Selective Electrochemical versus Chemical Oxidation of Bulky Phenol

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S Supporting Information

ABSTRACT: The electrochemical oxidation of selected *tert*-butylated phenols 2,6-di-*tert*-butyl-4-methylphenol (1), 2,6-di-*tert*-butylphenol (2), 2,4,6-tri-*tert*-butylphenol (3), 2-*tert*-butylphenol (4), and 4-*tert*-butylphenol (5) was studied in an aprotic environment using cyclic voltammetry, square-wave voltammetry, and UV-vis spectroscopy. All compounds exhibited irreversible oxidation of the corresponding phenol or phenolate ion. Compound 2 was selectively electrochemically oxidized, while other phenol analogues underwent mostly chemical oxidation. The electrochemical oxidation of 2 produced a highly absorbing product, 3,5,3',5'-tetra-*tert*-butyl-4,4'-diphenoquinone, which was characterized by X-ray crystal diffraction. The electrochemical oxidation was monitored as a function of electrochemical parameters and concentration. Experimental and theoretical data indicated that the steric hindrance, phenoxyl radical stability, and hydrogen bonding influenced the outcome of the electrochemical oxidation.



The absence of the substituent at the *para* position and the presence of the bulky substituents at *ortho* positions were structural and electrostatic requirements for the selective electrochemical oxidation.

1. INTRODUCTION

Phenolic compounds have a wide range of applications, from automotive and food industries to biological function. Antioxidant activity of phenol is related to its ability to donate electrons to a substrate. Under oxidative conditions, phenols may react to yield a variety of products including hemiacetals, quinones, biphenyl quinones, etc., depending on the structure of the parent phenol and experimental conditions.

Chemical oxidation of phenols is the most common synthetic route toward products of interest. Bisphenol and diphenoquinone were formed from hindered phenols under various chemical conditions, which include base-catalyzed oxidation under O₂ atmosphere,¹ base-catalyzed oxidation in the presence of K₃Fe(CN)₆,² or heterogeneous catalysis under basic conditions.³ 2,6-Di-*tert*-butyl-4-methylphenol (1) was also shown to undergo dimerization in the presence of an oxidant and O₂.⁴ Oxidation of 1,3-dimethoxyphenol and 2,4,6-trimethylphenol produced dimeric products leading to diphenoquinone and stilbenequinone, respectively.^{5–7}

The electrochemical oxidation of a phenol is initiated at largely positive potentials. Phenols were electrochemically oxidized in solution by anodic oxidation in the presence of metals such as Zn, Cd, and Hg.⁸ The oxidation products of catechols, dopamine, hydroquinone, and *para*-substituted phenols such as tyrosine, tyramine, and 4-ethylphenol were mostly *o*- or *p*-quinones.⁹

Based on the phenoxyl radical intermediate, the oxidation mechanism of phenol involves loss of an electron alongside deprotonation in a radical mechanism. Because the mechanism for this class of compounds proceeds via a radical intermediate, certain phenol derivatives exhibit unique properties. For example, phenoxyl radicals with bulky *tert*-butyl groups at 2'-, 4'-, and 6'-positions exhibited limited biomolecular interactions but underwent rapid reversible reactions to form dimers.¹⁰ Oxidation of other phenolic compounds produced unstable phenoxyl radicals that were further oxidized to quinones or reacted to produce dimers and polymeric aromatic species. α -Tocopherol underwent electrochemical oxidation involving two electron transfer and one proton transfer to produce phenoxonium cation.¹¹ The lifetime of a phenoxonium cations was between milliseconds and hours depending on the structure of the parent tocopherols, but in general the reaction was chemically reversible.¹⁰

Here we report on the oxidative transformation of *tert*butylphenol into biphenoquinone via C–C coupling by electrochemical oxidation. Exclusively, the 2,6-di-*tert*-butylphenol (2), unlike other phenol analogues, selectively produced corresponding biphenylquinone when electrochemically oxidized. The mechanism of electrochemical oxidation was evaluated by cyclic voltammetry and square-wave voltammetry to contrast with the mechanism of chemical oxidation. The electrochromic product from 2 was characterized by UV–vis spectroscopy and single-crystal X-ray diffraction. This is, to the best of our knowledge, the first example of this class of compounds exhibiting unique reactivity alongside oxidative dimerization, under electrochemical conditions. The aim of this

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work is to understand electrochemical behavior of *tert*-butylsubstituted phenols and elucidate the mechanisms through which they undergo electrochemical oxidations.

2. EXPERIMENTAL SECTION

Reagents and Materials. Butylated hydroxytoluene (1), 2,6-di-*tert*-butylpheno (2), 2,4,6-tri-*tert*-butylphenol (3), 2-*tert*-butylphenol (4), 4-*tert*-butylphenol (5), silver nitrate, and tetrabutylammonium perchlorate (TBAP) were all obtained from Sigma-Aldrich (USA). Acetonitrile (ACN) and copper perchlorate were purchase from Alta Aesar and used as received. Trifluoroacetic acid was obtained from Fischer Scientific.

