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# Biomimetic Oxidative Dimerization of Anodically Generated Stilbene Radical Cations: Effect of Aromatic Substitution on Product Distribution and Reaction Pathways

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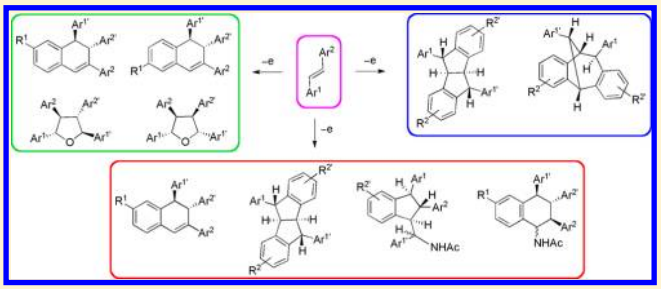
Supporting Information

**ABSTRACT:** A systematic study of the electrochemical oxidation of 1,2-diarylalkenes was carried out with the focus on detailed product studies and variation of product type as a function of aromatic substitution. A reinvestigation of the electrochemical oxidation of 4,4′-dimethoxystilbene under various conditions was first carried out, and all products formed were fully characterized and quantitated. This was followed by a systematic investigation of the effect of aromatic substitution on the nature and distribution of the products. The aromatic substituents were found to fall into three main categories, viz., substrates in which the nature and position of the aromatic substituents gave rise to essentially the same products as 4,4′-dimethoxystilbene, for example, tetraaryltetrahydrofurans, dehydrotetralins, and aldehydes (*p*-MeO or *p*-$NMe_2$ on one ring and X on the other ring, where X = *o*-MeO or *p*-alkyl, or *m*- or *p*-EWG; e.g., 4-methoxy-4′-trifluoromethylstilbene); those that gave rise to a mixture of indanyl (or tetralinyl) acetamides and dehydrotetralins (or pallidols) (both or one ring substituted by alkyl groups, e.g., 4,4′-dimethylstilbene); and those where strategic placement of donor groups, such as OMe and OH, led to the formation of ampelopsin F and pallidol-type carbon skeletons (e.g., 4,3′,4′-trimethoxystilbene). Reaction pathways to rationalize the formation of the different products are presented.




## INTRODUCTION

Electrochemically mediated processes have always constituted a useful option in organic synthetic methodology, both for functional group manipulations as well as for C−C bond formation.[1,2] The technique usually produces ion radicals in the first instance as a result of the initial electron transfer step. Anodic oxidation has attracted recent interest as a means for accessing radical cations for investigating the nature and reactivity of these highly reactive species, as well as for their utilization for carbon−carbon bond formation in organic synthesis.[2,3] This is in spite of potential difficulties due to the nature of the species itself, which is associated with its high reactivity and its inherent ambident or dualistic nature.[4,5] This inherent dualism poses a difficulty with respect to how best to interpret the reactivity of the radical cation, whether by analogy with radicals, cations, or both. This dualistic aspect of its nature, however, also confers an advantage on radical ion reactions, viz., the possibility of effecting umpolung processes (e.g., by reversal of polarity in the radical cations generated from enol ethers for coupling with electron-rich alkenes).[3,5] Indeed, recent developments in cation-radical chemistry have opened up new and exciting vistas that hold promise for more significant discoveries to emerge in the near future. Moeller, for example, has carried out systematic studies of intramolecular radical cation-mediated cyclizations based on anodic oxidation of various electron-rich alkenes and trapping of the resulting radical cations with various nucleophiles.[3] These studies have shed valuable light on radical cation reactivity and have also led to applications in synthesis.[6] Radical cations can also be accessed via non-electrochemical methods, for example, by electron-transfer using suitable one-electron oxidants,[4,5,7,8] or more recently, via visible light photocatalysis based on the use of transition metal polypyridyl complexes as facile SET agents.[9] These relatively recent developments have made radical cations (and radical anions) readily accessible for a wide range of applications in organic transformations, including asymmetric synthesis, and in a number of recent instances, radical cations (generated by the various methodologies mentioned) have been instrumental in forging key C−C bonds in natural product total syntheses.[6,10] Our own limited work on the anodic oxidation of indole derivatives and its applications prompted our interest in anodic oxidation of other substrates, which might lead to transformations into products incorporating natural product skeletons.[11] One such class of compounds is the stilbenes; recent reports of oxidative transformations employing one-electron oxidants or enzymes have led to a number of interesting products, including oxidized dimers.[12] In view of the paucity of electrochemical studies, except for several early kinetic investigations of the anodic oxidation of 4,4′-dimethoxystilbene,[13] we decided to initiate a systematic study of the electrochemical oxidation of 1,2-diarylalkenes, which we

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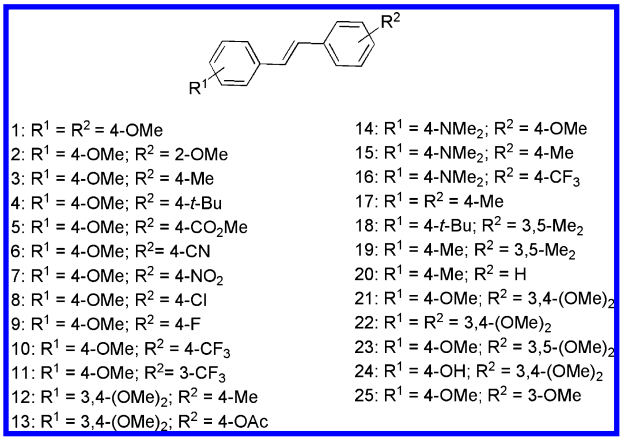
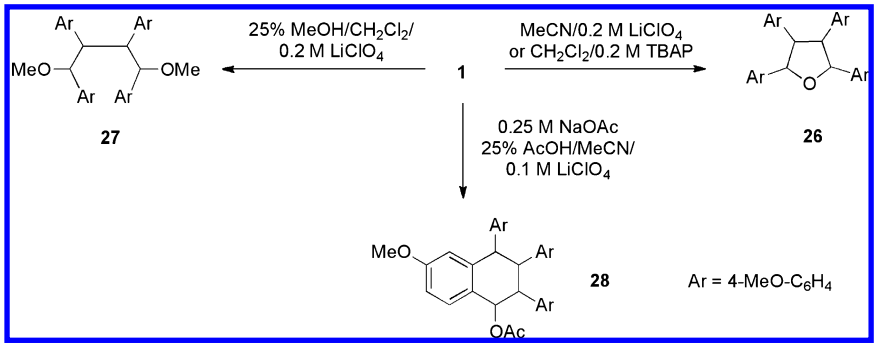
**Table 1. Synthesis of Stilbenes (1−25), Yield, Melting Point, and Anodic Half-Peak Potential**




| entry | stilbene | method[a] | % yield | mp (lit.) (°C) | $E_{p/2}$ (V)[b] |
|---|---|---|---|---|---|
| 1 | **1** | A | 77 | 203−204 (207−210)[18] | +0.68 |
| 2 | **2** | B | 89 | 80−82 (92)[19] | +0.72 |
| 3 | **3** | B | 87 | 156−158 (166−167)[20] | +0.82 |
| 4 | **4** | B | 64 | 168−169 (162−163)[21] | +0.84 |
| 5 | **5** | B | 86 | 170−173 (168−170)[13e] | +0.96 |
| 6 | **6** | B | 64 | 138−139 (133−141)[22] | +1.00 |
| 7 | **7** | B | 68 | 123−124 (130−131)[22] | +1.00 |
| 8 | **8** | C | 79 | 176−177 (196)[20] | +0.84 |
| 9 | **9** | C | 70 | 143−145 (147−149)[23] | +0.83 |
| 10 | **10** | C | 90 | 170−172 (171−172)[13e] | +0.92 |
| 11 | **11** | C | 78 | 66−68 | +0.94 |
| 12 | **12** | B | 86 | 111−112 | +0.76 |
| 13 | **13** | acetylation of **24** | 79 | 120−123 (125−126)[24] | +0.75 |
| 14 | **14** | B | 70 | 175−176 (171.9−173.4)[25] | +0.20 |
| 15 | **15** | B | 90 | 160−162 (163−165)[26] | +0.26 |
| 16 | **16** | B | 84 | 217−219 | +0.30 |
| 17 | **17** | A | 70 | 176−178 (179−180)[18] | +0.94 |
| 18 | **18** | B | 75 | 67−69 | +1.03 |
| 19 | **19** | B | 73 | 39−40 | +1.01 |
| 20 | **20** | B | 80 | 111−113 (116−118)[18] | +1.10 |
| 21 | **21** | B | 58 | 132−134 (138)[27] | +0.62 |
| 22 | **22** | A | 83 | 145−148 (154.6−155.0)[28] | +0.61 |
| 23 | **23** | B | 70 | 51−52 (55−56)[19] | +0.83 |
| 24 | **24** | B | 87 | 176−178 (180−182)[29] | +0.60 |
| 25 | **25** | B | 90 | 100−101 (104−105)[27] | +0.81 |

[a]Method of preparation: A = McMurry coupling; B = Heck coupling; C = Wittig reaction. [b]$E_{p/2}$ = anodic half-peak potential (Pt anode, Pt cathode, vs $Ag/AgNO_3$, $MeCN/LiClO_4$).

**Scheme 1. Products from Anodic Oxidation of 1 As Reported by Steckhan and Eberson[13a,c]**




hope will provide useful information on the reactivity of the radical cations generated from anodic oxidation of these substrates. Because the kinetics of the anodic oxidation of 4,4′-dimethoxystilbene has been previously thoroughly investigated, particularly by the work of Steckhan,[13a] our focus in this report is on the effect of aromatic substitution on the


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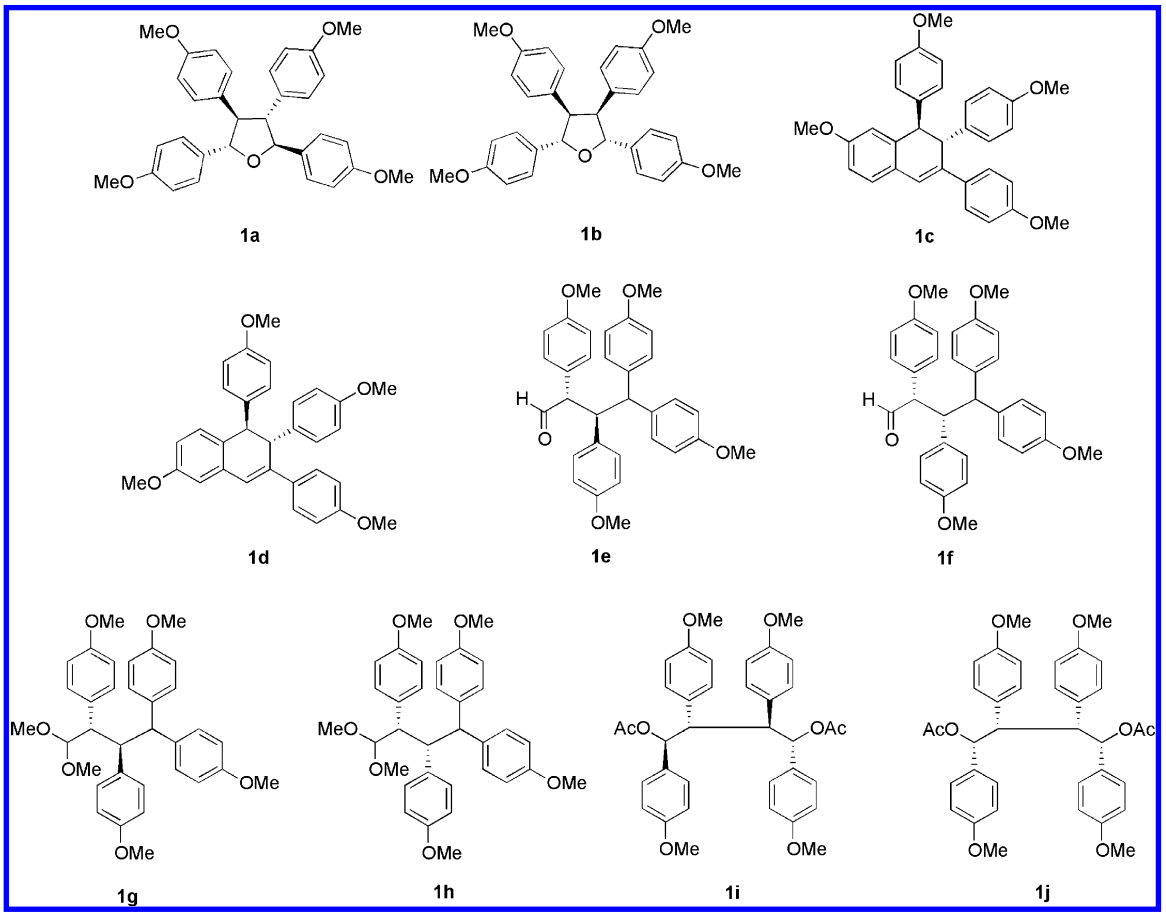
**Table 2. Products from the Anodic Oxidation of 1 under Different Conditions[a]**

| | | % yield[b] | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| entry | conditions | 1a | 1b | 1c | 1d | 1e | 1f | 1g | 1h | 1i | 1j | total |
| 1 | MeCN/0.2 M $LiClO_4$, +0.84 V | 56 | 22 | 1 | 5 | 5 | | | | | | 89 |
| 2 | MeCN/0.2 M LiClO4,[c] +0.84 V | 17 | 8 | 4 | 22 | | | | | | | 51 |
| 3 | 1% $H_2O$/MeCN/0.2 M $LiClO_4$,[c] +0.88 V | 38 | 20 | 2 | 7 | 3 | | | | | | 70 |
| 4 | 25% MeOH/$CH_2Cl_2$/0.2 M $LiClO_4$, +0.80 V | | | | | 11 | 3 | 28 | 14 | | | 56 |
| 5 | 25% MeOH/$CH_2Cl_2$/0.2 M $LiClO_4$,[c] +0.80 V | | | | | | | 40 | 10 | | | 50 |
| 6 | 0.25 M NaOAc, 25% AcOH/MeCN/0.1 M $LiClO_4$, +0.80 V | | | | | | | | | 40 | 22 | 62 |

[a]Pt anode, Pt cathode, vs Ag/$AgNO_3$. [b]Isolated yields. [c]Nonaqueous workup.

