Intramolecular Anodic Carbon–Carbon Bond-Forming Reactions of Oxidized Phenol Intermediates Leading to Spirodienones. Structural Effects on Reactivity and Evidence for a Phenoxonium Ion Intermediate

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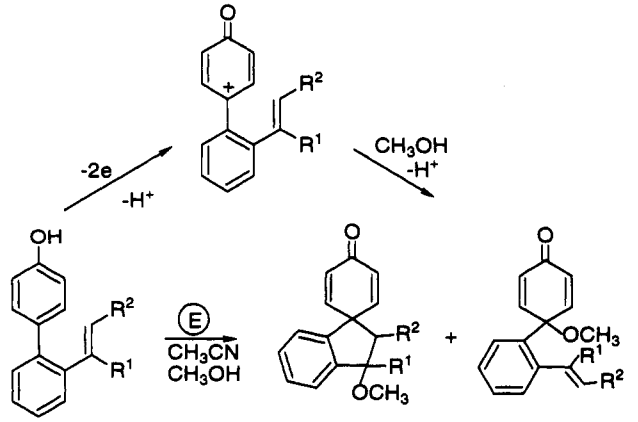
Anodic oxidation of 4-phenylphenol in methanol leads to 4-methoxy-4-phenylcyclohexa-2,5-dienones whereas anodic oxidation of 4-(2-alkenylphenyl)-phenols leads to spirocyclic 2,5-cyclohexadienones in competition with methanol addition to the 4-position. Using 4-phenylphenol and 4-(2-propenylphenyl)phenol as model systems, the optimum conditions for solvent addition versus carbon–carbon bond formation have been studied. The yield of the anodic cyclization reaction shows a dramatic dependence on olefin structure. Whereas 4-(2-propenylphenyl)phenol gives the spirocyclic 2,5-cyclohexadienone in high yield, 4-(2-vinylphenyl)phenol affords the analogous product in only 16% yield. This low yield of intramolecular carbon–carbon bond-forming reactions can be markedly improved if the vinyl substituent is forced closer to the 4-position of the phenol by the buttressing effect of a *o*-methyl group. Coloumetric studies as well as the oxidation chemistry of a (4-hydroxyphenyl)(2-propenylaryl)methane derivative support the involvement of a phenoxonium ion as the intermediate in these carbon–carbon bond-forming reactions. Finally, non-oxidative generation of a phenoxonium ion by reaction of 4-hydroxy-4-(2-propenylphenyl)2,5-cyclohexadieneone with methanesulfonyl chloride/triethylamine leads to spirodienones related to those isolated in the anodic oxidation chemistry. Although a slightly acidic media is critical for obtaining good yields of spirodienones for the propenyl system, anodic oxidation of the trimethylsilyl derivatives of the phenol allows this reaction to be performed in neutral or slightly basic media.

Introduction

Electroreductive methods for carbon–carbon bond formation have been extensively studied.[1] However, when this work was initiated,[3] except for phenolic coupling reactions,[2] much less effort had been focused on anodic carbon–carbon bond-forming reactions.[4] Several years ago the anodic oxidation of 4-(2-alkenylphenyl)phenols was investigated as a model system to explore reaction conditions and structural limitations on the reaction of oxidized phenol intermediates with electrophilic carbon substrates[3,5] (see Scheme I for representative examples). The working hypothesis was that a phenoxonium ion would be generated leading to product(s) arising from carbon–carbon bond formation. Hopefully, the information gained in this work would then be applied to bimolecular anodic carbon–carbon bond forming reactions involving olefinic substrates.[5]

Scheme I. Anodic Oxidations of 4-(2′-Alkenylphenyl)phenols



1a $R^1 = CH_3$; $R^2 = H$	2a (85%)	3a --
1b R^1, $R^2 = -(CH_2)_3-$	2b (70%)	3b --
1c $R^1 = R^2 = H$	2c (16%)	3c (19%)

We reported earlier on the effect of olefinic substituents on the preparative yields of the chemistry summarized in Scheme I.[6] An intriguing aspect of the results was the dramatic effect of a simple methyl group on the yield of the anodic cyclization reaction; whereas **1a** gave **2a** in 85% yield, **1c** afforded **2c** in 16% yield. This paper addresses several points of general interest concerning this chemistry. First, what reactions are competing with the anodic cyclization **1** → **2** and why does alkyl substitution on the double bond have such a dramatic effect on product yield? Second, does the reaction involve a two-electron oxidation

(1) For reviews, see: Rifi, M. R. *Organic Electrochemistry*; Dekker Publishing: New York, 1973; Chapter VI, pp 279–314. Baizer, M. M. *Ibid.* Chapter XIX, pp 679–704.

(2) (a) For a review of phenolic oxidations in general, see: Scott, A. J. *Quart. Rev.* **1965**, *19*, 1. *Oxidative Coupling of Phenols*; Taylor, W. I., Battersby, A. R., Eds.; Dekker: New York, 1967. (b) Yoshida, K. *Electrooxidation in Organic Chemistry*; John Wiley and Sons: New York, 1984; pp 99–156. (c) Torii, S. *Electroorganic Chemistry*; Kodansha Limited; Tokyo (Japan); VCH: Verlagsgesellschaft (Federal Republic of Germany), 1985; pp 97–149.

(3) Morrow, G. W.; Swenton, J. S. *Tetrahedron Lett.* **1987**, *28*, 5445.

(4) For recent examples of and leading references to anodic carbon–carbon bond coupling reactions see: (a) Maki, S.; Asaba, N.; Kosemuar, S.; Yamamura, S. *Tetrahedron Lett.* **1992**, *33*, 4169. (b) Yamamura, S.; Shizuri, Y.; Shigemori, H.; Yoshishige, O.; Mitsuru, O. *Tetrahedron* **1991**, *47*, 635. (c) Moeller, K. D.; Tinao, L. V. *J. Am. Chem. Soc.* **1992**, *114*, 1033.

(5) For extensions of these model studies to bimolecular anodic carbon–carbon bond formation via phenol oxidations see: (a) Wang, S.; Gates, B. D.; Swenton, J. S. *J. Org. Chem.* **1991**, *56*, 1979. (b) Gates, B. D.; Dalidowicz, P.; Tebben, A.; Wang, S.; Swenton, J. S. *Ibid* **1992**, *57*, 1992.

(6) Morrow, G. W.; Chen, Y.; Swenton, J. S. *Tetrahedron* **1991**, *45*, 655.

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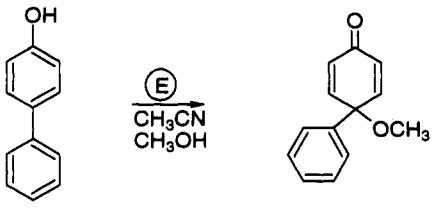
to a phenoxonium ion and what is the chemistry of this ion generated by nonelectrochemical methods? These points and mechanistically informative examples of the reaction are reported herein.

Factors Influencing Anodic Cyclization versus Methanol Addition to the Aromatic Ring. The anodic cyclizations studied previously, **1** → **2**, were conducted in 4:1 acetonitrile/methanol; for compounds such as **1c**, the quinol ether, **3c**, was obtained in addition to **2c**. Methanol is required in the reaction because it not only traps the reactive intermediate leading to the formation of **2** but also reacts with the lithium generated at the cathode. If methanol is not present, the cathode becomes coated with lithium, raising the potential required for the oxidation in addition to serving as a reducing agent for products generated from the oxidation. It would have been preferable to study the effect of variables on the ratio of anodic cyclization versus quinol ether formation, i.e., **2**:**3**, in one system. However, systems which afforded a mixture of **2** and **3** did not give a good overall accounting of material. Thus, we chose to study the effect of reaction variables for two different compounds: **1a** and *p*-phenylphenol, **4**. Both



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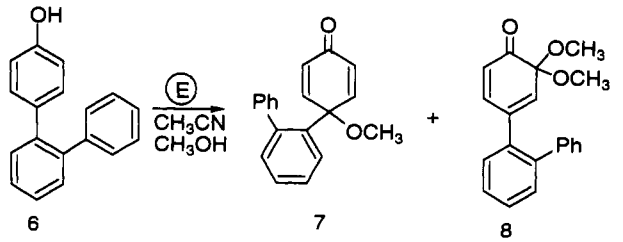
of these substrates gave clean anodic oxidation mixtures which were convenient to analyze by HPLC: **1a** gave the anodic cyclization product **2a**, and **4** produced the quinol ether **5**.[7]

For both **1a** → **2a** and **4** → **5** reactions, a cylindrical platinum anode of area 60 cm^2 was used with 4:1 acetonitrile/methanol as solvent and 1–2% lithium perchlorate as the supporting electrolyte. (Tables I–III in the supplementary material give the details of these studies; only the conclusions are presented here.) The reactions were studied with currents from 0.1 to 1.6 A which corresponded to current densities of 1.7–16 mA/cm^2. While a copper cathode led to decreased yields of product, little difference was noted between a tungsten and platinum cathode. These studies showed that different conditions maximized the yields of spirodienone and quinol ether. The **4** → **5** reaction proceeded very inefficiently at low current densities whereas at a current density of about 5 mA/cm^2 (0.3 A), **5** was formed in 71% yield with a current efficiency of 44%. By contrast, the anodic cyclization **1a** → **2a** gave the best yields (87–91%) and current efficiencies (50–60%) at lower current densities, 1.7 mA/cm^2 (0.1 A).

Interestingly, the **4** → **5** reaction conducted in a single cell never went to completion: 5–10% of starting material always remained in the reaction mixture. This is undoubtedly due to reduction of the quinol ether to *p*-phenylphenol at the cathode; two experiments support this contention. First, the quinol ether **5** under the electrolysis conditions formed *p*-phenylphenol, **4**, although the amount of phenol produced was not equal to the amount of **5** that had disappeared. Furthermore, in a divided cell, where the product is not in contact with the cathode, the **4** → **5** reaction did go to completion. Thus, the failure to detect minor amounts of quinol ethers such as **3a** in anodic cyclization reactions could be due to their instability under the reaction conditions. Finally, addition of 5–30 equiv of acetic acid to the reaction mixture is beneficial to the yield of the **1a** → **2a** reaction but does not have much effect on the yield of **4** → **5** process. These model studies show that low current density optimizes the anodic cyclization **1a** → **2a**, and this has been true for all of the systems we have studied. However, a variation of anodic reaction conditions never led to an improvement on the **2c**:**3c** ratio or the overall accounting of material for **1c** oxidation.

