

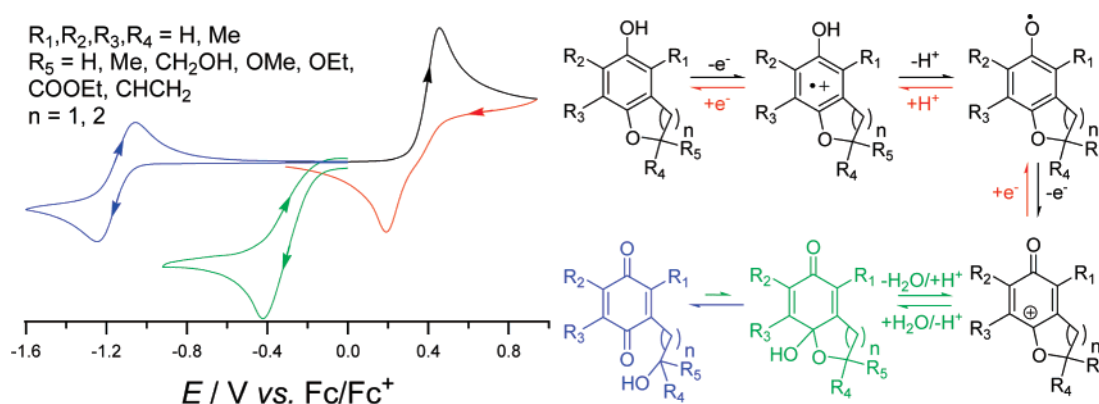
Investigation into Phenoxonium Cations Produced during the Electrochemical Oxidation of Chroman-6-ol and Dihydrobenzofuran-5-ol Substituted Compounds

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A series of chroman-6-ol and dihydrobenzofuran-5-ol based compounds with structures similar to vitamin E were examined by cyclic voltammetry and controlled potential electrolysis. The compounds displayed characteristic voltammetric features that enabled their electrochemical behavior to be interpreted in relation to the oxidation mechanism for vitamin E. The electrochemical experiments indicated the presence of several oxidized species: cation radicals, phenoxyl radicals, phenoxonium ions, hemiketals, and *p*-quinones, whose lifetimes varied depending on the extent of methylation of the aromatic ring (R_1 , R_2 , R_3) and the nature of substituents R_4 and R_5 .

1. Introduction

Phenoxonium cations (**1**) are thought to be involved as key intermediates during the oxidation of phenols, although evidence for their existence is most often based on proposed mechanistic pathways,¹ trapping experiments,^{2a-d} or the detection of UV-vis spectra of transients from laser flash photolysis experiments.^{2e}

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There currently exist only a few examples of phenoxonium cations whose lifetimes are long enough to enable detailed characterization by electrochemical or spectroscopic methods.^{3–7}

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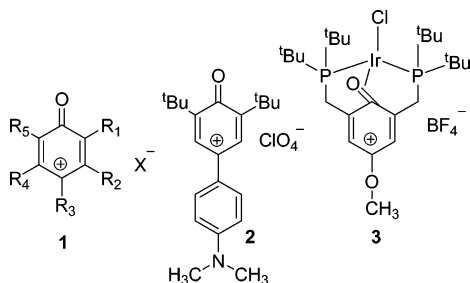
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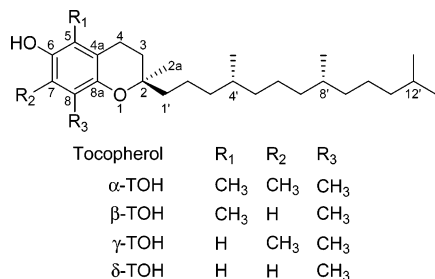
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SCHEME 1. One Resonance Structure Is Displayed for Each Phenoxonium Cation



SCHEME 2. Structures and Atomic Numbering System of the Tocopherol Forms of Vitamin E



Reports of phenols that form stable phenoxonium ions include two organic compounds with bulky groups in the 2- and 6-positions and an aromatic group in the 4-position (**2**),^{3,4} and a metal stabilized phenoxonium complex (**3**), also with bulky groups in the 2- and 6-positions (Scheme 1).⁵

There exists one interesting class of phenoxonium cations that are formed by oxidation of the natural 6-chromanol compounds comprising vitamin E (TOH) (Scheme 2), which have recently been extensively electrochemically and spectroscopically characterized.^{6,7} The phenoxonium cation derived from the α-tocopherol (α-TOH) model compound was particularly stable, even enabling X-ray structures to be determined from salts crystallized with non-nucleophilic [B(C₆F₅)₄]⁻ and (CB₁₁H₆Br₆)⁻ anions.^{7e} Due to the scarcity of long-lived phenoxonium cations, it is a remarkable observation that one obtained from a natural compound is stable (especially in light of the number of new non-antioxidant functions recently discovered that have been assigned specifically to the α-TOH vitamer⁸), and raises questions as to whether the cation has any biological importance.^{7d,7f}