**Chart 1**




course of the electrooxidation from the viewpoint of the nature of the products formed and the reaction pathways involved.

## RESULTS AND DISCUSSION

The required stilbenes were synthesized by employing either McMurry coupling of the appropriately substituted benzaldehydes (for symmetric stilbenes),[14,15] Heck coupling of aryl halides and styrenes,[16] or Wittig reaction of the appropriate benzaldehydes and phosphonium ylide.[17] The results are presented in Table 1, which also lists the anodic half-peak potentials (Pt anode, Pt cathode, vs Ag/$AgNO_3$) for these stilbenes (**1**–**25**).

We commenced with a detailed reinvestigation of the electrochemical oxidation of 4,4′-dimethoxystilbene **1** under different conditions. Steckhan reported the quantitative formation of 2,3,4,5-tetraanisyltetrahydrofuran **26** (without stereochemical assignment) as the sole product when the anodic oxidation was carried out in acetonitrile, followed by aqueous workup.[13a] When the electrooxidation was carried out in MeOH/$CH_2Cl_2$, the main product was dimethoxylated open-chain dimer **27** (Scheme 1). Eberson, on the other hand, reported the isolation of acetylated tetralin **28** when the reaction was carried out in 25% AcOH/MeCN/0.10 M $LiClO_4$ in the presence of 0.25 M NaOAc but did not furnish full characterization details or a mechanism to explain the formation of the tetralin product (Scheme 1).[13c,d] We have repeated all three reactions.

Anodic oxidation of **1** (Pt anode, MeCN/0.2 M $LiClO_4$) showed the presence of two irreversible waves at +0.74 and +1.37 V versus Ag/$AgNO_3$ in the potential range investigated as revealed by cyclic voltammetry. Controlled potential electrolysis (Pt gauze anode, Pt cathode; MeCN/0.2 M $LiClO_4$) at the first anodic wave (+0.84 V) was allowed to proceed until consumption of 1 F $mol^{-1}$.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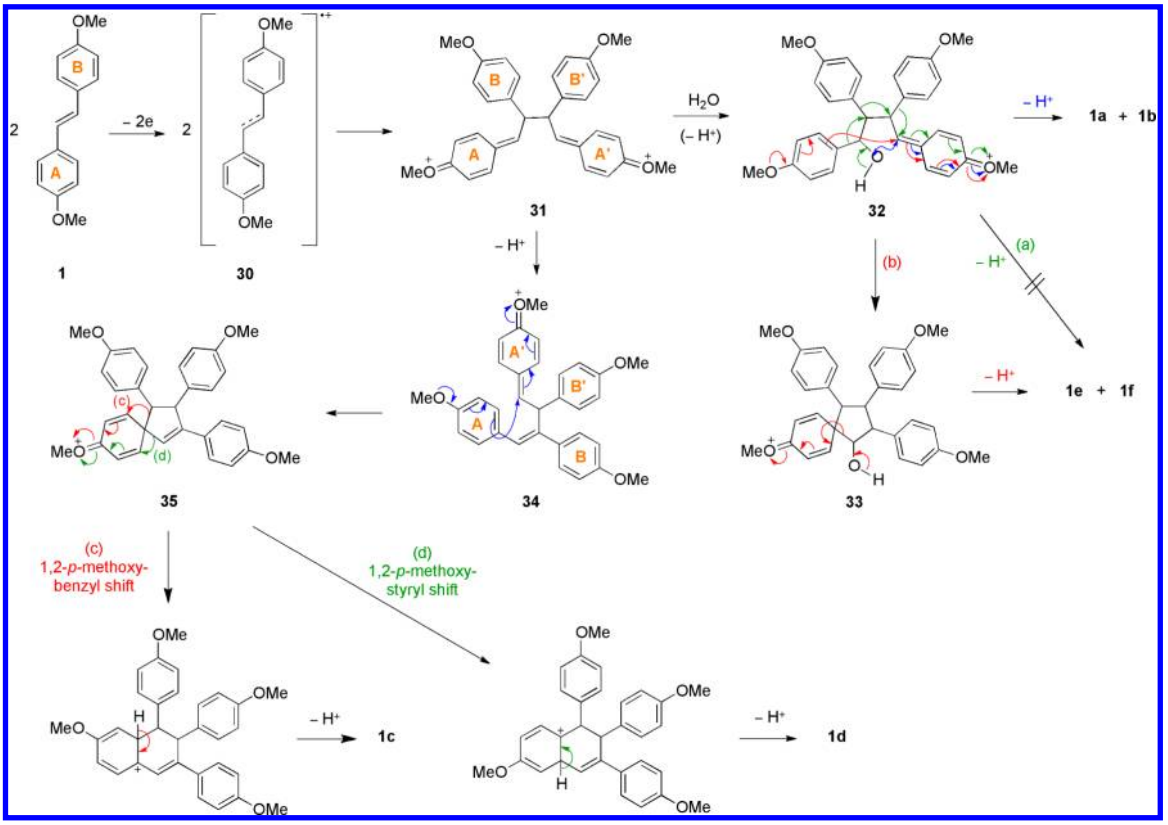
**Scheme 2. Proposed Mechanism for the Formation of the Products in the Anodic Oxidation of 1 in MeCN/$LiClO_4$**




A mixture of products was obtained (Table 2, Chart 1) comprising stereoisomeric tetraanisyltetrahydrofurans as the major products in combined yields of ca. 78% (**1a**, 56%; **1b**, 22%), accompanied by 6% of regioisomeric dehydrotetralins (**1c**, 1%; **1d**, 5%) and an aldehyde (**1e**, 5%). The product mixture was separated by a combination of centrifugal preparative TLC and HPLC. The two stereoisomeric tetrahydrofurans **1a** and **1b** could not be unambiguously distinguished by NMR spectroscopy alone, and complete stereochemical assignment was provided by X-ray diffraction analysis.

Separation of the dehydrotetralins (**1c** and **1d**) required resort to chiral-phase HPLC, and as in the case of the tetrahydrofurans, unambiguous and complete configurational assignment of these dehydrotetralins required X-ray diffraction analysis. While dehydrotetralin **1c** formed suitable crystals from EtOH for X-ray analysis, regioisomeric **1d** resisted crystal formation in most of the solvents tested. Eventually, treatment of **1d** with $Br_2/CH_2Cl_2$ led to the dibromo naphthalene derivative 1,6-dibromo-7-methoxy-2,3,4-tris(4-methoxyphenyl)naphthalene (a result of benzylic bromination, electrophilic aromatic substitution, electrophilic addition, and dehydrohalogenation; see Supporting Information), for which the structure could be deduced from the spectroscopic data and confirmed by X-ray diffraction analysis.

In the event, the methoxy-migrated dehydrotetralins **2d** and **6d** resulting from the oxidation of stilbenes **2** (4,2′-dimethoxystilbene) and **6** (4-methoxy-4′-cyanostilbene), respectively, provided suitable crystals for X-ray analysis. These data provided additional confirmation regarding the change in the position of methoxy substitution as shown in **1d**. The structure of aldehyde **1e** was also confirmed indirectly by X-ray analysis of the acetal **1h**.

Anodic oxidation of **1** in 25% $MeOH/CH_2Cl_2/LiClO_4$ (Steckhan's conditions) gave a mixture comprising the diastereomeric aldehydes (**1e**, 11%; **1f**, 3%) and the corresponding acetals (**1g**, 28%; **1h** 14%; for the X-ray structure of **1h**, see Supporting Information) as the major products (Table 2, entry 4). This is in contrast to Steckhan's observation of dimethoxylated open-chain dimer **27** as the main product of the electrooxidation. When the electrooxidation was carried out in 25% $AcOH/MeCN/LiClO_4$ in the presence of NaOAc (0.25 M) (Eberson's conditions), isomeric acetate derivatives **1i** and **1j** were obtained in combined yields of 62% (**1i**, 40%; **1j**, 22%; Table 2, entry 6; X-ray structures available for both products in Supporting Information). This is also in contrast to Eberson's observation of acetylated tetralin **28** as the main product obtained under these conditions.

The predominance of tetrahydrofuran products **1a** and **1b** (accompanied by a minor amount of aldehyde **1e**) from the oxidation of **1** is likely the result of aqueous workup subsequent to the completion of electrolysis and formation of the primary product of the electrooxidation. The same applies to the formation of the aldehyde products (**1e** and **1f**) in addition to the major acetal products (**1g** and **1h**) when oxidation was carried out in $MeOH/CH_2Cl_2$. The aldehyde products were likely the result of acetal hydrolysis during the aqueous workup. Additional control experiments were therefore carried out to establish this. For the oxidation of **1** in MeCN, where the reaction mixture was processed in the absence of water (standard nonaqueous workup: reaction mixture concentrated by evaporation of solvents under reduced pressure until a slurry was obtained, and the residue was then dissolved in $CH_2Cl_2$ and eluted through a short $SiO_2$ column with $CH_2Cl_2$), the amount of the tetrahydrofuran products was markedly reduced, while the yield of the dehydrotetralin products increased (Table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2, entry 2; a small amount of tetrahydrofuran products due to water present in $SiO_2$).[30]

When electrooxidation was carried out in MeCN/$LiClO_4$ containing 1% of water, followed by a nonaqueous workup of the reaction mixture as described above, the tetrahydrofuran products were obtained as the major products, together with the isomeric dehydrotetralins and the aldehyde (Table 2, entry 3). These experiments confirmed the origin of the tetrahydrofuran and aldehyde products as arising from attack by added water on the dication, formed as the primary and stable product of the anodic oxidation. In the case of the oxidation in MeOH/$CH_2Cl_2$, repeating the oxidation followed by nonaqueous workup gave only the diastereomeric acetals (Table 2, entry 5), indicating that the aldehydes formed from hydrolysis of the acetals during aqueous workup.

We propose the following mechanism to explain the formation of the products for the oxidation of 4,4′-dimethoxystilbene **1** (Scheme 2). One-electron oxidation gave the cation radical **30**, which in the absence of strong nucleophiles and under the conditions of preparative electrolysis undergoes cation radical dimerization to give the dicationic intermediate **31** as the dominant step, as previously demonstrated by the kinetic studies of Steckhan.[13a] Subsequent attack of the dicationic intermediate **31** by water leads to the cationic intermediate **32**, which on intramolecular trapping by OH furnishes tetrahydrofuran products (**1a** and **1b**).

The two stereoisomeric tetrahydrofuran products (**1a** and **1b**) arise as a consequence of the two possible modes of cation radical coupling, one giving rise to the "*threo*"-dication **31a**, which is characterized by a $C_2$ axis, and which gives rise to the major $C_2$-symmetric tetrahydrofuran product **1a**, and the other a "*meso*"-dication **31b**, which gives rise to the *meso*-tetrahydrofuran product **1b** (Figure 1).

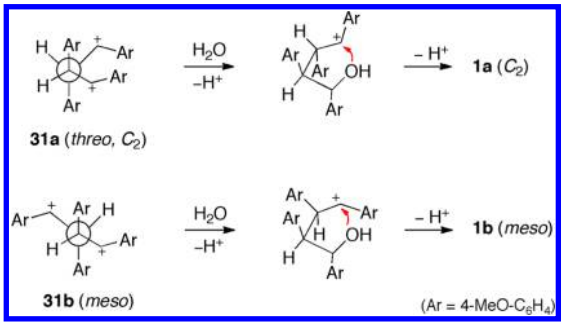


**Figure 1.** Formation of stereoisomeric tetrahydrofurans **1a** and **1b**.

It was initially thought that the minor aldehyde product **1e** originated from 1,2-shifts of aryl groups in the open chain carbocation intermediate **32** (Scheme 2, path a), but this had to be amended to path b from the results of other stilbenes (vide infra). The origin of the regioisomeric dehydrotetralins (especially **1d** where methoxy migration has occurred) appears to be less clear-cut, and we rationalize its formation as follows.

