

Voltammetric Reductions of Ring-Substituted Acetophenones. 1. Determination of an Electron-Transfer Mechanism Using Cyclic Voltammetry and Computer Modeling: The Formation and Fate of a Radical Anion.

Grant N. Holder*, David G. Farrar and Laurel L. McClure

A. R. Smith Department of Chemistry, Appalachian State University, Boone, NC 28608, holdergn@appstate.edu

Received July 12, 2001. Accepted August 27, 2001

Abstract: In a sophomore/junior-level experiment suitable for intermediate organic or instrumental analysis, ring-substituted acetophenones were electrochemically reduced to form radical anions that then decompose in a manner determined by the ring substituent. Cyclic voltammetry was used to identify the electron-transfer (ET) mechanism, which was an electron transfer followed by a chemical reaction (EC). The product of the reaction was often electroactive (ECE) in the potential window defined by the acetonitrile/ Bu_4NPF_6 solvent/supporting electrolyte. Products of the following decomposition were estimated with computer modeling (DFT) to estimate the likelihood of various decomposition pathways. Selection of the ring substituent or switching potential (E_{sw}) allows the instructor to ask students to assign the mechanism for a single reduction or a complete ET mechanism, matching the difficulty of this experiment to the level of audience preparation.

Introduction

Cyclic voltammetric determination of an electron-transfer mechanism is an electrochemical method likely to be encountered by synthetic chemists. There are many classic treatises on the subject that contain examples of the wide applicability of the technique to diffusion-controlled and surface ET processes [1]. Specifically, its use comes from the desire to assay the stability of reduced or oxidized forms of a compound in order to discern the stability of charged or multiply charged states. As an undergraduate experiment, cyclic voltammetry (CV) is well known due to its simplicity, adaptability, and low cost. Many publications detail cyclic voltammetric experiments useful in senior-level classes, including ET studies of biologically relevant molecules, surface processes, and other molecular behaviors [2].

We have recently become interested in incorporating electrochemistry into the curriculum in all levels except introductory classes as an effective tool to teach principles that are not efficiently demonstrated through other means. For example, our initial experiments have concentrated on sophomore-level exercises in linear free energy relationships [3]. In the intermediate-level experiment described herein, reactivity of anion radicals is investigated using classical CV diagnostic criteria to assign a mechanism of electron-transfer(s) and associated chemical reactions [4].

Cyclic voltammetry, while able to classify ET mechanisms with coupled chemical reactions, imparts no special insight into the identity of the products formed. One must rely on further experimentation, guided by experience and chemical intuition, to estimate the product(s) of the chemical reaction that follows. This is often not possible during a three-hour laboratory. We have chosen a compound series that exhibits useful structure–function variation and is amenable to

molecular modeling for estimation of the species formed via the postulated decomposition pathways.

Many compounds would serve adequately. The final choice is governed by the need to make the experiment challenging and relevant to as many as possible while still allowing DFT calculations in a reasonable time. We have been pleased with the results of our choice of substituted acetophenones for this exercise. These compounds are widely available, inexpensive, and of low or moderate toxicity. Additionally, they are simple enough to be encompassed by the physical organic concepts of the intermediate-level audience. The appearance of the cyclic voltammograms offers excellent contrast with variation of the ring substituent, even though the electron-transfer mechanisms are similar. The instructor can present a full or partial mechanism, depending on selection of switching potential (E_{sw}). In general, there is a reaction following the formation of the radical anion that is either slow or fast depending on the ability of the substituent to stabilize the radical anion through extended resonance.

Experimental

Acetophenone was used along with its 2'-nitro, 3'-nitro, 4'-nitro, 4'-chloro, 4'-bromo, 4'-iodo, 4'-fluoro, 4'-hydroxy, 4'-methoxy, 4'-methyl, 4'-cyano, 4'-trifluoromethyl, and 4'-(methyl)thio derivatives. Additionally, 4,4'-diacetyl biphenyl was examined. All were purchased commercially and used as received. Most are classified as irritants; contact with skin should be minimized. These make safer choices than α -substituted acetophenones, which are often corrosive and lachrymatory. Aprotic solvents were used for electrochemical studies to prevent complications involved with hydrogen-ion transfer. Acetonitrile was the most generally satisfactory, as it is unreactive and offers a wide potential window. The supporting electrolyte was 0.1 M in $n\text{-Bu}_4\text{NPF}_6$.

