# Rearrangements of Radical Ions: What It Means To Be Both a Radical *and* an Ion

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In mechanistic studies, unimolecular rearrangements of radical ions are often employed as "probes" for single-electron transfer: A structural feature (e.g., a cyclopropyl group) is incorporated into the substrate which (in principle) will lead to rearrangement if a radical or radical ion intermediate is involved. The use of a cyclopropyl group is predicated on the expectation that the rearrangement will be rapid, in analogy to the cyclopropylcarbinyl → homoallyl radical rearrangement (eq 1) which is fast ($k \approx 10^8$ s^{-1}) and essentially irreversible.[1]

$$\triangleright\!-\!\bullet \quad \xrightarrow{\; k_o \;} \quad \bullet\!\diagup\!\diagdown\!\diagup \qquad\qquad (1)$$
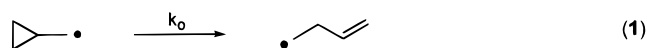
Although rate constants for unimolecular rearrangement of many *neutral* free radicals are known,[2] little is known regarding the rearrangement of structurally similar radical *ions*. Frequently, it is assumed that structural features which lead to facile rearrangement of neutral free radicals will do the same for radical ions.

To address this issue, rearrangements of radical anions derived from aliphatic ketones **1a**, **1b**, and **1c** (Scheme 1) were studied using electrochemical techniques. Preparative scale electrolysis (DMF or NMP solvent, gold electrode, ^{n}Bu$_4$NClO$_4$ supporting electrolyte) of all these substrates leads to ring-opened products (2-pentanone from **1a**, a 2.5:1 mixture of 5-methyl-2-pentanone and 4-methyl-2-pentanone from **1b**, and 2-hexanone from **1c**), results which are consistent with ring opening of **1**$^{\bullet-}$ as depicted in Scheme 1.

The technique of *homogeneous redox catalysis*, developed by Savéant,[3] was employed to learn more about the kinetics of these rearrangements. The premise of these experiments is outlined in Scheme 2: An electron is transferred (heterogeneously) from the electrode surface to a mediator species (**M**), rather than directly to substrate **1**. The mediator subsequently diffuses into solution, where it transfers an electron to the substrate. Finally, the reduced form of the substrate (**1**$^{\bullet-}$) undergoes ring opening, forming **2**$^{\bullet-}$. Kinetic information is obtained from changes in the cyclic voltammogram of the **M/M**$^{\bullet-}$ couple.

In principle, either ii or iii may be rate limiting. In the former case, the rate constant for electron transfer between **M**$^{\bullet-}$ and **1** (k_1) can be determined. If iii is rate limiting, then the composite rate constant $k_{obs} = (k_1/k_{-1})*k_2 = K_1k_2$ ensues. The rate constant k_2 can be readily extracted if the reduction potential of **1** ($E°_{1/1}{}^{\bullet-}$) is known. (There is an additional complication: After ring opening, **2**$^{\bullet-}$ may further react with **M**$^{\bullet-}$ via a *second* electron transfer (k_{et}: **2**$^{\bullet-}$ + **M**$^{\bullet-}$ → **2**$^{-2}$ + **M**) or by coupling (k_{add}: **2**$^{\bullet-}$ + **M**$^{\bullet-}$ → **2-M**$^{-2}$). The rate constant ratio $\rho = k_{et}/(k_{add} + k_{et})$ is also derived from the experimental data.)[4]

Scheme 1

1 (**a**; R = H, n = 1)
(**b**; R = CH$_3$, n = 1)
(**c**; R = H, n = 2)

Scheme 2

M + e$^\ominus$ ⇌ M$^{\bullet-}$ *i*: heterogeneous electron transfer

M$^{\bullet-}$ + **1** $\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}}$ M + **1**$^{\bullet-}$ *ii*: homogeneous electron transfer

1$^{\bullet-}$ $\xrightarrow{k_2}$ **2**$^{\bullet-}$ *iii*: rearrangement

Procedures for determining whether k_1 or k_2 is rate-limiting and for extracting the pertinent rate constants have been described by Savéant;[3] the specific procedures utilized in this study are similar to those described by us in an earlier publication.[5] For **1a** and **1b**, electron transfer was found to be rate-limiting for all mediators examined, and the pertinent kinetic information is summarized in the Supporting Information.