The competition between anodic cyclization and methanol addition at the *ortho* position of the oxidized phenol is a more difficult question to answer. This product could tautomerize to an *o*-methoxyphenol which would undergo further oxidation to give the monoketal of an *o*-benzoquinone. Unless these moieties are appropropriately substituted, they dimerize.[8] The electrochemistry of **6** was studied to investigate the possibility of methanol addition at the *ortho* position of a phenol because the aryl group in **6** would probably not undergo the anodic cyclization reaction. Indeed, the anodic oxidation of **6** afforded a 1:1 mixture of **7** and **8** in nearly quantitative yield. This offers clear evidence that oxidative addition



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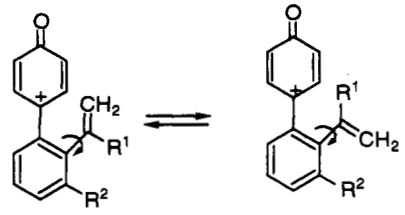
of methanol at the *ortho* position is a viable reaction pathway in these systems. The stability of **8** is probably due to steric inhibition of the dimerization reaction; no corresponding products were isolated from anodic oxidation of **1c**. However, the vinyl substituent in **1c** is less sterically demanding than the bulky phenyl group in **6**, and the corresponding adducts may have dimerized and/or reacted further, accounting for the tars and oils that made up the balance of the reaction products from the **1c** oxidation. In the absence of isolated reaction byproducts, this result serves as indirect experimental evidence that *ortho*-oxidation could be partly responsible for the low yields and current efficiencies observed in the anodic oxidation of **1c**.

Buttressing Effects on the Oxidative Cyclization. An understanding of the dramatic contrast in the yields of anodic cyclization product from **1a** (80–90%) versus **1c** (16%) is of major mechanistic interest. The difference in yield could be attributed to increased nucleophilicity of the methyl-substituted double bond or the methyl stabilization of a cation intermediate formed in the anodic cyclization reaction. A second possibility is that the double bond in **1c** is poorly situated to interact with the short-lived anodic oxidation intermediate. Models suggest that the preferred orientation of the double bond in **1c** is directed from the 4-position of the phenol as shown in

(7) Ronlan, A.; Palmquist, U.; Pettersson, T.; Nillson, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 696.
(8) Andersson, G.; Bertsson, *Acta Chem. Scand., Ser. B* **1975**, *29*, 948. Andersson, G. *Ibid.* **1976**, *30*, 64.

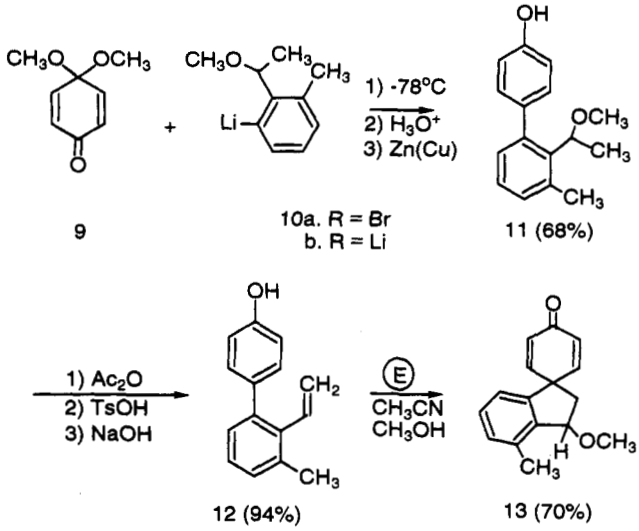
Scheme II. Reactive and Nonreactive Conformations for Anodic Cyclization



1a-1 $R^1 = CH_3$, $R^2 = H$ 1a-2
1c-1 $R^1 = R^2 = H$ 1c-2

1c-2 (Scheme II). However, in **1a** the orientation is directed toward the 4-position of the phenol (Scheme II, **1a-1**).

To establish if a good yield anodic cyclization could be effected in a compound in which the double bond was more suitably situated for cyclization, the electrochemistry of phenol **12** was studied. This compound was prepared from **9** and **10a** by the route shown below; **10a** was available in three steps from 2-amino-6-methylbenzoic acid. Although acid-catalyzed dehydration of phenol **11** led to a low yield of **12**, conversion of the phenol to its acetate followed by acid-catalyzed elimination of methanol and then acetate hydrolysis led to **12** in excellent yield. Interestingly, anodic oxidation of the simple vinyl-substituted system gave **13** in 70% yield. A major factor in

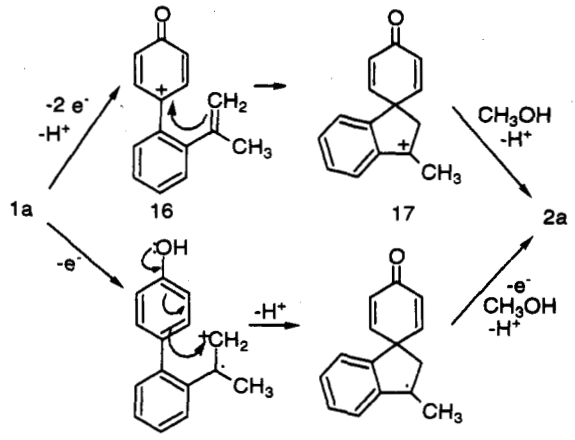


9 10a. R = Br b. R = Li 11 (68%) 12 (94%) 13 (70%)

the increase in yield from 16% (**1c**) to 70% (**12**) is the buttressing effect of the methyl group which forces the vinyl linkage closer to the 4-position of the oxidized phenol. Thus, high yields of anodic cyclization can occur with an unsubstituted vinyl substituent in appropriate systems.

Evidence for the Two-Electron Oxidation and the Nature of the Oxidized Species. This chemistry was conceived as arising from a two-electron oxidation of the phenol to generate an intermediate best pictured as a phenoxonium ion. Coulometry can furnish evidence on the number of electrons transferred under the anodic conditions. First, cyclic voltammetry measurements were made on **1a** and **4** in 4:1 acetonitrile/methanol containing 1% lithium perchlorate, the solvent/electrolyte system used in the preparative reactions. Under these conditions **1a** showed an irreversible wave with $E_{pa/2}$ at 1.23 V relative to Ag/AgCl, a value comparable to that of *p*-phenylphenol, **4** ($E_{pa/2}$ = 1.18 V). The number of electrons involved in the oxidation was determined by controlling the potential

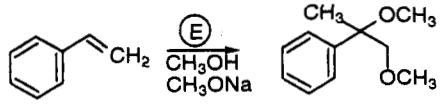
Scheme III. Two Mechanistic Perspectives on the Anodic Cyclization Reaction



1a 16 17 2a 18 19

at a value higher than the oxidation peak potential and conducting electrolysis until the starting material was consumed. The area under the plot of time versus current, *Q*, is directly related to the number of electrons consumed per mole of electroactive substance.[9] The *n* values for **1a** and **4** calculated from the equation $n = Q$ (mmol)(96480) were 2.19 ± 0.3 and 1.94 ± 0.3, respectively. Under these conditions oxidation of **1a** and **4** involves a two-electron transfer from the phenolic compounds.

The anodic cyclization reaction **1a** → **2a** can be viewed in two ways. One of these is the reaction of an olefinic side chain with a phenoxonium intermediate, **1a** → **16** → **17** → **2a**, and the second is nucleophilic attack of a phenol on an oxidized styrene double bond, **1a** → **18** → **19** → **2c**, as illustrated in Scheme III. Precedent exists for both of



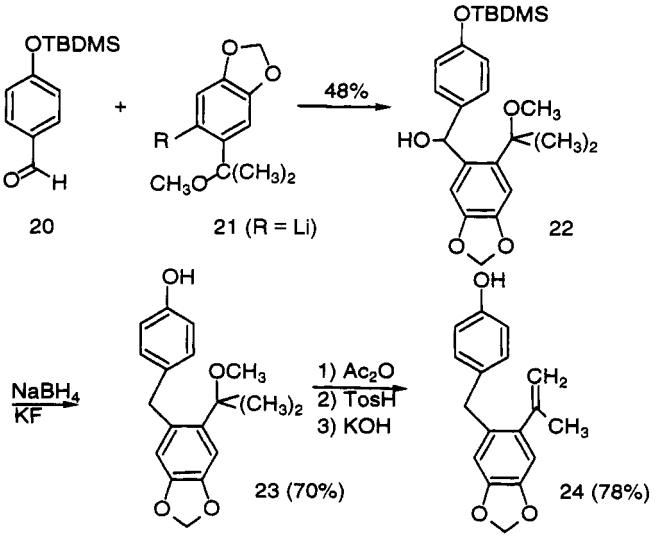
14 15

these processes. The oxidative addition of oxygen nucleophiles to the 4-position of oxidized phenols, i.e., **4** → **5**, serves as a precedent for the first possibility while the anodic addition of methanol to styrenes,[10] **14** → **15**, serves as a precedent for the latter view of the chemistry. Although the phenolic and propenylbenzene rings of **1a** are not planar, the conjugation present complicates making a decision between these two alternatives.

