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## Cyclopropylcarbinyl → Homoallyl-Type Ring Opening of Ketyl Radical Anions. Structure/Reactivity Relationships and the Contribution of Solvent/Counterion Reorganization to the Intrinsic Barrier

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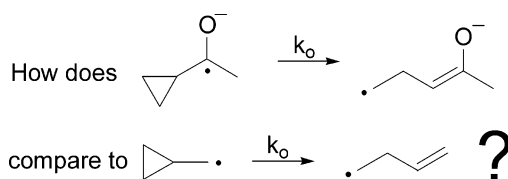
Following a protocol developed by Mathivanan, Johnston, and Wayner (*J. Phys. Chem.* **1995**, *99*, 8190−8195), the radical anions of several cyclopropyl- and oxiranyl-containing carbonyl compounds were generated in an effort to measure the rate constants for their ring opening (k_o) by laser flash photolysis. The results of these experiments are compared to those obtained from earlier electrochemical studies, and the combined data set is used to rationalize the kinetics of radical anion ring opening in a general context by using Savéant's theory pertaining to stepwise dissociative electron transfer (*Acc. Chem. Res.* **1993**, *26*, 455−461). Compared to cyclopropylcarbinyl → homoallyl rearrangements of neutral free radicals, at comparable driving force, the radical anion ring openings are slightly slower. The small difference in rate is attributed to the contribution of an additional, approximately 2 kcal/mol, solvent reorganization component for the radical anion rearrangements. The solvent reorganization energy for ring opening of these radical anions is believed to be small because the negative charge does not move appreciably in the progression reactant → transition state → product.

In direct analogy to the chemistry of cyclopropylcarbinyl neutral free radicals,[1-6] radical anions generated from the one-electron reduction of cyclopropyl ketones and related moieties undergo unimolecular rearrangement, **2** → **3**, as depicted in eq 1. By varying the substituent(s) on the α-carbon and cyclopropyl group, as well as examining several classes of carbonyl compounds (aliphatic ketones, enones, etc.), the nature of the structure/reactivity relationships in these systems has been explored.[7-15]

$$ \text{(1)} $$
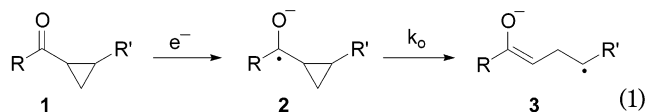
Briefly, the rates of rearrangement depend on the importance of charge- and spin-delocalization in the ring-closed and ring-opened (distonic) forms of the radical ions, which can be accounted for qualitatively and quantitatively in terms of the following structural properties: the thermodynamic stability of the ring-closed radical anion as reflected by the reduction potential of the parent carbonyl compound, the ability of substituents on the cyclopropyl group (R′) to stabilize the radical portion of distonic radical anion **3**, and the thermodynamic stability of the enolate portion of radical anion **3**.[9,15] On the basis of these principles, a thermochemical cycle can be constructed to estimate the free energy for the conversion **2** → **3**, which when coupled with the kinetic data, allows these rearrangements to be quantitatively treated in the context of a Marcus-based theory pertaining to stepwise dissociative electron transfer.[15]

Of course, the successful application of this theory requires good kinetic data for several substrates which span a broad range of reactivities. Virtually all of the kinetic data obtained up until now have been obtained by using electrochemical methods such as cyclic- or linear-sweep voltammetry and homogeneous redox catalysis.[16] While these methods are incredibly powerful tools for studying electron-transfer processes, problems arise in certain situations. Specifically, when the ring-opening reaction is extremely rapid, kinetic control shifts to the electron-transfer step and it is impossible to measure k_o (i.e., the rate-determining step occurs before the reaction of interest).[8,9] Consequently, alternative kinetic methods are needed to study exceptionally rapid ring-opening reactions.

A means of photochemically generating ketyl anions that avoids direct excitation of the ketone was reported

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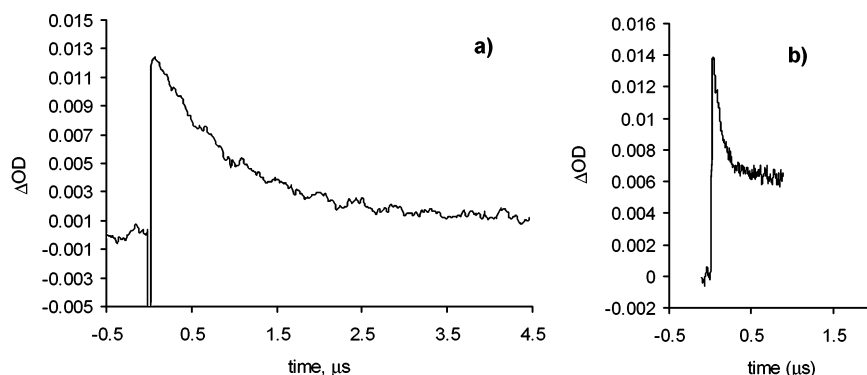
FIGURE 1. Transient signals for the decay of the radical anions generated from phenyl cyclopropyl ketone (**6**, a) and 1-benzoyl-2-phenylcyclopropane (**7**, b) in CH$_3$CN (0.01 M n-Bu$_4$NN$_3$ present to trap DMS$^{\bullet+}$).