The fact that ring opening is *not* the rate-limiting step for **1a** or **1b** is noteworthy because this means that ring opening is very fast. These results do not permit k_2 to be measured directly (although it is likely that $k_2 \gg 10^7$ s^{-1}, vide infra). The variation of k_1 with the reduction potential of the mediator allows an estimate of the reduction potentials of **1a** and **1b** via the application of Marcus theory.[6–8] Accordingly, the reduction potentials of **1a** and **1b** were determined to be -3.215 ± 0.068) and -3.196 ± 0.067) V (vs 0.1 M Ag$^+$/Ag), respectively. The fact that within experimental error the reduction potentials of **1a** and **1b** are identical means that substituents on the cyclopropyl group have little effect on the stability of **1a**$^{\bullet-}$ and **1b**$^{\bullet-}$.

Cyclobutyl ketone **1c** was selected for study because it was envisioned that ring opening would be slower than for the cyclopropyl derivatives, thus increasing the likelihood that ring opening would be rate-limiting for this substrate. Utilizing naphthalene and biphenyl as electron-transfer mediators, ring opening was found to be rate-limiting, and the composite rate constant $k_{obs} = (K_1k_2)$ was determined. Assuming that the reduction potential of **1c** is the same as that for **1a** and **1b**, k_2 can be abstracted from k_{obs} because $K_1 = \exp[F/(2.303RT)(E°_{1/1}{}^{\bullet-} - E°_{M/M}{}^{\bullet-})$. Identical values for k_2 were obtained using naphthalene and biphenyl as mediators ($k_2 = (3.3 \pm 0.2) \times 10^4$ s^{-1}).

The results discussed above indicate that ring opening of **1**$^{\bullet-}$ occurs with a rate constant $>10^7$ s^{-1}, with a modest preference
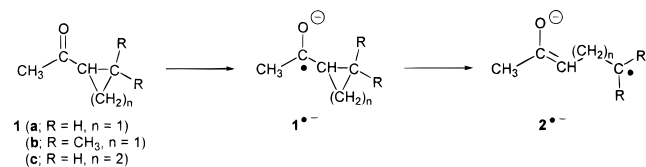
(1) (a) Effio, A.; Griller, D.; Ingold, K. U.; Beckwith, A. L. J.; Serelis, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 1734. (b) Mathew, L.; Warkentin, J. *J. Am. Chem. Soc.* **1986**, *108*, 7981. (c) Beckwith, A. L. J.; Bowry, V. W. *J. Org. Chem.* **1989**, *54*, 2681. (d) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275.

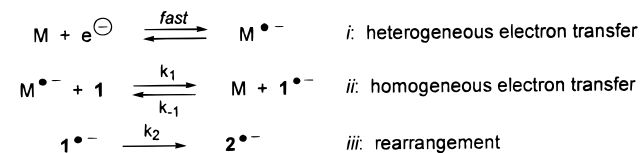(2) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.

(3) (a) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J. M.; M'Halla, F.; Savéant, J.-M. *J. Electroanal. Chem.* **1980**, *113*, 12. (b) Savéant, J.-M.; Su, K. B. *J. Electroanal. Chem.* **1985**, *196*, 1. (c) Andrieux, C. P.; Hapiot, P.; Savéant, J.-M. *Chem. Rev.* **1990**, *90*, 723.

(4) Nadjo, L.; Savéant, J.-M.; Su, K. B. *J. Electroanal. Chem.* **1985**, *196*, 23.

(5) Phillips, J. P.; Gillmore, J. G.; Schwartz, P.; Brammer, L. E., Jr.; Berger, D. J.; Tanko, J. M. *J. Am. Chem. Soc.* **1998**, *120*, 195.

