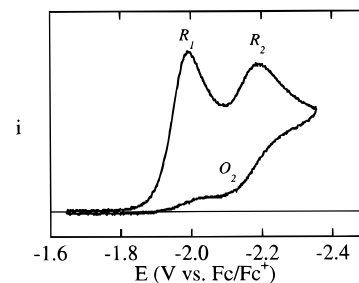


Figure 2. Cyclic voltammogram of **IIg** in DMF containing 0.1 M TEAP. HMDE, scan rate = 1 V·s⁻¹, T = 25 °C.

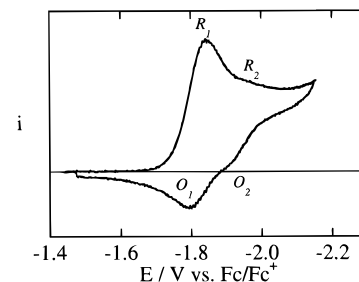
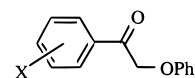


Figure 3. Cyclic voltammogram of **IIi** in DMF containing 0.1 M TEAP. HMDE, scan rate = 1 V·s⁻¹, T = 25 °C.

barrier and, indirectly, to the bond dissociation free energy of the neutral, unsubstituted α -phenoxyacetophenone.



IIa: *p*-MeO

IIb: *p*-Me

IIc: H

IId: *m*-MeO

IIe: *m*-Ac

IIf: *m*-CF₃

IIg: *m*-CN

IIh: *p*-CF₃

IIi: *p*-CN

IIj: *p*-Ac

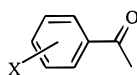
IIk: *p*-MeOOC

Results

Characterization of the Cathodic Reduction. The voltammetric behavior of the reduction of the α -phenoxyacetophenones **IIa–k** in DMF containing 0.1 M tetraethylammonium perchlorate (TEAP) depends strongly on the substituent on the acetophenone ring. The cyclic voltammograms (CV) of the reduction of the α -phenoxyacetophenones **IIa–g** at scan rates, ν , up to 1000 V s⁻¹ at a mercury electrode exhibited the same characteristics as found for α -aryloxyacetophenones with substituents on the phenoxy ring (Figures 1–3).^{13,29} The voltammograms consist of an irreversible cathodic peak, R_1 , which was found to correspond to a one-electron reduction process, and a reversible couple, R_2/O_2 , at a more negative potential which is due to the correspondingly substituted acetophenone

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IIa–k. The current of the R_1 -peak increases to the equivalent of a two-electron process in the presence of 2,6-di-*tert*-butylphenol (DBP), while the height of the peak at R_2 increases and the anodic peak O_2 disappears.



IIa: <i>p</i> -MeO	IIb: <i>p</i> -Me	IIc: H
IIId: <i>m</i> -MeO	IIe: <i>m</i> -Ac	IIIf: <i>m</i> -CF ₃
IIg: <i>m</i> -CN	IIh: <i>p</i> -CF ₃	IIi: <i>p</i> -CN
IIj: <i>p</i> -Ac	IIk: <i>p</i> -MeOOC	

The voltammetric behavior is changed gradually when the substituent is made more and more electron-withdrawing. An anodic peak, O_1 , that was associated with the cathodic R_1 peak can be observed at scan rates higher than 200 V s⁻¹ in the case of **IIg**. Furthermore, this anodic peak is unaffected by the presence of DBP. This reversibility of the R_1/O_1 couple can be observed at lower and lower scan rates as the substituent is made more electron-withdrawing. The CV of **IIj** is completely reversible at 1 V s⁻¹, and the O_1 peak disappears completely at $\nu < 0.05$ V s⁻¹. The separation between the R_1 and R_2 peaks at $\nu = 1$ V s⁻¹ changed from 390 mV (**IIa**) down to 120 mV (**IIk**). The R_2 peak was barely visible at $\nu = 1$ V s⁻¹ in the case of **IIi** and **IIj**.

Tetrabutylammonium perchlorate (TBAP) was also tested as a supporting electrolyte, but it was generally found that the half-peak widths, $E_{p/2} - E_p$, of all the α -phenoxyacetophenones were larger when TBAP was used as the supporting electrolyte than when TEAP was used. This is consistent with the rates of heterogeneous electron transfer being faster in the presence of tetraethylammonium ions than in the presence of the larger tetrabutylammonium ions.³⁰ The working electrode was a hanging mercury drop electrode, HMDE, which was found to give highly reproducible results. Glassy-carbon and gold electrodes gave the same qualitative results however, the values of the half-peak widths were found to be larger than in the case of the HMDE, which indicates the heterogeneous electron transfer is slower on those surfaces.