by Mathivanan, Johnston, and Wayner in 1995:[17] laser-induced photoionization of 4,4′-dimethoxystilbene (DMS) at 355 nm (third harmonic of a Nd:YAG laser) in acetonitrile yields solvated electrons which are trapped by aromatic ketones to yield ketyl anions. Utilizing this kinetic method based upon the photoionization of DMS, we studied the radical anions generated from several carbonyl compounds (see below). In conjunction with the results of earlier electrochemical investigations, we are now in a position to compare and contrast the nature of structure/reactivity trends for cyclopropylcarbinyl-type ring openings of neutral free radicals vs radical anions quantitatively, and discuss the contribution of solvent and counterion reorganization to the reaction barrier for the latter systems.

4: R = CH$_3$
5: R = ^{t}Bu
6: R = H
7: R = Ph
8: R = H
9: R = CH$_3$
10
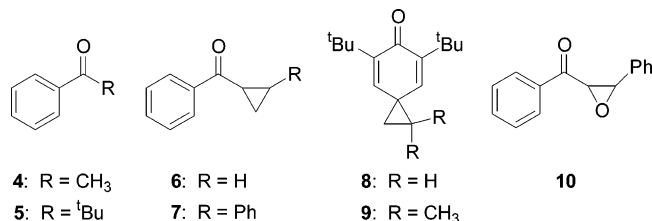
The transient absorption spectrum for the radical anion of phenyl cyclopropyl ketone (**6**$^{\bullet-}$) generated by the DMS photoionization protocol showed λ_{max} = 480 nm, identical with that reported for acetophenone radical anion (**4**$^{\bullet-}$) and other structurally related ketyls anions, generated using the DMS method and other well-established procedures.[17] Although the observed absorption spectrum of **6**$^{\bullet-}$ was consistent with the formation of an aromatic ketyl anion, the unusually high rate of decay (Figure 1, a) was unexpected.

Previous electrochemical experiments revealed that **6**$^{\bullet-}$ was considerably longer lived, *with a lifetime on the order of seconds*, under similar conditions (DMF solvent, n-Bu$_4$N$^+$ counterion)[10,11] leading to the suspicion that the observed rate constant for decay cannot be attributed to cyclopropane ring opening. This was further confirmed by examining aromatic ketones whose radical anions were known to be persistent. (For example, generated electrochemically, **5**$^{\bullet-}$ is known to persist for well over an hour at room temperature!)[11] Ketyl anions **4**$^{\bullet-}$ → **6**$^{\bullet-}$

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were all found to decay with an *apparent* first-order rate constant on the order 10^6 s^{-1}. The temperature dependence of the apparent first-order rate constants for decay of these "persistent" radical anions were similar, as were the apparent activation energies (6 kcal/mol) and log(A) values (9.5−10).

In their experiments, Mathivanan et al. observed a similar decay of **4**$^{\bullet-}$ on the order of microseconds, which was attributed to "quenching by residual oxygen that is difficult to completely remove from flow samples, or reaction of the radical anions with $^{\bullet}$DMS−Nu, produced by nucleophilic trapping of DMS$^{\bullet+}$".[17] It is clear that in order for this method to yield meaningful results for the radical anions of interest, the ring-opening process must occur with a rate constant significantly greater than 10^6 s^{-1}.

Cognizant of this limitation, the radical anions generated from **7** → **10** emerge as excellent candidates for obtaining meaningful kinetic data via the photoionization of DMS. Previous electrochemical investigations revealed that the radical anion generated from 1-benzoyl-2-phenylcyclopropane (**7**) undergoes cyclopropane ring opening with a rate constant estimated to be on the order of 10^7 s^{-1}.[12,15] The electrochemistry of **8** and **9** revealed that ring opening of their corresponding radical anions is so fast that the electron-transfer step is rate limiting; a lower limit of 10^7 s^{-1} was estimated for k_o.[8,13]

With use of the DMS photoionization method, the radical anion of 1-benzoyl-2-phenylcyclopropane (**7**) was successfully generated (λ_{max} = 530 nm). The observed red shift for **7**$^{\bullet-}$ is attributed to extended conjugation through the cyclopropyl group (discussed in more detail in the Supporting Information for this paper). As anticipated, the kinetic trace for this species (Figure 1b) indicates that **7**$^{\bullet-}$ decays in well under 1 μs, consistent with a ring-opening process. The data pertaining to the radical anions generated from **7** → **9** are summarized in Table 1.

