Characterization of a 'Hypersensitive' Probe for Single Electron Transfer to Carbonyl Compounds

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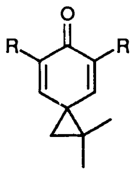
The radical anion generated from 1,1-dimethyl-5,7-di-*tert*-butylspiro[2.5]octa-4,7-dien-6-one (**1**) undergoes facile ring opening yielding both the 3° and 1° distonic radical ions in a ratio of 9 : 1 with a rate constant $\geq 10^7$ s^{-1} (relief of cyclopropane ring strain and the generation of an aromatic ring provide the thermodynamic driving force for this rearrangement), the facility of C–C bond cleavage in this radical anion and the observed electrochemistry are reminiscent of the reductive cleavage of carbon–halogen bonds in alkyl and benzylic halides: on the basis of these results, **1** emerges as a viable substrate for use as a hypersensitive SET probe in mechanistic studies.

A popular approach for the experimental detection of single electron transfer pathways in organic (and bioorganic) systems[1] involves the use of rearrangeable 'probes' based upon the well-characterized cyclopropylcarbinyl (CPC) free radical rearrangement.[2] The rationale behind this type of experiment is that introduction of a cyclopropyl group adjacent to a paramagnetic centre will lead to ring opening in direct analogy to the CPC radical.

In a recent series of papers, we have demonstrated that this analogy is not directly applicable to radical ions. Specifically, there are two factors which must be taken into account in the design of a suitable rearrangement probe, namely, strain energy (which provides the thermodynamic impetus for ring opening), and resonance energy.[3,4] Based upon the results obtained from these studies, we reasoned that the radical anion generated from 1,1-dimethyl-5,7-di-*tert*-butylspiro[2.5]octa-4,7-dien-6-one (**1**) should undergo facile ring opening because strain energy and resonance energy would work in concert to drive the rearrangement.[5]

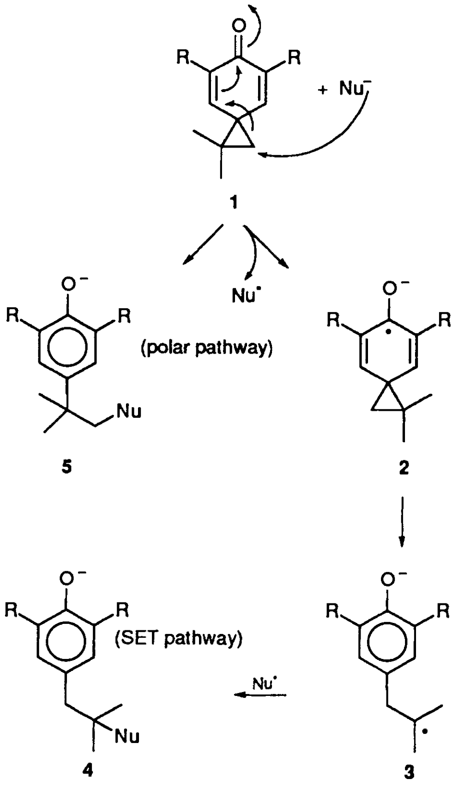


R = Bu^t

1

AM1 SCF-MO calculations (UHF) predict ΔH° for ring opening of the radical anion generated from **1** to be exothermic by over 84 kJ mol^{-1}.[6] Moreover, the geminal dimethyl groups on the cyclopropane ring of **1** should allow a clear distinction between ring-opened products formed by SET *vs.* competing polar pathways based upon the observed regiochemistry of the product(s) (Scheme 1). The successful use of this substrate as an SET probe in reactions with RMgX, RLi, and R_2CuLi has recently been demonstrated.[7] In this paper, we report our results pertaining to the electrochemical reduction of this compound.

The cyclic voltammogram of **1** is characterized by an irreversible reduction wave at −2.35 V, and a reversible oxidation wave at −0.7 V. A detailed study of this system was complicated by the fact that the results obtained using a gold electrode were erratic and irreproducible (presumably because of adsorption onto the electrode surface). More reproducible results were obtained using a glassy carbon electrode. Several determinations revealed that the peak potential of the reduction wave varies linearly with the log of the sweep rate ($\partial E_p/\partial \log(v) = -56 \pm 5$ mV decade^{-1}). Furthermore, this reduction wave is broad and the peak width does not vary significantly with the sweep rate ($E_p - E_{p/2} = 105 \pm 8$ mV over the range $v = 25$–2500 mV s^{-1}; representative voltammograms are presented in Fig. 1). Constant current electrolysis of **1** (0.98 e$^-$/molecule) yields **6**, **7** and **8** in yields of 47, 36 and 11%, respectively.