Electrochemical Setup. Electrochemical measurements were obtained using a CHI660D potentiostat (CH Instruments, Inc., USA) with the single-cell three-electrode setup. All electrodes were purchased from CH Instruments, Inc. (USA), and include glassy carbon electrode (GCE) as working electrode, Ag/AgNO₃ as reference electrode, and platinum wire as counter electrode. All compounds were measured at concentration of 10 mM in ACN, unless otherwise stated, in the presence of 0.1 M TBAP. The electrochemical oxidation was carried out by applying electrochemical potential during cyclic voltammetry (CVs) in a specific potential window. The onset potential used was open circuit potential. The positive direction in CV was used during measurements, unless otherwise mentioned. The electrochemical oxidation was carried out as a function of number of CV scans or concentration of compound 2. The potential scan rate was 100 mV s⁻¹ unless otherwise mentioned. All potentials reported were referred to the formal potential of 5 mM ferrocene (Fc/ Fc⁺) in 0.1 M TBAP in acetonitrile ($E_{1/2} = 5$ mV vs Ag/ AgNO₃).

UV–Vis Spectroscopy. UV–vis spectra were obtained with a Cary 100 UV–vis spectrophotometer from Agilent Technologies and 1 cm quartz cuvette from Starna Cells, Inc. (USA). Spectra were carried out with a baseline correction (0.1 M TBAP in acetonitrile). The UV–vis spectra were collected after consecutive four full CV scans for the cycling-dependent measurements. For concentration-based measurements, UV– vis spectra were collected after a full 32 scans.

Scan Rate Experiments. The CVs were collected for all compounds at 10 mM concentration as a function of scan rates: 10, 20, 40, 60, 80, 100, 200, 300, 400, 500, 600, 700, 800, 900, and 1000 mV s⁻¹. The first oxidation peak (E_{pa}), at a more positive potential, was used to generate a plot of current versus square root of scan rate, v. The oxidation peak, E_{pa} , at positive potential, was also used to plot potential versus ln v.

CV-Dependent Electrochemical Oxidation. Compound 2 was electrochemically oxidized in the presence of 0.1 M TBAP as a function of full CV scans: 2, 7, 12, 17, 22, 27, 32, 37, 47, 57, 67, and 72. The onset potential was open circuit potential. UV–vis spectroscopy was measured after each respective CV set.

Concentration-Dependent Electrochemical Oxidation. Compound 2 was electrochemically oxidized in the presence of 0.1 M TBAP with 32 CV scans in -3 to 3 V range (100 mV s⁻¹ scan rate). The following concentrations were used: 1, 5, 8, 10, 20, 40, 50, and 100 mM. UV–vis spectroscopy was measured after CV for each concentration.

Chemical Oxidation. All compounds at 5 mM were chemically oxidized by addition of equimolar amount of

 $\text{Cu}(\text{ClO}_4)_2$ and UV–vis spectroscopy measured over time from 0 to 60 min.

Single Crystal X-ray Diffraction. The brown needleshaped crystals of 3,5,3',5'-tetra-*tert*-butyl-4,4'-diphenoquinone were recrystallized from ACN by slow evaporation. A suitable crystal was selected and mounted on a nylon loop with paratone oil on a Bruker APEX-II CCD diffractometer. The crystal was kept at T = 173(2) K during data collection. Using Olex2, the structure was solved with the ShelXS structure solution program, using the Direct Methods solution method. The model was refined with version 2014/6 of XL using leastsquares minimization.

Theoretical Calculations. Calculations were performed using density functional theory (DFT) with the B3LYP functional and 6-31G* basis set using the Gaussian 09 suite of programs. The highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO), singly occupied molecular orbital (SOMO), and electrostatic potential maps were generated for compounds **2** and **4** using the cubegen utility. The spin density map was used to visualize the SOMO.

3. RESULTS AND DISCUSSION

The electrochromic ability of four derivatives of 2,6-di-tertbutyl-4-methylphenol (1), depicted in Figure 1, 2,6-di-tertbutylphenol (2), 2,4,6-tri-tert-butylphenol (3), 2-tert-butylphenol (4), and 4-tert-butylphenol (5), was evaluated under electrochemical or chemical oxidizing conditions by both electrochemical and spectroscopic methods. Selected compounds were chosen based on the location and number of tertbutyl substituents around the phenol core. Compound 2 lacks the substituent at the para position, similarly to compound 4. In contrast, compounds 1, 3, and 5 do have para-substituted tert-butyl substituents.