The anodic oxidation of a compound containing both the phenolic and styrene moieties, but separated by a methylene group, would not only explore the generality of the anodic cyclization chemistry but could also give information on the question raised above. The methylenedioxy derivative **24** was prepared as outline below. The desilylation/reduction of **22** → **23** undoubtedly proceeds via desilylation of **22** by fluoride ion followed by elimination of the hydroxide to form the quinone methide which is reduced by sodium borohydride to give **23**. The phenol **24** was used immediately after preparation because it

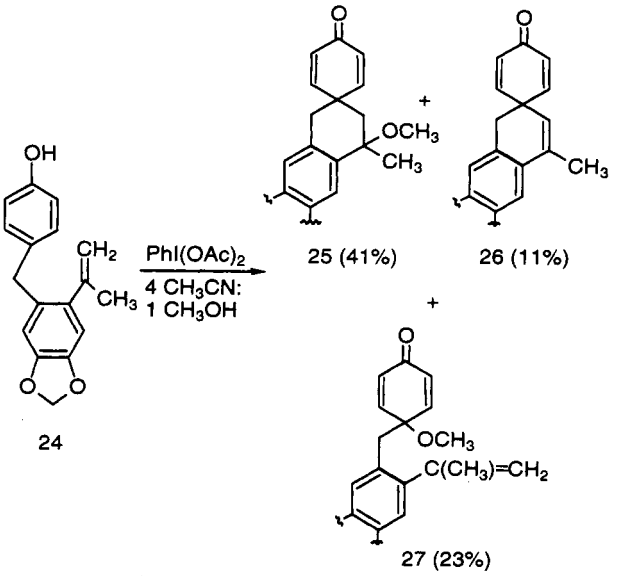
(9) Fry, A. J. *Synthetic Organic Electrochemistry*; Harper & Row Publishers: New York, 1972; pp 104–106.
(10) (a) Inoue, I.; Koyama, K.; Matsuoka, T.; Matsuoka, K.; Tsutsumi, S. *Tetrahedron Lett.* **1963**, 1409. (b) Inoue, T.; Koyama, K.; Matsuoka, T.; Tsutsumi, S. *Bull. Chem. Soc. Jpn.* **1967** *40*, 162. (c) Fichter, F.; Christen, A. *Helv. Chim. Acta* **1925**, 332. (d) O'Connor, J. J.; Pearl, I. A. *J. Electroanal. Soc.* **1964**, *111*, 335.

developed an orange color on exposure to UV or visible light. The cyclic voltammogram of **24** in 4:1 acetonitrile/methanol did not show distinct maxima in the range 1.0–1.6 V. Two inflection points in the oxidation wave corresponded to approximate $E_{pa/2}$'s of 1.28 and 1.35 V. These values closely approximate the identical $E_{pa/2}$'s of 1.33 V for *p*-methylphenol and 1-methyl-2-propenyl-4,5-(methylenedioxy)benzene (**21**, R = CH_3), compounds which mimic the electroactive segments of **24**.



The anodic oxidation of **24** gave a complicated reaction mixture under a variety of both constant current and controlled potential conditions. Except for recovered starting material, no products could be isolated pure from the tarlike product mixture formed in these anodic oxidations. Two factors may contribute to the complex electrochemistry exhibited by **24**. First, even under controlled potential conditions, both the phenolic and styrene segments of **24** will be oxidized. If oxidation of only the phenol moiety leads to a cyclization product, then the reaction mixture would be complicated by products from oxidation of the styrene segment of **24**. Second, a phenoxonium ion intermediate in this system has a reaction pathway not available to phenols such as **1**: loss of a proton to afford a quinone methide. The high reactivity of a quinone methide formed in the reaction could account for the formation of tarry reaction products.

Although the anodic oxidation of **24** resulted in a complex product mixture, different results were obtained using a chemical oxidant. Previously, it was shown that iodobenzene diacetate oxidation served as a complementary reagent for effecting the oxidative cyclization **1a** → **2a**.[5,11-13] Mechanistically, it has been suggested that the first step in this oxidation is the exchange reaction between the phenol and iodobenzene diacetate. If this is the case, then iodobenzene diacetate could selectively oxidize the phenol moiety of **24** in spite of the similar oxidation potentials of the phenol and styrene moieties. Indeed, reaction of **24** with iodobenzene diacetate in 4:1 acetonitrile/methanol gave a mixture of cyclization products **25** (41%) and **26** (11%) in addition to the quinol ether **27** (23%). Acid-catalyzed loss of methanol from **25** formed



26, and this could be the source of **26** in the reaction. This experiment not only reemphasizes the complementary nature of anodic and iodobenzene diacetate oxidation of phenols but also is suggestive that the anodic cyclization reaction **1** → **2** is best viewed as cyclization of an olefinic side chain on a phenoxonium ion intermediate. However, it is not necessarily true that the same intermediate is involved in both the anodic and iodobenzene diacetate oxidation. Unfortunately, we do not have experimental evidence for the complete failure of the electrochemical oxidation of **24**.

Nonoxidative Generation of Phenoxonium Ions. Ionization of a leaving group from an appropriate carbon center is a classic method for generation of a carbonium ion. As final evidence for the intermediacy of a phenoxonium ion in these anodic cyclization reactions, we studied the generation of this proposed carbonium ion intermediate by ionization of an appropriate quinol intermediate. The required quinol intermediate was prepared as outlined below. It was essential that the *tert*-butyldimethylsilyl methyl ketal, **28**,[14] be used in this reaction mixture because attempted acid hydrolysis of the dimethyl ketal analogous to **30** led to phenanthrene formation, a process noted in earlier work.[15] However, using the fluoride deblocking procedure and the *tert*-butyldimethylsilyl methyl protected carbonyl group, the preparation of **31** proceeded as expected.

Not unexpectedly, attempts to effect ionization of the hydroxyl group in **31** under acidic conditions led to the corresponding phenanthrene. It would have been ideal to generate the phenoxonium ion from **31** in methanol so that the product would be **2a**, the same compound formed in the anodic oxidation. However, this would require conversion of the quinol hydroxyl group to a stable derivative which would then function as a good leaving

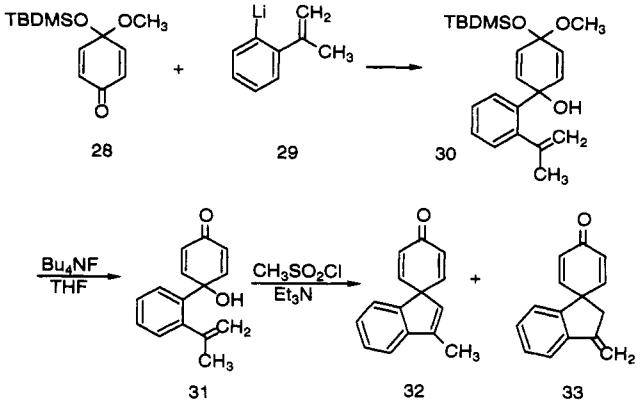
(11) Callinan, A.; Chen, Y.; Morrow, G. W.; Swenton, J. S. *Tetrahedron Lett.* **1990**, *31*, 4551.

(12) For iodobenzene diacetate oxidation of phenols to quinone monoketals, see: (a) Pelter, A.; Elgendy, S. *Tetrahedron Lett.* **1988**, *29*, 677. (b) Tamura, Y.; Yakura, T.; Haruta, J.; Kita, Y. *J. Org. Chem.* **1987**, *52*, 3927. (c) Fleck, A. E.; Hobart, J. A.; Morrow, G. W. *Synth. Commun.* **1992**, *22*, 179.

(13) For phenolic coupling reactions with positive iodine reagents, see: Szantay, C.; Blasko, G.; Barczai-Beke, Pechy, P.; Dornyei, G. *Tetrahedron Lett.* **1980**, *21*, 3509. Rama Krishna, K. V.; Sujatha, K.; Kapil, R. S. *Ibid.* **1990**, *31*, 1351. Kita, Y.; Yakura, T.; Tohma, H.; Kikuchi, K. *Tetrahedron Lett.* **1989**, *30*, 1119.

(14) Stern, A. J.; Swenton, J. S. *J. Org. Chem.* **1987**, *52*, 2763.

(15) Stern, A. J.; Swenton, J. S. *Ibid.* **1988**, *53*, 2465. For the use of this chemistry in phenanthrene synthesis see: Marks, T. M.; Morrow, G. W. *Tetrahedron. Lett.* **1992**, *33*, 2269.



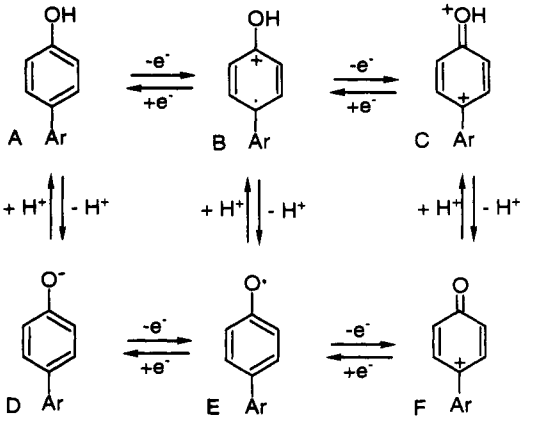
group in methanol; we knew of no stable quinol derivatives of this type. Thus, we employed the procedure used by Thomas[16] to generate an intermediate most reasonably formulated as a phenoxonium ion. Reaction of **31** with methanesulfonyl chloride in the presence of triethylamine gave two products in a ratio of ca. 2:3 (62% yield based on reacted **31**) in addition to starting **31**. These compounds were assigned as **32** and **33** based on spectroscopic and analytical data summarized in the Experimental Section. Furthermore, **32** was obtained in 86% yield by acid-catalyzed elimination of methanol from **2c**. The conversion of **31** to **32** and **33** under these conditions most reasonably involves conversion of the quinol hydroxyl to a mesylate derivative, ionization of the mesylate to afford a phenoxonium ion, followed by intramolecular carbon–carbon bond formation and loss of a proton to give **32** and **33**. *This result supports the intervention of the same type of intermediate in the oxidative carbon–carbon bond forming reactions discussed above* but does not rule out a mechanism involving oxidation of the styrene moiety.

Discussion

The chemistry reported here furnishes evidence on several features of the **1** → **2** reaction. First, optimum conditions for effecting this carbon–carbon bond-forming reaction involve platinum electrodes, low current density, and a slightly acidic medium. The low yield of anodic cyclization product for **1c**, in which cyclization involves an unsubstituted vinyl group, may be partly due to an unfavorable conformation of the vinyl group relative to the short-lived phenoxonium ion intermediate. For a system in which buttressing brings the vinyl group closer to the phenoxonium center, a good yield of cyclization product resulted, **12** → **13**. Circumstantial evidence was presented that in cases in which intramolecular cyclization of the vinyl group to the phenoxonium ion is slow, 1,2- as well as 1,4-oxidative addition of methanol to the phenoxonium ion is a competing reaction, **6** → **7** + **8**.