Scheme 1

A mechanism consistent with these observations is summarized in Scheme 2. Ring opening of **2** yields 3° and 1° distonic radical ions **3** and **9** ($k_3/k_1 = 9$) which disproportionate to yield phenolate ions **10**, **11** and **12**. The oxidation wave at −0.7 V is assigned to the reversible oxidation of the phenolate ions. Acidic work-up yields the observed products.

The broadness of the reduction wave and the observed

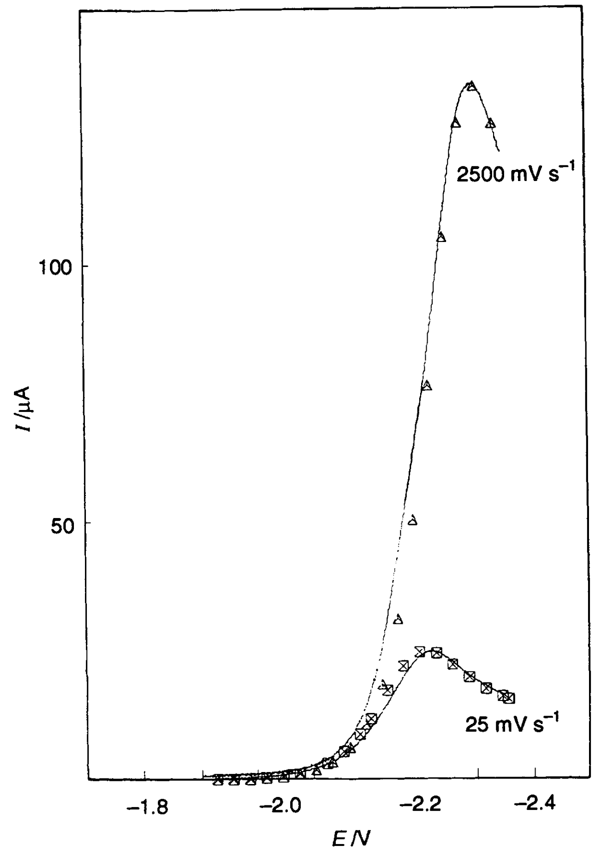
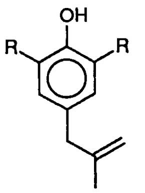


Fig. 1 Linear sweep voltammograms of 1,1-dimethyl-5,7-di-*tert*-butylspiro[2.5]octa-4,7-dien-6-one (**1**) (Me_2SO solvent; 0.5 mol dm^{-3} $Bu^n_4NClO_4$; GCE and 0.1 mol dm^{-3} Ag^+/Ag as working and reference electrodes, respectively)



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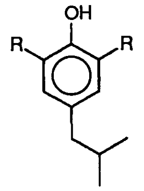

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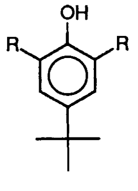

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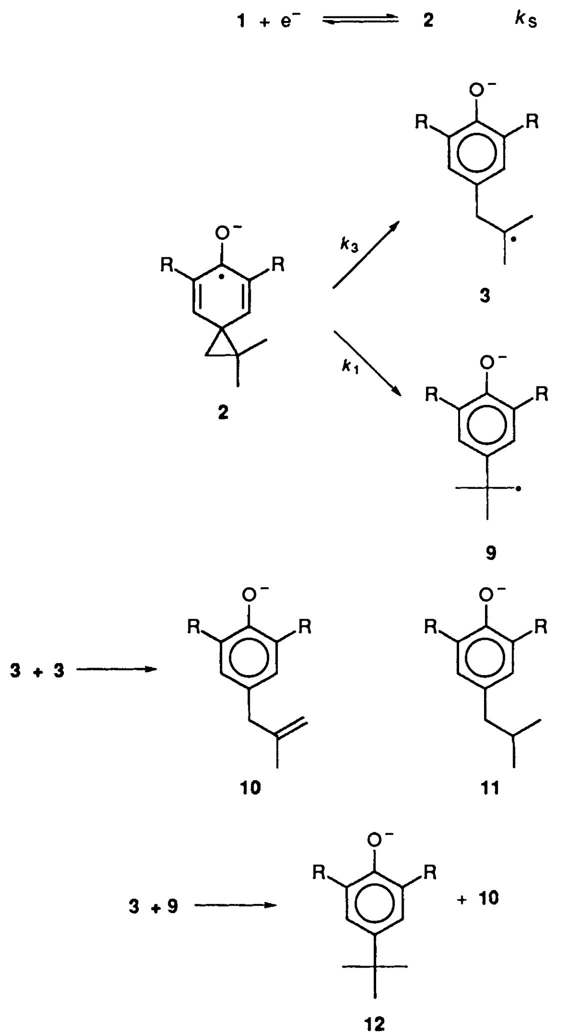
variation of E_p with sweeprate suggest that heterogeneous electron transfer (k_s, Scheme 2) is the rate-limiting step for this reaction. Within experimental error, the transfer coefficient (α) calculated from either the variation of E_p with sweep rate [eqn. (1)] or from the observed peak width [eqn. (2)][8] is the same (0.52 ± 0.04 and 0.45 ± 0.04, respectively). (The simulated voltammograms in Fig. 1 were generated assuming rate-limiting electron transfer and α = 0.49).[9]