Constant current coulometry of **IIa**, **c**, **e**, **i**, and **j** was carried out in the presence of 4–6 mM DBP gave values of n , the number of electrons consumed per substrate molecule, of 2.0 ± 0.1 . Following electrolysis and acidification with acetic acid analysis by HPLC showed that in all cases that the products were phenol and the corresponding acetophenones. The voltammetric and coulometric results are all consistent with an ECE/DISP-type reduction mechanism similar to that which has been found for the α -aryloxyacetophenones, **I**, Scheme 1, where the rate determining step is the cleavage of the radical anion.¹³

E° Values of the α -Aryloxyacetophenones. The standard potentials, E° , of the α -phenoxyacetophenones **IIe** and **IIg–k** were calculated as the midpoint between the cathodic and anodic peak potentials of the redox couple R_1/O_1 . The E° values of **IIc** have been determined previously from the E_p values of the R_1 peak by digital simulation of the kinetic peak shift, $E_p - E^\circ$, and with the use of the rates of cleavage of the radical anion which are available from a laser flash photolysis (LFP) study.^{13,31,32} The digital simulation was based on a mixed ECE/DISP mechanism consisting of steps (a)–(d) in Scheme 1 that

Table 1. E° Values for the Reduction of Substituted Acetophenones^a

substituent -X	E° (V) versus Fc/Fc ⁺		
	X-PhCOCH ₃	X-PhCOCH ₂ OMe	X-PhCOCH ₂ OPh
<i>p</i> -MeO	-2.654	-2.512	(-2.43 ₀)
<i>p</i> -Me	-2.567		-2.36 ₀ ^b
-H	-2.488	-2.364	-2.28 ₂ ^{b,c}
<i>m</i> -MeO	-2.468	-2.343	-2.27 ₄ ^b
<i>m</i> -Ac	-2.250		-2.14 ₄
<i>m</i> -CF ₃	-2.244	-2.136	(-2.08 ₅)
<i>m</i> -CN	-2.168		-2.03 ₀
<i>p</i> -CF ₃	-2.144	-2.051	-2.00 ₁
<i>p</i> -MeOCO	-1.997		-1.88 ₄
<i>p</i> -CN		-1.941	-1.88 ₄
<i>p</i> -Ac		-1.923	-1.82 ₈

^a Values in parentheses are interpolated/extrapolated, see text. Cyclic voltammetric measurements in DMF, 0.1 M TEAP, Hg-electrode, $T = 25$ °C. Experimental errors for the acetophenones, α -methoxyacetophenones, and the chemically reversible α -phenoxyacetophenones are ± 0.005 V. Those for the chemically irreversible α -phenoxyacetophenones are ± 0.01 V. ^b Obtained by digital simulation, see text. ^c Reference 32.

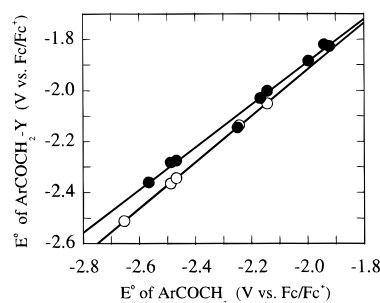


Figure 4. Plot of E° values of X-PhCOCH₂OMe, **IVa–e**, (○) and X-PhCOCH₂OPh, **IIa–i**, (●) versus E° values of the corresponding acetophenones **IIa–k**. The slopes of the lines are 0.904 for **IV** and 0.841 for **II**.

also included the heterogeneous electron transfer rate, k° . The rates of cleavage of the radical anions of **IIb** and **d** also were determined previously,³¹ so the E° values could therefore be determined in a similar manner. The data are given in Table 1. It was found that the reductions of **IIb** were best described by the mixed ECE/DISP mechanism, whereas the digital simulation of the mixed ECE/DISP mechanism and a DISP mechanism (steps (a), (b) and (d) in Scheme 1) gave similar results in case of **IIc** and **IId**.