In the absence of spectroscopic detection of the phenoxonium ion, it is difficult to rigorously establish that it is an intermediate in the cyclization reaction. However, coulometric experiments have established that the reaction involves a two-electron oxidation, and the oxidative chemistry observed for **24** is best interpreted as involving a phenoxonium ion intermediate. Finally, nonoxidative

Scheme IV. Acid–Base Equilibria Involved in Phenol Oxidations



generation of the phenoxonium ion from the quinol **31** and isolation of **32** and **33** indicates that such a phenoxonium ion can react to give products derived from carbon–carbon bond formation. Viewing the chemistry reported here as a carbon–carbon bond-forming reaction between a nucleophilic double bond and a phenoxonium ion is a convenient working mechanism for predicting structural effects on reactivity.

An intriguing aspect of the **1a** → **1c** reaction is the effect of acidic media on yield.[17] Thus, the HPLC yield of **1c** is 70% in the absence of acetic acid and is nearly quantitative in an identical reaction except for the presence of acetic acid (5–20 equiv). It is well-known that the electrochemistry of phenols is dramatically pH dependent, see Scheme IV,[18] and that the radical cation of phenol is a strong acid, $pK_a \sim 2$.[19a,b] The **B** → **E** → **F** process is inefficient in basic media as the **1a** → **2a** reaction did not occur in methanolic hydroxide. However, it is unlikely that the weakly acidic acetic acid ($pK_a \sim 5$) suppresses the ionization of the phenol radical cation ($pK_a \sim 2$), **B** → **E**.

Waters'[19c] studies suggest an interesting explanation for the beneficial effect of acetic acid on the anodic cyclization. He points out that of the two oxidation steps shown in Figure 1 (eqs 1 and 2), only the first is pH dependent. A plot of the oxidation potential of these two steps versus pH is shown in Figure 1. The point at which the two lines cross is termed the equipotential pH. At a pH higher than the equipotential value, the reaction described by eq 1 is more favorable and a high concentration of phenoxy radicals results. Thus, under these conditions, phenoxy radical coupling products would be favored. At a pH below the equipotential value, one-electron oxidation still occurs to give the highly acidic radical cation which ionizes to a phenoxy radical and a proton (eq 1). However, further oxidation of the phenoxy radical to the phenoxonium ion (eq 2) is energetically favorable at this pH. Thus, the concentration of phenoxy radicals remains low, minimizing phenoxy radical coupling reactions and maximizing the formation of the phenox-

(16) Mortlock, S. V.; Seckington, J. K.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2305. For nonoxidative methods for generating phenoxonium ions see: Abramovitch, R. A.; Alvernhe, G.; Bartnik, R.; Dassanayake, N. L.; Inbasekaran, M. N.; Kato, S. *J. Am. Chem. Soc.* **1981**, *103*, 4558. Shudo, K.; Orihara, Y.; Ohta, T.; Okamota, T. J. Am. Chem. Soc., **1981**, *103*, 943 and references cited therein.

(17) The beneficial effect of acid has also been noted in the cycloaddition reactions of oxidized phenols. Shizuri, Y.; Nakamura, K.; Yamamura, S. *J. Chem. Soc., Chem. Commun.* **1985**, 530.

(18) This scheme is adapted from: Reiker, A.; Beisswenger, R.; Regier, K. *Tetrahedron* **1991**, *47*, 645.

(19) (a) Dixon, W. T.; Murphy, D. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 432. (b) Holton, D. M. Murphy, D. *Ibid.* **1979**, *75*, 1637. (c) Waters, W. A. *J. Chem. Chem. Soc. B* **1971**, 2026 and references cited therein.

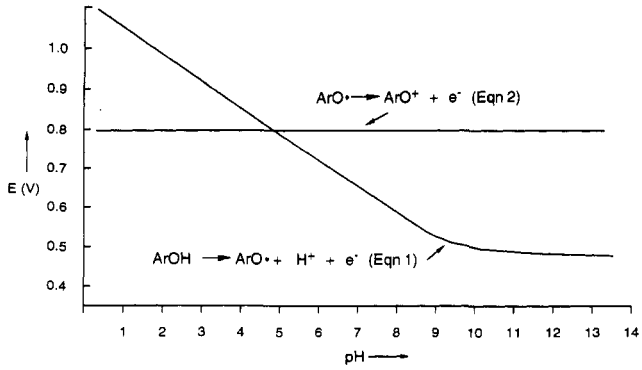
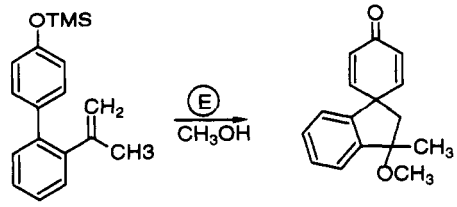


Figure 1. Plot of phenol oxidation potential vs pH for eqs 1 and 2.

onium ion. Interestingly, the equipotential pH for phenol is only slightly acidic.[19c] Although Waters' results are rigorous only for aqueous solutions, addition of acetic acid to the anodic oxidation reaction mixtures studied here could adjust the pH to a value lower than the equipotential value, thus favoring formation of the phenoxonium ion. Although not extensively studied, there is no dependence of the styrene oxidation potential on the pH.

Finally, if this anodic cyclization reaction could be performed under neutral or weakly basic conditions, this chemistry would be applicable to substrates having acid-sensitive functionality. Scheme IV suggests that replacement of the proton of the phenol with a group which does not markedly alter the oxidation potential of the molecule but ionizes less readily would favor the formation of **F** under nonacidic conditions. Miller and co-workers[20] noted that silyl ethers of phenols underwent oxidation in methanol to give quinone monoketals in high yield. Presumably, the oxidation of silyl ethers circumvented the side reactions of the phenoxy radical intermediate, **E**, generated in phenol oxidations. Thus, we briefly examined the anodic oxidation chemistry of the silyl ether derived from **1a**. Anodic oxidation of **34** in methanol gave **2a**



34 2a (73%)

(73%), and the identical reaction in the presence of 2,6-lutidine gave **2a** (60%). Although this chemistry was not optimized, these experiments establish that the anodic cyclization chemistry can be performed under neutral or mildly basic conditions.

In summary, a variety of factors influence the yields of carbon–carbon bond formation in the intramolecular cyclization of unsaturated substrates to the oxidized phenol intermediate. The high yield of products and the mild conditions for the reaction establish that this chemistry could be applied to substrates having base- or acid-sensitive functionalities.

Experimental Section[21]

4-(2-Biphenylyl)phenol, 6. To a solution of 2-bromobiphenyl (2.0 g, 8.6 mmol) in THF (30 mL) at −78 °C was added n-BuLi (5.9 mL of a 1.6 M solution) dropwise over 10 min, and the resulting mixture was stirred for 2 h. Next, a solution 4,4-dimethoxy-2,5-cyclohexadienone[22] (1.32 g, 1.2 mL) in THF (5 mL) was added dropwise, and the resulting mixture was stirred at −78 °C for 1 h and then allowed to warm to rt over 16 h. Extractive workup (saturated NH_4Cl, 5 mL; Et_2O (100 mL)) gave a light brown residue which was dissolved in a mixture of $(CH_3)_2CO$ (75 mL) and 5% HOAc (20 mL) and stored at 0 °C for 48 h. The mixture was then poured into saturated $NaHCO_3$ (50 mL), and the bulk of the $(CH_3)_2CO$ was removed in vacuo. Extractive workup (Et_2O, 2 × 50 mL) gave a yellow solid (2.03 g), mp 185–189 °C. This quinol was then dissolved in THF (9 mL), zinc–copper couple was added (0.885 g), followed by 5% HOAc (9 mL), and the resulting mixture was heated to reflux for 1 h. Extractive workup (Et_2O, 75 mL; 5% HCl, 50 mL) gave a solid, mp 105–110 °C, which was homogeneous by TLC but yellow in color. Slow recrystallization from Et_2O/PE gave white crystals: mp 127–128.5 °C; IR (KBr) 3400-3100 (br, s), 1350 cm^{-1}; ^1H NMR δ 7.38 (s, 5 H), 7.18 (br s, 4 H), 6.8 (AB q, $\Delta\nu$ = 21 Hz, J_{AB} = 8.7 Hz, 4 H), 4.6 (s, 1 H); mass spectrum, exact mass calcd for $C_{18}H_{14}O$ *m/e* 246.1045, obsd 246.1039.

Anodic Oxidation of 6. A solution of **6** (0.25 g, 1 mmol) in 4:1 CH_3CN/CH_3OH (75 mL) containing 1% by wt of $LiClO_4$ was anodically oxidized at 0 °C in a single cell using a platinum sheet anode and copper wire cathode at a constant current of 0.1 A for 65 min (50% current efficiency). Extractive workup with (Et_2O, 100 mL) gave a yellow residue (0.283 g) which by ^1H NMR was a ca. 1:1 mixture of compounds. A small amount of each component was isolated from the difficultly separable mixture as follows. Slow recrystallization from 4:1 PE/Et_2O afforded **7** (13 mg) as a white crystalline solid: mp 128–130 °C; IR (KBr) 1670 cm^{-1}; ^1H NMR (80 MHz) δ 8.0-7.9 (m, 1 H), 7.5–7.1 (str m, 8 H), 6.2 (AB q, $\Delta\nu$ = 47 Hz, J_{AB} = 10 Hz, 4 H), 3.15 (s, 3 H); mass spectrum, exact mass calcd for $C_{19}H_{16}O_2$ *m/e* 276.1150, obsd 276.1170.