This study is devoted to determining what aspects of the structure of vitamin E and structurally related chroman-6-ol and dihydrobenzofuran-5-ol based compounds (phenols) are important in increasing the lifetime of their related phenoxonium cations. It has already been determined that the phenoxonium ion of the most fully methylated form of vitamin E, α-tocopherol (α-TO⁺), has the longest lifetime in solution.^{7d} In dry CH₃CN or CH₂Cl₂, α-TO⁺ has a lifetime of at least several hours, β-TO⁺ persists for a few minutes, while γ-TO⁺ and δ-TO⁺ have lifetimes < 1 s.^{7d} In this study, a number of phenols with similar structures to vitamin E were prepared and their electrochemical

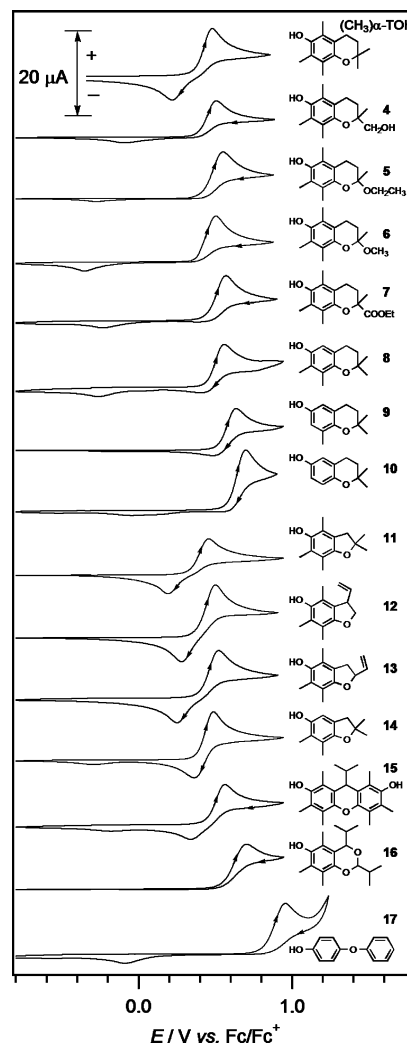


FIGURE 1. Cyclic voltammograms of 2.0 mM substrates in CH₃CN with 0.2 M *n*-Bu₄NPF₆ recorded at a 1 mm diameter Pt electrode at a scan rate of 0.1 V s⁻¹ at *T* = 293 K.

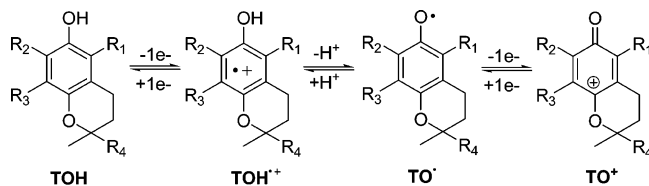
behavior examined by cyclic voltammetry (CV) and controlled potential electrolysis (CPE).

2. Results and Discussion

2.1. Cyclic Voltammetry. Cyclic voltammograms (CVs) of solutions containing a variety of phenols are given in Figure 1. The tocopherols have previously been extensively studied in CH₃CN and CH₂Cl₂ and their electrochemical behavior is well-understood,^{6,7,9} enabling CV to be used as a means of assessing the lifetimes of oxidized species. For example, the CV of the model compound of α-TOH with a methyl group in position 1' (Scheme 2), [(CH₃)α-TOH], shows an oxidation process with an anodic peak (*E*_p^{ox}) at approximately +0.5 V vs Fc/Fc⁺, and a reverse reduction process with a cathodic peak (*E*_p^{red}) at approximately +0.2 V vs Fc/Fc⁺ when the scan direction is switched (Figure 1). The voltammetric processes are associated with two chemically reversible heterogeneous one-electron transfers and a homogeneous chemically reversible proton transfer (an ECE mechanism, where E represents an electron transfer and C a chemical step) (Scheme 3).

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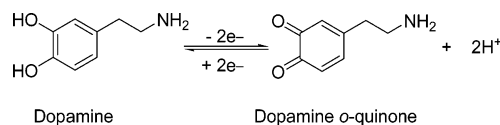
SCHEME 3. Electrochemical Oxidation Mechanism for Tocopherols in CH₃CN or CH₂Cl₂.^{7,a}

^a One resonance structure is displayed for each compound. R₁, R₂, R₃ = H or Me. R₄ = alkyl.