The standard potentials of the remaining α -phenoxyacetophenones were estimated from a correlation between the known values and the standard potentials of the analogous acetophenones **IIa–k**. The rationale behind this correlation was the assumption that the E° values of α -substituted acetophenones would be determined predominantly by the substituents on the acetophenone ring, whereas the α -substituent could give rise to only a minor attenuating effect since it must transmit electronic effects through a methylene group. Furthermore, the acetophenones **IIa–k** form long lived radical anions on the time scale of our CV experiments, and it is therefore possible to determine their E° values accurately (i.e., ± 5 mV, Table 1).

This correlation was tested by plotting the known E° -values of the α -methoxyacetophenones, **IVa–e**, which also form long lived radical anions on the CV time scale, against the E° -values of the acetophenones **IIa–k** (Figure 4). Both series of compounds give excellent linear correlations when the acetyl-substituted α -phenoxyacetophenones are excluded. It is noteworthy that both slopes are less than one which indicates the substituents have a smaller effect on the E° value of the two series of α -substituted acetophenones than in the acetophenones

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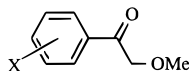
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Table 2. Rate Constants, k , for the Cleavage of α -Phenoxyacetophenone Radical Anions, and Rate Constants, k° , for the Heterogeneous Electron Transfer^a

substituent	k (s ⁻¹)	k° (cm ² s ⁻¹)
<i>p</i> -MeO	1.2×10^7	1.2
<i>p</i> -Me	2.6×10^6 ^b	1.5
-H	7.0×10^5 ^b	1.0
<i>m</i> -MeO	6.3×10^5 ^b	1.1
<i>m</i> -Ac	4.0×10^4	0.7
<i>m</i> -CF ₃	1.8×10^4	1.1
<i>m</i> -CN	5.1×10^3	0.6
<i>p</i> -CF ₃	1.0×10^3	0.4
<i>p</i> -MeOCO	15 ^c	
<i>p</i> -CN	1.1	
<i>p</i> -Ac	0.4	

^a DMF, 0.1 M TEAP, Hg-electrode, $T = 25$ °C. ^b Determined by LFP (ref 29). ^c Glassy carbon working electrode (diameter = 3 mm).

themselves. This is clearly a result of the inductive effect of the methoxy and phenoxy groups (which act as electronegative substituents) stabilizing the radical anions compared to the acetophenone. This intrinsic stability difference is reflected in the corresponding E° values. The α -methoxyacetophenone correlation line (slope = 0.90) is steeper than the α -phenoxyacetophenone line (slope = 0.84), which is consistent with the phenoxy group being slightly more electron withdrawing than the methoxy group (σ_1 (MeO-) = 0.23 and σ_1 (PhO) = 0.38).³³



Ia: H, **I**b: *p*-MeO, **I**c: *m*-MeO, **I**d: *m*-CF₃, **I**e: *p*-CF₃.

The correlation between the E° values for the α -phenoxyacetophenones and those for the acetophenones were used to interpolate/extrapolate the E° values of **I**a and **f** for which direct determination from the electrochemical data was not possible, Table 1.

Rate Constants. By having reasonable estimates of the E° values of the α -phenoxyacetophenones it is possible to determine the rate constants for the cleavage of the radical anions. Except in the case of **I**ii and **I**jj (*vide infra*) the rate constants of the radical anion cleavage and the rate of the heterogeneous electron transfer, k° , were obtained by fitting working curves obtained by digital simulation to experimental values of $E_p - E^\circ$ and $E_{p/2} - E_p$ (obtained by linear sweep voltammetry at several different scan rates in the range 0.2–10 V s⁻¹).^{13,32} The results are shown in Table 2. The heterogeneous electron transfer rates were found to be in the range 0.3–1.5 cm²s⁻¹, which are typical values for the reduction of aromatic compounds at a mercury electrode in DMF.³⁴ The cathodic reductions of **I**c–**k** were best described by the DISP mechanism (i.e., digital simulation of the DISP and the mixed ECE/DISP mechanisms gave identical results). In the case of **I**a and **I**b which have the fastest cleaving radical anions the mixed ECE/DISP mechanism gave the best results.³²