Chromatography of the mother liquors from the above crystallization on silica gel (6-in. × 1/2-in. column, $CHCl_3$ as eluant) afforded a single fraction containing pure **8**, 4-(2-biphenylyl)-6,6-dimethoxy-2,4-cyclohexadien-1-one (5 mg) as a yellow oil with the following spectral properties: IR (NaCl plates) 1680 cm^{-1}; ^1H NMR (80 MHz) 7.42 (s, 4 H), 7.35 (s, 5 H), 6.35 (s, 1 H), 6.25 (AB q with *meta* coupling, $\Delta\nu$ = 54 Hz, J_{AB} = 2, 10 Hz, with lower field component partially obscured, 2 H), 3.33 (s, 6 H); mass spectrum, exact mass calcd for $C_{20}H_{18}O_3$ *m/e* 306.1256, obsd 306.1250.

2-Bromo-6-methylbenzoic Acid. Cuprous bromide was prepared by heating a deep purple solution of $CuSO_4 \cdot 5H_2O$ (16.5 g, 66 mmol) and NaBr (13.5 g, 132 mmol) in HBr (66 mL, 48%) and adding Cu powder (8.4 g, 132 mmol) in portions until the purple solution became colorless. This solution was then added in portions to a hot solution (ca. 90 °C) of 2-amino-6-methylbenzoic acid (10 g, 66 mmol) in H_2O (160 mL) and HBr (23 mL, 48%). This was followed by the dropwise addition of a solution

(20) Stewart, R. F.; Miller, L. L. *J. Am. Chem. Soc.* **1980**, *102*, 4999.

(21) **General Procedures.** Melting points were determined in capillaries and are uncorrected. Only strong absorptions are reported for IR spectra unless otherwise noted. ^1H NMR spectra were measured at 200 MHz in $CDCl_3$ unless noted otherwise. All reagents or compounds not explicitly referenced were obtained from commercial sources. Alumina and silica gel (Kieselgel 60 230–400 mesh) were obtained from E. Merck Co. TLC was done using Merck silica gel 60 F_{254} precoated aluminum backed plates, 0.2-mm thickness. All organometallic reactions were done under N_2 or Ar. Visualization was by UV or by spraying with 5% ethanolic phosphomolybdic acid and then heating. THF was purifed by distillation from benzophenone ketyl. Throughout the Experimental Section the following abbreviations are used: petroleum ether, bp 35–60 °C (PE), *p*-toluenesulfonic acid (*p*-TsOH). Extractive workup refers to extraction of the material into the indicated solvent, washing the organic layer with brine solution, drying over Drierite ($CaSO_4$), concentration in vacuo, and drying to constant weight under vacuum (1–2 Torr). The anodic oxidations employed a Kepco Model JQE 0–36-V direct-current power supply. The anode in all cases was a cylindrical, perforated platinum sheet (4.8-cm × 2.5-cm diameter) with an estimated surface area of 60 cm^2. Using a current of 0.05 A corresponded to a current density of 0.84 mA/cm^2. The cathode was either a coil of copper wire (~2.5 cm length) or a platinum wire (approximately 2 cm in length) as specified. All anodic oxidations were performed at 0–10 °C. The current efficiencies are based on the theoretical number of Coulombs required to consume the starting phenol and are probably only accurate to ±15%.

(22) Swenton, J. S.; Bradin, D.; Gates, B. D. *J. Org. Chem.* **1991**, *56*, 6156.

of $NaNO_2$ (13.7 g, 198 mmol) in H_2O (40 mL) to this stirred heated solution over a period of 25 min. The dark-brownish reaction mixture was heated at ca. 90 °C for 1 h and then was heated at reflux for another 0.5 h before it was cooled to rt and stirred for 2 h. The mixture was poured into ice (1000 g), 5% NaOH solution was added until pH 14 was reached, and the resulting dark suspension was filtered through Celite. The yellowish filtrate was acidified with concd HCl to pH 1. Extractive workup (Et_2O, 3 × 300 mL) gave a dark residue which was dissolved in Et_2O (100 mL), charcoal was added, and the resulting solution was heated to reflux. Filtration and concentration gave a solid compound which was recrystallized in Et_2O/PE to afford the bromo acid as a crystalline solid (9.28 g, 65%): mp 109–110.5 °C; IR (KBr) 3089-2555 (br), 1714, 1680, 1450, 1302, 1282, 771 cm^{-1}; ^1H NMR (200 MHz) δ 7.42 (t, J = 5 Hz, 1 H), 7.1–7.2 (m, 2 H), 2.43 (s, 3 H); mass spectrum, exact mass calcd for $C_8H_7BrO_2$ m/e 213.9630, obsd 213.9632.

2-Bromo-6-methylacetophenone. To a solution of the above acid (9.28 g, 43 mmol) in CH_2Cl_2 (200 mL) was added oxalyl chloride (7.6 g, 86 mmol), and the resulting solution was stirred at rt for 24 h. The reaction mixture was then concentrated in vacuo, and the residue was purified via a Kugelrohr distillation at 80–100 °C/0.2 Torr to afford the 2-bromo-6-methylbenzoic acid chloride as a light yellow oil (7.8 g). This freshly prepared acid chloride was dissolved in toluene (108 mL), the resulting solution was cooled to 0 °C, and dimethylaluminum chloride (43 mL, 1 M solution in hexane) was added over a period of 20 min. The resulting solution was stirred at 0 °C for 1 h, stirred for 18 h at rt, and then treated with H_2O (90 mL). Extractive workup (Et_2O, 3 × 90 mL) gave a light yellow oil (7.5 g), which was purified via a Kugelrohr distillation at 60–80 °C/0.2 Torr to afford the ketone as a colorless oil (7.1 g, 99%): IR (neat) 1709, 1447, 1422, 1355, 1254, 1239, 774, 607 cm^{-1}; ^1H NMR (200 MHz) δ 7.3–7.4 (m, 1 H), 7.05–7.15 (m, 2 H), 2.53 (s, 3 H), 2.24 (s, 3 H); mass spectrum, exact mass calcd for C_9H_9BrO m/e 211.9837, obsd 211.9876.

2-Bromo-6-methyl-α-methylbenzyl Alcohol. To a solution of 2-bromo-6-methylacetophenone (5.0 g, 23 mmol) in EtOH/H_2O (9:1, 55.5 mL) at 0 °C was added $NaBH_4$ (3.6 g, 94 mmol) in several portions. The resulting white suspension was stirred at 0 °C for 1 h before it was warmed to rt and stirred for 16 h. After addition of H_2O (60 mL), extractive workup (Et_2O, 4 × 30 mL) gave the alcohol as a white crystalline solid (4.76 g, 94%): mp 72–73.5 °C; IR (KBr) 3317, 1449, 1081, 1067, 775 cm^{-1}; ^1H NMR (200 MHz) δ 7.35 (dd, J = 1, 8 Hz, 1 H), 7.10 (dd, J = 1, 7 Hz, 1 H), 6.95 (pseudo t, 1 H), 5.47 (q, J = 6.8 Hz, 1 H), 2.48 (s, 3 H), 2.36 (s, 1 H), 1.55 (d, J = 6.8 Hz, 3 H); mass spectrum, exact mass calcd for $C_9H_{11}OBr$ m/e 213.9988, obsd 213.9993.

Methyl Ether of 2-Bromo-6-methyl-α-methylbenzyl Alcohol, 10a. To a suspension of NaH (1.58 g, 40 mmol, 60% dispersion in mineral oil) in THF (30 mL) was added the above alcohol (4.26 g, 20 mmol) in THF (20 mL). The resulting solution was heated at reflux for 4 h and cooled to rt, CH_3I (3.4 g, 26 mmol) was added, and the resulting mixture was stirred overnight. Addition of H_2O (20 mL) and extractive workup (Et_2O, 2 × 40 mL) gave the ether as a light yellow oil (4.5 g), which was further purified via a Kugelrohr distillation at 60–90 °C/0.2 Torr to afford the pure ether (4.21 g, 92%): IR (neat) 2978, 2930, 1449, 1115, 771, cm^{-1}; ^1H NMR (200 MHz) δ 7.42-6.95 (m, 3 H), 5.11 (q, J = 6.8 Hz, 1 H), 3.21 (s, 3 H), 2.49 (s, 3 H), 1.49 (d, J = 6.8 Hz, 3 H); mass spectrum, exact mass calcd for $C_{10}H_{13}BrO$ m/e 230.0129, obsd 230.0104.

2′-(1-Methoxyethyl)-3′-methyl-4-biphenylol, 11. To a stirred solution of **10a** (2.0 g, 8.7 mmol) in THF (30 mL) at −78 °C was added a solution of n-BuLi (4.4 mL, 2.4 M in hexane) over a period of 10 min. The resulting yellow solution was stirred at −78 °C for 3 h, 4,4-dimethoxy-2,5-cyclohexadienone[22] (1.6 g, 10 mmol) in THF (5 mL) was added dropwise, and the reaction mixture was stirred at −78 °C for 1 h. Addition of H_2O (20 mL) and extractive workup (Et_2O, 3 × 40 mL) afforded a light yellow oil (3.2 g). Purification by chromatography (1 × 10 in. diameter column, flash silica gel, 20–50% Et_2O/PE as eluants) gave the quinol ketone (1.7 g, 75%): mp 143–144 °C; IR (KBr) 3448, 1658, 867 cm^{-1}; ^1H NMR (200 MHz) δ 7.26–6.93 (m, 5 H), 6.25 (str d, J ~ 10 Hz, 1 H), 6.05 (str d, J = 10 Hz, 1 H), 4.97 (q, J = 6.6 Hz, 1 H), 3.45 (s, 3 H), 2.41 (s, 3 H), 1.69 (d, J = 6.6 Hz, 3 H); mass spectrum, exact mass calcd for $C_{16}H_{18}O_3$ m/e 258.1255, obsd 258.1241.

To a suspension of Zn/Cu couple (75 mg, 0.59 mmol) in THF (10 mL) was added the above product (100 mg, 0.39 mmol) in THF (10 mL) followed by 5% HOAc (5 mL). The resulting suspension was heated at reflux for 1 h. After filtration and extractive workup (EtOAc, 3 × 10 mL) there was obtained a white solid, which was chromatographed (0.2- × 20-in. diameter column, silica gel, 10–20% Et_2O/PE as eluants) to give **11** (86 mg, 91%) as a white crystalline solid: mp 162–163 °C; IR (KBr) 3261, 1513, 1460, 1268, 1214, 1087 cm^{-1}; ^1H NMR (200 MHz) δ 7.13 (d, J = 5.2 Hz, 2 H), 7.04 (d, J = 8.5 Hz, 2 H), 6.95 (t, J = 5.25 Hz, 1 H), 6.82 (d, J = 8.5 Hz, 2 H), 4.52 (q, J = 6.7 Hz, 1 H), 3.05 (s, 3 H), 2.53 (s, 3 H), 1.43 (d, J = 6.7 Hz, 3 H); mass spectrum, exact mass calcd for $C_{16}H_{18}O_2$ m/e 242.1307, obsd 242.1326.