All electrochemical measurements were made with a BAS, Inc. 100B Electrochemical Workstation. Working electrodes were

composed of glassy carbon ($A = 0.109 \text{ cm}^2$), gold ($A = 0.0305 \text{ cm}^2$), platinum ($A = 0.0307 \text{ cm}^2$), or palladium ($A = 0.0977 \text{ cm}^2$) disks (BAS), while auxiliary electrodes were platinum coils. All potentials are referenced to Ag/Ag^+ and were not corrected for liquid junction; instead, an internal standard (ferrocene) was used to correct for day-to-day drift. For consistency, all potentials reported were taken at a scan rate (ν) = 0.300 V s^{-1} unless otherwise noted. A static mercury-drop electrode was not utilized in this experiment, even though the large potential window for reductions makes it a viable alternative. The disadvantages of the SMDE are the hazards of mercury, associated disposal costs, and frustrations associated with cleaning and using such a device. A major advantage involves faster data acquisition for compounds that tend to adsorb on the electrode surface. Mercury has been used to investigate compounds of this sort [9] with great success.

Molecular modeling was performed with PC Spartan Pro (Wavefunction, Inc.) using a full-basis-set perturbative Becke-Perdew Density Functional Theory model.

Results

The experiment consists of three distinct phases:

1. acquisition of cyclic voltammetric (scan-rate dependence) data and estimation of electron-transfer mechanism from observed trends,
2. estimation of the some products of the following chemical reactions and rationalization of the ET mechanism according to physical organic principles, and
3. Computer modeling to lend support to the conclusions reached in step 2.

Students are assigned an acetophenone(s) to examine reductively ($E_{\text{sw}} = -2.7 \text{ V}$) between 0.050 and 2 V s^{-1} . The window may be shortened to allow for investigation of individual reductive processes for compounds exhibiting more than one. A complete study takes about 20 min. We have no difficulty with two potentiostats processing 15–18 students in a 3-hr period.

Cyclic voltammetric behavior naturally divides these compounds into classes of similar reactivity/complexity (Table 1). For HOMO/LUMO/linear-free energy lessons, examination of first reduction peak potentials for the entire series gives satisfying results [3]. For instructive physical organic lessons in stability and structure, pick 2'-, 3'-, 4'-nitro, 4'-CN and 4'-CF₃. Even acetophenones classified as simple are instructive in that their mechanism is not obvious. For best results, we allow students to take data on "their" compound, but each gets one set from each category for interpretation.

Nitroacetophenones are the most versatile group as these exhibit the largest number of resolved waves. The chloro and bromo compounds have the most accessible ET mechanism, and useful contrasts are possible when comparing these compounds with 4'-iodo, which is similar but has significant complications involving surface adsorption, and 4'-fluoro, which appears markedly different. The 4'-CH₃, 4'-OCH₃, 4'-SCH₃, and 4'-F derivatives all show one reduction and are followed by a fast chemical reaction. The 4'-CN and 4'-CF₃ derivatives exhibit a pair of reductions and represent a nicely instructive pair in that these substituents are similar in their electron-withdrawing strength and ET mechanism but differ significantly in the rate of decomposition following reduction (Figure 1).

Alternately, the instructor may designate a lower switching potential in order to reduce the complexity of the accessible ET mechanism or to demonstrate a particular chemical concept. The number of electrons in the initial reduction of each compound can be determined by comparing current magnitudes to an internal standard (ferrocene), which can be added at any point as no oxidative scans are made in the study and the presence of ferrocene does not affect the reduced acetophenone. Data for representative examples grouped by similar substituent class are shown in Figure 2(a–h). After acquiring their cyclic voltammograms, students will examine them for relevant diagnostic criteria [4]. Though current-potential data may be obtained by "point-and-click" on the computer screen, it is desirable to obtain a hardcopy so that tangent lines (Figure 1) may be drawn for manual tabulation of data, as this allows more precise determination of current at the switching potential, i_{sw} . The corrected current ratio can be calculated according to [5]

$$\frac{i_{p,a}}{i_{p,c}} = \frac{(i_{p,a})_o}{i_{p,c}} + \frac{0.485(i_{\text{sw}})_o}{i_{p,c}} + 0.086 \quad (1)$$

Where $i_{p,a}$ is the anodic peak current, $i_{p,c}$ is the cathodic peak current, and i_{sw} is the current at the switching potential. These calculations are easily made by a spreadsheet into which students place current and potential data derived from their voltammograms.

Results of the Scan Rate Dependence Study by Substituent Group

Complexes can be separated into those showing multiple and those showing single one-electron reductions.

Multiple Reductions: 2', 3', 4'-NO₂, 4'-CN, 4'-Cl, 4'-Br, 4'-I, 4'-CF₃, 4'-OH.

Single Reductions: 4'-F, 4'-OMe, 4'-SMe, 4'-Me, H

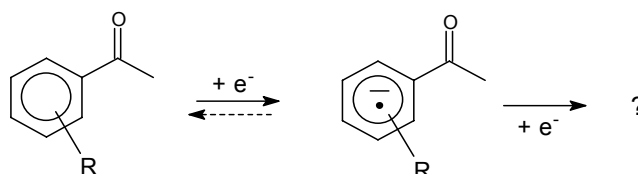
Full discussion is given in the supplementary material. In general, waves corresponding to formation of the radical anion show the characteristics as listed in Tables 2 and 3.