The cleavage of the **I**kk radical anion was studied using a 3 mm glassy-carbon working electrode. This made it possible to use scan rates as slow as to 20 mV s⁻¹ and thereby obtain reasonable values for the shift of the peak potential. The cleavage of the **I**ii and **I**jj radical anions were too slow to cause any significant shift of the cathodic peak potential. The determination of the cleavage rates of the radical anions were instead determined by digital simulation of the complete cyclic

voltammogram (Digisim Version 2.0). The errors in $\log(k)$, estimated to be ca. ± 0.3 , are mainly associated with the errors in determining the E° values (± 10 mV for the chemically irreversible systems).¹³

Discussion

Thermodynamics of the Cleavage of the α -Phenoxyacetophenone Radical Anions. We consider the cleavage of the α -phenoxyacetophenone radical anions to be heterolytic, i.e., the SOMO (and the charge) of the radical anion is mainly located on the acetophenone ring-system, whereas the charge after the fragmentation is located on the phenolate anion.^{12,13,35} This mode of cleavage also has been viewed as an intramolecular dissociative electron transfer, where the electron is transferred from a π^* orbital on the acetophenone moiety to a σ^* orbital of the breaking bond between the phenacyl and phenoxy groups.¹⁴ The free energy of a heterolytic cleavage of radical anions, $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$, can be calculated from the thermochemical cycle given by eq 3, where $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ is obtained as the free energy of the homolytic cleavage of the bond in the neutral substrate molecule, BDFE(RX), plus the difference between $E^\circ(\text{RX})$ and the reduction potential of the radical, $E^\circ(\text{X}^\bullet)$.^{24,25}

$$\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-}) = \text{BDFE}(\text{RX}) + F\{E^\circ(\text{RX}) - E^\circ(\text{X}^\bullet)\} \quad (3)$$

In order to determine the effect of substitution on the acetophenone-ring on $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$, the effect on BDFE(RX) must first be understood. While the substituent effect on C–O bond energies in these systems has not been reported, it has been found the C–H homolytic bond energies of methyl ketones (RCHOCH₂H) are independent of the R-group.²⁸ Furthermore, ESR studies have shown that there is very little interaction between the carbonyl methyl and the phenyl π -system in substituted phenacyl radicals and that there is very little delocalization of the spin into the aromatic ring.^{36,37} It is therefore reasonable to assume that both the strength of the C–OPh bond in the α -phenoxyacetophenones and the change in entropy upon cleavage should also be independent of the substituent. Since $E^\circ(\text{X}^\bullet)$, the standard reduction potential of the phenoxy radical, is constant, $E^\circ(\text{RX})$ is the only term in eq 3 that depends on the substituent. Thus, changes in $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ are determined by changes in the standard potentials of the α -phenoxyacetophenones. Consequently, $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ increases by 17 kcal/mol from **I**a to **I**jj.

We have studied the thermodynamics of the cleavage of the radical anions of the substituted α -aryloxyacetophenones, **I**, and found that the substituent effects on $\Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$ could be determined using eqs 1 and 2.¹³ Since the unsubstituted α -phenoxyacetophenone is a member of both groups of compounds **I** and **II** eqs 1–3 can be used to calculate the free energies of the cleavage of the radical anions relative to the unsubstituted compound, $\Delta \Delta G^\circ_{\text{het}}(\text{RX}^{\bullet-})$, and thereby compare the thermodynamics of the two series of α -aryloxyacetophenones on the same relative energy scale. The main difference between the two series of compounds is that in **I** the substituents modulate the energy of the products of the cleavage (i.e., the phenolate ions), whereas in **II** they modulate the energy of the reacting radical anion.

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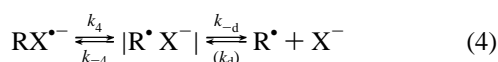
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Relation between the Kinetics and the Thermodynamics of the Radical Anion Fragmentation. A plot of the logarithm of the rate constants for fragmentation of the two series of compounds versus $\Delta\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ gives a correlation that consists of two linear portions, Figure 5. It is noteworthy that the two series of compounds fall on the same correlation line, which suggests that the intrinsic barrier, ΔG_0^{\ddagger} , is similar for all of the compounds or that the intrinsic barriers also vary with substitution.¹⁴ It is more likely that the intrinsic barrier is nearly constant for the entire series of compounds since there is no reason to believe that the substitution in either aromatic ring would have the same influence on ΔG_0^{\ddagger} .