Dicationic intermediate **31** upon deprotonation gives cation **34**, which then forms spirocyclic carbocation intermediate **35**, a step that is assisted by the appositely substituted *p*-methoxy substituent in ring A.[31−33] Ring expansion from **35** via path c involving a 1,2-*p*-methoxybenzyl shift followed by deprotonation leads to the expected regioisomer **1c**. The alternative 1,2-*p*-methoxystyryl shift (Scheme 2, path d), on the other hand, leads after deprotonation to the "unusual" or methoxy-migrated, regioisomeric dehydrotetralin, **1d**. In view of the observation that the product from path d predominates (by a factor of about 5-fold), it seems likely that in the case of **1**, the 1,2-*p*-methoxystyryl shift (path d) is preferred over the alternative 1,2-*p*-methoxybenzyl shift (path c).

The formation of the aldehyde (**1e**; Table 2, entry 1) as well as the acetals (**1g**, **1h**; Table 2, entry 4; oxidation in MeOH/$CH_2Cl_2$) also required the intermediacy of a similar spirocyclic carbocation, as shown in Scheme 2, for the reaction of **1** in MeCN with aqueous workup because, in these instances, aryl group migration has occurred. Although initially thought to result from 1,2-shifts of aryl groups in an open-chain carbocation intermediate, on the basis of the results for the reaction of the symmetrically substituted 4,4′-dimethoxystilbene (Scheme 2, path a), the aldehydes (and acetals) obtained for the oxidation of unsymmetrically substituted stilbenes (e.g., 4-OMe, 4′-$CF_3$; Table 3, entry 11) indicated that migration of an anisyl group has occurred en route, which clearly ruled out the operation of the open chain carbocation pathway. The result can be rationalized by the formation of the corresponding spirocationic intermediate **33**, which on subsequent ring-opening, leads to the aldehyde products **1e** and **1f** (Scheme 2, path b). In reactions in the presence of methanol, intermediacy of the corresponding methoxylated spirocation **36** is invoked to explain the rearranged acetal products **1g** and **1h** (Scheme 3).

Anodic oxidation of **1** in 25% AcOH/MeCN/0.1 M $LiClO_4$ in the presence of stronger nucleophiles (NaOAc, 0.25 M; Table 2, entry 6; Eberson's conditions) gave the diastereomeric acetate products **1i** and **1j**, which, following Steckhan, arise from facile nucleophilic capture of the radical cation intermediate **30** preceding radical dimerization. (Although the above pathway predominates in the presence of added nucleophiles, the possibility that under conditions of preparative electrolysis, where the cation radical concentration is high, some competition by the alternative pathway involving radical cation dimerization preceding attack by the nucleophile cannot be completely ruled out.)

Following the thorough reinvestigation of the products formed from the anodic oxidation of **1**, a series of differentially disubstituted stilbenes were investigated to determine the effect of aromatic substitution on the course of the electrooxidation. These oxidations were carried out in MeCN/0.2 M $LiClO_4$ with standard aqueous workup, unless otherwise stated. From the viewpoint of product type, the aromatic substituents appear to fall into three main categories, viz., substrates in which the nature and position of the aromatic substituents give rise to essentially the same products as 4,4′-dimethoxystilbene **1** (i.e., tetraaryltetrahydrofurans, dehydrotetralins, and aldehydes); those that give rise to a mixture of indanyl (or tetralinyl) acetamides and dehydrotetralins (or pallidols); and those where strategic placement of donor groups, such as OMe and OH, leads to the formation of ampelopsin F and pallidol-type carbon skeletons.

The results for the stilbenes of the first group are summarized in Table 3 and Chart 2. It can be seen that for stilbenes of the type $R^1-C_6H_4-CH{=}CH-C_6H_4-R^2$, where $R^1$ = 4-OMe; $R^2$ = 2-OMe, 4-Me, 4-*t*-Bu, 4-$CO_2$Me, 4-CN, 4-$NO_2$, 4-Cl, 4-F, 4-$CF_3$, or 3-$CF_3$ (i.e., **1**−**11**), the products are the tetraaryltetrahydrofurans (major), dehydrotetralins, and aldehydes.[34,35] Several additional features were noted. First, all the stilbenes from the above list (**1**−**11**) gave the unusual dehydrotetralin regioisomer (analogous to **1d**), and in the


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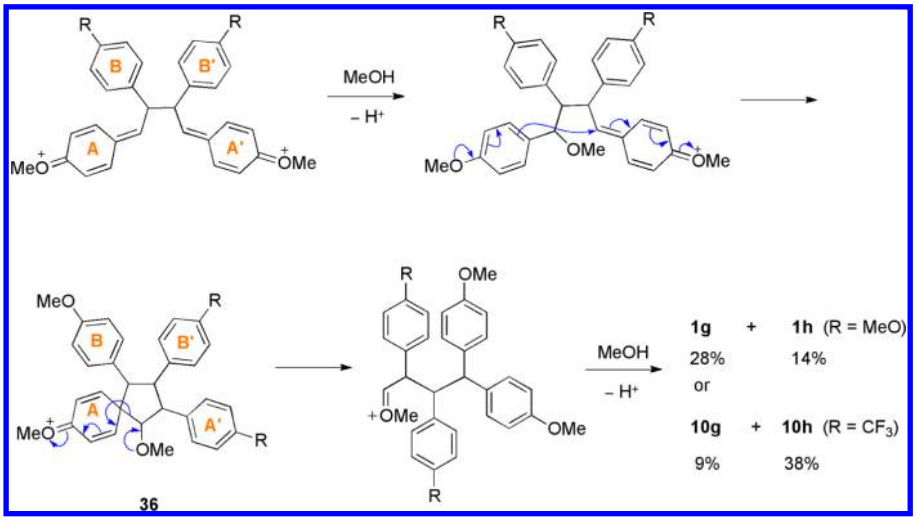
**Scheme 3. Formation of Acetals in the Anodic Oxidation of 1 and 10 in $MeOH/CH_2Cl_2/LiClO_4$**




majority of instances were accompanied by traces of the aldehydes. In all cases, a *p*-methoxy group is present in ring A, which provides the crucial assistance for the formation of the spirocyclic carbocation similar to **35**, from which both the dehydrotetralin regioisomers arise. For stilbenes **1** (4,4′-dimethoxystilbene) and **2** (2′,4-dimethoxystilbene), the unusual methoxy-migrated dehydrotetralin (analogous to **1d**) was the major regioisomer formed (X-ray structure for **2d** is in Supporting Information).

In all the other stilbenes of the type 4-MeO−$C_6H_4$CH═$CHC_6H_4$−$R^2$, where $R^2$ (ring B) is an electron-withdrawing group or an alkyl group (as exemplified by 4-MeO−$C_6H_4$CH═$CHC_6H_4$−$CF_3$-4′), both regioisomers were obtained but with the "normal" dehydrotetralin (analogous to **1c**) obtained as the major product.

It would appear that when the substituent in the other ring ($R^2$, ring B) is a strong donor, such as 4′-OMe or 2′-OMe, ring-expansion of the spirocationic intermediate (analogous to **35**) via a 1,2-*p*-methoxystyryl (in the case of 4′-OMe-substituted ring B, **1**) or 1,2-*o*-methoxystyryl (in the case of 2′-OMe-substituted ring B, **2**) shift is favored over the alternative 1,2-*p*-methoxybenzyl shift (see Scheme 2). In contrast, for stilbenes of the type 4-MeO−$C_6H_4$CH═$CHC_6H_4$−$R^2$ where $R^2$ (ring B) is an electron-withdrawing group or an alkyl group, the 1,2-*p*-methoxybenzyl shift is now preferred over the alternative 1,2-*p*-$R^2$-styryl shift ($R^2$ = alkyl or EWG). It would also appear that the primary product of the electrooxidation in these stilbenes is the dication (analogous to **31**, because the tetrahydrofurans constituted the major products). The dication, in addition to being exceptionally stable in the highly polar medium, is also strongly stabilized via through-resonance by the two 4- and 4′-methoxy substituents. A portion of these stable dications react to give the dehydrotetralins, with the bulk persisting until completion of the electrolysis, following which, attack by water during the aqueous workup leads mainly to the tetrahydrofuran products.

In the case of stilbenes **12** and **13**, where $R^1$ = 3,4-$(MeO)_2$ and $R^2$ = Me (**12**) or OAc (**13**), the normal dehydrotetralin was the major product (ca. 60%) while the tetrahydrofuran products were either absent (as in the case of **13**) or minor products (in the case of **12**). In these stilbenes, it would appear that the presence of the appositely placed *m*-OMe substituent in ring A resulted in a facile cyclization to the dehydrotetralin product as shown in Scheme 4. This is in contrast to stilbene **3** ($R^1$ = 4-OMe, $R^2$ = 4-Me, lacking an additional *m*-MeO substituent in ring A) where the tetrahydrofurans constitute the major products and the dehydrotetralins constitute the minor products.

The stilbenes in entries 15−18 (**14**−**16**, Table 3) are of the type where $R^1$ = 4-$NMe_2$ and $R^2$ = 4′-OMe, 4′-Me, or 4′-$CF_3$. Oxidation of these stilbenes gave mainly the tetrahydrofuran products accompanied by traces of aldehyde products. The tetrahydrofuran products formed from the reaction of stilbene **14** revealed another important feature of these reactions, namely, the inversion in the regioselectivity of the tetraarylte-trahydrofuran products as exemplified by the oxidation of a stilbene where the substituent in one ring is *p*-OMe ($\sigma^+$ = −0.78), while the substituent in the other ring is a stronger donor than *p*-OMe, e.g., *p*-$NMe_2$ ($\sigma^+$ = −1.70). In such a case, in the tetrahydrofuran products, the $\alpha$- and $\alpha'$-aryl groups are 4-$NMe_2$−$C_6H_4$−, while the $\beta$- and $\beta'$-aryl groups are 4-OMe−$C_6H_4$−. This is in contrast to all the other stilbenes examined thus far, where the reverse is the case, that is, where the $\alpha$- and $\alpha'$-aryl groups are 4-OMe−$C_6H_4$− ($R^1$ = OMe), whereas the $\beta$- and $\beta'$- aryl groups are 4-$R^2$−$C_6H_4$− ($R^2$ = 2-OMe, 4-Me, 4-*t*-Bu, 4-$CO_2$Me, 4-CN, 4-$NO_2$, 4-Cl, 4-F, 4-$CF_3$, 3-$CF_3$, etc.).

This constitutes another piece of evidence in support of the proposed mechanism involving cation radical dimerization as the dominant step following one-electron oxidation: coupling occurs in the position where a positive charge would be least stabilized according to resonance theory; consequently, the stronger donor substituent is attached to the aromatic moiety associated with the benzylic carbon with greater carbocation character. Similar results from two other related examples were also consistent with this conclusion (**15**, $R^1$ = $NMe_2$, $R^2$ = Me; **16**, $R^1$ = $NMe_2$, $R^2$ = $CF_3$). In these three examples, an additional tetrahydrofuran diastereomer was also isolated (**14k**, **15k**, **16k**; X-ray structures of **14k** and **16k** are in Supporting Information), while the dehydrotetralin products were not detected. Presumably, the dications are so highly stabilized by the *p*-$NMe_2$ groups that they persist until quenched by water during workup.