Typical data obtained for a scan-rate dependence study is shown in Table 4.

Following their analyses, student should be able to postulate general mechanistic details such as

1. all acetophenones are reduced to their radical anions via a one-electron process,
2. all radical anions decompose either quickly or slowly based on their ring substituent, and species with additional low-lying orbitals exhibit a second one-electron reduction in the solvent window.

In other words, what is known now is



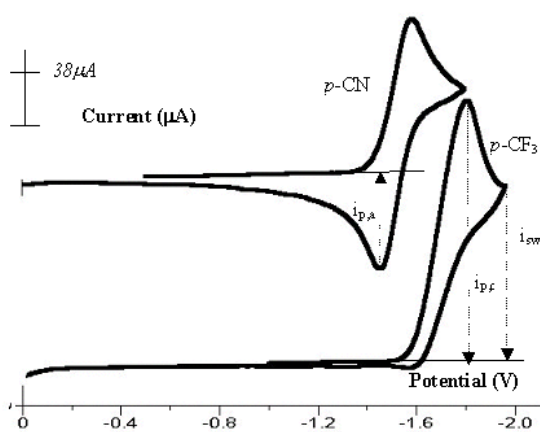


Figure 1. Cyclic voltammograms (0.300 V s^{-1} , MeCN, $0.1 \text{ M } n\text{-Bu}_4\text{NPF}_6$, gold disk electrode) of initial *p*-cyanoacetophenone and 4'-trifluoromethylacetophenone reduction, demonstrating the stabilization of the radical anion by extended resonance.

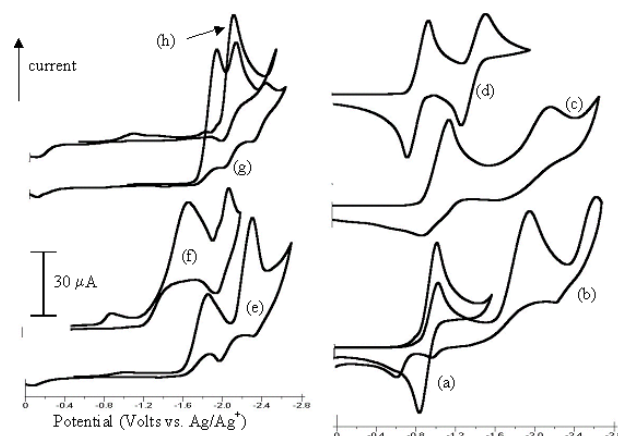


Figure 2. Reductive CV scans (0.300 V s^{-1} , MeCN, $0.1 \text{ M } n\text{-Bu}_4\text{NPF}_6$, gold disk electrode) of selected acetophenones. (a) 2'-nitroacetophenone, scan reversal after first reduction; (b) 2'-nitroacetophenone, full scan (note change in anodic portion of the first reduction as a result of the second); (c) 3'-nitroacetophenone; (d) 4'-nitroacetophenone; (e) 4'-bromoacetophenone; (f) 4'-iodoacetophenone; (g) 4'-chloroacetophenone; (h) 4'-fluoroacetophenone.

Table 1. Classification of Substituted Acetophenones on the Basis of Difficulty of Interpretation of Cyclic Voltammetric ET Mechanism

| Classification | Acetophenones | Comments |
|--|--|--|
| Very Challenging | 4'-OH, 4'-I | Adsorption, indistinct E_p values which shift with time and electrode material. |
| Very Challenging or Simple (depending on E_{sw} selection) | 4'-, 3'-, 2'-NO ₂ , 4'-CF ₃ , 4'-CN | Initial reduction has appearance of reversibility; diagnostic color appears in double layer (except CF ₃); subsequent reductions are more complex. |
| Challenging | 4'-Cl, 4'-Br, 4'-F | Reaction following dissociation of X ⁻ can be theoretically difficult. Fluoro compound appears to students to have unrelated ET mechanism. |
| Simple | 4'-OCH ₃ , 4'-CH ₃ , 4'-SCH ₃ , 4,4'-diacetylbiphenyl | Formation of radical anion + poor leaving group gives only one reduction. For 4,4'-diacetylbiphenyl, overlapping sequential reductions can be observed. |