The slopes of the two lines drawn in Figure 5, when expressed using the dimensionless coefficient $\alpha = \partial\Delta G^{\ddagger}/\partial\Delta G^{\circ}$ ($= -RT \cdot 2.303 \cdot \partial\log(k)/\partial\Delta G^{\circ}$), have values of -0.5 and -1 . The transition between these two linear regions is reminiscent of the change from activation control to equilibrium control of electron transfer as described by Marcus theory.³⁸ Recently, Savéant and co-workers pointed out that the kinetics of a number of radical anion and radical cation reactions fall into the region of equilibrium or counterdiffusion control.¹⁷ In the context of the unimolecular fragmentation of radical ions, the latter term refers to the fact that the fragmentation is completely reversible on the time scale of diffusional separation of the radical/anion pair (hence counterdiffusion). A simple scheme describing this competition is shown in eq 4. The possibility of diffusional reencounter is shown to avoid confusion (i.e., diffusion is bimolecular while counterdiffusion is unimolecular) although it is unlikely that this will occur.



The observed rate constant, k_{obs} , is according to this model given by eq 5, where k_4 and k_{-4} are the rate constants for the cleavage and recombination reactions inside the solvent cage, respectively, and k_{-d} is the rate constant for the diffusion out of the solvent cage. This model predicts that $k_{\text{obs}} = k_4$ when

$$k_{\text{obs}} = \frac{k_4 k_{-d}}{k_{-4} + k_{-d}} \quad (5)$$

$k_{-4} \ll k_{-d}$ and that $k_{\text{obs}} = k_d k_{-d}/k_{-4}$ when $k_{-4} \gg k_{-d}$. Since $k_4/k_{-4} = \exp(-\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})/RT)$ and k_{-d} is a constant (usually taken to be ca. 10^{10} s^{-1}), the latter case leads to a linear plot of $\log(k_{\text{obs}})$ versus $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ with a slope that corresponds to $\alpha = -1$. Furthermore, when $k_{\text{obs}} = k_{-d}$ then $k_4 = k_{-4}$ and so $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ must be equal to zero. Thus, the intersection between the extended line (which corresponds to $\alpha = -1$) and the horizontal line at $\log(k) = 10$ defines the point at which $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-}) = 0$ and allows the relative thermodynamic scale to be put on an absolute scale. In Figure 5 this occurs at $\Delta\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-}) = -3 \text{ kcal/mol}$ and leads to the result that $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-}) = \Delta\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-}) + 3 \text{ kcal/mol}$.

Since Savéant has shown that the Marcus equation (eq 6) can be applied to fragmentation reactions of radical ions,^{14,17} these absolute values of $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ and the apparent activation free energies, $\Delta G_0^{\ddagger}(\text{RX}^{\bullet-})$ (from the Eyring equation, eq 7, setting the preexponential factor to the usual value of 10^{13} s^{-1}), can be used to determine a value for the intrinsic barrier, ΔG_0^{\ddagger} . Nonlinear regression gives a value of 8 kcal/mol (0.35 eV), Figure 6.³⁹ It is the relatively large intrinsic barrier (presumably a result of the significant charge reorganization

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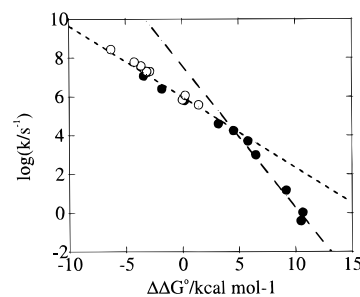


Figure 5. Logarithm of the rate constants for the cleavage of anion radicals of **I** (○) (data taken from ref 13) and **IIa–k** (●) plotted versus $\Delta\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$. The slope of the dashed lines correspond to α values equal to -0.5 and -1 .