3′-Methyl-2′-vinyl-4-biphenylol, 12. To **11** (260 mg, 1.07 mmol) and DMAP (10 mg, 0.0819 mmol, 7.65 mol %) in CH_2Cl_2 (20 mL) was added acetic anhydride (218 mg, 2.13 mmol), and the solution was stirred at rt for 2 h. Extractive workup gave the acetate as a white crystalline solid (286 mg, 99%): mp 103–104 °C; IR (KBr) 1771, 1212 cm^{-1}; ^1H NMR (200 MHz) δ 7.24–6.95 (m, 7 H), 4.59 (q, J = 6.8 Hz, 1 H), 3.05 (s, 3 H), 2.53 (s, 3 H), 2.32 (s, 3 H), 1.42 (d, J = 6.8 Hz, 3 H); mass spectrum, exact mass calcd for $C_{18}H_{20}O_2$ m/e 284.1407, obsd 284.1412.

The above acetate (0.314 g, 1.17 mmol), benzene (50 mL), and p-TsOH (30 mg) were heated to reflux for 6 h with the condenser packed with 4-Å molecular sieves. After addition of saturated $NaHCO_3$ (20 mL), extractive workup (EtOAc, 3 × 30 mL) gave the unsaturated acetate as a clear oil (0.283 g), which was used directly in the next step. This material was dissolved in 1% KOH/MeOH (20 mL), and TLC analysis indicated nearly immediate acetate hydrolysis. After addition of saturated NH_4Cl (35 mL) extractive workup (EtOAc, 3 × 15 mL) gave a clear oil, which was chromatographed (0.5- × 16-in. diameter silica gel column, 5–8% Et_2O/PE as eluants) to afford **12** as a white crystalline solid (233 mg overall yield for the two steps: 94%): mp 73.5–74.0 °C; IR (KBr) 3166 (br), 1512, 1217 cm^{-1}; ^1H NMR (200 MHz) δ 7.24–7.06 (m, 5 H), 6.71 (d, J = 8.6 Hz, 2 H), 6.54 (dd, J = 11.6, 18 Hz, 1 H), 5.32 (dd, J = 1.8, 11.6 Hz, 1 H), 5.08 (dd, J = 1.8, 18.0 Hz, 1 H), 2.39 (s, 3 H); mass spectrum, exact mass calcd for $C_{15}H_{14}O$ m/e 210.1039, obsd 210.1045.

Anodic Oxidation of 12. Oxidation of **12** (90 mg, 0.43 mmol) in 1:4 CH_3OH/CH_3CN (100 mL) at 0 °C with added HOAc (0.28 g, 4.3 mmol) was conducted at a constant current of 0.05 A for 0.5 h. Addition of H_2O (20 mL) and extractive workup (EtOAc, 3 × 20 mL) gave a light yellow crystalline solid (110 mg), which was chromatographed (16- × 0.2-in. diameter column, 10–20% Et_2O/PE as eluants) to afford **13**, 3′-methoxy-4-methylspiro[2,5-cyclohexadiene-1,1′-indan]-4-one, as a white crystalline solid (72 mg, 70%): mp 87.0–87.2 °C; IR (KBr) 1664, 1087 cm^{-1}; ^1H NMR (200 MHz) δ 7.24–7.03 (m, 3 H), 6.80–6.71 (m, 2 H), 6.36 (dd, J = 1.9, 10.0 Hz, 1 H), 6.15 (dd, J = 1.9, 10.0 Hz, 1 H), 4.97 (t, J = 3.9 Hz, 1 H), 3.47 (s, 3 H), 2.41 (s, 3 H), 2.40 (d, J = 3.9 Hz, 2 H).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Obsd: C, 79.95; H, 6.56.

4-(*tert*-Butyldimethylsiloxy)benzaldehyde, 20. To a solution of imidazole (3.2 g, 47.4 mmol) and 4-hydroxybenzaldehyde (4.8 g, 39.3 mmol) in THF (100 mL) was added TBDMS chloride (6.5 g, 43.4 mmol), resulting in the formation of a white precipitate. The suspension was stirred overnight and vacuum filtered and the filtrate was concentrated in vacuo. Extractive workup with CH_2Cl_2 (2 × 50 mL) gave a mixture of product and starting phenol. This material was dissolved in THF (50 mL) and reacted further [imidazole (0.5 g, 7.3 mmol) TBDMS chloride (1 g, 6.6 mmol) for 48 h]. Workup as above gave a yellow oil (7.56 g, 81%) which after Kugelrohr distillation (110 °C, 0.8 mmHg) gave a pure water-white liquid (6.95 g, 75%): IR (NaCl) 1695, 1600, 1290–1240 (br), 895, 830, 780, 540 cm^{-1}; ^1H NMR δ 9.9 (s, 1 H), 7.8 (d, J = 8 Hz, 2 H), 6.9 (d, J = 8 Hz, 2 H), 1.0 (s, 9 H), 0.25 (s, 6 H); exact mass calcd for $C_{13}H_{20}O_2Si$ m/e 236.1233, obsd 236.1218.

6-Bromopiperonylic Acid. To the vigorously stirred suspension of 6-bromopiperonal (40.0 g) in t-BuOH (400 mL) and H_2O (1000 mL) at 83 °C was slowly added $KMnO_4$ (38.5 g) in H_2O (500 mL) over 45 min. The brown suspension was stirred

overnight at 83 °C, and then KOH (10% aq, 200 mL) was added, raising the pH to 10–11. The brown suspension was then filtered hot, and the cooled filtrate was extracted with Et_2O (2 × 400 mL). The aqueous layer was then acidified with concd HCl (80 mL) to give a white chalky solid (28.38 g, 66%, mp 199–201 °C (lit.[23] mp 201–202 °C)).

5-(Methoxycarbonyl)-6-bromo-1,3-benzodioxole. A mixture of 6-bromopiperonylic acid (12.0 g, 49.2 mmol) in CH_3OH (450 mL) containing trimethylorthoformate (26 g, 246 mmol) and H_2SO_4 (3 mL) was heated at reflux for 3 days. Solid $NaHCO_3$ and H_2O were added to neutralize the acid, and the reaction mixture was concentrated in vacuo to give a light tan solid. The solid was washed with water to give white crystals (12.1 g, 95%): mp 84–85 °C (lit.[24] mp 87–88 °C); IR (KBr) 1725, 1490, 1240 cm^{-1}; ^1H NMR δ 7.33 (s, 1 H), 7.09 (s, 1 H), 6.05 (s, 2 H), 3.89 (s, 3 H).

5-(1-Hydroxy-1-methylethyl)-6-bromo-1,3-benzodioxole. To a solution of 4-(methoxycarbonyl)-6-bromo-1,3-benzodioxole (6.0 g, 23.3 mmol) in dry Et_2O (200 mL) at 9 °C was added dropwise CH_3MgI (2.9 M, 24.0 mL, 69.6 mmol). The cloudy solution was stirred overnight and slowly poured into saturated aqueous NH_4Cl (100 mL) with the evolution of gas and the formation of a pale yellow solid. Extractive workup (Et_2O, 3 × 75 mL) gave a light yellow solid (5.58 g, 93%) which was used for the next step without further purification. An analytical sample was obtained by recrystallization from PE to afford a white solid (4.83 g, 80%): mp 58–63 °C: IR (KBr) 3500–3150 (br, s), 1480, 1240, 1038 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (s, 1 H), 7.03 (s, 1 H), 5.97 (s, 2 H), 2.70 (s, 1 H), 1.71 (s, 6 H); mass spectrum, exact mass calcd for $C_{10}H_{11}O_3Br$ *m/e* 257.9888, obsd 257.9891.

4-Bromo-5-(2-methoxy-2-propyl)-1,3-benzodioxole, 21 (R = Br). Sodium hydride (6.0 g, 248 mmol) was added slowly to a solution of 5-(1-hydroxy-1-methylethyl)-6-bromo-1,3-benzodioxole (16.0 g, 62.0 mmol) in THF (200 mL) at rt. The mixture was stirred for 5.0 h, CH_3I (17 mL, 38.0 g, 260 mml) was added to the brown suspension, and the mixture was stirred overnight. Extractive workup (NH_4Cl, 300 mL) followed by Et_2O (2 × 300 mL) and Kugelrohr distillation (0.5 mmHg, 120 °C) gave **21** (R = Br) as a clear, pale yellow oil (15.49 g, 92%): IR (NaCl) 1480, 1230, 1035 cm^{-1}; ^1H NMR δ 7.07 (s, 1 H), 6.95 (s, 1 H), 5.98 (s, 2 H), 3.10 (s, 3 H), 1.64 (s, 6 H); mass spectrum, exact mass calcd for $C_{11}H_{13}O_3Br$ *m/e* 272.0044, obsd 272.0031.

4′-(*tert*-Butyldimethylsiloxy)-2-(1-methoxy-1-methylethyl)-4,5-(methylenedioxy)benzhydrol, 22. A THF (80 mL) solution of **21** (3.2 g, 11.8 mmol) was cooled to −78 °C, *n*-BuLi (5.12 mL, 2.3 M, 11.8 mmol) was added dropwise, and the solution was stirred for 1.75 h. Then, 4-(tert-butyldimethylsiloxy)-benzaldehyde dissolved in THF (80 mL) was added dropwise to the solution at −78 °C, and the reaction mixture was stirred overnight. Extractive workup (5 × 50 mL Et_2O) of the brown solution, followed by chromatography (6-in. × 2-in. diameter column, silica gel, gradient eluted with 5–30% E/PE) afforded **22** as a yellow solid (2.39 g, 48%) which could be recrystallized from Et_2O/PE: mp 119–120 °C; IR (KBr) 3450, 1510, 1490, 1250, 1060, 1030, 910 cm^{-1}; ^1H NMR δ 7.21 (d, J = 8.6 Hz, 2 H), 6.85–6.72 (m, 4 H), 5.93 (s, 2 H), 3.05 (s, 3 H), 2.48 (d, J = 4.1 Hz, 1 H), 1.66 (s, 3 H), 1.58 (s, 3 H), 0.97 (s, 9 H), 0.18 (s, 6 H); exact mass calcd for $C_{24}H_{34}O_5Si$ *m/e* 430.2176, obsd 430.2162.