(6) (a) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 966. (b) Marcus, R. A. *Faraday Discuss. Chem. Soc.* **1960**, *29*, 21. (c) Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155. (d) Marcus, R. A. *J. Chem. Phys.* **1965**, *43*, 679. (e) Marcus, R. A. *Faraday Discuss. Chem. Soc.* **1982**, *74*, 7. (f) For an excellent review see ref.

(7) Eberson, L. *Electron-Transfer Reactions in Organic Chemistry*; Springer-Verlag: Berlin, 1987; pp 25−34.

(8) According to Marcus theory, the relationship between k_1 and the free energy of electron transfer ($\Delta G°$) is

$$\frac{1}{k_1} = \frac{1}{k_d} + \frac{1}{K_d Z \exp\left(\frac{-\lambda}{4RT}(1 + \Delta G°/\lambda)^2\right)} + \frac{1}{k_d \exp(-\Delta G°/RT)} \qquad (2)$$

where $\Delta G° = F(E°_{M/M}{}^{\bullet-} - E°_{1/1}{}^{\bullet-})$. Assuming $k_d = 1.0 \times 10^{10}$ M^{-1} s^{-1} (the diffusion-controlled rate constant in DMF), $K_d = 0.16$ M^{-1}, and the frequency factor $Z = 6 \times 10^{11}$ s^{-1}, the rate constants were fit to eq 2 via nonlinear regression analysis, with $E°_{1/1}{}^{\bullet-}$ and the reorganization energy λ as the only adjustable parameters. For a more detailed description of this treatment, see ref 5.
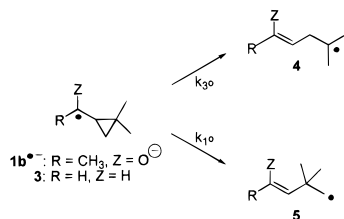
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Scheme 3

1b•⁻: R = CH₃, Z = O⁻
3: R = H, Z = H

Table 1. Effect of Substituents on the Rate of Ring Opening of Radicals and Radical Ions

rearrangement reaction		k_1 (s⁻¹)		$k_{relative}$[a]
		X = H	X = O⁻	
a)		$5 \times 10^{2\,b}$	$3.3 \times 10^{4\,c}$	66
b)		$1 \times 10^{6\,d}$	$<2^{\,e}$	< 0.00006
c)		$3.6 \times 10^{8\,f}$	$3 \times 10^{5\,g}$	0.00083

[a] $k_{relative} = k_1(X = O^-)/k_1(X = H)$. [b] R = H, ref 11. [c] R = CH₃, this work. [d] Reference 12. [e] Reference 10. [f] Reference 14. [g] Reference 13 (see also ref 10).

for the more-substituted (stable) distonic radical anion (Scheme 3, with $k_3°/k_1° = 2.5$ based upon product studies). For the 2,2-dimethylcyclopropylcarbinyl radical (**3**), $k_3°/k_1° = 6.7$.[9] Assuming the reactivity/selectivity principle pertains, the lower selectivity observed for ring opening of **1•⁻** suggests that this rearrangement is *faster* than that of the neutral free radical (**3**). The rate constant for ring opening of **3** is greater than 10^8 s⁻¹, and on this basis, we suggest that the rate constant for ring opening of **1•⁻** is of similar or greater magnitude.

Until now, results pertaining to the rearrangements of radical anions derived from carbonyl compounds (Scheme 1) suggested that these reactions are *radical-like* in terms of substituent effects: With alkyl substituents on the cyclopropyl group, ring opening occurs to generate the more substituted (and more stable) distonic radical anion; radical-stabilizing substituents (e.g., phenyl or vinyl) on the cyclopropyl group enhance the overall rate of ring opening.[10]

This study demonstrates that there are additional factors which govern radical ion reactivity. The cyclobutylcarbinyl radical undergoes ring opening with a rate constant of 5×10^2 s⁻¹.[11] The analogous radical anion undergoes ring opening at a *faster* rate (entry a, Table 1). Although k for ring opening of **1a•⁻** and **1b•⁻** could not be measured in these experiments, it is likely that ring opening of these radical anions occurs with a rate constant similar to (or perhaps greater than) that of the cyclopropylcarbinyl neutral free radical.

