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

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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, dehydratetralins, and aldehydes (p-MeO or p-NMe2 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 dehydratetralins (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. 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. 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. 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). 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. These studies have shed valuable light on radical cation reactivity and have also led to applications in synthesis. Radical cations can also be accessed via non-electrochemical methods, for example, by electron-transfer using suitable one-electron oxidants or more recently, via visible light photocatalysis based on the use of transition metal polypyridyl complexes as facile SET agents. 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. 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. 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. In view of the paucity of electrochemical studies, except for several early kinetic investigations of the anodic oxidation of 4,4′-dimethoxystilbene, we decided to initiate a systematic study of the electrochemical oxidation of 1,2-diarylalkenes, which we...
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

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

<table>
<thead>
<tr>
<th>entry</th>
<th>stilbene</th>
<th>methoda</th>
<th>% yield</th>
<th>mp (lit.) (°C)</th>
<th>(E_{p/2}) (V)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>A</td>
<td>77</td>
<td>203–204 (207–210)18</td>
<td>+0.68</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>B</td>
<td>89</td>
<td>80–82 (92)19</td>
<td>+0.72</td>
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<tr>
<td>3</td>
<td>3</td>
<td>B</td>
<td>87</td>
<td>156–158 (166–167)20</td>
<td>+0.82</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>B</td>
<td>64</td>
<td>168–169 (162–163)21</td>
<td>+0.84</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>B</td>
<td>86</td>
<td>170–173 (168–170)15a</td>
<td>+0.96</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>B</td>
<td>64</td>
<td>138–139 (133–141)22</td>
<td>+1.00</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>B</td>
<td>68</td>
<td>123–124 (130–131)22</td>
<td>+1.00</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>C</td>
<td>79</td>
<td>176–177 (190)20</td>
<td>+0.84</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>C</td>
<td>70</td>
<td>143–145 (147–149)23</td>
<td>+0.83</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>C</td>
<td>90</td>
<td>170–172 (171–172)15a</td>
<td>+0.92</td>
</tr>
<tr>
<td>11</td>
<td>11</td>
<td>C</td>
<td>78</td>
<td>66–68</td>
<td>+0.94</td>
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<tr>
<td>12</td>
<td>12</td>
<td>B</td>
<td>86</td>
<td>111–112</td>
<td>+0.76</td>
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<td>13</td>
<td>13</td>
<td></td>
<td>79</td>
<td>120–123 (125–126)24</td>
<td>+0.75</td>
</tr>
<tr>
<td>14</td>
<td>14</td>
<td>B</td>
<td>70</td>
<td>175–176 (171.9–173.4)25</td>
<td>+0.20</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
<td>B</td>
<td>90</td>
<td>160–162 (163–165)26</td>
<td>+0.26</td>
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<tr>
<td>16</td>
<td>16</td>
<td>B</td>
<td>84</td>
<td>217–219</td>
<td>+0.30</td>
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<td>17</td>
<td>17</td>
<td>A</td>
<td>70</td>
<td>176–178 (179–180)15a</td>
<td>+0.94</td>
</tr>
<tr>
<td>18</td>
<td>18</td>
<td>B</td>
<td>75</td>
<td>67–69</td>
<td>+1.03</td>
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<tr>
<td>19</td>
<td>19</td>
<td>B</td>
<td>73</td>
<td>39–40</td>
<td>+1.01</td>
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<tr>
<td>20</td>
<td>20</td>
<td>B</td>
<td>80</td>
<td>111–113 (116–118)18</td>
<td>+1.10</td>
</tr>
<tr>
<td>21</td>
<td>21</td>
<td>B</td>
<td>58</td>
<td>132–134 (138)27</td>
<td>+0.62</td>
</tr>
<tr>
<td>22</td>
<td>22</td>
<td>A</td>
<td>83</td>
<td>145–148 (154.6–155.0)28</td>
<td>+0.61</td>
</tr>
<tr>
<td>23</td>
<td>23</td>
<td>B</td>
<td>70</td>
<td>51–52 (55–56)29</td>
<td>+0.83</td>
</tr>
<tr>
<td>24</td>
<td>24</td>
<td>B</td>
<td>87</td>
<td>176–178 (180–182)29</td>
<td>+0.60</td>
</tr>
<tr>
<td>25</td>
<td>25</td>
<td>B</td>
<td>90</td>
<td>100–101 (104–105)27</td>
<td>+0.81</td>
</tr>
</tbody>
</table>

aMethod 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/AgNO₃, MeCN/LiClO₄).