Thus, the forward oxidative process for (CH₃) α -TOH in Figure 1 is associated with two one-electron oxidations and one proton loss to form the phenoxonium cation (CH₃) α -TO⁺, while the reductive process detected when the scan direction is reversed is associated with the reverse reaction to regenerate the starting phenol. The anodic to cathodic peak-to-peak separation (ΔE_{pp}) for the CV of (CH₃) α -TOH is much wider than expected for a two-electron electrochemically reversible transfer, because of the presence of the chemically reversible deprotonation/protonation step shifting the E_p^{ox} and E_p^{red} peaks.^{7f} The phenoxyl radicals (TO[•]) can also be produced by one-electron oxidation of the phenolate anions (that can be prepared by adding base to a solution of the phenols).^{7a,b,9} However, for the conditions used in this study, the phenoxyl radicals only have a short lifetime in solution: either being immediately further oxidized to form the phenoxonium cations, or undergoing protonation then being reduced back to the phenols, depending on the applied potential.⁷

The chemically reversible nature of the two one-electron and one-proton process is unusual compared to what is observed for most phenols, which generally undergo chemically irreversible oxidations to form reaction products that are not readily converted back to the starting material. Therefore, CVs performed on phenols do not usually display a reverse cathodic peak when the scan directions are reversed.^{7b} Some exceptions are (i) hydroquinones that can reversibly form quinones during oxidation/reduction cycling, via a two-electron, two-proton process,^{1b} (ii) phenols with amine groups adjacent to the hydroxyl group that undergo a chemically reversible proton coupled one-electron transfer,¹⁰ and (iii) in organic solvents containing strong acids some phenol cation radicals can be stabilized against deprotonation resulting in chemically reversible one-electron transfer.¹¹

The observation of a reverse reductive peak detected during CV experiments, within 0.3–0.4 V of the oxidation process, appears to be characteristic of the existence of phenoxonium cations, as observed for α -TOH and β -TOH at $\nu = 0.1$ V s⁻¹ and γ -TOH and δ -TOH at $\nu = 10$ V s⁻¹ ($\nu =$ scan rate).^{7d} The wide separation between the forward and reverse peaks is similar to that observed during CV experiments on hydroquinones, such as dopamine (a two-electron and two-proton process) (Scheme 4).¹² However, phenols with one hydroxy group (and an ether

SCHEME 4. Electrochemical Oxidation Mechanism for Hydroquinones, Such as Dopamine, in Acidic Aqueous Conditions

group in the para-position) cannot form quinones without breaking an oxygen–carbon bond, which decreases the likelihood of chemical reversibility on the CV time scale. Therefore, the detection of a reverse (reductive) peak during CV experiments on phenols that undergo two-electron oxidation (and only contain one hydroxy group) is good evidence for the presence of persistent phenoxonium cations.

The electrochemical responses observed for the compounds in Figure 1 can be interpreted based on the mechanism in Scheme 3, with the lifetime of the phenoxonium cations determining whether reverse cathodic peaks are detected within 0.3–0.4 V of the oxidation process. The degree of chemical reversibility of the oxidation process in Scheme 3 can be estimated by the anodic (i_p^{ox}) to cathodic (i_p^{red}) peak current ratio (i_p^{ox}/i_p^{red}). For compounds where the oxidized forms are stable (within the time scale of the CV), the i_p^{ox}/i_p^{red} ratio approaches unity (although this relationship is complicated and strictly depends upon the equilibrium constant for the proton-transfer reaction).^{7f} Compounds **4–10** show only very small reverse cathodic peaks when the scan directions are reversed (at a scan rate of 100 mV s⁻¹), therefore, their i_p^{ox}/i_p^{red} ratios are $\gg 1$, indicating that their associated phenoxonium cations are relatively short-lived and decompose/react before they can be reduced back to the starting material. Many of the compounds also displayed a small cathodic peak at ca. –0.2 to –0.4 V vs Fc/Fc⁺ that was evident only when the scan direction was reversed after the main oxidation process at ca. +0.5 V. The peak at ca. –0.2 to –0.4 V vs Fc/Fc⁺ is due to a secondary reaction product (but not the phenoxonium cations which occur at ca. +0.2 V vs Fc/Fc⁺) and will be discussed in section 2.2. The secondary reaction product does not show a reverse oxidative peak when the scan direction is applied in the positive potential direction (i.e., when the CV is conducted over three scans), indicating that its reduced form is short-lived.

The conclusion that the observation of only a small reverse peak (E_p^{red}) at potentials 0.3–0.4 V less positive than the oxidation peak (E_p^{ox}) for compounds **4–10** is because their phenoxonium cations are short-lived is supported by variable scan rate studies. For example, Figure 2 shows variable scan rate CVs of compound **7** between $\nu = 0.1$ and 5 V s⁻¹. As the scan rate is progressively increased, the cathodic peak at ca. +0.2 V becomes bigger, so that at a scan rate of 5 V s⁻¹, the CV of **7** has a very similar appearance to that observed for (CH₃) α -TOH at $\nu = 0.1$ V s⁻¹ (compare Figures 1 and 2). The close similarity in the voltammetry supports the presence of the phenoxonium cation of **7** (albeit with a lesser lifetime compared to (CH₃) α -TO⁺). Concomitantly to the reductive peak in Figure 2 at ca. +0.2 V vs Fc/Fc⁺ increasing with increasing scan rate, the reductive peak at ca. –0.2 V becomes smaller due to the faster scan rates outrunning the formation of the secondary oxidized product. Similar variable scan rate results were obtained for compounds **8** and **9** (the model compounds of γ -TOH and δ -TOH), with the reverse reductive peaks at ca. +0.2–0.3 V vs Fc/Fc⁺ increasing in size as the scan rate was increased, so that at a scan rate of 10 V s⁻¹, the voltammograms