In contrast, ring opening of the cyclopropylbenzyl radical occurs with a rate constant of 1×10^6 s⁻¹.[12] Replacement of an α-hydrogen in the radical by O⁻ results in more than a 6 orders

Scheme 4
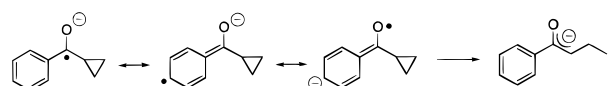
of magnitude *diminution* in the rate of ring opening (entry b, Table 1). Placement of a phenyl group on the cyclopropyl ring accelerates both rearrangements attributable to stabilization of the unpaired electron of the ring-opened form by resonance (entry c, Table 1), but rearrangement of the radical anion[13] is 3 orders of magnitude slower than the neutral free radical.[14]

The results summarized herein demonstrate that the relationship between rearrangement rates of neutral free radicals and similarly structured radical anions is not simple. Delocalization of spin is certainly an important consideration affecting the rates of rearrangement of paramagnetic intermediates in general. However, these results reveal *that for radical ions, charge also plays an important role*.

For radical anions generated from aliphatic ketones, rearrangement is actually *faster* than that of the analogous neutral free radical. Placement of a phenyl group on the α-carbon of either a neutral radical or radical ion retards the rate of rearrangement because of delocalization of spin. However for the radical ion, delocalization of charge is *also* important (Scheme 4). In the ring-opened form, the negative charge no longer enjoys stabilization afforded by the aromatic ring. (Semiempirical molecular orbital calculations[15] reveal that in the ring-closed form, 62% of the total charge is associated with the aromatic ring. In the ring-opened form, 80% of the charge is associated with the oxygen and α-carbon of the enolate anion).

In summary, stabilization of both charge and spin are important factors pertaining to substituent effects on the rates of radical anion rearrangements. Although this work focused specifically on radical *anion* rearrangements, there is little doubt that the same considerations pertain to rearrangements of radical cations as well. Although the chemistry of radical ions is more complex than is generally appreciated, it is important to emphasize that they do not appear to defy established principles of organic reactivity. The complexity arises because these species are both radicals *and* ions, and their chemistry is reminiscent of *both* types of reactive intermediates. As more systems are studied and patterns regarding the role played by stabilization (or destabilization) of charge and spin are revealed, it is likely that an excellent understanding of the chemistry of this unique class of reactive intermediates will be achieved.

(9) Beckwith, A. L. J.; Bowry, V. W. *J. Org. Chem.* **1989**, *54*, 2681.

(10) (a) Tanko, J. M.; Drumright, R. E. *J. Am. Chem. Soc.* **1990**, *112*, 5362. (b) Tanko, J. M.; Drumright, R. E. *J. Am. Chem. Soc.* **1992**, *114*, 1844. (c) Tanko, J. M.; Drumright, R. E.; Suleman, N. K.; Brammer, L. E., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 1785.

(11) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1083. See also Ingold, K. U.; Maillard, B.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1981**, 970.

(12) (a) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Chem. Soc., Chem. Commun.* **1990**, 923. (b) Beckwith, A. L. J.; Bowry, V. W. *J. Am. Chem. Soc.* **1994**, *116*, 2710.

(13) Tanner, D. D.; Chen, J. J.; Luelo, C.; Peters, P. M. *J. Am. Chem. Soc.* **1992**, *114*, 713.

(14) Hollis, R.; Hughes, L.; Bowry, V. W.; Ingold, K. U. *J. Org. Chem.* **1992**, *57*, 4284.

(15) AM1: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.