There is additional experimental support for the proposed cation radical coupling as the dominant step under the conditions of preparative electrolysis. One useful technique in preparative electroorganic chemistry is the selective oxidation


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**Table 3. Products from the Anodic Oxidation of Stilbenes 1−16[a]**

| | | % yield[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| entry | stilbene | a | b | c | d | e | f | k | total |
| 1 | **1** | **1a** | **1b** | **1c** | **1d** | **1e** | | | |
| | | 56 | 22 | 1 | 5 | 5 | | | 89 |
| 2 | **2**[c] | **2a** | **2b** | | **2d** | | | | |
| | | 35 | 19 | | 18 | | | | 72 |
| 3 | **3**[c] | **3a** | **3b** | **3c** | **3d** | | | | |
| | | 28 | 14 | 11 | 3 | | | | 56 |
| 4 | **4** | **4a** | **4b** | **4c** | **4d** | **4e** | | | |
| | | 43 | 35 | 4 | 1 | 4 | | | 87 |
| 5 | **5**[c] | **5a** | **5b** | **5c** | **5d** | | | | |
| | | 30 | 25 | 6 | 3 | | | | 64 |
| 6 | **6**[c] | **6a** | **6b** | **6c** | **6d** | | | | |
| | | 30 | 28 | 7 | 2 | | | | 67 |
| 7 | **7**[c] | **7a** | **7b** | **7c** | **7d** | | | | |
| | | 34 | 34 | 3 | 1 | | | | 72 |
| 8 | **8**[c] | **8a** | **8b** | **8c** | **8d** | | | | |
| | | 36 | 33 | 5 | 1 | | | | 75 |
| 9 | **9**[c] | **9a** | **9b** | **9c** | **9d** | | | | |
| | | 38 | 30 | 5 | 1 | | | | 74 |
| 10 | **10**[c] | **10a** | **10b** | **10c** | **10d** | | | | |
| | | 31 | 31 | 8 | 2 | | | | 72 |
| 11 | **10**[c,d] | | | | | **10g** | **10h** | | |
| | | | | | | 9 | 38 | | 47 |
| 12 | **11**[c] | **11a** | **11b** | **11c** | **11d** | | | | |
| | | 30 | 27 | 4 | 2 | | | | 64 |
| 13 | **12** | **12a** | | **12c** | | | | | |
| | | 13 | | 76 | | | | | 89 |
| 14 | **13** | | | **13c** | | | | | |
| | | | | 57 | | | | | 57 |
| 15 | **14** | **14a** | **14b**[f] | | | **14e**[c] | **14f** | **14k** | |
| | | 31 | | | | | 1 | 27 | 59 |
| 16 | **14**[e] | **14a** | **14b** | | | **14e**[c] | **14f** | **14k** | |
| | | 30 | 12 | | | | 20 | 22 | 84 |
| 17 | **15**[c] | **15a** | **15b** | | | | **15f** | **15k** | |
| | | 21 | 6 | | | | 10 | 21 | 58 |
| 18 | **16** | **16a** | **16b** | | | **16e** | **16f** | **16k** | |
| | | 14 | 4 | | | 12 | 9 | 14 | 53 |

[a]Pt anode, Pt cathode, vs $Ag/AgNO_3$ in MeCN/0.2 M $LiClO_4$, unless otherwise stated. [b]Isolated yields. [c]Traces of aldehyde products observed in NMR spectra of product mixtures. [d]Electrolysis in 25% $MeOH/CH_2Cl_2$/0.2 M $LiClO_4$. [e]Electrolysis in 5% $H_2O$/MeCN/0.2 M $LiClO_4$. [f]Traces of tetrahydrofuran products observed in NMR spectra of product mixtures.

of a substrate (A) to generate an electrophilic species (cation, cation radical, dication, etc.), which then reacts with an acceptor substrate (B) present in the electrolyte solution. A prerequisite for this technique to work is that the anodic peak potential of B must be higher than that of A by at least 0.2 V, so that oxidation of A can proceed in the presence of B without affecting B. An impressive demonstration of this principle was the partial synthesis of anhydrovinblastine via anodic oxidation of catharanthine in the presence of vindoline.[36] In the present case, anodic oxidation of 4,4′-dimethoxystilbene **1** ($E_{pa}$ = +0.74 V) in the presence of **10** (4-$MeOC_6H_4CH{=}CHC_6H_4{-}CF_3$-4′, $E_{pa}$ = +0.98 V), gave the same products as those obtained by anodic oxidation of **1** alone. No "cross-coupled" products were detected, and **10** was recovered virtually intact after electrolysis. The same results were obtained for the oxidation of **1** in the presence of 4,4′-dimethylstilbene **17** ($E_{pa}$ = +0.99 V). These experiments provide indirect support for cation radical coupling, as opposed to attack of cation radical on a native stilbene, as the dominant step following the initial one-electron oxidation.

The results for oxidation of stilbenes of the second group are summarized in Table 4 and Chart 3. These are stilbenes substituted in both rings by alkyl groups (**17**, $R^1 = R^2$ = 4-Me; **18**, $R^1$ = 4-*t*-Bu, $R^2$ = 3,5-$Me_2$; **19**, $R^1$ = 4-Me, $R^2$ = 3,5-$Me_2$; **20**, $R^1$ = 4-Me, $R^2$ = H). The products are the "normal" dehydrotetralin (for **17** and **20**) or pallidol (for **18** and **19**), and the epimeric indanyl acetamides (or tetralinyl acetamide in the case of **20**), whose structures indicated incorporation of MeCN. The indanyl acetamides (**17m** and **17n**) were isolated as an unresolvable mixture of the epimers (1:1 mixture). Single crystals were obtained from solutions ($MeOH{-}CH_2Cl_2$) containing the mixture of the epimers, and the X-ray crystal structure obtained (see Supporting Information) showed that the epimers had cocrystallized. The epimers (in the case of oxidation of 4,4′-dimethylstilbene **17**) could be separated by chiral-phase HPLC to give the individual pure epimers, which


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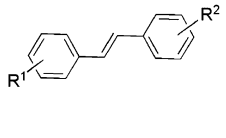
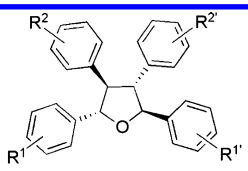
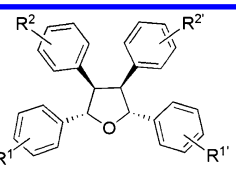
**Chart 2**



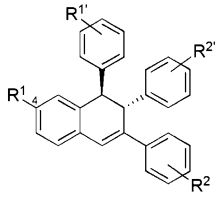
**1**: $R^1 = R^2 = 4\text{-OMe}$
**2**: $R^1 = 4\text{-OMe}$; $R^2 = 2\text{-OMe}$
**3**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-Me}$
**4**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-}t\text{-Bu}$
**5**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-CO}_2\text{Me}$
**6**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-CN}$
**7**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-NO}_2$
**8**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-Cl}$
**9**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-F}$
**10**: $R^1 = 4\text{-OMe}$; $R^2 = 4\text{-CF}_3$
**11**: $R^1 = 4\text{-OMe}$; $R^2 = 3\text{-CF}_3$
**12**: $R^1 = 3,4\text{-(OMe)}_2$; $R^2 = 4\text{-Me}$
**13**: $R^1 = 3,4\text{-(OMe)}_2$; $R^2 = 4\text{-OAc}$
**14**: $R^1 = 4\text{-NMe}_2$; $R^2 = 4\text{-OMe}$
**15**: $R^1 = 4\text{-NMe}_2$; $R^2 = 4\text{-Me}$
**16**: $R^1 = 4\text{-NMe}_2$; $R^2 = 4\text{-CF}_3$



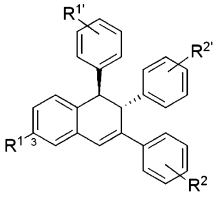
**1a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-OMe}$
**2a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 2\text{-OMe}$
**3a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Me}$
**4a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-}t\text{-Bu}$
**5a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CO}_2\text{Me}$
**6a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CN}$
**7a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-NO}_2$
**8a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Cl}$
**9a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-F}$
**10a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CF}_3$
**11a**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 3\text{-CF}_3$
**12a**: $R^1 = R^{1'} = 3,4\text{-(OMe)}_2$; $R^2 = R^{2'} = 4\text{-Me}$
**14a**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-OMe}$
**15a**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-Me}$
**16a**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-CF}_3$



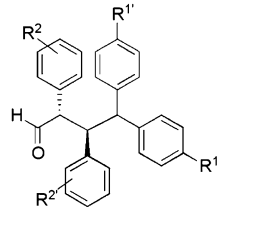
**1b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-OMe}$
**2b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 2\text{-OMe}$
**3b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Me}$
**4b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-}t\text{-Bu}$
**5b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CO}_2\text{Me}$
**6b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CN}$
**7b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-NO}_2$
**8b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Cl}$
**9b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-F}$
**10b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CF}_3$
**11b**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 3\text{-CF}_3$
**14b**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-OMe}$
**15b**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-Me}$
**16b**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-CF}_3$



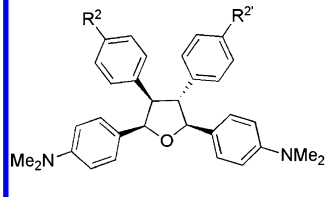
**1c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-OMe}$
**2c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 2\text{-OMe}$
**3c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Me}$
**4c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-}t\text{-Bu}$
**5c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CO}_2\text{Me}$
**6c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CN}$
**7c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-NO}_2$
**8c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Cl}$
**9c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-F}$
**10c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CF}_3$
**11c**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 3\text{-CF}_3$
**12c**: $R^1 = R^{1'} = 3,4\text{-(OMe)}_2$; $R^2 = R^{2'} = 4\text{-Me}$
**13c**: $R^1 = R^{1'} = 3,4\text{-(OMe)}_2$; $R^2 = R^{2'} = 4\text{-OAc}$



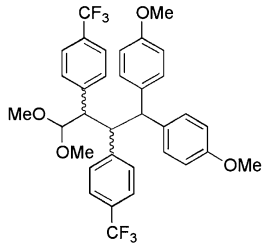
**1d**: $R^1 =$ 3-OMe; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-OMe}$
**2d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 2\text{-OMe}$
**3d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Me}$
**4d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-}t\text{-Bu}$
**5d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CO}_2\text{Me}$
**6d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CN}$
**7d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-NO}_2$
**8d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-Cl}$
**9d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-F}$
**10d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-CF}_3$
**11d**: $R^1 = 3\text{-OMe}$; $R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 3\text{-CF}_3$



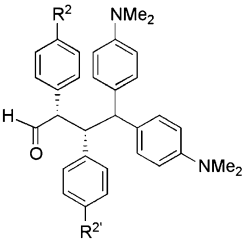
**1e**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-OMe}$
**4e**: $R^1 = R^{1'} = 4\text{-OMe}$; $R^2 = R^{2'} = 4\text{-}t\text{-Bu}$
**16e**: $R^1 = R^{1'} = 4\text{-NMe}_2$; $R^2 = R^{2'} = 4\text{-CF}_3$



**14k**: $R^2 = R^{2'} = 4\text{-OMe}$
**15k**: $R^2 = R^{2'} = 4\text{-Me}$
**16k**: $R^2 = R^{2'} = 4\text{-CF}_3$



**10g**: *anti*
**10h**: *syn*



**14f**: $R^2 = R^{2'} = 4\text{-OMe}$
**15f**: $R^2 = R^{2'} = 4\text{-Me}$
**16f**: $R^2 = R^{2'} = 4\text{-CF}_3$

**Scheme 4. Formation of Dehydrotetralins 12c and 13c in Anodic Oxidation of Stilbenes 12 and 13**

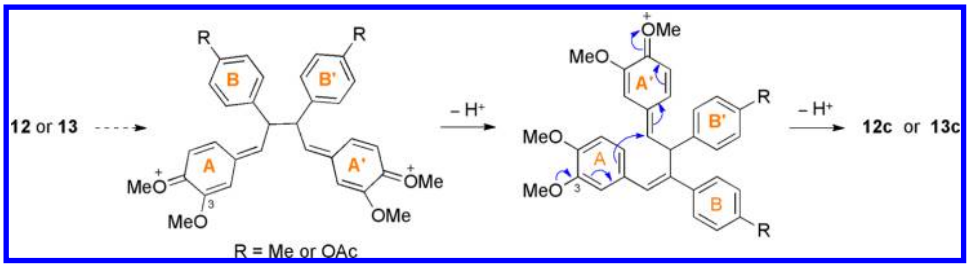




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**Table 4. Products from the Oxidation of Stilbenes 17−21**[a]

| | | % yield[b] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| entry | stilbene | m | n | c | p | q | r | total |
| 1 | **17** | **17m** | **17n** | **17c** | | | | |
| | | 32 | 32 | 15 | | | | 79 |
| 2 | **18** | **18m** | **18n** | | **18p** | | | |
| | | 34 | 34 | | 8 | | | 76 |
| 3 | **19** | **19m** | **19n** | | **19p** | | | |
| | | 15 | 15 | | 27 | | | 57 |
| 4 | **20** | | | **20c** | | **20q** | **20r** | |
| | | | | 22 | | 19 | 19 | 60 |

[a]Pt anode, Pt cathode, vs $Ag/AgNO_3$ in MeCN/0.2 M $LiClO_4$. [b]Isolated yields.

unfortunately did not provide crystals suitable for X-ray diffraction analysis.[37]

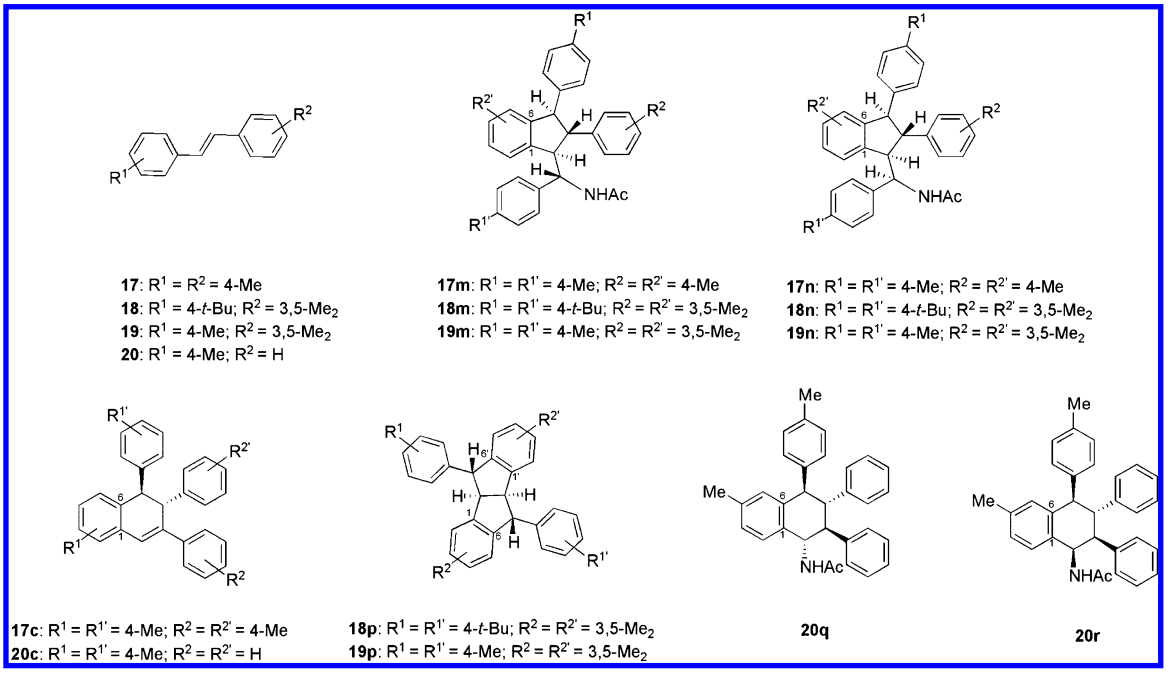
The nature of the products obtained is determined by the position of alkyl substitution in the stilbene. We propose the following mechanism (Scheme 5) to account for the products based on the oxidation of 4,4′-dimethylstilbene **17**. Radical cation coupling following one-electron oxidation gives the dication, the key intermediate from which the other products (dehydrotetralin and indanyl acetamides) are derived. For all these alkyl-disubstituted substrates, only the normal dehydrotetralin (e.g., **17c**) was obtained. No methyl-migrated dehydrotetralins were detected because the 4-methyl substituent (compared to 4-methoxy) was unable to provide the crucial assistance required to form the spirocyclic cation. We propose that in these alkyl-substituted stilbenes, the formation of the dehydrotetralins is via cyclization of an open-chain carbocation as shown in Scheme 5. An alternative cyclization of the dication via electrophilic attack of the cations on the aromatic moieties as shown leads eventually to the epimeric indanyl acetamide products.