Table 2. Voltammetric Characteristics for Compounds Exhibiting Multiple Reductions

| Nitroacetophenones | Diagnostic | With Increasing Scan Rate |
|---|---|---|
| Notes: Near-reversible radical anion formation for all isomers with intense discoloration observed at electrode surface. Second reduction is followed by fast chemical reaction. | $E_{p,c}$ and $E_{1/2}$ | Shifts cathodically |
| | Peak potential separation (ΔE_p) | Increases |
| | Current ratio ($i_{p,a}/i_{p,c}$) _{corr} for radical anion formation | Increases from 0.85 (0.050 V s^{-1}) to unity (higher scan rates) |
| | Current function ($i_{p,c}/\nu^{1/2}C$) | Decreases |
| Haloacetophenones | Diagnostic | With Increasing Scan Rate |
| Non-reversible anion radical formation followed by halide dissociation; E_p a function of halide. Second reduction E_p is similar. Iodo shows surface interaction, esp. on Au; 4'-F shows only one reduction. | $E_{p,c}$ and $E_{1/2}$ | Shifts cathodically |
| | Peak potential separation (ΔE_p) | Increases |
| | Current ratio ($i_{p,a}/i_{p,c}$) _{corr} for radical anion formation | No anodic current at any scan rate |
| | Current function ($i_{p,c}/\nu^{1/2}C$) | Relatively insensitive; decreases or increases slightly. |
| 4'-CN, 4'-CF ₃ | Diagnostic | With Increasing Scan Rate |
| Radical anion formation near-reversible for 4'-CN, not for 4'-CF ₃ . Both show following chemical reactions; rate constant for 4'-CN is much smaller. | $E_{p,c}$ and $E_{1/2}$ | Shifts cathodically |
| | Peak potential separation (ΔE_p) | Increases |
| | Current ratio ($i_{p,a}/i_{p,c}$) _{corr} for radical anion formation | Unity for <i>p</i> -CN; zero for <i>p</i> -CF ₃ |
| | Current function ($i_{p,c}/\nu^{1/2}C$) | Decreases slightly. |

Table 3. Voltammetric Characteristics for Compounds Exhibiting Single Reductions

| Single-wave compounds | Diagnostic | With Increasing Scan Rate |
|---|---|---------------------------|
| Pronounced cathodic shifts with some variation in rate constant for following chemical reaction. Small return waves seen in some. | $E_{p,c}$ and $E_{1/2}$ | Shifts cathodically |
| | Peak potential separation (ΔE_p) | Increases |
| | Current ratio ($i_{p,a}/i_{p,c}$) _{corr} for radical anion formation | Increases |
| | Current function ($i_{p,c}/\nu^{1/2}C$) | decreases |

Table 4. Cyclic Voltammetric Diagnostic Criteria for the First Reduction of *m'*-Nitroacetophenone on Gold and Glassy Carbon Electrodes