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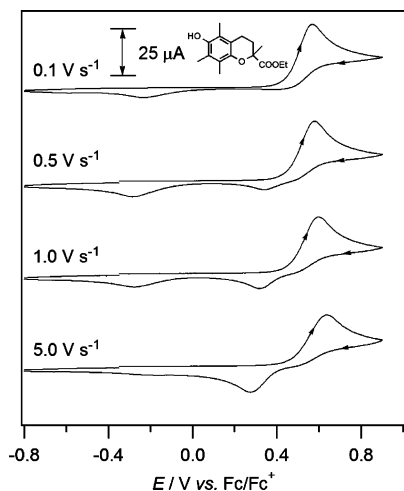


FIGURE 2. Cyclic voltammograms of 2.0 mM **7** in CH_3CN with 0.2 M $n\text{-Bu}_4\text{NPF}_6$ recorded at a 1 mm diameter Pt electrode at $T = 293\text{ K}$. The current data were scaled by multiplying by $\nu^{-0.5}$ ($\nu = \text{scan rate}/\text{V s}^{-1}$).

of **8** and **9** appeared similar to that of $(\text{CH}_3)\alpha\text{-TOH}$ at a slow scan rate of 0.1 V s^{-1} .

In contrast to **7–9**, variable scan rate studies on **4–6** up to $\nu = 200\text{ V s}^{-1}$ showed no evidence of chemical reversibility of the oxidation processes, indicating that the phenoxonium cations of **4–6** were considerably less stable than **7–9** (variable scan rate CVs are provided in the Supporting Information).

The voltammetry and peak shapes of the dihydrobenzofuran-5-ol substituted compounds containing a five-membered ring (compounds **11–14**) at a scan rate of 0.1 V s^{-1} were also examined and showed similar electrochemical behavior to that observed for $(\text{CH}_3)\alpha\text{-TOH}$ (Figure 1) at the same scan rate, indicating that their phenoxonium cations were stable for at least several seconds (compound **11** reportedly has antioxidant properties that exceed those of $\alpha\text{-TOH}$ ¹³). Compounds **12** and **13**, with hydrogen atom(s) bonded to the α -carbons adjacent to the ether oxygen (the equivalent of position 2 in Scheme 2), also showed chemically reversible voltammetry, indicating that carbon atoms in positions 1' and 2a (Scheme 2) are not essential for the formation of long-lived phenoxonium cations. Compound **14**, with the least methyl groups (of compounds **11–14**) in the aromatic ring, displayed a smaller reverse reductive peak close to the oxidation process suggesting that its phenoxonium cation was less stable than the other dihydrobenzofuran-5-ol based compounds.

Compound **15** displayed voltammetric behavior similar to $(\text{CH}_3)\alpha\text{-TOH}$ indicating the reversible formation of its phenoxonium ion, while **16** and **17** displayed chemically irreversible voltammetry indicating that their oxidized states were unstable. Compounds **16** and **17** showed no evidence for the formation of the phenoxonium cations at scan rates up to 200 V s^{-1} . (Compound **17** is included to illustrate the typical oxidative behavior of phenols, which generally display chemically irreversible cyclic voltammograms.)

2.2. Electrolysis Experiments. CV experiments performed in isolation only provide mechanistic information about oxidized or reduced species that have lifetimes on the time scale of the experiment (usually less than a few seconds). In order to gain information about the lifetime of the oxidized compounds over

longer time scales (minutes), controlled potential electrolysis (CPE) experiments were performed and the reaction solutions monitored with CV. It was found that the compounds could be divided into two classes based on their behavior under CPE conditions. Class 1 systems were compounds where their associated phenoxonium cations were detectable during bulk electrolysis experiments indicating that they were stable for at least several minutes. Class 2 compounds were those where their phenoxonium cations were undetectable after electrolysis indicating that they were unstable or reactive. Both of these classes of compounds showed voltammetric evidence of an additional secondary oxidized compound (not the phenoxonium cation) that could be partly reduced back to the starting material under electrolysis conditions. It is difficult to provide accurate kinetic data for the stability of the cations since most were continually decaying during the time scale of the electrolysis. One factor that greatly decreases the lifetime of the cations is the presence of water. Ultra-dry conditions are difficult to achieve under CPE conditions because of the requirement of multicompartments cells to separate the different electrodes. However, since the electrolysis experiments were all performed under identical conditions, the relative stabilities and subsequent division into Class 1 and Class 2 systems is valid.