Electrochemical Characterization of Substituted Phenols 1–5. Solutions of compounds 1–5 in acetonitrile (ACN) were characterized by cyclic voltammetry (CV) and squarewave voltammetry (SWV) in the presence of 0.1 M TBAP as an electrolyte, using a glassy carbon electrode (GCE) as the working electrode. CV was used to compare the oxidation/ reduction potentials and electrochemical reversibility between all compounds. The CVs acquired in the –3 to 3 V potential window vs Ag/AgNO₃ (reference electrode) in the positive direction are given in Figure 1.

All compounds exhibited anodic peak potential values, $E_{\rm pa}$, at negative and positive potentials in addition to an irreversible oxidation due to the lack of a corresponding reduction peak in the cathodic direction. The lack of reduction wave for all compounds indicates that, following oxidation, they are rapidly transformed into their products and became unavailable for reduction back to the original parent phenols. A single cathodic peak potential value, $E_{\rm pc}$ at ~-1.7 V was noted for all compounds. Table 1 indicates $E_{\rm pa}$ and $E_{\rm pc}$ values for all substituted phenols as determined from CVs. Compounds 1–3 exhibited similar CV profiles, but 2 had an additional oxidation peak at 1.70 ± 0.08 V. Compounds 4 and 5 had a negative $E_{\rm pa}$ peak shifted to a more positive potential value (~450 mV) compared to other compounds.

Similar behavior was reported for α -tocopherol which produced a single oxidation wave and lacked the corresponding reduction wave.¹² Irreversible oxidation was also reported for other substituted phenols including 2,4,6-trimethylphenol, compound **3**, and 2,6-di-*tert*-butyl-4-methoxyphenol.¹²



Figure 1. CVs of compounds 1-5 (10 mM, ACN, 0.1 M TBAP, 100 mV/s, arrow indicates scan direction).

All compounds exhibited similar linear dependence of $E_{\rm pa}$ on the square root of scan rate from 10 to 500 mV/s, as illustrated for **2** in Figure 2. However, at higher scan rates, deviation from linearity was observed pointing to the electrochemical–chemical mechanism, or a combination thereof.¹³ The non-

Table 1. Electrochemical Parameters for Compounds 1–5 (-3 to 3 V Potential Window, 100 mV/s)

| compound | $E_{\rm pa}^{a,b}$ (V) | $E_{\rm pc}^{\ a,b}$ (V) |
|----------|------------------------|--------------------------|
| 1 | -0.67 ± 0.02 | -1.64 ± 0.04 |
| | 1.11 ± 0.02 | |
| 2 | -0.54 ± 0.02 | -1.70 ± 0.04 |
| | 1.28 ± 0.01 | |
| | 1.70 ± 0.08 | |
| 3 | -0.58 ± 0.02 | -1.72 ± 0.68 |
| | 0.78 ± 0.01 | |
| 4 | -0.14 ± 0.04 | -1.62 ± 0.45 |
| | 1.46 ± 0.04 | |
| 5 | -0.13 ± 0.02 | -1.75 ± 0.09 |
| | 1.24 ± 0.02 | |

 ${}^{a}E_{\rm pa}$ and $E_{\rm pc}$ values were determined from cyclic voltammetry measurements. All potentials were reported vs Fc/Fc⁺. ${}^{b}Mean$ of triplicates \pm standard deviation.

linearity of anodic potential as a function of the ln of scan rate, at higher scan rates, confirms chemical reaction following electron transfer.¹⁴ The E_{pa} of compound 2 was plotted as a function of the ln of scan rate and exhibited linearity from 10 to 400 mV, as seen in Figure 2C. The shift in anodic peak potential with the ln of scan rate was indicative of the irreversible oxidation process and may be described by the Laviron equation. The lack of the reduction peak after oxidation of 2 during CV indicates that the oxidized species underwent chemical reaction to form other products before being reduced back to the parent compound 2. Similar CV behavior was commonly observed for compounds that underwent an electrochemical-chemical mechanism and were characterized by a very large chemical rate constant. Both an increase in the oxidation current as well as a shift of E_{pa} peaks toward higher potential was observed for all compounds with increasing concentration of analyte, which indicated minimal electrode fouling. Notably, for compound 1, at concentrations above 8 mM a second E_{pa} peak (at positive potential) was observed. Similarly, compound 2 exhibited a third E_{pa} peak (at positive potential) above 10 mM. Other compounds did not exhibit significant dependence of CV profiles on concentration.