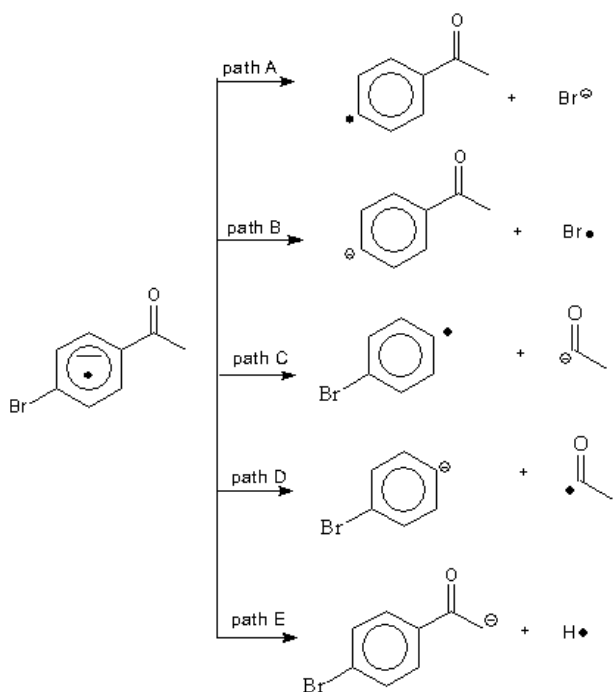
| Gold disk electrode (area = 0.0305cm ²) | | | | | | | | | | | | |
|--|-------------------------------|------------------|--------------|------------------|-----------------|--------------|-------------------------------|------------------|-----------------|--|--|--|
| ν (V s ⁻¹) | ^a E _{p,c} | E _{p,a} | ΔE_p | E _{1/2} | E _{sw} | τ^b (s) | ^c i _{p,c} | i _{p,a} | i _{sw} | ^d (i _{p,a} /i _{p,c}) | ^e (i _{p,c} / $\nu^{1/2}$) | |
| 0.050 | -1.007 | -0.895 | 0.112 | -0.951 | -1.600 | 12.9800 | 5.984 | 3.464 | 3.769 | 0.9704 | 0.8463 | |
| 0.100 | -1.016 | -0.888 | 0.128 | -0.952 | -1.600 | 6.4800 | 8.119 | 4.879 | 4.836 | 0.9758 | 0.8119 | |
| 0.200 | -1.032 | -0.877 | 0.155 | -0.955 | -1.600 | 3.2275 | 11.04 | 6.826 | 5.84 | 0.9609 | 0.7806 | |
| 0.300 | -1.045 | -0.870 | 0.175 | -0.958 | -1.600 | 2.1417 | 13.13 | 8.265 | 6.593 | 0.9590 | 0.7581 | |
| 0.400 | -1.053 | -0.862 | 0.191 | -0.958 | -1.600 | 1.6063 | 14.96 | 9.822 | 6.681 | 0.9591 | 0.7480 | |
| 0.500 | -1.061 | -0.857 | 0.204 | -0.959 | -1.600 | 1.2820 | 16.35 | 10.56 | 7.537 | 0.9554 | 0.7312 | |
| 0.750 | -1.073 | -0.845 | 0.228 | -0.959 | -1.600 | 0.8547 | 19.57 | 13.45 | 8.114 | 0.9744 | 0.7146 | |
| 1.003 | -1.091 | -0.833 | 0.258 | -0.962 | -1.600 | 0.6361 | 21.89 | 15.48 | 9.164 | 0.9962 | 0.6912 | |
| 2.007 | -1.122 | -0.809 | 0.313 | -0.966 | -1.600 | 0.3161 | 29.04 | 20.07 | 12.81 | 0.9911 | 0.6482 | |
| Glassy carbon disk electrode (area = 0.109 cm ²) | | | | | | | | | | | | |
| ν (V s ⁻¹) | ^a E _{p,c} | E _{p,a} | ΔE_p | E _{1/2} | E _{sw} | τ^b (s) | ^c i _{p,c} | i _{p,a} | i _{sw} | ^d (i _{p,a} /i _{p,c}) | ^e (i _{p,c} / $\nu^{1/2}$) | |
| 0.050 | -1.231 | -0.863 | 0.368 | -1.047 | -1.700 | 13.0600 | 74.72 | 27.25 | 44.44 | 0.7392 | 10.5670 | |
| 0.100 | -1.296 | -0.806 | 0.490 | -1.051 | -1.700 | 6.4900 | 96.8 | 52.62 | 59.21 | 0.9263 | 9.6800 | |
| 0.200 | -1.367 | -0.696 | 0.671 | -1.033 | -1.700 | 3.3425 | 123.33 | 70.42 | 72.85 | 0.9435 | 8.7207 | |
| 0.300 | -1.429 | -0.702 | 0.727 | -1.066 | -1.700 | 2.1150 | 141.9 | 82.02 | 93.74 | 0.9844 | 8.1926 | |
| 0.400 | -1.488 | -0.679 | 0.809 | -1.084 | -1.700 | 1.5413 | 155.6 | 87.98 | 113 | 1.0036 | 7.7800 | |
| 0.500 | -1.508 | -0.676 | 0.832 | -1.092 | -1.700 | 1.2160 | 171.6 | 92.85 | 132.7 | 1.0021 | 7.6742 | |
| 0.750 | -1.618 | -0.570 | 1.048 | -1.094 | -1.900 | 1.0747 | 191.7 | 100.6 | 137 | 0.9574 | 6.9999 | |
| 1.003 | -1.672 | -0.481 | 1.191 | -1.077 | -2.000 | 0.9207 | 212.2 | 106.2 | 150.9 | 0.9314 | 6.7003 | |
| 2.000 | -1.861 | -0.307 | 1.554 | -1.084 | -2.150 | 0.5330 | 268.7 | 130.4 | 215.3 | 0.9599 | 6.0083 | |

^aAll potentials (E) have units of V. ^b $\tau = (E_{1/2} - E_{sw})\nu$; τ is the time necessary to scan between half-wave and switching potentials. ^cUnits are microamperes, but for this laboratory exact current readings are unnecessary; this column can be reported as distance measured from the extended baseline drawn on the i-E curve. ^dCorrected value according to eq 1. ^eTypical units of $\mu\text{A s}^{-1/2}$.

Formation of the radical anion occurring in the initial one-electron step is postulated from comparing current magnitude to that observed for ferrocene, an externally added standard. This step is reversible in some compounds, not in others. Those exhibiting reversible initial ET are, predictably, those able to stabilize the radical anion. Without the stabilizing ring substituent, the radical anion is probably more localized on the carbonyl group. In compounds exhibiting more than one, the second reduction is either the radical anion or the product of its decomposition. Now the goal is to refine the choices by making some predictions as to the identity of products formed and species further reduced.

DFT Calculations. Some speculations can be aided by using molecular modeling software. Once CV data are analyzed and reasonably cogent and mechanistic hypotheses presented, students set up DFT calculations for the various fragments that could be formed following decomposition of the radical anion. The students need to calculate the total energy of their own radical anion and then subtract it from the sum of products resulting from its decomposition. The probabilities of various decomposition pathways can be compared in this way to estimate the most likely reaction to follow the electrochemical reduction. For example, consider possible decomposition pathways of the 4'-bromoacetophenone radical anion (Scheme 1). Some are chemically reasonable, involving the dissociation of the best leaving group present. Some are, to the practiced eye, rather fanciful. The student may also be guided by past experience in organic class, though we urge complete examination of all possibilities. This has never caused a problem as the technique is new and students can be uncertain as to what may be happening at the unfamiliar heterogeneous interface.