Two alternative modes of cyclization (Scheme 5, paths b and c) both yield the same indanyl cation intermediate in the first instance. Subsequent attack by the acetonitrile solvent followed by hydrolysis furnished the epimeric indanyl acetamides.[38] It would appear that the first cyclization is immediately followed by acetonitrile capture of the carbocation leading eventually to the acetamide product following hydrolysis. A second cyclization to the fused bisindanyl product or pallidol derivative was not observed in this instance, but in the oxidation of stilbenes **18** ($R^1$ = 4-*t*-Bu, $R^2$ = 3,5-$Me_2$) and **19** ($R^1$ = 4-Me, $R^2$ = 3,5-$Me_2$), pallidol products were formed in place of the dehydrotetralin, in addition to the indane acetamides. In these stilbenes, the presence of methyl substituents in the meta positions provided the required activation for aromatic substitution leading to the pallidol products (**18p** and **19p**) as shown in Scheme 6.

The oxidation of stilbene **20** (where only one ring is substituted by a methyl group) also showed a departure compared to the other dialkyl-substituted stilbenes (**17**−**19**). In this instance, the epimeric indanyl acetamides were not obtained. Instead, in addition to the expected dehydrotetralin product **20c**, two epimeric tetralinyl acetamides (**20q** and **20r**) were obtained. Although initially isolated as a nonresolvable mixture, the **20r** epimer could eventually be separated by fractional crystallization from EtOH solution, which provided suitable crystals for X-ray diffraction analysis. The proposed pathway to these products is shown in Scheme 7. The absence of an activating alkyl group in the unsubstituted ring (B) resulted in path a not being favored, hence the absence of the indane products. Cyclization to the dehydrotetralin product in the usual manner (path c) gave **20c** except that, in this case, trapping of the intermediate cation by acetonitrile solvent (path b) competed to give the epimeric tetralinyl acetamide products.

The stilbenes of the third group correspond to those where strategic placement of donor groups, such as OMe and OH, leads on electrooxidation to the formation of ampelopsin F and pallidol-type carbon skeletons.[39,40] The structures of both products were confirmed by X-ray diffraction analysis (X-ray structures of **21p**, **22p**, **22s**, **23p**, **23s**, and **25p** are in

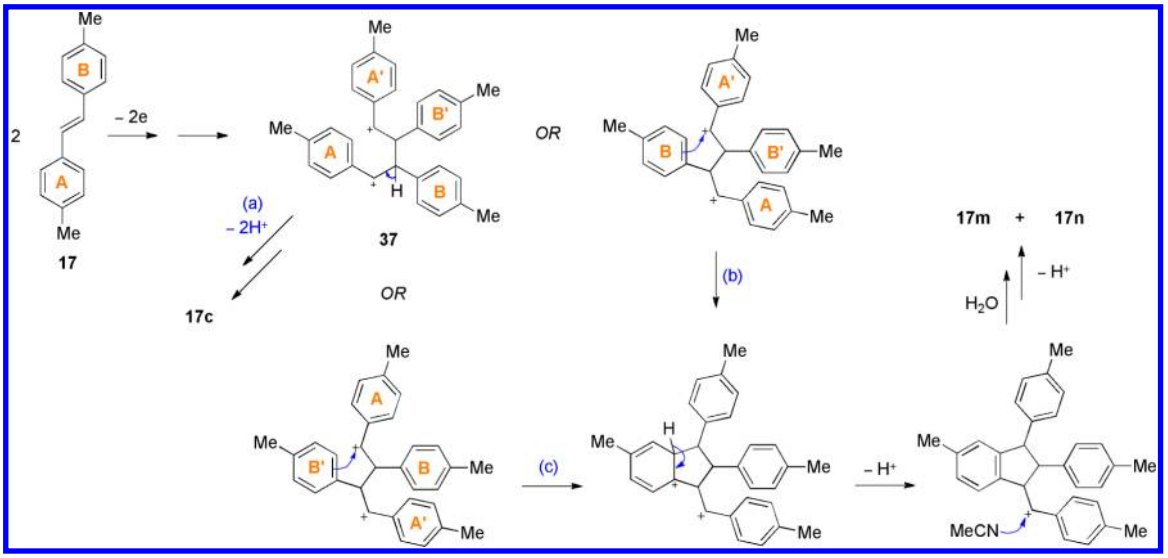
**Chart 3**



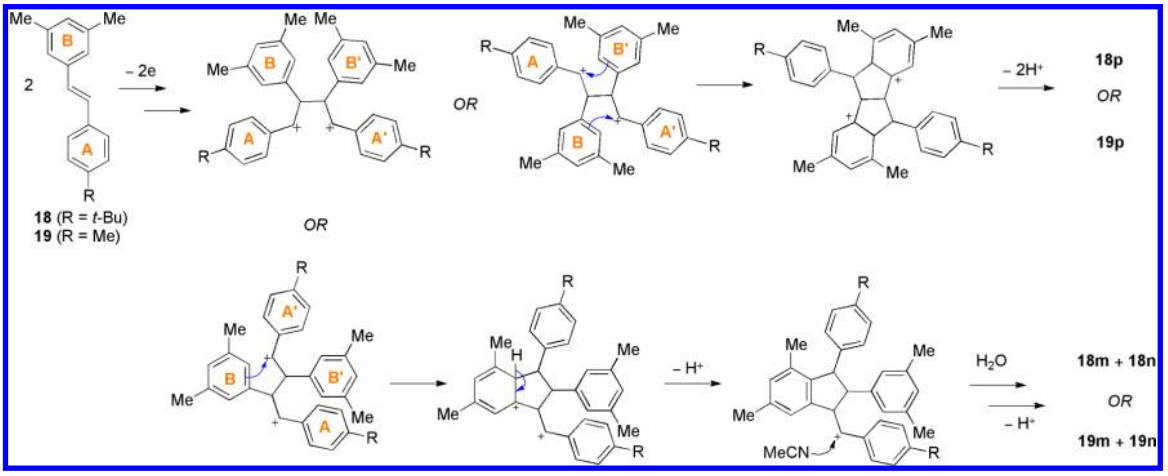


dx.doi.org/10.1021/jo500559r | J. Org. Chem. 2014, 79, 4528−4543

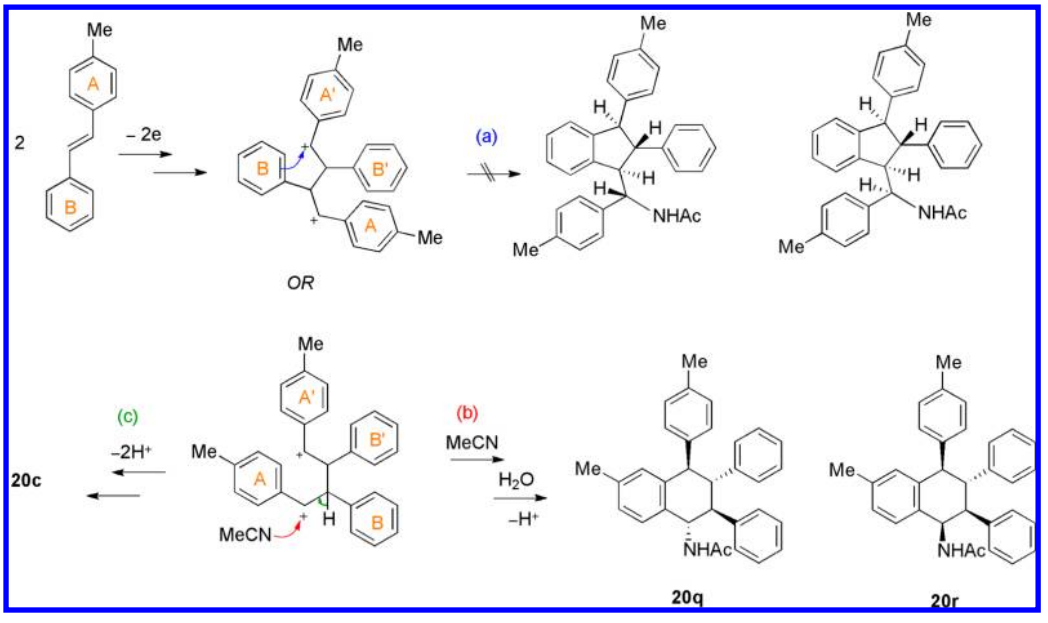
Scheme 5. Proposed Mechanism for the Formation of the Products in the Anodic Oxidation of Stilbene 17




Scheme 6. Proposed Mechanism for the Formation of the Products in the Anodic Oxidation of Stilbenes 18 and 19




Scheme 7. Proposed Mechanism for the Formation of the Products in the Anodic Oxidation of Stilbene 20





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Supporting Information). The results are shown in Table 5 and Chart 4. In stilbenes of this type, the position of methoxy or hydroxy substitution is such as to provide the right directing and activating effects for facile aromatic substitution by the cationic electrophiles, resulting in a double cyclization to yield the two products that possess the ampelopsin F and pallidol-type carbon skeletons. The mechanism (Scheme 8) is illustrated for the case of stilbene **21** (entry 1, Table 5).

**Table 5. Products from the Anodic Oxidation of Stilbenes 21−25**[a]

| | | % yield[b] | | | |
|---|---|---|---|---|---|
| entry | stilbene | a | p | s | total |
| 1 | **21** | | **21p** | **21s** | |
| | | | 30 | 51 | 81 |
| 2 | **22** | | **22p** | **22s** | |
| | | | 13 | 29 | 42 |
| 3 | **23** | | **23p** | **23s** | |
| | | | 14 | 8 | 22 |
| 4 | **24** | **24a** | **24p** | **24s** | |
| | | 6 | 16 | 36 | 58 |
| 5 | **25** | **25a** | **25p** | **25s** | |
| | | 33 | 12 | 5 | 50 |

[a]Pt anode, Pt cathode, vs $Ag/AgNO_3$ in MeCN/0.2 M $LiClO_4$. [b]Isolated yields.

In this case, two types of cation radical coupling occur because there is little difference between the 4-OMe versus the 3,4-OMe substituents from the viewpoint of benzylic carbocation stabilization. The "symmetrical" coupling at the benzylic carbons, both of which are associated with 3,4-dimethoxyaryl groups, leads to a dication, which, following electrophilic aromatic substitution, furnishes the pallidol-type product **21p**. The alternative "unsymmetrical" coupling between the benzylic carbon associated with a 3,4-dimethoxyaryl group and another benzylic carbon associated with a 4-methoxyaryl group leads in the same manner to the ampelopsin F-type product, **21s**.

The same regiochemistry of the initial coupling was observed for the other stilbenes **23**−**25**. In the symmetrically substituted tetramethoxystilbene **22**, both pallidol and ampelopsin F products derive from the same dication (Scheme 9). On the basis of the mechanism presented, substitution of two donor (methoxy) groups, one at the para position in one ring and another at the meta position in the other ring, would represent the minimum requirement (in terms of aromatic substitution, for the required activating and directing effects for electrophilic substitution), for the formation of the pallidol- and ampelopsin F-type products, as a result of double intramolecular cyclization of the dicationic intermediate. This is shown in the case of stilbene **25** (4-MeO-$C_6H_4$CH=CH$C_6H_4$−OMe-3′), where although both the ampelopsin F and pallidol products were formed (Table 5, **25p** and **25s**, respectively), the tetrahydrofuran product (**25a**) was also obtained in this case (Scheme 10).