Scheme 1. Products from Anodic Oxidation of 1 As Reported by Steckhan and Eberson13a,c
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/AgNO₃) 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/CH₂Cl₂, 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/0.1 M LiClO₄ 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 LiClO₄) showed the presence of two irreversible waves at +0.74 and +1.37 V versus Ag/AgNO₃ in the potential range investigated as revealed by cyclic voltammetry. Controlled potential electrolysis (Pt gauze anode, Pt cathode; MeCN/0.2 M LiClO₄) at the first anodic wave (+0.84 V) was allowed to proceed until consumption of 1 F mol⁻¹.

### Table 2. Products from the Anodic Oxidation of 1 under Different Conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>1a</th>
<th>1b</th>
<th>1c</th>
<th>1d</th>
<th>1e</th>
<th>1f</th>
<th>1g</th>
<th>1h</th>
<th>1i</th>
<th>1j</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeCN/0.2 M LiClO₄, +0.84 V</td>
<td>56</td>
<td>22</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>MeCN/0.2 M LiClO₄, +0.84 V</td>
<td>17</td>
<td>8</td>
<td>4</td>
<td>22</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1% H₂O/MeCN/0.2 M LiClO₄, +0.88 V</td>
<td>38</td>
<td>20</td>
<td>2</td>
<td>7</td>
<td>3</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>25% MeOH/CH₂Cl₂/0.2 M LiClO₄, +0.80 V</td>
<td>11</td>
<td>3</td>
<td>28</td>
<td>14</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>25% MeOH/CH₂Cl₂/0.2 M LiClO₄, +0.80 V</td>
<td>40</td>
<td>10</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0.25 M NaOAc, 25% AcOH/MeCN/0.1 M LiClO₄, +0.80 V</td>
<td>40</td>
<td>22</td>
<td>62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*aPt anode, Pt cathode, vs Ag/AgNO₃.* Isolated yields. *Nonaqueous workup.*
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 Br₂/CH₂Cl₂ 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/CH₂Cl₂/LiClO₄ (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/LiClO₄ 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/CH₂Cl₂. 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 CH₂Cl₂ and eluted through a short SiO₂ column with CH₂Cl₂), the amount of the tetrahydrofuran products was markedly reduced, while the yield of the dehydrotetratin products increased (Table
2, entry 2; a small amount of tetrahydrofuran products due to water present in SiO2.\textsuperscript{30}

When electrooxidation was carried out in MeCN/LiClO\textsubscript{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\textsubscript{3}Cl\textsubscript{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 dicarboxylic intermediate 31 as the dominant step, as previously demonstrated by the kinetic studies of Steckhan.\textsuperscript{31a} Subsequent attack of the dicarboxylic 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\textsubscript{2} axis, and which gives rise to the major C\textsubscript{2}-symmetric tetrahydrofuran product 1a, and the other a "meso"-dication 31b, which gives rise to the meso-tetrahydrofuran product 1b (Figure 1).

![Diagram of the formation of stereoisomeric tetrahydrofurans 1a and 1b.](Image)

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 regiosomeric dehydrotetralins (especially 1d where methoxy migration has occurred) appears to be less clear-cut, and we rationalize its formation as follows.