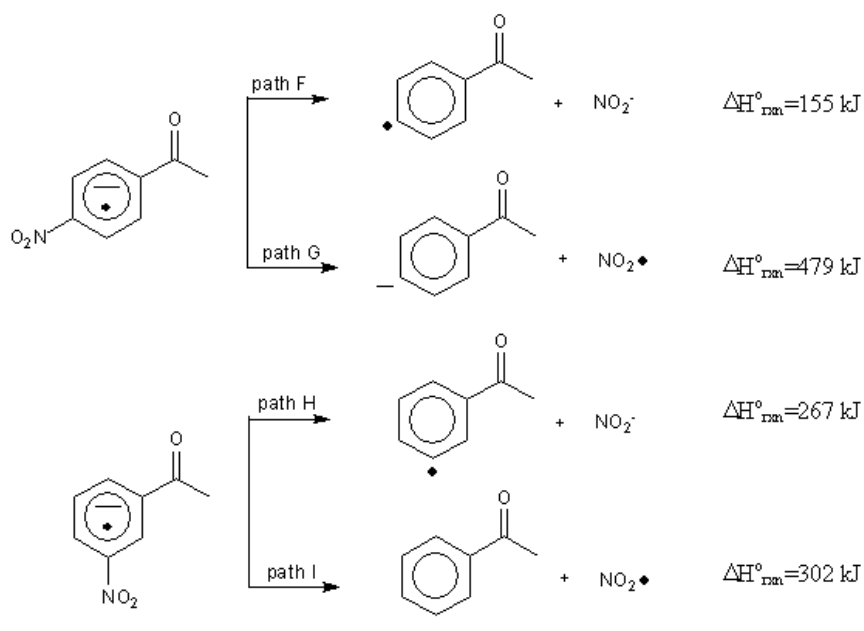
Regardless of the degree of incredulity, the student can estimate the likelihood of each from DFT calculations. Density Functional Theory is chosen over other models because it



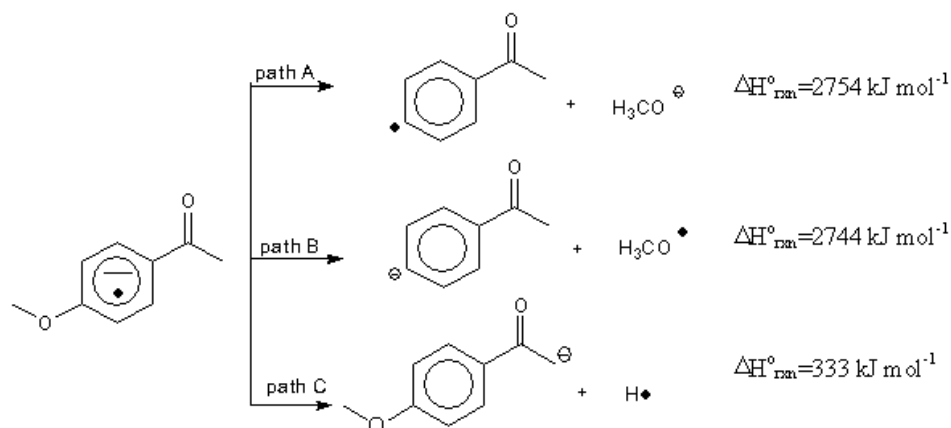
Scheme 1. Postulated pathways for the decomposition of *p*-bromoacetophenone following reduction (as determined by cyclic voltammetry). These homolytic bond dissociations are put forth by students as possible identities for the species formed.

produces the best reproduction of homolytic bond-dissociation energies.

Using path A as an example, students setup their calculations using the full-polarization basis set perturbative Becke-Perdew modification of Density Functional Theory.



Scheme 2. Postulated pathways for the decomposition of 4'- and 3'-nitroacetophenone following reduction (as determined by cyclic voltammetry). The more unlikely guesses from Scheme 1 are omitted.



Scheme 3. Postulated pathways for the decomposition of 4'-methoxyacetophenone following reduction (as determined by cyclic voltammetry) showing likely mechanisms for poor leaving groups.

Starting from initial geometry, one selects the appropriate charge and multiplicity (neutral or anionic, singlet or doublet). Selecting orbitals and energies gives all the information necessary, though any combination of HOMO/LUMO/SOMO orbitals, electron density surfaces, electrostatic potential surfaces, electron density slice, or other surfaces can be selected as well.

As paths A through E are all homolytic bond dissociations, the question becomes "where does the added electron end up?" or "does the ring substituent dissociate, or is an α -hydrogen lost?" Any additional pathways would involve the breaking of more than one bond. Because there is no direct electrochemical evidence for this, Occam's Razor should apply.