4′-Hydroxy-2-(1-methoxy-1-methylethyl)-4,5-(methylenedioxy)diphenylmethane, 23. A mixture of **22** (4.0 g, 9.6 mmol), $NaBH_4$ (1.08 g, 28.8 mmol), KF (0.56 g, 9.6 mmol), and 18-crown-6 (2.72 g, 9.6 mmol) was dissolved in freshly distilled CH_3CN (160 mL) and stirred for 5 days at reflux. The suspension was concentrated in vacuo, and the resulting red oil was chromatographed on flash silica gel (6-in. × 2-in. diameter, gradient eluted with 20–40% Et_2O/PE) to give **23** as a white solid (2.07 g, 70%). Recrystallization from MeOH gave a white solid: mp 143–145 °C; IR (KBr) 3310 (br, s), 1500, 1035 cm^{-1}; ^1H NMR δ 6.98 (d, J = 8 Hz, 2 H), 6.84 (s, 1 H), 6.74 (d, J = 8 Hz, 2 H), 6.53 (s, 1 H), 5.91 (s, 2 H), 4.89 (s, 1 H), 4.28 (s, 2 H), 3.04 (s, 3 H), 1.58 (s, 6 H); exact mass calcd for $C_{18}H_{20}O_4$ *m/e* 300.1362, obsd 300.1364.

(23) Bottcher, K. *Chem. Ber.* **1909**, *42*, 265.
(24) Oertly, M.; Pictet, A. *Chem. Ber.* **1910**, *43*, 1339.

4′-Hydroxy-2-isopropenyl-4,5-(methylenedioxy)diphenylmethane, 24. Acetic anhydride (1.28 g, 12.5 mmol), DMAP (77 mg, 0.63 mmol), and **23** (1.92 g, 6.26 mmol) were dissolved in CH_2Cl_2 (100 mL). After 10 min, extractive workup using saturated aqueous $NaHCO_3$ (100 mL) and CH_2Cl_2 (3 × 50 mL) gave the acetate as a brown oil which slowly solidified (2.14 g, 100%). Although the crude material was judged pure enough for the next step, a portion was purified by chromatography (8-in. × 0.5-in. diameter column, silica gel, gradient eluted with 2% Et_2O/PE) to give the pure acetate: mp 85–86 °C; IR (KBr) 1765, 1500, 1480, 1245, 1190, 1170 cm^{-1}; ^1H NMR δ 7.05 (AB q, J = 8 Hz, $\Delta\nu$ = 26 Hz, 4 H), 6.84 (s, 1 H), 6.54 (s, 2 H), 4.37 (s, 2 H), 3.02 (s, 3 H), 2.29 (s, 3 H), 1.57 (s, 6 H); exact mass calcd for $C_{20}H_{22}O_5$ *m/e* 342.1468, obsd 342.1433.

The acetate from above (320 mg, 0.96 mmol) was stirred for 15 min in CH_2Cl_2 (24 mL) containing *p*-toluenesulfonic acid (40 mg, 0.20 mmol, dehydrated at 100 °C under vacuum). The solution changed from yellow to orange-red, and after 15 min the reaction was quenched by adding saturated $NaHCO_3$ (aqueous 25 mL). Extractive workup with CH_2Cl_2 (3 × 24 mL) gave a crude red oil (0.27 g, 94%) which could be used for the next step without purification. An analytical sample was obtained by flash chromatography (7-in. × 0.5-in. diameter, silica gel, gradient eluted with 5–10% Et_2/PE) as a clear yellow oil: IR (neat, NaCl) 1762, 1503, 1484, 1221 cm^{-1}; ^1H NMR δ 7.04 (AB q, J = 8 Hz, $\Delta\nu$ = 26 Hz, 4 H), 6.63 (s, 1 H), 6.57 (s, 1 H), 5.91 (s, 2 H), 5.15 (s, 1 H), 4.80 (s, 1 H), 3.92 (s, 2 H), 2.28 (s, 3 H), 1.94 (s, 3 H); mass spectrum, exact mass calcd for $C_{19}H_{18}O_4$ *m/e* 310.1205, obsd 310.1204.

The unsaturated acetate from above (280 mg, 0.90 mmol) was dissolved in THF (5 mL), and KOH (200 mg, 2.7 mmol) and H_2O (2 drops) were added, resulting in a dark red reaction mixture. After 4 h of stirring at rt, the reaction was quenched with aqueous NH_4Cl, lowering the pH to 7. Extractive workup (CH_2Cl_2, 4 × 20 mL) afforded a crude red oil which was chromatographed (silica gel, 7-in. × 0.5-in diameter, gradient eluted with 10–20% Et_2O/PE) to give **24** as a clear, water-white oil (202 mg, 84%): IR (neat, NaCl) 3396, 1511, 1502, 1483, 1040 cm^{-1}; ^1H NMR δ 6.97 (d, J = 12 Hz, 2 H), 6.73 (d, J = 12 Hz, 2 H), 6.63 (s, 1 H), 6.57 (s, 1 H), 5.90 (s, 2 H), 5.15 (s, 1 H (fine splitting)), 4.81 (s, 1 H (fine splitting)), 3.86 (s, 2 H), 1.94 (s, 3 H (fine splitting)); mass spectrum, exact mass calcd for $C_{17}H_{16}O_3$ *m/e* 268.1100, obsd 268.1092.

Oxidation of 24 with Iodobenzene Diacetate. To a stirred solution of **24** (0.200 g, 0.746 mmol) in CH_3CN (8 mL) and CH_3OH (2 mL) at rt was added $PhI(OAc)_2$ (264 mg, 0.82 mmol). After 15 min, the solution was concentrated in vacuo, and the resulting amber oil was chromatographed (8-in. × 0.5-in. diameter column, silica gel, gradient eluted with 10–20% Et_2O/PE) to give **27** as a clear, light yellow oil (51 mg, 23%), **25** as light yellow crystals (90 mg, 41%), and **26** as white crystals (24 mg, 11%). Also collected from the final wash with CH_3OH was a brown tar (41 mg, 18%). Spectral data of 4-(6-isopropenylpiperonyl-4-methoxy-2,5-cyclohexadien-1-one, **27**, showed: IR (neat, NaCl) 1671, 1504, 1486, 1225, 1080, 1041 cm^{-1}; ^1H NMR δ 6.86 (s, 1 H), 6.70 (d, J = 10 Hz, 2 H), 6.56 (s, 1 H), 6.27 (d, J = 10 Hz, 2 H), 5.92 (s, 2 H), 5.18 (s, 1 H), 4.74 (s, 1 H), 3.19 (s, 3 H), 3.05 (s, 2 H), 1.93 (s, 3 H); mass spectrum, exact mass calcd for $C_{18}H_{18}O_4$ *m/e* 298.1205, obsd 298.1205.

7,8-Dihydro-8′-methoxy-8′-methylspiro[2,5-cyclohexadiene-1,6′(5′*H*)-naphtho[2,3-d]-1,3-dioxol]-4-one, 25, was recrystallized from MeOH to give pure white crystals: mp 139–140 °C; IR (KBr) 1667, 1499, 1483, 1244, 1036, 855 cm^{-1}; ^1H NMR ($(CD_3)_2CO$) δ 7.19 (dd, J = 1, 10 Hz, 1 H), 7.03 (s, 1 H), 6.91 (dd, J = 1, 10 Hz, 1 H), 6.67 (s, 1 H), 6.19–6.09 (m, 2 H), 6.01 (s, 2 H), 3.04 (s, 3 H), 2.93–2.84 (m, 2 H), 2.28 (d, J = 16 Hz, 1 H), 1.83 (d, J = 16 Hz, 1 H), 1.54 (s, 3 H); mass spectrum exact mass calcd for $C_{18}H_{18}O_4$ *m/e* 298.1205, obsd 298.1205. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.26; H, 6.30.

8′-Methylspiro[2,5-cyclohexadiene-1,6′(5′H)-naphtho[2,3-*d*]-1,3-dioxol]-4-one, 26, was recrystallized from CH_3OH to give pure white crystals: mp 159–160 °C; IR (KBr) 1670, 1486, 1248, 1041, 855 cm^{-1}; ^1H NMR δ 6.86 (d, J = 13 Hz, 2 H), 6.84 (s, 1 H), 6.65 (s, 1 H), 6.21 (d, J = 12 Hz, 2 H), 5.96 (s, 2 H), 5.17 (s, 1 H), 2.85 (s, 2 H), 2.05 (s, 3 H); mass spectrum, exact mass calcd for

$C_{17}H_{14}O_3$ *m/e* 266.0943, obsd 266.0942. Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.45; H, 5.57.

5-(2-Methoxy-2-propyl)-6-methyl-1,3-benzodioxole. A solution of 5-(1-methoxy-1-methylethyl)-6-bromo-1,3-benzodioxole (0.8 g, 2.9 mmol) in THF (25 mL) was cooled to −78 °C, and *n*-BuLi (1.28 mL, 2.5 M, 3.2 mmol) was added dropwise. The solution was stirred for 1 h, and then iodomethane (0.28 mL, 0.60 g, 4.44 mmol, 1.5 equiv) was added and stirring continued for 6 h at −78 °C. Extractive workup (4 × 15 mL Et_2O) afforded a clear, pale-yellow oil (0.53 g, 88%): IR (neat, NaCl) 2977, 1504, 1487, 1242, 1073, 1041 cm^{-1}; ^1H NMR δ 6.79 (s, 1 H), 6.64 (s, 1 H), 5.91 (s, 2 H), 3.03 (s, 3 H), 2.45 (s, 3 H), 1.55 (s, 6 H); mass spectrum, exact mass calcd for $C_{12}H_{16}O_3$ *m/e* 208.1099, obsd 208.1096.