2.2.1. Class 1 Compounds. Figure 3 shows CV and coulometry data obtained during CPE experiments on **11**. Compounds **11–15**, $(\text{CH}_3)\alpha\text{-TOH}$,^{6,7c-e} $\alpha\text{-TOH}$,⁷ and $\beta\text{-TOH}$ ^{7d} are examples of Class 1 compounds. All CPE experiments were performed at $-20\text{ }^\circ\text{C}$ in order to improve the stability of the phenoxonium cations, which are known to have longer lifetimes at lower temperatures (likely due to slowing down the reaction with trace water that is usually present in mM levels in organic solvents).⁷ The black line in Figure 3a is the CV of **11** prior to the CPE, the red line is the CV obtained of the oxidized solution at the completion of the CPE at $+0.6\text{ V vs Fc/Fc}^+$ (after the transfer of 2 electrons per molecule), and the dashed line is the CV obtained after the oxidized species had been reduced back to the starting material under CPE conditions at 0.0 V vs Fc/Fc^+ .

Panels b and c of Figure 3 are the current (black line) and coulometry data (red line) (plotted as the number of electrons transferred per molecule) for the forward oxidation and reverse reduction processes, respectively. The total experiment time was around 2100 s (35 min) excluding the time to run the CVs, with the electrochemical data confirming that the phenoxonium cation of **11** was stable for at least several minutes in CH_3CN . There is a small shift in potential between the first scan (solid black line) and final scan (dashed line) possibly due to a change in solution composition during the electrolysis affecting the equilibrium of the homogeneous proton-transfer reaction (a similar effect is observed during the electrolysis of $\alpha\text{-TOH}$ ^{7b}). The i_p^{ox} -value recorded in the CV of the final product (dashed line) was approximately 80% of the initial i_p^{ox} -value in the CV recorded prior to the electrolysis (black line), indicating that $\sim 20\%$ of the phenoxonium cation was lost during the reaction, which is supported by the coulometry data which indicated the transfer of ~ 1.6 electrons for the reverse reduction reaction (Figure 3c). A small reductive peak was evident at ca. -0.4 V vs Fc/Fc^+ that was due to a secondary oxidation product. All compounds showed a reductive peak at ca. -0.4 V after their exhaustive oxidative electrolysis, which became progressively larger in relation to the phenoxonium cation peak as the systems changed from Class 1 to Class 2 systems. Class 2 systems only

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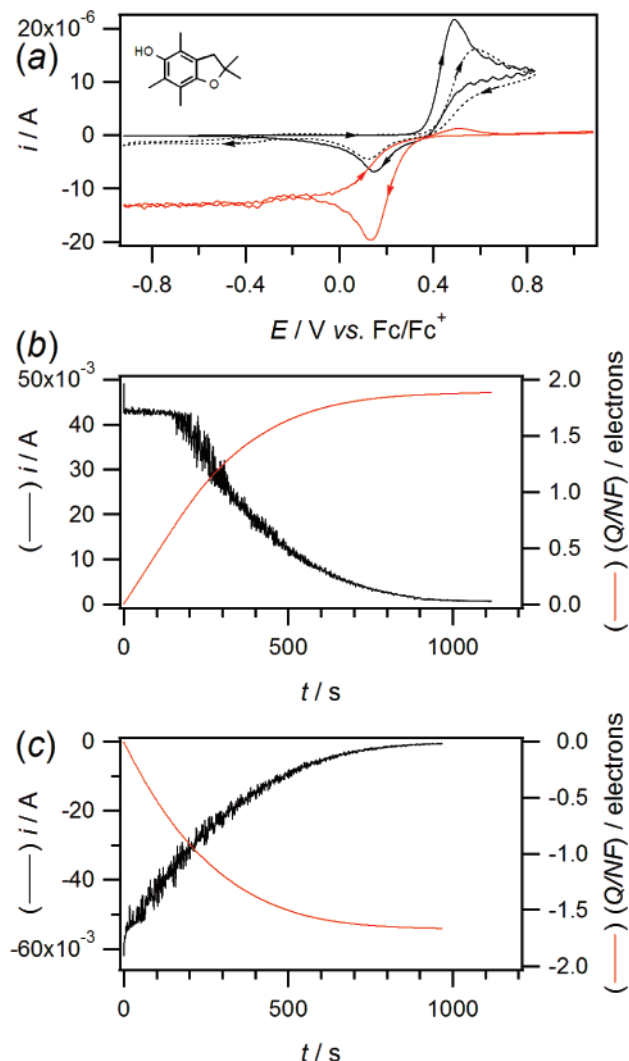


FIGURE 3. Voltammetric and coulometric data obtained at 253 K during the controlled potential electrolysis of 5 mM **11** in CH_3CN with 0.2 M Bu_4NPF_6 . (a) Cyclic voltammograms recorded at a scan rate of 0.1 V s^{-1} with a 1.0 mm diameter Pt electrode: (black line) prior to the bulk oxidation of **11**; (red line) after the exhaustive oxidation of **11**; (dashed line) after the exhaustive reduction of the oxidized product. (b) Current/coulometry vs time data obtained during the exhaustive oxidation of **11** at $+0.6 \text{ V vs Fc/Fc}^+$. (c) Current/coulometry vs time data obtained during the reverse exhaustive reduction of the oxidized product at 0.0 V vs Fc/Fc^+ .

showed the peak at ca. -0.4 V at the completion of the electrolysis. A summary of the data from CPE experiments is given in Table 1.