$$\alpha = \frac{RT}{2F}\frac{\partial \ln v}{\partial E_p} \qquad (1)$$

$$\alpha = \frac{RT}{F}\frac{1.85}{E_{p/2} - E_p} \qquad (2)$$

For an EC mechanism, the competition between heterogeneous electron transfer and a follow-up chemical step (k_s and k) for kinetic control depends upon the parameter p [eqn. (3)].[10] Making the assumptions that for kinetic control by k_s, $\log(p) \le -1$,[10] using the value of the transfer coefficient determined above (α = 0.49), and assuming typical values for D and k_s ($D = 1 \times 10^{-5}$ cm^2 s^{-1}; $k_s = 1$ cm s^{-1}), we estimate that $k \ge 10^7$ s^{-1}.



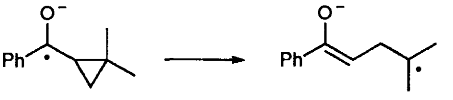
Scheme 2

$$p = [\alpha nF\nu/RT]^{(\alpha-1)/2\alpha}[k_s^{1/\alpha}/k^{\frac{1}{2}}]D^{-\frac{1}{2\alpha}} \qquad (3)$$

Because the electrochemical reduction of **1** proceeds *via* an EC mechanism and electron transfer is rate limiting, $E°$ for this compound could not be obtained directly using cyclic voltammetry. For such a process, however, the peak potential (E_p) is related to $E°$ by eqn. (4) [where $\Lambda = k_s(DnF/RT)^{-\frac{1}{2}}$].[10] At 100 mV/sec, $E_p = -2.35$ V (*vs.* 0.1 mol dm^{-3} Ag^+/Ag). Again, assuming typical values for D and k_s, and using the experimentally determined value for the transfer coefficient (α = 0.49), $E°$ is estimated to be in the order of −2.5 V (*vs.* 0.1 mol dm^{-3} Ag^+/Ag).

$$E_p = E° - \frac{RT}{nF\alpha}(0.78 - \ln \Lambda\alpha^{-\frac{1}{2}}) \qquad (4)$$

The regiochemistry of ring opening of **2** deserves comment. Based upon the product yields, $k_3/k_1 = 9$, which is reminiscent of that observed for the 2,2-dimethylcyclopropylcarbinyl radical, which ring opens to 3° and 1° radicals in a ratio of 7 : 1 at 60 °C. The rate constant for ring opening to the 3° radical is 2×10^9 s^{-1} at this temperature.[11] In contrast, ring opening of the radical anion generated from 1-benzoyl-2,2-dimethylcyclopropane (**13**) yields exclusively products derived from ring opening to the most-stable radical [eqn. (5)].[3] The observed difference in the regiochemistry of ring opening of **2** and **13** is explicable on the basis of the Hammond postulate. We infer a late transition state for the ring opening of **13** because this process is endothermic.[3] Hence the kinetics of ring opening are much more sensitive to the stability of the resulting radical. In contrast, because ring opening of **2** is so exothermic, an early transition state is likely and the thermodynamic stability of the ring-opened radicals is far less important.



13 **14** (5)

In summary, the radical anion generated from **1** undergoes facile ring opening, driven by both the relief of cyclopropane ring strain and by the generation of an aromatic ring, yielding both the 3° and 1° distonic radical ions in a ratio of 9:1 with a rate constant $\geq 10^7$ s^{-1}. The facility of C–C bond cleavage in this radical anion and the observed electrochemistry is analogous to the reductive cleavage of carbon–halogen bonds in alkyl and benzylic halides.[12] C–X bond cleavages in these systems are so facile that (*a*) the electrochemistry is governed by the kinetics of charge transfer, and (*b*) the lifetime of C–X$^{\bullet -}$ is extremely short.[13] Future work in our laboratory will centre on obtaining a better estimate of the standard reduction potential of **1** and the rate constant for ring opening of **2**.

In summary, **1** is likely the best probe for single electron transfer characterized to date. Ring opening of the corresponding radical anion is sufficiently rapid such that detection of SET pathways (based upon the appearance of rearranged products) is kinetically feasible.

Acknowledgements

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