The E_{pa} located at a negative value in CV may be ascribed to oxidation of the phenolate ion to the phenoxyl radical via oneelectron oxidation, as has been shown in the literature.¹⁵ The oxidation potential for phenoxyl radicals has been noted at potentials similar to that of parent phenol.¹⁰ The more positive E_{pa} peak was associated with oxidation of parent phenol compound to phenoxonium cation via two-electron and oneproton loss mechanism, which was reported for compound 1.15 The phenoxonium cation, for most phenols, is short-lived, and the reduction peak in 0.2-0.5 V is seldom observed.¹⁶ Alternatively, a parent phenol, such as compound 1, may be oxidized to PhOH^{•+} (one-electron process) followed by proton loss to give phenoxyl radical and further oxidation to produce PhO⁺ cation.^{9,13,15} All CVs show a major anodic oxidation peak located at a largely positive potential, associated with substituted phenol, thus indicating that the concentration of phenolate anion was much lower in solution (smaller E_{pa} at negative potential).

Characterization of Electrochemical Oxidation of 1–5. Compounds **1–5** were characterized in solution by UV–vis spectroscopy prior to electrochemical oxidation. All compounds exhibited absorption below 300 nm due to π – π * electronic



Figure 2. (A) CVs of 2 as a function of scan rates (arrow indicates the scan direction). (B) Plot of oxidation current as a function of square root of scan rate (current associated with largest E_{pa} peak from CV). (C) Plot of potential as a function of ln scan rate (largest E_{pa} from CV).

transitions, as expected for phenols. The electrochemical oxidation was carried out by using CV in the presence of 0.1 M TBAP in ACN with a GCE. For electrochemical oxidation, the voltage was swept in the positive direction and was used alongside the onset potential, which was equivalent to the open circuit potential. UV–vis spectroscopy was subsequently used to measure the absorption associated with each compound post electrochemical oxidation. Upon cycling from -3 to 3 V, compound 2 changed from colorless to yellow in solution after only two complete CV scans, as shown in Figure 3A.

The remaining substituted phenols 1 and 3-5 displayed minimal change in their UV-vis absorption after only two CV scans. No absorption was noted above 320 nm for 2, but following electrochemical cycling, a new absorption peak appeared at $\lambda_{max} = 420$ nm with a slight shoulder at $\lambda = 399$ nm (Figure 3A). The oxidation product of 2, 3,5,3',5'-tetra-tertbutyl-4,4'-diphenoquinone (TTBDQ), was crystallized from solution post electrochemical oxidation. Absorption at λ_{max} = 420 nm is ascribed to the oxidation product, TTBDQ; this is in line with the reported value for this compound.¹⁷ TTBDQ crystallized in the orthorhombic space group P-1. Figure 4A depicts the X-ray crystal structure of electrochemically synthesized TTBDQ from 2. The packing of TTDBQ along the a-axis (Figure 4B) or b-axis (Figure 4C) indicates lack of hydrogen bonding but significant $\pi - \pi$ interactions. Additional intermediates may contribute to absorption above 300 nm as well. In previous report, TTBDQ was synthesized by electrochemical anodic oxidation of compound 2 in the presence of metals, such as Zn, Cd, or Hg.

Herein, TTDBQ was generated by electrochemical oxidation of 2 in the absence of metal ions. TTBDQ and its X-ray crystal structure prepared by the chemical oxidation of 2 have also been reported.¹⁹

The formation of TTBDQ was monitored as a function of electrochemical CV scanning. As shown in Figure 3A, with an increasing number of full CV scans from 0 to 32, the absorption band at $\lambda_{\text{max}} = 420$ nm increased. A plot of $\lambda_{\text{max}} = 420$ nm versus number of CV scans showed maximum absorption after 32 scans (Figure 3B). However, upon further scanning (up to 72 CV scans), the TTBDQ-associated absorption decreases, resulting in the broadening of its own absorption band. This decrease in absorption with additional cycling may indicate scattering in solution; however, no physical precipitation was observed. Additionally, degradation of TTBDQ may contribute to the changing shape of the UV-vis spectra above 32 CV scans. The solution of 2 at 20 mM was electrochemically oxidized with 72 full CV scans, and the brown crystals were formed as well, indicating that TTBDQ was also successfully formed.

The UV–vis absorption was also measured as a function of initial concentration of **2** after 32 CV scans. Absorption at λ_{max} = 420 nm of **2** increased after 32 electrochemical cycles, along with increasing concentration (Figure 3C). At concentrations below 1 mM no absorption was observed above 300 nm. The maximum absorption was detected at 20 mM (Figure 3D); at higher concentrations absorption saturation was observed.

Because of the electrochemical behavior of 2, several E_{pa} and E_{pc} peaks may be contributing to the formation of species

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Figure 3. (A) UV–vis spectra of compound **2** as a function of CV scans (5 mM, ACN, 0.1 M TBAP, potential window: -3 to 3 V). (B) Plot of absorbance at $\lambda_{max} = 420$ nm as a function of number of CV scans. (C) UV–vis spectra of compounds **2** as a function of concentration (32 CV scans, ACN, 0.1 M TBAP, potential window: -3 to 3 V). (D) Plot of absorbance at $\lambda_{max} = 420$ nm as a function of concentration (32 CV scans, ACN, 0.1 M TBAP, potential window: -3 to 3 V). (D) Plot of absorbance at $\lambda_{max} = 420$ nm as a function of concentration of **2**.