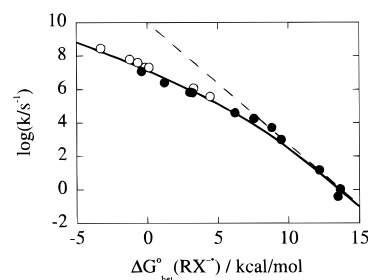


Figure 6. Logarithm of rate constants for the cleavage of anion radicals of **I** (○) (data taken from ref 13) and **IIa–k** (●) plotted versus $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$. The slope of the dashed line correspond to $\alpha = 1$. The regression line is calculated from eqs 5–7 by using $A = 10^{13} \text{ s}^{-1}$, $k_{-d} = 10^{10} \text{ s}^{-1}$, and $\Delta G_0^{\ddagger} = 8 \text{ kcal/mol}$.

that must occur at the transition state¹⁷) that allows the transition from activation control ($\alpha = 0.5$) to counterdiffusion control ($\alpha = 1.0$) to be so clearly observed.

$$\Delta G^{\ddagger}(\text{RX}^{\bullet-}) = \Delta G_0^{\ddagger} \left(1 + \frac{\Delta G^{\circ}(\text{RX}^{\bullet-})}{4\Delta G_0^{\ddagger}} \right)^2 \quad (6)$$

$$k_{\text{obs}} = A \exp(-\Delta G^{\ddagger}/RT) \quad (7)$$

Savéant and co-workers¹⁷ reported reactions of radical cations of NADH model compounds that were clearly under counterdiffusion control. In addition, they reanalyzed data from Maslak and co-workers¹² and showed that the majority of the data in that work also were in the counterdiffusion regime. It is only for the fastest reactions that the change over from counterdiffusion to activation control begins to be evident. The fragmentation of the α -aryloxyacetophenone radical anions in this work is the first unequivocal observation of such a transition and lends strong support to the model proposed by Savéant.

The intrinsic barrier that we derive (8 kcal mol^{-1}) using this analysis is significantly smaller than that reported by Savéant and his co-workers (16 kcal mol^{-1}).¹⁸ Both groups obtained the same rate constant and standard potential for the α -(3-methoxyphenoxy)acetophenone radical anion. On inspection of the data, the different ΔG_0^{\ddagger} values appear to be rooted in the value for the homolytic bond dissociation energy of the neutral aryloxyacetophenone used in a thermochemical cycle by

(39) The preexponential factor equal to 10^{13} s^{-1} , which is the value of kT/h at 298 K , is commonly used in the case of adiabatic unimolecular reactions. However, large variations in the preexponential factor have been observed for the fragmentation of radical anions (Meot-Ner, M.; Neta, P.; Norris, R. K.; Wilson, K. *J. Phys. Chem.* **1986**, *90*, 168). Changing the preexponential factor to 10^{15} s^{-1} , for the present case, gives $\Delta G_0^{\ddagger} = 11 \text{ kcal/mol}$, while using 10^{11} s^{-1} gives $\Delta G_0^{\ddagger} = 5 \text{ kcal/mol}$. Both sets of constants give the same excellent fits to the experimental data in Figure 6.

Savéant. The value they used (40 kcal mol^{-1}) is based on an electrochemical determination of the C–Br bond energy of phenacyl bromide and assuming that the difference between C–Br and C–X bond energies in the phenacyl and benzyl systems are the same.¹⁸ Thermolysis⁴⁰ of α -phenoxyacetophenone leads to an estimate of 56 kcal mol^{-1} , while group additivities predict a slightly higher value of 57 kcal mol^{-1} . Since the cleavage of this radical anion is under activation control, half of the difference in the bond energies must be subtracted from the derived intrinsic barrier (i.e., $\alpha = -0.5$). It should be noted that the driving force for the radical anion fragmentation that we have determined is independent of the neutral α -aryloxyacetophenones; i.e., it relies only on the kinetic data for the radical anions and assumes that the intrinsic barrier is independent of substituent. In order to derive an intrinsic barrier as high as 16 kcal mol^{-1} , we would require a preexponential term in eq 7 of ca. 10^{19} . We are currently attempting to understand the discrepancy between the bond energy determinations from the electrochemical and thermolysis measurements.⁴¹

Our values of $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ can be used in the thermochemical cycle given by eq 3 to estimate the bond dissociation free energy (BDFE) of the C–OPh bond in the unsubstituted α -phenoxyacetophenone, **IIc**. Using $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-}) = 3 \text{ kcal/mol}$ and $E^{\circ}(\text{PhO}^{\bullet}) = -0.19 \text{ V vs Fc/Fc}^{+}$ ^{13,42} gives BDFE(PhCOCH₂–OPh) = 51 kcal/mol . This leads to a reasonable estimate of the entropy change associated with the fragmentation of $+17 \text{ cal mol}^{-1} \text{ K}^{-1}$ when combined with the bond dissociation enthalpy⁴⁰ of 56 kcal mol^{-1} . A bond dissociation enthalpy as low as 40 kcal mol^{-1} leads to a value of ΔS° for the fragmentation of $-37 \text{ cal mol}^{-1} \text{ K}^{-1}$.