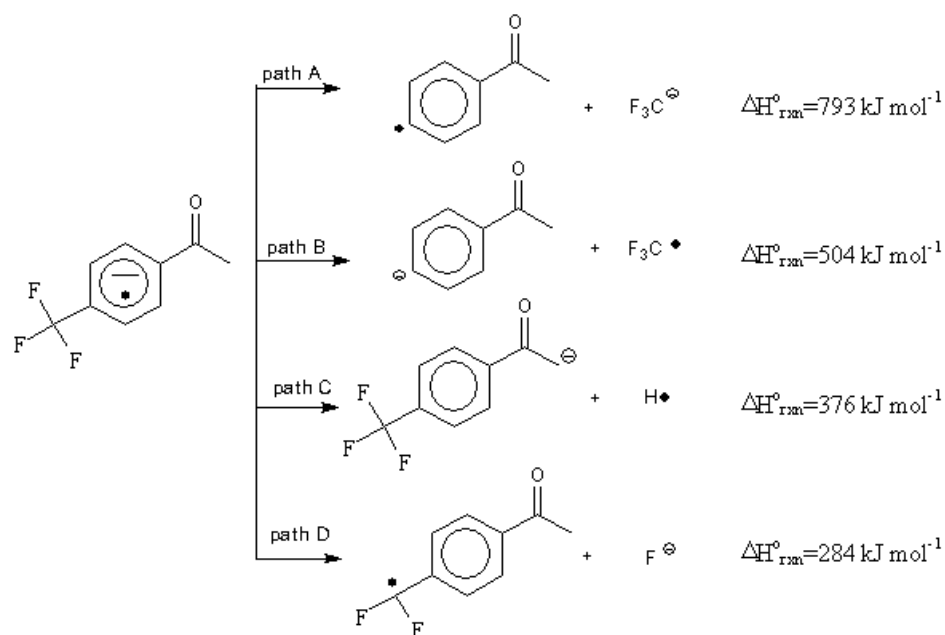
We can calculate reaction energy according to

$$\Delta H_{rxn}^0 = \sum H_f^0(\text{products}) - \sum H_f^0(\text{reactants})$$

For our p-bromoacetophenone example (see above), the following results are obtained:

| Path | ΔH_{rxn}^0 |
|------|---|
| A | 93.71 kJ mol ⁻¹ |
| B | 1.03×10^4 kJ mol ⁻¹ |
| C | 470.26 kJ mol ⁻¹ |
| D | 355.23 kJ mol ⁻¹ |
| E | 355.679 kJ mol ⁻¹ |

As expected, these calculations suggest that the first step in the reaction following radical anion formation is probably dissociation of ring bromine as Br⁻. Quantum mechanical calculations utilizing DFT can be very time-consuming for many molecules; however, many of these species are recurrent (such as acetophenone radical) or very small (like Br⁻ or Br•). Calculations for these small fragments take only a few minutes



Scheme 4. Postulated pathways for the decomposition of 4'-(trifluoromethyl)acetophenone following reduction (as determined by cyclic voltammetry). The complication here is that the substituent itself contains a potential leaving group.

on a Pentium computer. What is rather lengthy is the calculation for the radical anion of each acetophenone. These can be set up to run overnight.

For the nitro compounds, Scheme 2 represents typical student postulations. These calculations yield a more ambiguous result than the halogenated acetophenones.

Calculation results for 4'-nitroacetophenone clearly show a preference for dissociation of nitrite. Students can prove this by controlled-potential electrolysis of a small amount of the compound followed by UV-vis spectroscopy of the resulting solution. This can be done as a special project. Using a double-beam instrument to subtract the MeCN/n-Bu₄NPF₆ background, an absorption at $\lambda_{\text{max}} = 362 \text{ nm}$ appears, which, upon comparison to a bonafide sample, proves to match the absorption by free NO₂⁻.

Similar calculations for the 3'-nitroacetophenone compound shows that the energy difference between pathways H and I is very small, which might indicate that both paths are occurring. Visual inspection of the electrode upon the first reduction clearly shows a brown color evolving instead of the blue seen for the 4'- (and 2'-) derivatives. This is identical to that observed upon the reduction of 2-nitro-5-chloropyridine, which is followed by dissociation of NO₂(g) [6]. For those with the capability, the application of spectroelectrochemical techniques, now widespread, can be useful to avoid time delays associated with electrolysis [7].

Reasonable estimations of decomposition pathways for acetophenones bearing poor leaving groups, such as 4'-methoxy, 4'-methyl, 4'-thiomethyl, and acetophenone, are given in Scheme 3. One can see that the most likely mode of decomposition is the loss of an α -hydrogen from the carbonyl-bound methyl group.

Scheme 4 describes the interesting case of 4'-trifluoromethyl, where the ring substituent itself contains a potential leaving group. Some students postulate, having

deduced fluorine dissociation from 4'-fluoroacetophenone, an equivalent possibility for 4'-trifluoromethylacetophenone. Following reduction, it becomes apparent that one fluoride is probably dissociating from the trifluoromethyl group, a mechanism that has been observed in aqueous solution as well [8].