2.2.2. Class 2 Compounds. Figure 4 shows CV and CPE data obtained during the electrolysis of **7**, a Class 2 compound. Figure 4a(ii) (black line) shows the CV of **7** prior to the electrolysis and (red line) immediately after the exhaustive transfer of 1.8 electrons per molecule. The red line CV in Figure 4a(ii) shows a reductive peak at ca. $-0.4 \text{ V vs Fc/Fc}^+$, due to the reduction of the main oxidation product of the electrolysis. The reductive peak at $-0.4 \text{ V vs Fc/Fc}^+$ is substantially shifted from where the phenoxonium ion peak occurs ($+0.2$ to $+0.4 \text{ V}$) and is therefore due to a secondary oxidized compound.

When the oxidized solution was reduced at $-0.5 \text{ V vs Fc/Fc}^+$ under CPE conditions, CV experiments indicated that the starting material could be partly regenerated in $\sim 50\%$ yield (see

TABLE 1. Calculated Number of Electrons Transferred Per Molecule (n -values) Obtained during the Controlled Potential Oxidation of Phenols, and in Some Cases the Reverse Reduction of Their Associated Phenoxonium Cations

compd	n -value ^a (oxidation) ^b	n -value ^a (reduction) ^c	class ^d
$(\text{CH}_3)_\alpha\text{-TOH}$	1.9	-1.5	1
4	1.9	<i>e</i>	2
5	1.8	<i>e</i>	2
6	1.8	<i>e</i>	2
7	1.8	<i>e</i>	2
8	1.9	<i>e</i>	2
9	1.9	<i>e</i>	2
10	2.1	<i>e</i>	2
11	1.9	-1.7	1
12	1.9	-1.2	1
13	1.6	-0.5	1
14	2.5	-0.3	1
15	2.1	-1.4	1
16	1.9	<i>e</i>	2
17	2.2	<i>e</i>	2

^a Calculated from coulometry data by using the equation $n = Q/NF$, where Q is the charge passed (coulombs), N is the number of moles, and F is the Faraday constant (96485 C mol^{-1}). ^b Applied potential is $+0.1 \text{ V}$ past oxidation peak potential (E_p^{ox}) of the phenol (see Figure 1). ^c Applied potential is -0.1 V past reduction potential of the phenoxonium cation (see Figure 1). ^d Class 1 systems are where the phenoxonium cations are voltammetrically detectable for several minutes, and Class 2 systems are where the phenoxonium cations cannot be detected after electrolysis (lifetimes < a few seconds). ^e Not measurable under present conditions.

the Supporting Information). In order for the phenol (**7**) to be regenerated, the reaction product at $-0.4 \text{ V vs Fc/Fc}^+$ cannot be too dissimilar from the starting material, thus a ring-opened form is unlikely. Therefore, the species at $-0.4 \text{ V vs Fc/Fc}^+$ has been assigned as the hemiketal chromenol (Figure 4a(ii)), which are known oxidation products of tocopherols that subsequently convert into the ring-opened p -quinones (Scheme 5).^{14a-c} Also evident in Figure 4a(ii) (red line) is a reductive peak at $-1.0 \text{ V vs Fc/Fc}^+$ that has been assigned to the p -quinone (**7a**) by comparison with the voltammetry of an authentic sample synthesized by chemical oxidation of the phenol.^{14c} (CVs of several p -quinones are provided in the Supporting Information section showing their voltammetric behavior that typically involves chemically reversible one-electron reduction processes.)