The present investigation has thus provided valuable insight into how subtle changes in the nature and position of the aromatic substituents can affect the course of the electrochemical oxidation of stilbenes. These effects are entirely consistent with the mechanistic rationalization of the results based on interpretation of the anodically generated radical cation intermediate, both as a radical (dimerization or coupling), as well as a cation (electrophilic aromatic substitution, trapping by solvent nucleophiles).

## EXPERIMENTAL SECTION

**Synthesis of Stilbenes.** Stilbenes were synthesized following literature procedures (vide supra).[14−17] Compound characterization data for new stilbenes are as follows:

*4-Methoxy-3′-trifluoromethylstilbene (**11**).* White solid (1.64 g, 78%); mp 66−68 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.83 (3H, s), 6.92 (2H, d, $J$ = 8.6 Hz), 6.95 (1H, d, $J$ = 16.3 Hz), 7.11 (2H, d, $J$ = 16.3 Hz), 7.45 (4H, m), 7.63 (1H, d, $J$ = 6.7 Hz), 7.72 (1H, s); HRESIMS $m/z$ 279.0980 $[M + H]^+$ (calcd for $C_{16}H_{13}OF_3$ + H, 279.0991).

*3,4-Dimethoxy-4′-methylstilbene (**12**).* White solid (32.1 mg, 86%); mp 111−112 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.34 (3H, s), 3.88 (3H, s), 6.83 (1H, d, $J$ = 8.3 Hz), 6.93 (1H, d, $J$ = 16.3 Hz), 6.99 (1H, d, $J$ = 16.3 Hz), 7.02 (1H, dd, $J$ = 8.3, 1.9 Hz), 7.05 (1H, d, $J$ = 1.9 Hz), 7.14 (2H, d, $J$ = 8.1 Hz), 7.38 (2H, d, $J$ = 8.1 Hz); HRESIMS $m/z$ 255.1372 $[M + H]^+$ (calcd for $C_{17}H_{18}O_2$ + H, 255.1380).

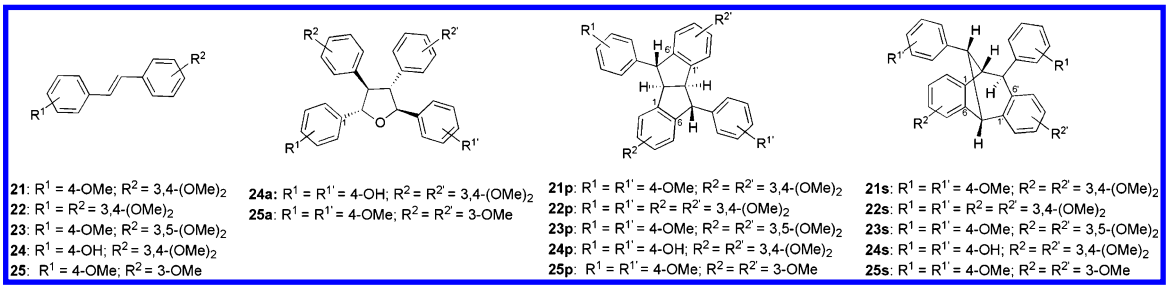
*4-N,N-Dimethylamino-4′-trifluoromethylstilbene (**16**).* Yellow solid (36.6 mg, 84%); mp 217−219 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.99 (6H, s), 6.71 (2H, d, $J$ = 8.8 Hz), 6.90 (1H, d, $J$ = 16.3 Hz), 7.11 (1H, d, $J$ = 16.3 Hz), 7.42 (2H, d, $J$ = 8.8 Hz), 7.54 (4H, s); HRESIMS $m/z$ 292.1307 $[M + H]^+$ (calcd for $C_{17}H_{16}F_3N$ + H, 292.1313).

*4-tert-Butyl-3′,5′-dimethylstilbene (**18**).* White solid (20.0 mg, 75%); mp 67−69 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.37 (9H, s), 2.36 (6H, s), 6.93 (1H, s), 7.04 (1H, d, $J$ = 16.4 Hz), 7.11 (1H, d, $J$ = 16.4 Hz), 7.17 (1H, s), 7.41 (2H, d, $J$ = 8.3 Hz), 7.47 (2H, d, $J$ = 8.3 Hz); HRESIMS $m/z$ 265.1964 $[M + H]^+$ (calcd for $C_{20}H_{24}$ + H, 265.1953).

*4,3′,5′-Trimethylstilbene (**19**).* Colorless crystals (24.3 mg, 73%); mp 39−40 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.41 (6H, s), 2.43 (3H, s), 3.94 (3H, s), 6.97 (1H, s), 7.08 (1H, d, $J$ = 16.3 Hz), 7.15 (1H, d, $J$ = 16.3 Hz), 7.21 (2H, s), 7.23 (2H, d, $J$ = 8.2 Hz), 7.48 (2H, d, $J$ = 8.2 Hz); HRESIMS $m/z$ 223.1476 $[M + H]^+$ ($C_{17}H_{18}$ + H).

**General Procedure for Cyclic Voltammetry.** All cyclic voltammetry experiments were carried out in a divided cell fitted with a Teflon cell top and a nitrogen inlet. The electrodes used were a Pt electrode (1.6 mm diameter) or a C electrode (3.0 mm diameter for

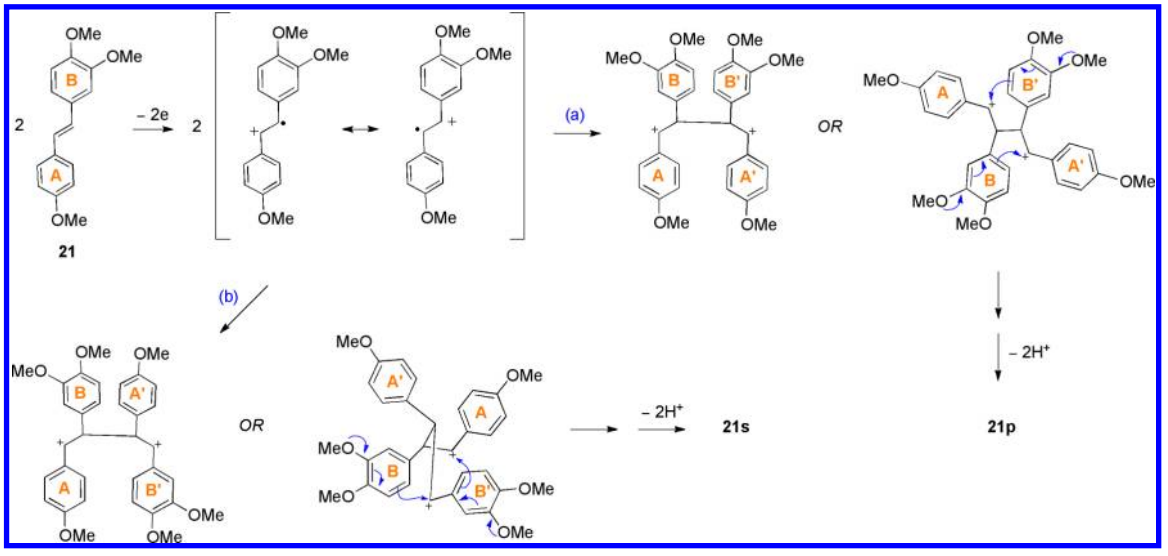
**Chart 4**



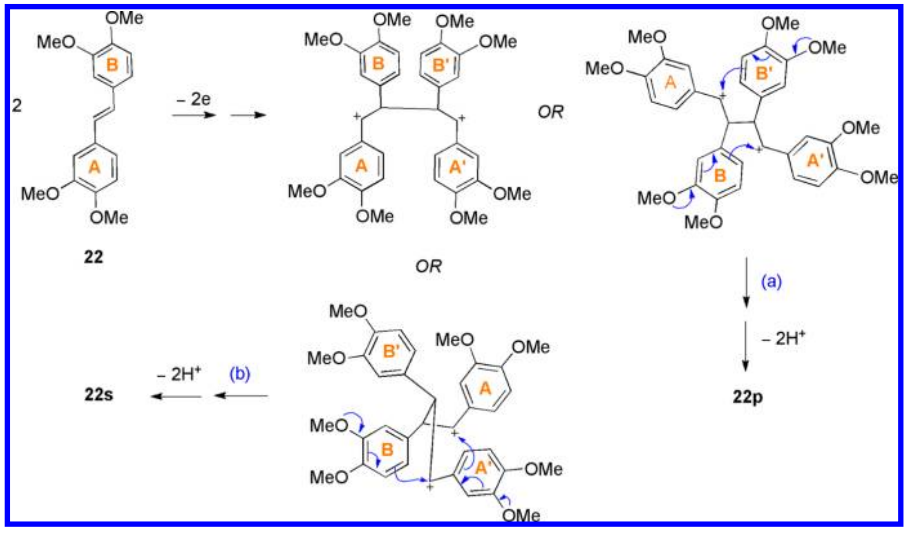


dx.doi.org/10.1021/jo500559r | J. Org. Chem. 2014, 79, 4528−4543

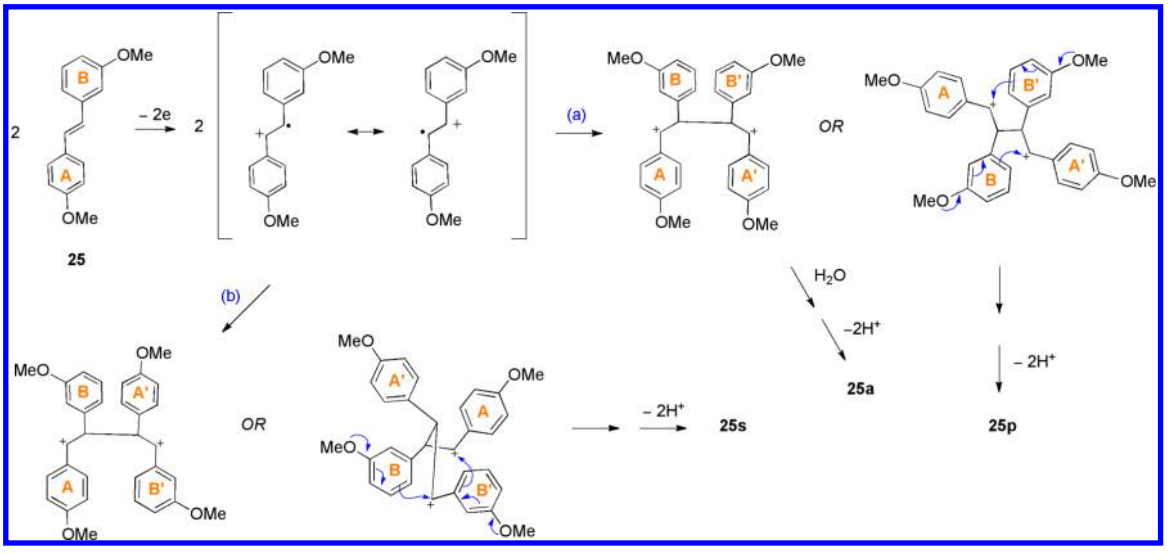
**Scheme 8. Formation of Products in the Anodic Oxidation of Stilbene 21**




**Scheme 9. Formation of Products in the Anodic Oxidation of Stilbene 22**




**Scheme 10. Formation of Products in the Anodic Oxidation of Stilbene 25**





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CV carried out in MeOH/$CH_2Cl_2$) as the working electrodes, with Pt as the counter electrode and Ag/$AgNO_3$ (0.01 M)/TEAP (0.1 M in MeCN) as the reference electrode.

**General Procedure for Electrochemical Oxidation (Controlled Potential Electrolysis).** To the electrochemical cell containing 0.2 M $LiClO_4$ in 25 mL of MeCN was added the corresponding stilbene (ca. 0.2 mmol) under nitrogen or argon. Bulk electrolysis was carried out using a Pt gauze electrode (working electrode), Pt (counter electrode), and Ag/$AgNO_3$ (0.01 M)/TEAP (0.1 M in MeCN) (reference electrode) with stirring, and the electrolysis was allowed to proceed until 1 F $mol^{-1}$ of charge had been transferred at the first anodic wave. The reaction mixture was then concentrated by evaporation under reduced pressure, and $CH_2Cl_2$ (10 mL) was then added. The mixture was then poured into $H_2O$ and extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic layer was then washed with $H_2O$, dried ($Na_2SO_4$), and concentrated under reduced pressure, and the resulting residue was then fractionated by various chromatographic methods until pure compounds were obtained. In cases requiring nonaqueous workup, the reaction mixture was concentrated by evaporation under reduced pressure until a slurry was obtained. The residue was then dissolved in $CH_2Cl_2$ and eluted through a short $SiO_2$ column with $CH_2Cl_2$ to give a crude product mixture, which upon further fractionation by various chromatographic methods (Centrifugal preparative TLC; HPLC; LH20) gave the pure products.