Figure 4. (A) ORTEP diagram of TTBDQ obtained by electrochemical oxidation of compound **2**. (B) View along the *a*-axis showing packing. (C) View along the *b*-axis showing packing with the diphenyl rings offset with respect to each other (crystals were grown from 100 mM **2** after 32 full CV scans).

which absorb at $\lambda_{max} = 420$ nm. Hence, electrochemical oxidation of **2** was carried out in the specific potential windows to determine which oxidation/reduction event contributed to formation of UV–vis absorbing species. Figure 5 shows respective CVs used to generate the corresponding UV–vis spectra (Figure 5).

UV-vis spectra generated in various potential windows resulted in identical absorption at $\lambda_{max} = 420$ nm with a slight shoulder at $\lambda = 399$ nm, indicating the formation of similar product(s) (Figure 5). Electrochemical oxidation in the largest potential window from -3 to 3 V (a) resulted in the greatest

UV-vis absorption (2.2 au). When a shorter potential window was used, including the E_{pa} at a negative potential (c), a significant absorption was observed (1.5 au). This data indicates that the absorbing species was predominantly formed during the oxidation of phenolate anion. The inclusion of the E_{pa} peak at positive potential (b) during electrochemical oxidation produced significant absorption as well (1.6 au) but was similar to that of (c). By contrast, the electrochemical oxidation in the narrow window 0.5 to 3 V (d) produced the smallest absorption (0.2 au).



Figure 5. CVs of compound 2 collected in various potential windows: (a) -3 to 3 V, (b) -3 to 1.4 V, (c) -3 to 0.5 V, and (d) 0.5 to 3 V. UV-vis spectra of compounds 2 after 32 full CV scans as a function of potential window (5 mM compound 2, 0.1 M TBAP, ACN, 100 mV s⁻¹ scan rate).

Absorption at $\lambda_{\text{max}} = 420$ nm which was associated predominantly with TTBDQ was monitored in the presence of chemical reducing agent, 1,4-dithiothriethiol (DTT). With addition of 1 equiv of DTT, the $\lambda_{\text{max}} = 420$ nm decreased completely after 30 min, indicating that TTBDQ may have been reduced to biphenyldiol analogue which absorbs at lower wavenumbers. The TD-DFT calculations for TTBDQ and its diol analogue were used to generate the UV–vis spectra showing that TTBDQ absorbed at lower energy relative to its diol analogue.

Other compounds did not produce significant color change under identical experimental conditions (72 CV scans), except compound 4. When compound 4 was electrochemically oxidized, it produced a small absorption $\lambda_{max} = 407$ nm, as in Figure 6A. The colored intermediate decomposed over time (within 24 h) yielding a colorless solution. A comparison of the λ_{max} versus number of CV scans during electrochemical cycling, presented in Figure 6B, indicated that 2 formed the colored product rapidly while 4 reacted slowly.

The maximum absorption for **2** was observed after only 32 CV scans, while absorption of **4** continued to increase slowly even after 72 CV scans.

Computational Studies. In order to gain further understanding of mechanistic differences between 2 and 4, the compounds were investigated using DFT. DFT calculations for compounds 2 and 4 were used to compare energies of their neutral and radical forms. Figure 7A depicts energy levels of the HOMO and LUMO of neutral and radical forms of compounds 2 and 4. The HOMO and LUMO levels of radical 4° were slightly stabilized compared to 2° , which may point to their difference in reactivity. Electrostatic potential maps for both the neutral and radical species were generated for compounds 2 and 4 and are depicted in Figure 7B. In neutral form, the electron density appears similarly distrubuted throughout both

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Figure 6. (A) UV–vis spectra of compound 4 as a function of CV scans (72 scans, 5 mM, acetonitrile, 0.1 M TBAP, potential window: -3 to 3 V). (B) Plot of absorbance as a function of number of CV scans during electrochemical oxidation for compound 2 ($\lambda_{max} = 420$ nm) and 4 ($\lambda_{max} = 407$ nm).



Figure 7. (A) Energy diagrams of HOMO and LUMO levels and (B) electrostatic potential maps and SOMO diagrams for neutral and radical of compounds 2 and 4.

compounds; while in the radical form, compound 2 has less electron density localized on the phenol O atom.