Preparation of 1-Methyl-2-propenyl-4,5-(methylenedioxy)benzene. To a solution of 5-(1-methoxy-1-methylethyl)-6-methyl-1,3-benzodioxole (148 mg, 0.74 mmol) in dry CH_2Cl_2 was added dry *p*-toluenesulfonic acid (29 mg, 0.15 mmol). After 30 min, saturated $NaHCO_3$ (aqueous, 20 mL) was added. Extractive workup with CH_2Cl_2 (3 × 18 mL) gave a crude brown oil (80 mg, 61%) which was chromatographed (7-in. × 0.5-in. diameter column, silica gel, 5% Et_2O/95% PE) to give the title compound as a clear, water-white oil (41 mg, 32%); IR (neat, NaCl) 1487, 1238, 1222, 1042, cm^{-1}; ^1H NMR δ 6.66 (s, 1 H, overlapping), 6.63 (s, 1 H, overlapping), 5.91 (s, 2 H), 5.17 (s, 1 H), 4.82 (s, 1 H), 2.23 (s, 3 H), 2.00 (s, 3 H); mass spectrum, exact mass calcd for $C_{11}H_{12}O_2$ *m/e* 176.0837, obsd 176.0838.

2-Bromo-α-methylstyrene. To a solution of 2-(1-hydroxy-1-methylethyl)bromobenzene (8.2 g, 38 mmol) in $CHCl_3$ (50 mL) was added thionyl chloride (4.1 mL), and the resulting mixture was heated to reflux for 2 h and then poured into cold water (100 mL). Workup gave a dark brown oil (7.6 g) which was chromatographed (silica gel, 6-in. × 2-in. column, hexane as eluant) to yield the title compound (4.1 g, 55%) as a water-white oil: IR (NaCl plates) 1475, 1440, 1030, 903, 760, 730 cm^{-1}; ^1H NMR (80 MHz) δ 7.7–7.0 (str m, 4 H), 5.2 (m, 1 H), 4.9 (m, 1 H), 2.1 (m, 3 H); mass spectrum, exact mass calcd for C_9H_9Br *m/e* 197.9867, obsd 197.9864.

Preparation of 4-Hydroxy-4-(2′-isopropenylphenyl)-2,5-cyclohexadienone, 31. To a solution of 2-bromo-α-methylstyrene (2.2 g, 11.2 mmol) in THF (30 mL) at −78 °C was added dropwise *n*-BuLi (6.07 mL of a 1.94 M solution in THF) over 10 min. After the solution was stirred for 2 h, a solution of 4-methoxy-4-(*tert*-butyldimethylsiloxy)-2,5-cyclohexadienone[14] (2.87 g, 0.0113 mol) in THF (10 mL) was added dropwise to the yellow solution. The resulting mixture was stirred for 1 h at −78 °C and then allowed to warm to rt over a period of 2 h. The reaction was quenched with saturated NH_4Cl (50 mL) and was diluted with Et_2O (150 mL). Extractive workup gave a yellow oil which was dissolved in THF (150 mL) and treated with $(n\text{-Bu})_4NF$ (0.0168 mol, 16.8 mL of a 1 M solution in THF) at 0 °C. After 30 min the reaction mixture was poured into cold brine (150 mL). Extractive workup (Et_2O, 150 mL) gave a deep red oil. The crude product was purified by chromatography (5-in. × 1-in. diameter column, silica gel, hexane, then 15% EtOAc/hexane as eluant) to afford 4-hydroxy-4-(2′-isopropenylphenyl)-2,5-cyclohexadienone (24%, 608 mg): mp 124–125 °C; IR (KBr) 3427 (br), 1659, 1620 cm^{-1}; ^1H NMR δ 7.55–7.48 (m, 1 H), 7.35–7.25 (m, 2 H), 7.12–7.04 (m, 1 H), 6.58 (AB q, Δν = 156 Hz, *J* = 9.7 Hz, 4 H), 5.15 (s, 1 H), 4.87 (s, 1 H), 3.06 (s, 1 H), 2.08 (s, 3 H); HRMS, exact mass calcd for $C_{15}H_{14}O_2$ *m/e* 226.0994, obsd 226.0998.

Nonoxidative Preparation of 32 and 33. Methanesulfonyl chloride (0.085 mL, 1.1 mmol) was added to a 0 °C solution of **31** (207 mg, 0.916 mmol) in dry CH_2Cl_2 (2 mL) containing triethylamine (0.303 mL, 2.18 mmol). The mixture was stirred for 2 h at 0 °C and then at rt for 15 h before being quenched with H_2O (5 mL). Extractive workup (CH_2Cl_2, 2 × 3 mL) gave a yellow oil (228 mg) which was triturated with Et_2O/hexane to remove most of the unreacted starting material as a solid. The remaining oil was chromatographed (silica gel, 0.25-in. × 5-in. column, 4:1 EtOAc/hexane as eluant) to yield a difficultly separable mixture of the exocyclic isomer **33** (38%) and endocyclic double bond isomer **32** (62%) (44 mg, 62% yield based on recovered starting material). The exocyclic isomer was converted to the endocyclic isomer **32** in acidic media, and the ^1H NMR spectrum of this compound was identical to the material prepared below. The exocyclic isomer was difficult to separate from **32**, and the separation was further compounded by the facile **32** → **33** isomerization. However, a fraction enriched in **33** was obtained by reversed-phase HPLC (3:1 H_2O/MeOH as eluant on a Microsorb RP octadecyldimethylsilyl C_{18} column, 10 × 250 mm), and this material showed: ^1H NMR δ 7.58 (d, *J* = 6.7 Hz, 1 H), 7.37-7.21 (m, 2 H), 6.99 (d, *J* = 6.8 Hz, 1 H), 6.86 (dd, *J* = 8.1, 1.9 Hz, 2 H), 6.29 (dd, *J* = 8.1, 1.9 Hz, 2 H), 5.60 (t, *J* = 2.3 Hz, 1 H), 5.19 (t, *J* = 2.3 Hz, 1 H), 3.03 (t, *J* = 2.3 Hz, 2 H).

3′-Methylspiro[2,5-cyclohexadiene-1,1′-inden]-4-one, 32. A solution of **2a** (0.214 g, 0.89 mmol) and *p*-TsOH (0.03 g, 0.2 mmol) in $CHCl_3$ (20 mL) was heated at 52 °C for 4 h and then poured into a saturated $NaHCO_3$ solution (30 mL). Extractive workup ($CHCl_3$, 2 × 20 mL) gave **32** (0.21 g) as white crystals, mp 134–137 °C. Chromatography of this material (0.2 × 10 in., base-washed silica gel, 5% EtOAc/PE as eluant) gave white crystals of **32** (0.16 g, 86%), which were analytically pure: mp 138–139 °C: IR (KBr) 1662, 810, 760 cm^{-1}; ^1H NMR (200 MHz) δ 7.39–7.12 (m, 4 H), 6.42 (AB q, Δν = 15.7 Hz, *J* = 10.4 Hz, 4 H), 5.7 (d, *J* = 1.5 Hz, 1 H), 2.22 (d, *J* = 1.5 Hz, 3 H); ^{13}C NMR (63 MHz) δ 186.2 (1 C), 148.7 (2 C), 145.8 (1 C), 144.1 (1 C), 142.8 (1 C), 130.0 (2 C), 129.3 (1 C), 128.3 (1 C), 126.5 (1 C), 123.4 (1 C), 119.9 (1 C), 57.6 (1 C), 13.0 (1 C); mass spectrum, exact mass calcd for $C_{15}H_{12}O$ *m/e* 208.0888, obsd 208.0895.

2-Isopropenyl-4′-(trimethylsiloxy)biphenyl, 34. A mixture of **1a** (500 mg, 2.38 mmol) in dry pyridine (7 mL) and freshly distilled hexamethyldisilazane (1 mL, 4.76 mmol) was heated at reflux for 2 h (ca. 112 °C). The excess hexamethyldisilazane was distilled under reduced pressure at 25–27 °C/0.2 Torr to afford a light yellow oil (660 mg, 98%): IR (neat) 1250, 902, 834 cm^{-1}; ^1H NMR (80 MHz, $(CD_3)_2CO$) δ 7.26–7.16 (m, 6 H), 6.70 (d, *J* = 8.7 Hz, 2 H), 5.00–4.93 (m, 2 H), 1.58–1.55 (m, 3 H), 0.21 (s, 9 H); mass spectrum, exact mass calcd for $C_{18}H_{22}OSi$ *m/e* 282.1440, obsd 282.1418.

Anodic Oxidation of 34 under Basic Conditions. To a solution of **34** (230 mg, 0.81 mmol) in methanol (100 mL) and 2,6-lutidine (0.2 mL, 1.6 mmol) was added $LiClO_4$ (1.06 g). The mixture was saturated with N_2, cooled to 0 °C, and anodically oxidized at a constant current of 0.2 A for 14 min on a Pt cylindrical gauze anode and a Pt wire cathode. TLC analysis of the resulting reaction mixture indicated a mixture of **2a** and **34**. The reaction mixture was poured into H_2O (50 mL) and concentrated in vacuo. Extractive workup (CH_2Cl_2, 3 × 30 mL) gave a yellow oil which was chromatographed (silica gel, 0.2- × 10-in. column, 15 Et_2O/PE as eluant) to provide **2a** as a white needle-like crystalline solid (104 mg, 53%) and **34** (20 mg, 12%) as an oil.

Anodic Oxidation of 34 under Neutral Conditions. A solution of **34** (106 mg, 0.38 mmol) in methanol (100 mL) containing $LiClO_4$ (1.07 g) was anodically oxidized under the same conditions as described above for 6 min. The same workup and purification procedure afforded **34** as an oil (13 mg, 17%) and **2a** as a white crystalline solid (55 mg, 61%).

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Supplementary Material Available: Details of the current, solvent, and concentration dependence of the anodic oxidations (Tables I–III) and ^1H NMR spectra of all new compounds (38 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.