**Anodic Oxidation of 1 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **1** (+0.84 V, 1 F $mol^{-1}$) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 2:1 hexanes/$CH_2Cl_2$ to 100% $CH_2Cl_2$) gave two fractions. HPLC of the first fraction (Chiralpak IA column, 10% *i*-PrOH/*n*-hexane, 1.0 mL/min) gave **1c** (0.5 mg, 1%) and **1d** (2.3 mg, 5%), while HPLC of the second fraction (Luna Phenyl-Hexyl column, 18% $H_2O$/MeCN, 15 mL/min) gave **1a** (29.0 mg, 56%), **1b** (11.5 mg, 22%), **1e** (3.0 mg, 5%). See Table 2 and Table 3, entry 1.

*(2S,3R,4R,5S)-2,3,4,5-Tetrakis(4-methoxyphenyl)tetrahydrofuran (**1a**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$Et_2O$; mp 118−122 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.52 (2H, dd, $J$ = 6.3, 2.7 Hz), 3.71 (6H, s), 3.78 (6H, s), 5.26 (2H, dd, $J$ = 6.3, 2.7 Hz), 6.73 (4H, d, $J$ = 8.6 Hz), 6.83 (4H, d, $J$ = 8.6 Hz), 6.98 (4H, d, $J$ = 8.6 Hz), 7.22 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 497.2327 $[M + H]^+$ (calcd for $C_{32}H_{32}O_5$ + H, 497.2323).

*(2R,3S,4R,5S)-2,3,4,5-Tetrakis(4-methoxyphenyl)tetrahydrofuran (**1b**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$CH_2Cl_2$; mp 100−102 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.66 (2H, dd, $J$ = 4.6, 1.6 Hz), 3.71 (6H, s), 3.77 (6H, s), 5.47 (2H, dd, $J$ = 4.6, 1.6 Hz), 6.63 (4H, d, $J$ = 8.8 Hz), 6.79 (4H, d, $J$ = 8.8 Hz), 6.83 (4H, d, $J$ = 8.8 Hz), 7.33 (4H, d, $J$ = 8.8 Hz); HRESIMS $m/z$ 497.2323 $[M + H]^+$ (calcd for $C_{32}H_{32}O_5$ + H, 497.2323).

*(1R,2R)-7-Methoxy-1,2,3-tris(4-methoxyphenyl)-1,2-dihydronaphthalene (**1c**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$CH_2Cl_2$; mp 138−142 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.70 (3H, s), 3.71 (6H, s), 3.72 (3H, s), 3.80 (2H, s), 6.53 (1H, d, $J$ = 2.7 Hz), 6.73 (6H, m), 6.74 (1H, m), 7.05 (1H, s), 7.09 (2H, d, $J$ = 8.2 Hz), 7.16 (2H, d, $J$ = 8.6 Hz), 7.22 (1H, d, $J$ = 8.2 Hz), 7.29 (2H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 501.2038 $[M + Na]^+$ (calcd for $C_{32}H_{30}O_4$ + Na, 501.2036).

*(1R,2R)-6-Methoxy-1,2,3-tris(4-methoxyphenyl)-1,2-dihydronaphthalene (**1d**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.69 (3H, s), 3.70 (3H, s), 3.72 (3H, s), 3.81 (3H, s), 4.12 (1H, br s), 4.16 (1H, br s), 6.63 (1H, dd, $J$ = 8.3, 2.7 Hz), 6.74 (6H, m), 6.86 (1H, d, $J$ = 2.7 Hz), 6.88 (1H, d, $J$ = 8.3 Hz), 7.05 (1H, s), 7.08 (2H, d, $J$ = 8.6 Hz), 7.16 (2H, d, $J$ = 8.6 Hz), 7.31 (2H, d, $J$ = 9.0 Hz); HRESIMS $m/z$ 479.2216 $[M + H]^+$ (calcd for $C_{32}H_{30}O_4$ + H, 479.2217).

*(2S,3R)-2,3,4,4-Tetrakis(4-methoxyphenyl)butanal (**1e**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.66 (3H, s), 3.72 (3H, s), 3.76 (1H, m), 3.77 (3H, s), 3.78 (3H, s), 3.84 (1H, m), 4.59 (1H, d, $J$ = 9.5 Hz), 6.61 (2H, d, $J$ = 8.6 Hz), 6.64 (2H, d, $J$ = 8.6 Hz), 6.82 (4H, m), 6.83 (4H, m), 6.93 (2H, d, $J$ = 8.6 Hz), 7.23 (2H, d, $J$ = 8.6 Hz), 9.54 (1H, d, $J$ = 3.2 Hz); HRESIMS $m/z$ 519.2142 $[M + Na]^+$ (calcd for $C_{32}H_{32}O_5$ + Na, 519.2142).

**Anodic Oxidation of 10 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **10** (+1.08 V) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 3:1 hexanes/$CH_2Cl_2$ to 100% $CH_2Cl_2$) gave **10a** (15.9 mg, 31%), **10b** (15.9 mg, 31%), and a mixture of dehydrotetralins (**10c** and **10d**). Fractional crystallization of the mixture from EtOH−$CH_2Cl_2$ gave **10c** (colorless crystals, 4.0 mg, 8%) and **10d** (1.0 mg, 2%). See Table 3, entry 10.

*(2S,3R,4R,5S)-2,5-Bis(4-methoxyphenyl)-3,4-bis(4-(trifluoromethyl)phenyl)tetrahydrofuran (**10a**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$Et_2O$; mp 140−142 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.71 (2H, dd, $J$ = 6.3, 2.7 Hz), 3.79 (6H, s), 5.35 (2H, dd, $J$ = 6.3, 2.7 Hz), 6.85 (4H, d, $J$ = 8.6 Hz), 7.18 (4H, d, $J$ = 8.2 Hz), 7.20 (4H, d, $J$ = 8.6 Hz), 7.46 (4H, d, $J$ = 8.2 Hz); HRESIMS $m/z$ 573.1842 $[M + H]^+$ (calcd for $C_{32}H_{26}F_6O_3$ + H, 573.1859).

*(2R,3S,4R,5S)-2,5-Bis(4-methoxyphenyl)-3,4-bis(4-(trifluoromethyl)phenyl)tetrahydrofuran (**10b**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$Et_2O$; mp 121−126 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.80 (6H, s), 3.92 (2H, br d, $J$ = 5.2 Hz), 5.58 (2H, br d, $J$ = 5.2 Hz), 6.91 (4H, d, $J$ = 8.4 Hz), 7.04 (4H, d, $J$ = 8.4 Hz), 7.38 (8H, d, $J$ = 8.4 Hz); HRESIMS $m/z$ 573.1860 $[M + H]^+$ (calcd for $C_{32}H_{26}F_6O_3$ + H, 573.1859).

*(1R,2R)-7-Methoxy-1-(4-methoxyphenyl)-2,3-bis(4-(trifluoromethyl)phenyl)-1,2-dihydronaphthalene (**10c**).* Light yellowish oil, and subsequently, colorless block crystals from EtOH/$CH_2Cl_2$; mp 130−136 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.73 (3H, s), 3.74 (3H, s), 4.20 (1H, br s), 4.28 (1H, br s), 6.57 (1H, d, $J$ = 2.7 Hz), 6.79 (2H, d, $J$ = 8.8 Hz), 6.83 (1H, dd, $J$ = 8.2, 2.7 Hz), 7.11 (2H, d, $J$ = 8.8 Hz), 7.30 (1H, s), 7.34 (1H, d, $J$ = 8.2 Hz), 7.39 (2H, d, $J$ = 8.5 Hz), 7.41 (2H, d, $J$ = 8.3 Hz), 7.47 (2H, d, $J$ = 8.3 Hz), 7.49 (2H, d, $J$ = 8.5 Hz); HRESIMS $m/z$ 555.1761 $[M + H]^+$ (calcd for $C_{32}H_{24}F_6O_2$ + H, 555.1753).

*(1R,2R)-6-Methoxy-1-(4-methoxyphenyl)-2,3-bis(4-(trifluoromethyl)phenyl)-1,2-dihydronaphthalene (**10d**).* Yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.72 (3H, s), 3.84 (3H, s), 4.16 (1H, br s), 4.27 (1H, br s), 6.70 (1H, dd, $J$ = 8.2, 2.7 Hz), 6.75 (2H, d, $J$ = 8.6 Hz), 6.89 (1H, d, $J$ = 8.2 Hz), 6.92 (1H, d, $J$ = 2.7 Hz), 7.05 (2H, d, $J$ = 8.6 Hz), 7.23 (1H, s), 7.28 (2H, d, $J$ = 8.4 Hz), 7.33 (2H, d, $J$ = 7.9 Hz), 7.46 (4H, br d, $J$ = 7.9 Hz); HRESIMS $m/z$ 555.1750 $[M + H]^+$ (calcd for $C_{32}H_{24}F_6O_2$ + H, 555.1753).

**Anodic Oxidation of 14 in MeCN/0.2 M $LiClO_4$ or 5% $H_2O$/MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **14** (+0.33 V, in MeCN) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 1:1 hexanes/$CH_2Cl_2$, $NH_3$-saturated to 100% $CH_2Cl_2$, $NH_3$-saturated) gave a semipure fraction. This fraction was loaded onto a Sephadex LH20 column and eluted with MeOH to give **14a** (16.0 mg, 31%), **14f** (0.5 mg, 1%), and **14k** (13.9 mg, 27%). Controlled potential electrolysis of **14** (+0.37 V, in 5% $H_2O$/MeCN) gave after similar fractionation **14a** (15.7 mg, 30%), **14b** (6.3 mg, 12%), **14f** (10.7 mg, 20%), and **14k** (11.3 mg, 22%). See Table 3, entries 15 and 16.

*4,4′-((2S,3R,4R,5S)-3,4-Bis(4-methoxyphenyl)tetrahydrofuran-2,5-diyl)bis(N,N-dimethylaniline) (**14a**).* Yellowish oil, and subsequently, yellowish block crystals from MeOH/$CH_2Cl_2$; mp 177−179 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.91 (12H, s), 3.54 (2H, dd, $J$ = 6.3, 3.2 Hz), 3.71 (6H, s), 5.23 (2H, dd, $J$ = 6.3, 3.2 Hz), 6.67 (4H, d $J$ = 8.6 Hz), 6.71 (4H, d $J$ = 8.6 Hz), 6.99 (4H, d, $J$ = 8.6 Hz), 7.18 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 523.2966 $[M + H]^+$ (calcd for $C_{34}H_{38}N_2O_3$ + H, 523.2961).

*4,4′-((2S,3R,4R,5S)-3,4-Bis(4-methoxyphenyl)tetrahydrofuran-2,5-diyl)bis(N,N-dimethylaniline) (**14b**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.92 (12H, s), 3.67 (2H, d, $J$ = 3.2 Hz), 3.71 (6H, s), 5.45 (2H, d, $J$ = 3.2 Hz), 6.63 (4H, d $J$ = 8.6 Hz), 6.69 (4H, d $J$ = 8.6 Hz), 6.81 (4H, d, $J$ = 8.6 Hz), 7.31 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 523.2958 $[M + H]^+$ (calcd for $C_{34}H_{38}N_2O_3$ + H, 523.2961).

*(2S,3R)-4,4-Bis(4-(dimethylamino)phenyl)-2,3-bis(4-methoxyphenyl)butanal (**14f**).* Yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.75 (6H, s), 2.92 (6H, s), 3.67 (3H, s), 3.78 (3H, s), 3.85 (1H, d, $J$ = 3.8 Hz), 4.03 (1H, d, $J$ = 12.0 Hz), 4.64 (1H, dd, $J$ = 12.0, 3.8 Hz), 6.43 (2H, d, $J$ = 8.5 Hz), 6.51 (2H, d, $J$ = 8.5 Hz), 6.54 (2H, d, $J$ = 8.5 Hz), 6.73 (6H, m), 6.98 (2H, d, $J$ = 8.5 Hz), 7.34 (2H, d, $J$ =


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8.7 Hz), 9.55 (1H, s); HRESIMS $m/z$ 523.2978 $[M + H]^+$ (calcd for $C_{34}H_{38}N_2O_3$ + H, 523.2961).

*4,4′-((2R,3R,4R,5S)-3,4-Bis(4-methoxyphenyl)tetrahydrofuran-2,5-diyl)bis(N,N-dimethylaniline) (**14k**).* Yellowish oil, and subsequently, yellowish needles from hexanes/$CH_2Cl_2$; mp 175−178 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.87 (6H, s), 2.96 (6H, s), 3.53 (1H, t, $J$ = 9.9 Hz), 3.67 (3H, s), 3.74 (3H, s), 4.02 (1H, dd, $J$ = 9.9, 8.5 Hz), 5.10 (1H, d, $J$ = 9.9 Hz), 5.54 (1H, d, $J$ = 8.5 Hz), 6.55 (4H, d, $J$ = 8.3 Hz), 6.72 (2H, d, $J$ = 8.7 Hz), 6.76 (2H, d, $J$ = 8.3 Hz), 6.78 (2H, d, $J$ = 8.3 Hz), 7.01 (2H, d, $J$ = 8.3 Hz), 7.10 (2H, d, $J$ = 8.3 Hz), 7.30 (2H, d, $J$ = 8.7 Hz); HRESIMS $m/z$ 561.2516 $[M + K]^+$ (calcd for $C_{34}H_{38}N_2O_3$+ K, 561.2520).