Finally, it is interesting to compare the rate constant for β -cleavage of the α -phenoxy-*p*-bromoacetophenone radical anion reported by Tanner et al. ($k = 4 \times 10^6 \text{ s}^{-1}$) with the values for our series of α -aryloxyacetophenones.² The standard reduction potential of *p*-bromoacetophenone was reported to be -1.84 V vs SCE in DMF,⁴³ which corresponds to $E^{\circ} = -2.31 \text{ V}$ versus the Fc/Fc⁺ couple. This leads to a value of $E^{\circ} = -2.14 \text{ V}$ for α -phenoxy-*p*-bromoacetophenone (Figure 4) and a value of $\Delta G_{\text{het}}^{\circ}(\text{RX}^{\bullet-})$ of 6.2 kcal/mol (Figure 6). Substitution of this value into eqs 5–7 (and using the constants derived above) leads to $k_4 \approx k_{\text{obs}} = 4 \times 10^4 \text{ s}^{-1}$, ca. 2 orders of magnitude slower than the previous estimate. The ratio of ring-cleavage (loss of bromide) to β -cleavage (loss of phenoxide) was found to be approximately 7, corresponding to a rate constant for loss of bromide of $5 \times 10^5 \text{ s}^{-1}$. The rate constant reported by Tanner et al. was based on the assumption that the substituent on the acetophenone ring did not affect on the rate constant for loss of the α -substituent (or vice versa). However, it appears from the correlations in Figure 5 that this is not the case.

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Conclusions

The kinetics of fragmentation of a number of substituted α -phenoxyacetophenone radical anions have been determined using linear sweep voltammetry over more than eight orders of magnitude in rate constant. When plotted as a function of the thermodynamic driving force, the transition from activation control to counterdiffusion control is clearly observed as predicted by a kinetic model recently proposed by Savéant and co-workers.¹⁷ This is, to our knowledge, the first clear demonstration of this phenomenon in the chemistry of radical anions and is completely analogous to the kinetic regimes observed in electron transfer reactions. Analysis of these data allows the intrinsic barrier to be determined to be 8 kcal mol^{-1} . It is this relatively large intrinsic barrier that allows the transition to be observed in a convenient kinetic window. The large intrinsic barrier is attributed to a significant degree of solvent reorganization at the transition state resulting from the flow of charge from the π^* of the acetophenone radical anion to the oxygen of the phenoxide leaving group. The clear relationship between the driving force for the fragmentation and the kinetics of the process (including consideration of the counterdiffusion effect) allows for the design of electron transfer probes based on aryloxyacetophenones over a very broad time range from seconds to subnanoseconds. The rate constant for fragmentation of the radical anion is easily estimated using only the pK_a of the protonated leaving group (i.e., the phenol) and the E° of the acetophenone (ArCOCH₃, from which the standard potential of the aryloxyacetophenone can be obtained from the correlation in Figure 4).

Experimental Section

The α -phenoxyacetophenones, **IIa–k**, were synthesized according to a known procedure.^{31,44} All the acetophenones, **IIIa–k**, were commercially available (Aldrich) and were used as received. α -Methoxyacetophenone, **IVa**, were commercially available (Aldrich), and the other α -methoxyacetophenones, **IVb**,⁴⁵ **IVc**, **IVd**, and **IVe**,⁴⁶ were synthesized according to a known procedure.⁴⁶

Electrochemistry. The electrochemical setup, experimental conditions, data analysis, coulometry experiments, and subsequent analysis of the catholytes were performed as previously described.¹³ The catholytes were acidified with acetic acid and analyzed by HPLC after 60–80% conversion of the substrate. However, the coulometry experiment of **IIj** were stopped after 40% conversion due to the small difference between the reduction potentials of **IIj** and **IIIj**. A BAS glassy-carbon electrode (3 mm diameter) was used as working electrode in the study of **IIIk** in order to use scan rates down to $20 \text{ mV}\cdot\text{s}^{-1}$ during the LSV-experiments.

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