SOMO maps for both radicals were also generated. The SOMOs of both compounds further indicate that the majority of radical electron density resides on the aromatic ring, with delocalization onto the *tert*-butyl groups. Since **2** has two *tert*-butyl groups, the radical is further delocalized, possibly leading to a longer lived species, thereby increasing reactivity. Similar delocalization has been attributed to increased radical scavanger activity of hydroxybenzohydroxamic acid derivatives.²⁰

Chemical versus Electrochemical Oxidation of 1–5. Chemical oxidation was compared with electrochemical oxidation to further elucidate mechanistic differences between substituted phenols. In general, chemical oxidation is considered to occur faster than the electrochemical oxidation.²¹ Chemical oxidation of 1–5 was carried out with 1 equiv of $Cu(ClO_4)_2$ in ACN and monitored by using UV–vis spectroscopy. Compound 1, when chemically oxidized, led to an increase in absorption below 300 nm, and the appearance of a small absorption band at 400 nm was noted alongside a weak band above 600 nm. Chemical oxidation of 2 was successfully carried out to produce a yellow/brown solution ($\lambda_{max} = 420$ nm), which was associated with the formation of TTBDQ, similar to electrochemical oxidation. was noted after only 5 min in addition to a weak band beyond 600 nm. Notably, no decrease in λ_{\max} for **2** was observed during chemical oxidation up to 60 min, unlike with electrochemical oxidation, which produced an increase in absorption followed by a subsequent decrease. Chemical oxidation of 3 led to an increase in absorption below 300 nm and an appearance of a small peak at 318 nm alongside a weak band above 600 nm. Compound 4 was only slightly electrochemically oxidized, as observed by UV-vis spectroscopy (Figure 6A). However, following chemical oxidation of 4, strong absorption at λ_{max} = 418 nm was observed after only 5 min. In addition, the UV-vis spectrum of 4 indicates formation of other products absorbing at higher wavelengths during chemical oxidation. As the reaction time proceeded to 60 min, absorption decreased dramatically. The chemical oxidation of 5 produced only an increase in absorption below 300 nm and a weak band beyond 600 nm.

The reactivity of substituted phenols was highly dependent on the experimental conditions. For example, the chemical oxidation of 1 and 3 produced new absorption peaks above 300 nm, which were absent in electrochemical oxidation. Only a small absorption band above 300 nm was observed after electrochemical oxidation of 4; however, significant new peaks developed above 300 nm upon chemical oxidation. In addition, the UV-vis spectra of compounds 1-5 after chemical oxidation possess a weak absorption band above 700 nm, which was absent after electrochemical oxidation. The transient species above 600 nm may be ascribed to a phenoxyl radical generated during chemical oxidation.²² Phenoxyl radicals also have an absorption band at 400 nm.^{22,23} Reportedly, the yield of phenoxyl radical was much higher in the presence of water in organic solvent due to deprotonation of phenol radical cation to give a phenoxyl radical. Hence, under chemical oxidation conditions, compounds 1-5 undergo a mechanism which involves formation of phenoxyl radicals, as detected spectrophotometrically. The long-lived phenoxyl radicals formed by all bulky phenols, under chemical oxidation conditions, may further react to generate a variety of products. Notably, the phenoxyl radicals of 1-3 and 5 were observed spectrophotochemically within 1 min of chemical oxidation reaction and were rapidly used up in the formation of species which absorbed in the 300-500 nm range. By contrast, the phenoxyl radical of 4 accumulated over time (6 min) and then decreased independently of species which absorb at higher energy. Under chemical and electrochemical oxidation conditions all compounds exhibited an increase in absorbance below 300 nm, indicating the formation of similar products.

Notably, during the electrochemical oxidation of the bulky phenols, no phenoxyl radicals were observed by UV-vis spectroscopy. The lack of an absorption band associated with the phenoxyl radical under electrochemical oxidation conditions does not definitively discount the presence of a phenoxyl radical in the oxidation mechanism. During the electrochemical oxidation of 2, the yellow solution color was noticed coming from the GCE surface and diffusing into the solution. Hence, the phenoxyl radical may be formed and react only within the Helmholtz layer, and the reaction may be largely driven by the electrode properties.²⁴ For example, factors such as the mass transfer of reactant/products to and from the electrode interface, electron transfer at the interface, and surface adsorption/desorption may influence reactivity of phenoxyl radicals.²⁵ In general, the radicals formed via electrochemical reactions may adsorb onto the electrode surface. During the electrochemical oxidation, the phenoxyl radicals formed may further react to produce a variety of products or be reduced back to the starting compound. In addition, differences in the rates between the electron-transfer reactions and direct hydrogen abstraction may explain the subtle trends observed for chemical and electrochemical oxidations of bulky phenols.²² In contrast, reduction of intermediates and product formation are not viable under chemically oxidizing conditions. Thus, the final products and stability of their intermediates during oxidation reactions differ upon the experimental conditions employed during oxidation process.²⁶