The hemiketal evident in the CVs at $-0.4 \text{ V vs Fc/Fc}^+$ is stable at 253 K for several hours but when the solution is warmed to 293 K, it quickly reacts further to form a species with a reduction potential peak (E_p^{red}) close to $-1.0 \text{ V vs Fc/Fc}^+$ (Figure 4a(iii)), which has been assigned to the p -quinone (**7a**). The voltammetric peak shape of the p -quinone is different when it is present in a pure solution of CH_3CN (Figure 4a(i)) because the presence of acid liberated during the oxidation effects the chemical reversibility of the reduction process. When a standard sample of **7a** is added to the solution, the peak at -1.0 V increases in size, supporting the assignment of the p -quinone in partial yield (Figure 4a(iv)). It is likely that other oxidation products also form at room temperature because the long-term oxidation products of phenols are usually complicated with one product seldom formed in 100% yield.^{1,14,15}

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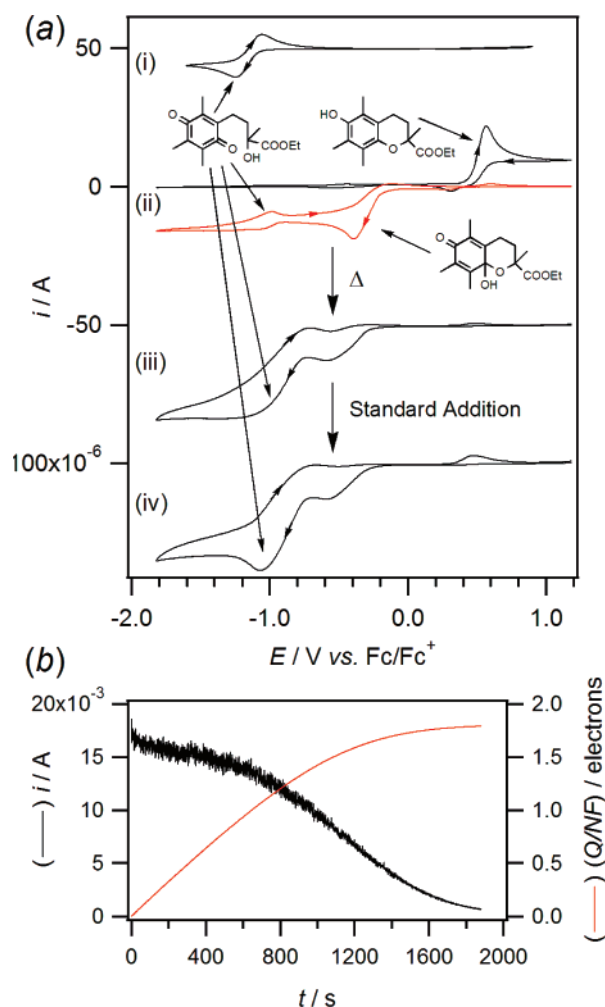
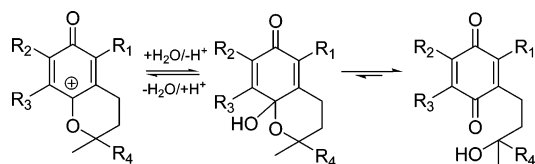


FIGURE 4. Voltammetric and coulometric data obtained in CH_3CN with 0.2 M Bu_4NPF_6 . (a) Cyclic voltammograms recorded at a scan rate of 0.1 V s^{-1} with a 1.0 mm diameter Pt electrode: (i) 2 mM of **7a** at 293 K; (ii) (black line) prior to the bulk oxidation of 5 mM **7** at 253 K and (red line) after the exhaustive oxidation of 5 mM **7** at 253 K; (iii) after the electrolyzed solution of **7** had warmed to 293 K; (iv) after **7a** was added to the oxidized solution of **7** at 293 K. (b) Current/coulometry vs time data obtained during the exhaustive oxidation of **7** at 0.8 V vs Fc/Fc^+ .

SCHEME 5. Conversion of Phenoxonium Cation into Hemiketals (chromenols) and Further Conversion into *p*-Quinones



A spiro-dimer has been identified as a common product formed via chemical oxidation of α -tocopherol in solvents with low dielectric constants such as benzene and chlorobenzene.^{14d,e} α -Tocopherol is thought to be initially chemically oxidized to the phenoxyl radical, which further reacts to form the *o*-quinone

methide, which subsequently undergoes a bimolecular reaction to form the spiro-dimer.^{14d} It is unknown whether quinone methides can form directly from phenoxonium cations, which theoretically would also lead to the formation of spiro-dimers.^{7f} However, it is unlikely that the species detected at -0.4 V vs Fc/Fc^+ could be a complicated product such as a dimer, because the CPE experiments indicated that the reaction is at least partially chemically reversible, while the formation of a spiro-dimer is a chemically irreversible process under the mild conditions used in this study.

The oxidation reaction occurs in two steps under electrolysis conditions: initial one-electron oxidation (and one-proton loss) to form the phenoxyl radical, followed by further one-electron oxidation to form the phenoxonium cation (Scheme 3). However, reactions that are performed with chemical oxidants will not necessarily undergo the same mechanism as the electrochemical oxidation reported in this study, because chemical oxidation reactions can result in higher concentrations of the phenoxyl radicals, especially when hydrogen atom abstracting agents are used.^{14c-e,15} Under electrochemical conditions, the phenoxyl radicals will always undergo immediate further oxidation to the phenoxonium cations. Thus, the conditions used in this study favor the formation of the phenoxonium cations in high yields. It is reasonable to expect the cationic compounds to be highly reactive with nucleophiles present in the solvent; therefore, the formation of hemiketals via reaction with low levels of water is consistent with the present data, but may not mimic the yields of the final products formed by chemical oxidation experiments.^{14,15}

Compounds **4–6**, **8–10**, **16**, and **17** behaved similarly under electrolysis conditions to **7** and so can also be considered Class 2 systems. A summary of the data from controlled potential electrolysis experiments is given in Table 1 and current–time and charge–time plots from the CPE experiments are provided in the Supporting Information. The coulometry data confirmed the transfer of close to two electrons per molecule over electrolysis time scales (Table 1), which is supportive of the initial oxidation product being the phenoxonium cations in each case.