Complete results of DFT calculations for relevant acetophenones, radicals, and fragments used in this study are provided as supplementary material.

With the voltammetric and thermodynamic information, students can present fairly complete mechanisms for radical anion decomposition. Acetophenones displaying more than one reduction become somewhat more ambiguous, though they can be discerned following the procedure above; it is likely the reduction of the ring radical to give an anion. In aprotic solvents, competing reaction mechanisms such as hydrogen-atom transfer need not be given serious consideration, though disproportionation can occur. Recognizing details of this sort, however, requires an experienced eye and one should not be surprised if the students miss them.

Conclusions

We have found ring-substituted acetophenones to be excellent for teaching students the basics of cyclic voltammetry while at the same time reinforcing concepts of structure and reactivity learned in organic lecture classes. These compounds give readily interpretable voltammograms and visual clues aiding in the deduction of associated ET mechanisms. Student throughput is rapid and simple potentiostats are quite inexpensive compared to other scientific equipment. The addition of DFT calculations adds some familiar chemical reactivity to the exercise and can give real examples of concepts like inductive effects versus resonance effects and the importance of ring substituents on dissociative

ET mechanisms, which are only classroom abstractions to this point. This experiment fits nicely into an organic, electrochemical, or instrumental analysis course. Instructors may choose to concentrate only on the first ET step (EC mechanism), choosing to forego the added complexity of examining additional reductions. This has some merit as DFT calculations often fail to converge for charged species.

Issues not addressed include the effect of ring substituent on the rate of electron transfer and chemical reaction, and the determination of whether the EC mechanism accompanying the first reduction is stepwise or concerted. Analysis of this question will require application of principles of free energy, cell thermodynamics, and electrode kinetics, as well as digital data simulation. This will be the subject of the second paper in this series.

Acknowledgment. We gratefully acknowledge funding from the National Science Foundation through the ILI program (DUE # 9750519), which allowed for purchase of our potentiostats and associated equipment.

Supporting Materials. One supporting file is available; Results of the Scan Rate Dependence Study by Substituent Group (<http://dx.doi.org/10.1007/s00897000522b>).

References and Notes

1. Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*, 2nd ed.; Wiley & Sons: New York, 2001; Chapter 6.
2. (a) Wang, Q.; Geiger, A.; Frias, R.; Golden, T. D. *Chem. Educator* **2000**, 5(2), 58–60; DOI [10.1007/s00897990364a](https://doi.org/10.1007/s00897990364a) (b) Petrovic, S. *Chem. Educator* **2000**, 5(5), 231–235; DOI [10.1007/s00897000416a](https://doi.org/10.1007/s00897000416a) (c) Hathcock, D.; Morris, J.; Madden, J.; Slattery, S. *Chem. Educator* **1997**, 2(3), 1–8; DOI [10.1007/s00897970125a](https://doi.org/10.1007/s00897970125a) (d) Gilles De Pelichy, L. D.; Smith, E. T. *Chem. Educator* **1997**, 2(2), 1–13; DOI [10.1007/s00897970116a](https://doi.org/10.1007/s00897970116a) (e) Sawyer, D. T.; Heineman, W. R.; Beebe, J. M. *Chemistry Experiments for Instrumental Methods*; Wiley & Sons: New York, 1984; pp 79.
3. Holder, G. N.; Farrar, D. G.; McClure, L. L. *Chem. Educator*, in preparation.
4. Nicholson, R. S.; Shain, I. *Anal. Chem.* **1964**, 36, 706. There are many others, but this landmark work is the most generally useful. For a less rigorous but very useful resource, we suggest Brown, E. R.; Large, R. F. *Techniques of Chemistry: Physical Methods of Chemistry, Part IIA, Electrochemical Methods*; Weissberger, A.; Rossiter, B. W., Eds.; Wiley & Sons: New York, 1971, p 423.
5. Nicholson, R. S. *Anal. Chem.* **1965**, 37, 1351–1355.
6. Werner, D.; Tomasik, P. *Ann. Chim. (Rome)* **1973**, 63(1-2), 135–140.
7. Babaei, A.; Connor, P. A.; McQuillan, A. J.; Umapathy, S. *J. Chem. Educ.* **1997**, 74(10), 1200–1204.
8. (a) Liotier, E.; Mousset, G.; Mousty, C. *Can. J. Chem.* **1995**, 73(9), 1488–1496.; (b) Combellas, C.; Kanoufi, F.; Thiebault, A. *J. Electroanal. Chem.* **1996**, 407(1-2), 195–202.
9. Andersen, M. L.; Mathivanan, N.; Wagner, D. D.M. *J. Am. Chem. Soc.*, **1996**, 118, 4871–4879 and many others.