Mechanistic Evaluation of Oxidation. The mechanisms of phenol oxidation differ slightly under neutral, basic, or acidic conditions.²⁷ When phenols undergo oxidation under basic conditions, the process may involve a phenolate anion and oneelectron loss to generate the phenoxyl radical, as was shown for compound 2.¹ These species subsequently may lose an electron, yielding a cation. Under acidic conditions, the phenol may undergo stepwise two-electron oxidation without proton loss to produce radical cation. In the absence of acid or base, the mechanism of phenol oxidation may involve a variety of different steps; it could be a hybrid of basic and acidic mechanisms. Under the given experimental conditions, the experimentally measured pH values for solution 0.1 M TBAP and 5 mM compound 2 in ACN were determined to be 7.3 and 8.8, respectively. The solution of 5 mM compound 2 with 0.1 M TBAP prior to electrochemical CV cycling was nearly neutral at pH 7.6, but following electrochemical oxidation the pH became 8.3. Even in the absence of TBAP, the electrochemical oxidation of 2 took place; this was not the case for compound 4. Hence, the electrochemical oxidation of compound 4 required the presence of TBAP. The electrochemical reaction may require an electrolyte in order to minimize the resistance between anode and cathode during the reaction. Given the experimental pH value of substituted phenols during the electrochemical oxidation reaction, the overall mechanisms may be similar to that of phenols under neutral conditions. The mechanism of electrochemical oxidation of 2 was further investigated under acidic conditions by using 1 equiv of trifluoroacetic acid and 0.1 M TBAP. CV of 2 in the range of -3 to 3 V lacked the $E_{\rm pa}$ peak at -0.54 V, which is associated with phenolate anion. Even in the absence of phenolate anion in solution under acidic conditions, the full 32 CV scans induced a color change with $\lambda_{max} = 420$ nm, which was similar to that of TTBDQ formation under basic conditions.

The electrode surface, specifically the GCE, may play a role in the electrochemical oxidation of phenols due to fouling of phenols onto the GCE.^{28,29} Notably, the electron transfer rates and adsorptive properties of the GCE for some electroactive analytes may be affected by surface modification of the GCE.^{28,29} Adsorption of analyte, such as substituted phenol, onto oxidized GCE may be driven by hydrogen bonding (-OH group of phenol and -COOH group of modified GCE electrode surface) and $\pi - \pi$ interactions between aromatic phenols and the modified GCE surface.³⁰ Because of the similarity in aromaticity and number of -OH groups in compounds 1-5, their adsorptivity and interactions with GCE may not fully explain differences in electro-oxidation. After oxidation of substituted phenols, no film was detected on the electrode surface, indicating that electrode activity was maintained. Fouling of the electrode surface was tested by characterizing the GCE electrode prior to and post electrochemical oxidation of compound 2 by measuring its activity. The electrode was tested by cyclic voltammetry, using a redox probe $[Fe(CN)_6]^{3-/4-}$, which is characterized by a reversible oxidation and reduction current. The current associated with $[Fe(CN)_6]^{3-/4-}$ remained largely unchanged after electrochemical oxidation, indicating no fouling of the electrode surface for experiments performed with compound 2. In addition, no new peaks were observed in CV or SWV, indicating that no redox active compounds were deposited on GCE surface after electrochemical oxidation of 2.

The hydrogen bonding between residual water in ACN and phenol, phenolate, or phenoxyl radical may also impact their stability and reactivity. The hydrogen bonding ability of a hydroxyl group of a butylated phenol with residual water also plays an important role in its electrochemical behavior. The bulky *tert*-butyl groups at the *ortho* positions of a phenol may reduce hydrogen-bonding interactions between a hydroxyl group and residual water, further affecting the oxidation potential of parent phenol.¹² Phenoxyl radical stability was increased due to hydrogen bonding with the hydrogen bond donors, such as residual water or solvent.³¹ The intramolecular hydrogen bonding in semiquinone radical derived from catechol also contributed to radical stability.³² Hence, in the present work the phenols, phenolate, and phenoxyl radicals

General scheme for substituted phenol oxidation



may also be stabilized by residual water molecules in the ACN, but to a different extent. Because of the bulky *tert*-butyl groups at both *ortho* positions, the hydrogen-bonding interactions with residual solvent may be minimized as in 1-3. But sterically unhindered phenols around hydroxyl group, such as 4 and 5, may give rise to the phenoxyl radicals which are easily complexed with residual water.