The rate constant for ring opening of **7**$^{\bullet-}$ obtained in this study (9.6 × 10^6 s^{-1}) agrees with recent estimates derived from electrochemical methods (3.0 × 10^6 s^{-1}), the latter of which was an indirect estimate, based upon the difference between the LSV peak potential and the estimated standard reduction potential of **7**.[12,15] For **8**$^{\bullet-}$ and **9**$^{\bullet-}$, electrochemical experiments defined a lower

TABLE 1. Summary of Results Obtained for the Transient Absorption Spectra and Rate Constants for Ring Opening of Radical Anions 7$^{\bullet-}$ → 10$^{\bullet-}$ (CH$_3$CN Solvent, 0.01 M *n*-Bu$_4$NN$_3$ Present to Trap DMS$^{\bullet+}$)

radical anion	$\lambda_{\max}$ (nm)	k_o (s^{-1})
7$^{\bullet-}$	530	9.6×10^6
8$^{\bullet-}$	400	$\geq 3 \times 10^8$
9$^{\bullet-}$	410	$\geq 3 \times 10^8$
10$^{\bullet-}$	530	1.4×10^7

limit of 10^7 s^{-1} for k_o,[8,13] though still too fast to measure accurately, the LFP results raise this lower limit to 10^8 s^{-1}.

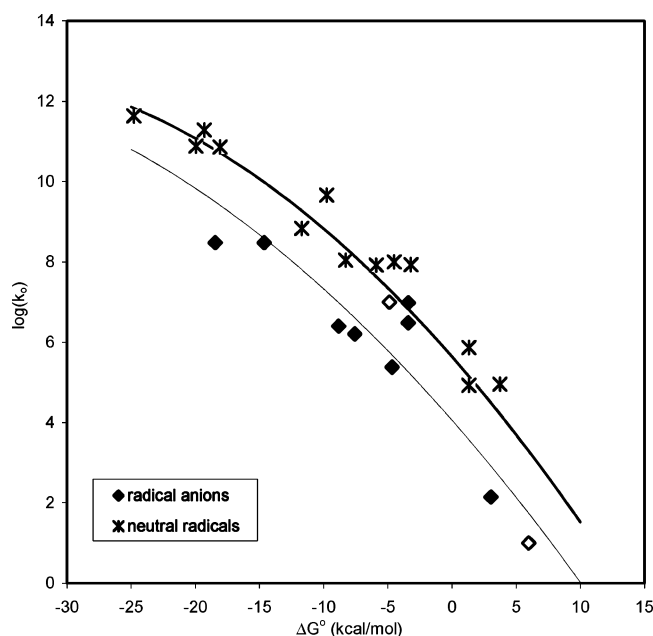In Figure 2, the relationship between log(k_o) and $\Delta G°$ is presented for the cyclopropane ring opening of the

FIGURE 2. Structure/reactivity relationships for the cyclopropylcarbinyl → homoallyl-type rearrangement of radical anions generated from carbonyl compounds and neutral free radicals (unshaded data points are based upon estimates of k_o).

subject radical anions, using kinetic results reported herein, and in previous studies. ($\Delta G°$ is obtained from a thermochemical cycle as described previously.[15]) In the same figure, we also include the data pertaining to cyclopropylcarbinyl → homoallyl ring openings of *neutral* free radicals. For the neutral free radicals, the rate constants are from the literature.[6,18−26] Thermodynamic

data for ring opening of the neutral radicals are not widely available, and were estimated. (Several papers do address the parent system in the context of experimental[27] and calculated values of ΔH.[27−30]) For the purposes of constructing Figure 2, the following procedure was followed to estimate $\Delta G°$. The temperature-dependent rate constants for the cyclopropylcarbinyl → homoallyl rearrangement are known in the forward[6] and reverse[2] directions, allowing $\Delta G°$ to be calculated at room temperature for the parent system. Assuming that the energetics of bond making and bond breaking, ring strain, etc. are the major contributors to the differences in $\Delta G°$ when substituents are introduced, these energies (ZPE-corrected) were obtained from molecular orbital calculations by using B3LYP/6-31G*, which has proven reliable for estimating the thermodynamic and kinetic parameters for these type of reactions.[27]