**Anodic Oxidation of 17 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **17** (+1.09 V) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 4:1 hexanes/$CH_2Cl_2$ to 100% $CH_2Cl_2$) gave **17c** (6.5 mg, 15%) and a mixture of acetamides (**17m** and **17n**). Crystals were obtained from MeOH/$CH_2Cl_2$, which were shown by X-ray analysis to be 1:1 cocrystals of the epimers. HPLC (Chiralpak IA column, 10% *i*-PrOH/*n*-hexane, 0.5 mL/min) of the acetamide mixture gave **17m** (16.5 mg, 32%) and **17n** (16.5 mg, 32%). See Table 4, entry 1.

*(1R,2R)-7-Methyl-1,2,3-tri-p-tolyl-1,2-dihydronaphthalene (**17c**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$Et_2O$; mp 134−139 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.24 (3H, s), 2.29 (9H, s), 4.22 (1H, s), 4.25 (1H, s), 6.84 (1H, s), 7.04 (1H, m), 7.05 (6H, m), 7.14 (2H, d, $J$ = 8.2 Hz), 7.21 (1H, m), 7.24 (2H, d, $J$ = 7.7 Hz), 7.25 (1H, d, $J$ = 7.7 Hz), 7.32 (2H, d, $J$ = 8.2 Hz); HRESIMS $m/z$ 415.2431 $[M + H]^+$ (calcd for $C_{32}H_{30}$ + H, 415.2420).

*N-((S)-((1R,2S,3R)-5-Methyl-2,3-di-p-tolyl-2,3-dihydro-1H-inden-1-yl)(p-tolyl)methyl)acetamide (**17m**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.54 (3H, s), 2.23 (3H, s), 2.33 (6H, s), 2.38 (3H, s), 3.35 (1H, t, $J$ = 9.3 Hz), 4.09 (1H, d, $J$ = 9.3 Hz), 4.17 (1H, d, $J$ = 9.3 Hz), 5.31, (1H, t, $J$ = 9.3 Hz), 5.44 (1H, br s), 6.34 (1H, d, $J$ = 7.4 Hz), 6.71 (1H, s), 6.83 (2H, d, $J$ = 7.4 Hz), 6.91 (2H, d, $J$ = 7.7 Hz), 7.02 (2H, d, $J$ = 8.2 Hz), 7.07 (4H, m), 7.17 (2H, d, $J$ = 7.7 Hz), 7.28 (2H, d, $J$ = 7.7 Hz); HRESIMS $m/z$ 474.2784 $[M + H]^+$ (calcd for $C_{34}H_{35}NO$ + H, 474.2791).

*N-((R)-((1R,2S,3R)-5-Methyl-2,3-di-p-tolyl-2,3-dihydro-1H-inden-1-yl)(p-tolyl)methyl)acetamide (**17n**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.94 (3H, s), 2.26 (3H, s), 2.30 (3H, s), 2.32 (6H, s), 3.25 (1H, t, $J$ = 10.0 Hz), 4.00 (1H, br d, $J$ = 9.0 Hz), 4.32 (1H, d, $J$ = 10.0 Hz), 5.48 (1H, dd, $J$ = 9.0, 2.3 Hz), 5.73 (1H, d, $J$ = 2.3 Hz), 6.75 (1H, br s), 6.84 (2H, d, $J$ = 7.9 Hz), 6.86 (1H, br d, $J$ = 8.2 Hz), 6.96 (1H, d, $J$ = 8.2 Hz), 7.03 (2H, d, $J$ = 7.9 Hz), 7.12 (8H, m); HRESIMS $m/z$ 474.2786 $[M + H]^+$ (calcd for $C_{34}H_{35}NO$ + H, 474.2791).

**Anodic Oxidation of 18 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **18** (+1.18 V) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 4:1 hexanes/$CH_2Cl_2$ to 100% $CH_2Cl_2$) gave **18p** (5.0 mg, 8%) and a mixture of acetamides (**18m** and **18n**). HPLC of the mixture (Chiralpak IB column, 2% EtOH/*n*-hexane, 0.7 mL/min) gave **18m** (20.0 mg, 34%) and **18n** (20.0 mg, 34%). See Table 4, entry 2.

*N-((S)-(4-(tert-Butyl)phenyl)((1R,2S,3R)-3-(4-(tert-butyl)phenyl)-2-(3,5-dimethylphenyl)-4,6-dimethyl-2,3-dihydro-1H-inden-1-yl)-methyl)acetamide (**18m**).* Colorless oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.31 (18H, s), 1.66 (3H, s), 1.88 (3H, s), 2.18 (6H, s), 2.20 (3H, s), 3.15 (1H, t, $J$ = 8.2 Hz), 3.68 (1H, t, $J$ = 8.2 Hz), 4.34 (1H, d, $J$ = 8.2 Hz), 5.29 (1H, t, $J$ = 8.2 Hz), 5.42 (1H, d, $J$ = 8.2 Hz), 6.31 (1H, s), 6.44 (2H, s), 6.78 (1H, s), 6.87 (1H, s), 6.88 (2H, d, $J$ = 7.8 Hz), 7.09 (2H, d, $J$ = 8.7 Hz), 7.26 (2H, d, $J$ = 7.8 Hz), 7.30 (2H, d, $J$ = 8.7 Hz); HRESIMS $m/z$ 586.4030 $[M + H]^+$ (calcd for $C_{42}H_{51}NO$ + H, 586.4049).

*N-((R)-(4-(tert-Butyl)phenyl)((1R,2S,3R)-3-(4-(tert-butyl)phenyl)-2-(3,5-dimethylphenyl)-4,6-dimethyl-2,3-dihydro-1H-inden-1-yl)-methyl)acetamide (**18n**).* Colorless oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.27 (9H, s), 1.30 (9H, s), 1.76 (3H, s), 1.80 (3H, s), 2.24 (3H, s), 2.26 (6H, s), 3.14 (1H, t, $J$ = 6.0 Hz), 3.80 (1H, t, $J$ = 6.0 Hz), 4.31 (1H, d, $J$ = 8.0 Hz), 5.43 (1H, dd, $J$ = 9.2, 6.0 Hz), 5.65 (1H, d, $J$ = 9.2 Hz), 6.46 (1H, s), 6.73 (2H, s), 6.76 (2H, d, $J$ = 8.7 Hz), 6.86 (1H, s), 6.87 (1H, s), 7.08 (2H, d, $J$ = 8.2 Hz), 7.19 (2H, d, $J$ = 8.7 Hz), 7.29 (2H, d, $J$ = 8.2 Hz); HRESIMS $m/z$ 586.4035 $[M + H]^+$ (calcd for $C_{42}H_{51}NO$ + H, 586.4049).

*(4bR,5R,9bR,10R)-5,10-Bis(4-(tert-butyl)phenyl)-1,3,6,8-tetramethyl-4b,5,9b,10-tetrahydroindeno[2,1-a]indene (**18p**).* Colorless oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.26 (18H, s), 1.94 (6H, s), 2.34 (6H, s), 4.00 (2H, s), 4.52 (2H, s), 6.76 (2H, s), 6.99 (4H, d, $J$ = 8.7 Hz), 7.20 (2H, s), 7.23 (4H, d, $J$ = 8.7 Hz); HRESIMS $m/z$ 527.3687 $[M + H]^+$ (calcd for $C_{40}H_{46}$ + H, 527.3678).

**Anodic Oxidation of 21 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **21** (+0.76 V) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 1:2 hexanes/$CH_2Cl_2$ to 100% $CH_2Cl_2$) gave a semipure fraction. This fraction was loaded onto a Sephedex LH20 column and eluted with 20% MeCN/MeOH to give **21p** (14.9 mg, 30%) and **21s** (25.4 mg, 51%). See Table 5, entry 1.

*(4bR,5R,9bR,10R)-2,3,7,8-Tetramethoxy-5,10-bis(4-methoxyphenyl)-4b,5,9b,10-tetrahydroindeno[2,1-a]indene (**21p**).* Light yellowish oil, and subsequently, colorless block crystals from hexanes/$Et_2O$; mp 181−183 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.73 (6H, s), 3.79 (6H, s), 3.92 (6H, s), 4.05 (2H, br s), 4.44 (2H, br s), 6.52 (2H, s), 6.86 (4H, d, $J$ = 8.6 Hz), 6.91 (2H, s), 7.09 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 539.2419 $[M + H]^+$ (calcd for $C_{34}H_{34}O_6$ + H, 539.2428).

*(5S,10S,11S,12R)-2,3,7,8-Tetramethoxy-11,12-bis(4-methoxyphenyl)-10,11-dihydro-5H-5,10-methanodibenzo[a,d][7]annulene (**21s**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.39 (1H, s), 3.64 (3H, s), 3.67 (3H, s), 3.80 (4H, s), 3.83 (3H, s), 3.87 (3H, s), 3.92 (1H, s), 3.93 (3H, s), 4.23 (1H, s), 6.41 (1H, s), 6.65 (2H, d, $J$ = 8.4 Hz), 6.74 (1H, s), 6.75 (1H, s), 6.85 (2H, d, $J$ = 8.4 Hz), 6.87 (2H, d, $J$ = 8.6 Hz),7.00 (1H, s), 7.18 (2H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 539.2406 $[M + H]^+$ (calcd for $C_{34}H_{34}O_6$ + H, 539.2428).

**Anodic Oxidation of 24 in MeCN/0.2 M $LiClO_4$.** Controlled potential electrolysis of **24** (+0.75 V) yielded a mixture, which on centrifugal preparative TLC ($SiO_2$, 100% $CH_2Cl_2$ to 5% MeOH/$CH_2Cl_2$), followed by HPLC (Luna Phenyl−Hexyl column, 60% $H_2O$/MeCN to 40% $H_2O$/MeCN in 7 min, 15 mL/min), gave **24a** (3.1 mg, 6%), **24p** (9.0 mg, 16%), and **24s** (18.0 mg, 36%). See Table 5, entry 4.

*4,4′-((2S,3R,4R,5S)-3,4-Bis(3,4-dimethoxyphenyl)-tetrahydrofuran-2,5-diyl)diphenol (**24a**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.50 (2H, dd, $J$ = 6.3, 2.7 Hz), 3.69 (6H, s), 3.79 (6H, s), 5.24 (2H, dd, $J$ = 6.3, 2.7 Hz), 5.32 (2H, br s), 6.47 (2H, d, $J$ = 1.5 Hz), 6.64 (2H, dd, $J$ = 8.4, 1.5 Hz), 6.69 (2H, d, $J$ = 8.4 Hz), 6.74 (4H, d, $J$ = 8.6 Hz), 7.17 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 529.2205 $[M + H]^+$ (calcd for $C_{32}H_{32}O_7$ + H, 529.2226).

*4,4′-((4bR,5R,9bR,10R)-2,3,7,8-Tetramethoxy-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-5,10-diyl)diphenol (**24p**).* Light yellowish oil; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.72 (6H, s), 3.90 (6H, s), 4.00 (2H, s), 4.39 (2H, s), 5.05 (2H, br s), 6.50 (2H, s), 6.77 (4H, d, $J$ = 8.6 Hz), 6.88 (2H, s), 7.00 (4H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 511.2121 $[M + H]^+$ (calcd for $C_{32}H_{30}O_6$ + H, 511.2115).

*4,4′-((5S,10S,11S,12R)-2,3,7,8-Tetramethoxy-10,11-dihydro-5H-5,10-methanodibenzo[a,d][7]annulene-11,12-diyl)diphenol (**24s**).* Light yellowish oil, and subsequently, light yellowish block crystals from hexanes/acetone; mp 164−166 °C; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 3.33 (1H, s), 3.61 (3H, s), 3.73 (1H, s), 3.79 (3H, s), 3.84 (3H, s), 3.87 (1H, s), 3.90 (3H, s), 4.18 (1H, s), 5.57 (1H, br s), 5.77 (1H, br s), 6.39 (1H, s), 6.56 (2H, d, $J$ = 8.6 Hz), 6.72 (2H, s), 6.75 (2H, d, $J$ = 8.6 Hz), 6.77 (2H, d, $J$ = 8.6 Hz), 6.96 (1H, s), 7.07 (2H, d, $J$ = 8.6 Hz); HRESIMS $m/z$ 511.2120 $[M + H]^+$ (calcd for $C_{32}H_{30}O_6$ + H, 511.2115).

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1$H and $^{13}$C NMR (except **3d**, **4d**, and **5d**) spectra for stilbenes and electrochemical oxidation products. Experimental procedure and compound characterization data for the synthesis and anodic oxidation of stilbenes. Representative cyclic voltammograms of selected stilbenes. X-ray structures and crystallo-


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graphic data in CIF format for compounds **1a**, **1b**, **1c**, **29**, **1h**, **1i**, **2a**, **2b**, **2d**, **4b**, **6d**, **7c**, **9a**, **10a**, **10b**, **10c**, **12c**, **14a**, **14k**, **15b**, **16a**, **16k**, **17c**, **17m** and **17n** (cocrystal), **19p**, **20c**, **20r**, **21p**, **22p**, **22s**, **23p**, **23s**, and **25p**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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