The stability of phenoxyl radicals may be associated with the presence of bulky tert-butyl substituents at 2- and 6- positions. Hence, from the chemical structures in Figure 1, compounds that lack these substituents may be forming less stable radicals or short-lived radicals, thus minimizing further reactivity. For example, compounds 4 and 5 lack one or both *tert*-butyl groups which may point to the lower stability of their radicals. The lack of the second *tert*-butyl group in 4 reduces the stability of the 4° radical such that a minimal amount of biphenoquinone is formed by the electrochemical method. The 5° radical may not dimerize due to steric hindrance at 4'-position, in addition to the instability resulting from lack of substitution at the 2'- and 6'-positions. It has been shown that the more stable secondary radicals, with ethyl or butyl substituent at the 4'-position, are more likely to undergo other reactions.³³ If compounds 1-3were to form stable phenoxyl radicals, due to stabilizing effects by tert-butyl substitutents at 2'- and 6'-positions, then they could participate in formation of a dimer. However, the resonance contributors of radicals 1° and 3° are unlikely to undergo dimerization due to steric effects associated with

methyl or tert-butyl group at 4'-position. Compound 1 underwent chemical oxidation to a 1,2-bis(3,5-di-tert-butyl-4hydroxyphenyl)ethane intermediate, followed by oxidation to 3,5,3',5'-tetra-tert-butylstilbene-4,4'-quinone, which appeared red in color.⁴ Under present electrochemical conditions, stilbenequinone from 1 was not made. Steric hindrance at the 4'-position of 3° may not lead to dimerization or other reactions at that site. Notably, the electrochemical oxidation of 3 did not result in formation of UV-vis absorbing species. This was not the case for compound 2. The 2° is stabilized by the tert-butyl groups at 2'- and 6'-positions and lacks a substituent at the 4'-position. The steric and electronic effects then allow for 2° to effectively dimerize into the product, TTBDO. Upon electrochemical oxidation, none of the compounds exhibited blue color that has been ascribed to the formation of stable and long-lived phenoxyl radical. Reportedly, the chemical oxidation of compound 3 produced intense blue color due to the formation of 2,4,6-tri-tert-butylphenoxy radical in solution, which reversibly generated parent phenol in the presence of iodide ion and molecular O2.34 A lack of blue color upon electrochemical oxidation of compounds 1-5 may be due the rapid reactivity of phenoxyl radicals with atmospheric O2, or in subsequent reactions, like dimerization. Because of the irreversibility of CVs performed with these phenols, the presence of phenoxonium cations is less likely.³⁵

All substituted phenols may undergo oxidation reactions as described in Scheme 1, which involves phenol or phenolate and

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subsequent formation of phenoxyl radical and/or cation.³⁶ Based on the experimental data and the literature precedence, the proposed mechanism for the formation of TTBDQ from compound **2** under electrochemical oxidation condition may involve phenoxyl radical formation, as in Scheme 1.

Compound 2 may form a phenoxyl radical, 2°, either via radical cation intermediate, $2^{\bullet+}$, in a one-electron oxidation and proton loss, or via phenolate anion, 2⁻, via one-electron oxidation (Scheme 1). Both species, parent phenol or phenolate anion, may produce phenoxyl radicals which may undergo further dimerization reactions via 4'-site of their respective resonance contributor to produce dimerized product TTBDQ. Both species, the phenolate anion and phenol, were observed in CV of 2, and they both contributed to the formation of TTBDQ, as evidenced by the potential rangedependent measurements. A similar mechanism, involving a phenoxyl radical, was proposed for the chemical formation of TTBDQ from 2 under alkaline conditions in the presence of O₂.^{1,37} This transformation was ascribed to the free-radical mechanism under thermal decomposition of nitrosophenol. Compounds 1 and 2 reportedly also formed stable benzyl radicals and underwent dimerization, upon chemical oxidation, into stilbenequinone and diphenoquinone, respectively.^{5–7} The formation of substituted benzyl radicals from substituted phenols has been previously reported.⁵⁻⁷ It has been shown that phenoxyl radicals, generated from phenolate anions, may dimerize or undergo disproportionation, among other reactions.¹⁰ The ionic mechanism, which would include the condensation reaction, was not the likely route in formation of TTBDQ.1 The electrochemical and spectroscopic data indicated that the number of bulky substitutents and their location play a critical role in reactivity of this class of compounds. Subsequently, the tunability of chemical structure and electronic effects may further expand their functional utility.

4. CONCLUSIONS

The electrochemical and spectroscopic evaluation of *tert*-butylsubstituted phenols revealed that most phenols were not easily oxidized under electrochemical conditions to generate an electrochromic product. Selective electrochemical oxidation of **2** to produce TTBDQ was associated with stability of the phenoxyl radical intermediate and a lack of steric hindrance at the 4'-site. By comparison, the chemical oxidation of all phenols resulted in the significant product formation. The data indicate that the utility of this class of compounds may be extended by carefully tuning the structural parameters and experimental conditions. Hence, a complete understanding of the selectivity of electrochromism may aid in designing new functional molecules.

ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpcb.6b06135.

CVs, SWVs, and UV-vis spectra (PDF)

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Notes

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ABBREVIATIONS

CV, cyclic voltammetry; SWV, square-wave voltammetry; TBAP, tetrabutylammonium perchlorate.

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