The plots in Figure 2 suggest that at a comparable driving force, the rate constant for cyclopropane ring opening of a radical anion is about an order of magnitude lower than that of a neutral free radical. These results can also be treated quantitatively. In an earlier paper, Savéant's theory pertaining to stepwise dissociative electron transfer[31,32] was applied to these radical anion ring openings.[15] Utilizing a Marcus-based approach, this theory describes the relationship between $\Delta G^{\ddagger}$ (the free energy of activation) and $\Delta G°$ (the free energy of reaction) according to eq 2: $\Delta G_o^{\ddagger}$ refers to the intrinsic barrier (activation free energy at zero driving force) and accounts for reorganization of the solvent and/or counterion (external reorganization) or changes in the molecule itself (internal reorganization) which may be required to reach the transition state. For the radical anions, fitting to the eq 2 yields $\Delta G_o^{\ddagger} = 12$ kcal/mol. Applying the same analysis to the neutral free radicals yields $\Delta G_o^{\ddagger} = 10$ kcal/mol. (The curved lines in Figure 2 are based upon these parameters and eq 2.) Making the reasonable assumption that the internal reorganization component of $\Delta G_o^{\ddagger}$ (bond making/breaking) is similar for neutral radicals and radical anions, the 2 kcal/mol difference is likely attributable to an additional solvent reorganization component in the radical anion ring openings.

$$\Delta G^{\ddagger} = \Delta G_o^{\ddagger} \left(1 + \frac{\Delta G°}{4 \Delta G_o^{\ddagger}} \right)^2 \qquad (2)$$

Despite the likely errors in the $\Delta G°$ estimates used in this analysis, it seems reasonable to conclude that the contribution of solvent reorganization to the intrinsic barrier for ring opening of the radical anions is quite small. Qualitatively, this result makes sense because for these ring openings, the negative charge is closely

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associated with the electronegative oxygen atom in the ring-closed and ring-opened forms (eq 3), and a major reorganization of solvent is not needed to stabilize the ion in the progression reactant → transition state → product.

$$(3)$$
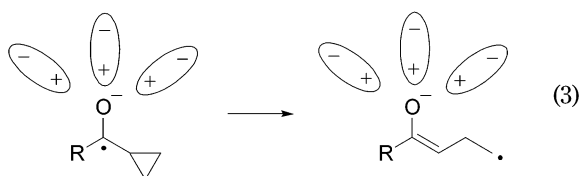
In contrast, for a system in which the charge migrates (e.g., the cleavage of α-substituted acetophenone radical anions, $Ph(C=O^{\bullet-})CH_2X \rightarrow Ph(C=O)CH_2^{\bullet} + X^-$, eq 4), a much larger reorganization energy is observed (ca. 16 kcal/mol), with solvent reorganization being the major contributor to the intrinsic barrier.[33]

$$(4)$$
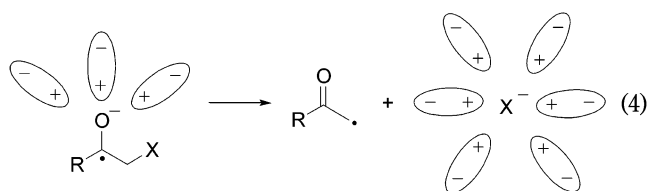
These results and conclusions are especially significant to the use of radical ion rearrangements as mechanistic probes for single-electron transfer. The mechanistic probe approach is essentially an *intramolecular* trapping ex-

periment. A structural feature, typically a cyclopropyl or cyclobutyl group, is incorporated into the substrate, which will lead to a rearrangement uniquely ascribed to radical ion intermediate. Compared to unimolecular rearrangements of *neutral* free radicals, until recently, very little was actually known regarding analogous rearrangement of radical ions. Frequently, it was (and is still) assumed that structural features which lead to facile rearrangement of neutral free radicals will do the same for radical ions, and that the rates will be comparable.

Structure/reactivity relationships for the radical anion rearrangements are governed by the relative importance of charge- and spin-delocalization in the ring-closed and ring-opened (distonic) forms of the radical ions. Of course, for the corresponding neutral free radicals, charge delocalization is not a factor. The results of this paper now suggest that despite this difference, the activation/driving force relationship is similar for both ring opening of radical anions and neutral free radicals (i.e., plots of $\log(k_o)$ vs $\Delta G°$ are parallel as shown in Figure 2). The small difference can be attributed to solvent/counterion reorganization, which is a factor for the radical anions which may slightly inhibit the rate of their ring opening.

Supporting Information Available: Experimental details and a detailed presentation of the results (including transient traces and spectra); rate constants and $\Delta G°$ values used to construct Figure 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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