3. Conclusions

A number of new compounds have been identified that form phenoxonium cations upon electrochemical oxidation in CH_3CN . By comparing the variable scan rate CV and CPE data obtained for the compounds in Figure 1, it is possible to make some observations about the lifetimes of the phenoxonium cations based on their structures. Both chroman-6-ol and dihydrobenzofuran-5-ol substituted compounds are able to form detectable phenoxonium cations upon oxidation in CH_3CN , several with lifetimes of at least a few seconds. In general, the lifetime of the phenoxonium cations increases with increasing methylation of the aromatic ring. The increased lifetime of the phenoxonium cations with increasing methylation can be rationalized by improved steric shielding from nucleophilic attack, and by the electron donating ability of the methyl groups aiding in stabilizing the increased positive charge.

Previously, results from ^{13}C NMR experiments and data from theoretical calculations indicated that the positive charge in the phenoxonium cation of α -TOH ($\alpha\text{-TO}^+$) was, surprisingly, mainly located on the quaternary carbon in the chromanol ring (position 2 in Scheme 2), with lesser delocalization into the aromatic ring.^{7c} Therefore, it would be expected that the

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properties of the group bonded to position 2 (positions 1' and 2a in Scheme 2) would have a pronounced affect on the lifetimes of the phenoxonium cations. Thus it was found that for the chroman-6-ol compounds with fully methylated aromatic rings and methyl groups in position 2a [(CH₃) α -TOH, **4–7**], the lifetime of their phenoxonium cations followed the order Me \gg CH₂OH \approx COOEt \gg OMe \approx OEt for the groups in position 1'.

The presence of a carbon atom or heteroatom in positions 1' or 2a (Scheme 2) is not a prerequisite for the stability of the phenoxonium cations. It was found that compounds **12** and **13** with hydrogen atom(s) bound to position 2 formed persistent phenoxonium cations upon electrochemical oxidation. Furthermore, compound **11**, containing a 5-membered ring, formed a phenoxonium cation upon oxidation whose lifetime in solution was as high as that of the 6-membered ring naturally occurring analogue, α -TO⁺.

4. Experimental Section

4.1. Chemicals. (CH₃) α -TOH,¹⁶ **4**,¹⁷ **5**,¹⁸ **6**,¹⁹ **7**,¹⁷ **8**,²⁰ **9**,²¹ **10**,²² **11**,^{23,24} **12**,²⁵ **13**,²⁵ **14**,^{23a} **15**,²⁴ **15a**,²⁴ **16**,²⁴ and **18**^{14c} were prepared by literature methods. Other compounds and reagents were from

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commercial sources, except **7a**, which is a new compound prepared by a standard method.^{14c}

7a: FeCl₃ hexahydrate (762 mg, 2.8 mmol) was added to a methanol/water/diethyl ether (40 mL, v/v/v = 19: 1: 20) solution of ethyl 6-hydroxy-2,5,7,8-tetramethyl-3,4-dihydro-2*H*-chromene-2-carboxylate (150 mg, 0.68 mmol) in an ice bath, and the resulting solution was stirred for 2 h. Water (20 mL) was added and the mixture was extracted with ether. The organic layer was washed with water and brine and dried over sodium sulfate. The residue was separated by column chromatography to give yellow oil product (125 mg, 76%). ¹H NMR (CDCl₃, 400 MHz) δ 4.33–4.23 (m, 2H), 3.31 (s, 1H), 2.65–2.58 (m, 1H), 2.43–2.35 (m, 1H), 2.02 (s, 3H), 2.00 (s, 6H), 1.88–1.81 (m, 1H), 1.74–1.67 (m, 1H), 1.42 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ¹³C {¹H} NMR (CDCl₃, 400 MHz) δ 187.6, 186.9, 176.9, 143.4, 140.6, 140.5, 140.4, 74.1, 62.1, 38.3, 26.0, 21.1, 14.2, 12.3, 12.2, 11.9.

4.2. General Experimental Methods. Procedures for all electrochemical experiments are provided in previous publications.⁷

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Supporting Information Available: Compound characterization data (¹H, ¹³C NMR, and HRMS) and electrochemical data from cyclic voltammetry and controlled potential electrolysis experiments. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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