Dicarboxylic 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.\textsuperscript{31f–33} Ring expansion from 35 via path c involving a 1,2-p-methoxybenzyl shift followed by deprotonation leads to the expected regiosomer 1c. The alternative 1,2-p-methoxystyril 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-methoxystyril 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\textsubscript{3}Cl\textsubscript{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\textsubscript{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 spirocatic 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 spirocatic 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\textsubscript{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\textsubscript{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 amelpolin 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\textsuperscript{1}=C\textsubscript{6}H\textsubscript{4}−CH=CH−C\textsubscript{6}H\textsubscript{4}−R\textsuperscript{2}, where R\textsuperscript{1} = 4-OMe; R\textsuperscript{2} = 2-OMe, 4-Me, 4-t-Bu, 4-CO\textsubscript{2}Me, 4-CN, 4-NO\textsubscript{2}, 4-Cl, 4-F, 4-Cl\textsubscript{2}CF\textsubscript{3} or 3-Cl\textsubscript{2}CF\textsubscript{3} (i.e., 1–11), the products are the tetraaryltetrahydrofurans (major), dehydrotetralins, and aldehydes.\textsuperscript{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
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 usual 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-CH=CH<sub>2</sub> (where R<sup>2</sup> = R<sup>2</sup> substituent), 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<sup>2</sup> 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-β-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-CH=CH<sub>2</sub> (where R<sup>2</sup> = 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<sup>2</sup>-styryl shift (R<sup>2</sup> = 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 as shown in Scheme 4. This is in contrast to stilbene 3 (R<sup>1</sup> = 4-OMe, R<sup>2</sup> = 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<sup>1</sup> = 4-NMe<sub>2</sub> and R<sup>2</sup> = 4′-OMe, 4′-Me, or 4′-CF<sub>3</sub>. 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 tetraarylcation radical as exemplified by the oxidation of a stilbene where the substituent in one ring is p-OMe (α = −0.78), while the substituent in the other ring is a stronger donor than p-OMe, e.g., p-NMe<sub>2</sub> (α = −1.70). In such a case, in the tetrahydrofuran products, the α- and α′-aryl groups are 4-NMe<sub>2</sub>−C<sub>6</sub>H<sub>4</sub>− and 4′-OMe−C<sub>6</sub>H<sub>4</sub>−. This is in contrast to all the other stilbenes examined thus far, where the reverse is the case, that is, where the α- and α′-aryl groups are 4′-OMe−C<sub>6</sub>H<sub>4</sub>− (R<sup>1</sup> = OMe), whereas the β- and β′-aryl groups are 4-OMe−C<sub>6</sub>H<sub>4</sub>−. 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 benzylidene carbon with greater carbocation character. Similar results from two other related examples were also consistent with this conclusion (15, R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = Me; 16, R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = CF<sub>3</sub>). 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<sub>2</sub> 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...
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_{6}H_{4}CH═CHC_{6}H_{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_{2}Cl_{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

### Table 3. Products from the Anodic Oxidation of Stilbenes 1−16

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**Notes:**
- Pt anode, Pt cathode, vs Ag/AgNO_{3} in MeCN/0.2 M LiClO_{4} unless otherwise stated.
- Isolated yields.
- Traces of aldehyde products observed in NMR spectra of product mixtures.
- Electrolysis in 25% MeOH/CH_{2}Cl_{2}/0.2 M LiClO_{4}.
- Electrolysis in 5% H_{2}O/MeCN/0.2 M LiClO_{4}.
- Traces of tetrahydrofuran products observed in NMR spectra of product mixtures.
Scheme 4. Formation of Dehydrotetralins 12c and 13c in Anodic Oxidation of Stilbenes 12 and 13
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 carboxation 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 (R1 = 4-t-Bu, R2 = 3,5-Me2) and 19 (R1 = 4-Me, R2 = 3,5-Me2), 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

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aPt anode, Pt cathode, vs Ag/AgNO3 in MeCN/0.2 M LiClO4.
bIsolated yields.
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
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 amelopsin F and pallidol-type carbon skeletons. The mechanism (Scheme 8) is illustrated for the case of stilbene 21 (entry 1, Table 5).

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-dimethoxystilbene, traps by solvent nucleophiles. The same regiochemistry of the initial coupling was observed for the other stilbenes 23–25. In the symmetrically substituted tetramethoxystilbene 22, both pallidol and amelopsin F products derive from the same dication (Scheme 9). On the basis of the mechanism presented, substitution of two donor sites, 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 amelopsin 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-CHCl2CH═CH2CH3=O-Me-3’), where although both the amelopsin F and pallidol products were formed (Table 5, 25p and 25s, respectively), the tetrahydropurpurin 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:

1. **4-Methoxy-3′-trifluoromethylstilbene (11).** White solid (1.64 g, 78%); mp 66–68 °C; H NMR (CDCl3, 400 MHz) δ 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 279.0990 [M + H]+ (calcd for C16H13OF3 +H , 279.0991).

2. **3,4-Dimethoxy-4′-methylstilbene (12).** White solid (321.2 mg, 86%); mp 111–112 °C; H NMR (CDCl3, 400 MHz) δ 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, 19.3 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 C16H14O2 +H , 255.1380).

3. **4-N,N-Dimethylamino-4′-methylstilbene (16).** Yellow solid (36.6 mg, 84%); mp 217–219 °C; H NMR (CDCl3, 400 MHz) δ 6.299 (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 C18H24F3 +H , 292.1313).

4. **4-tert-Butyl-3′,5′-dimethylstilbene (18).** White solid (20.0 mg, 75%); mp 67–69 °C; H NMR (CDCl3, 400 MHz) δ 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 C19H24 +H , 265.1983).

5. **3,5′-Trimethylstilbene (19).** Yellow solid (24.3 mg, 73%); mp 39–40 °C; 1H NMR (CDCl3, 400 MHz) δ 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]+ (C13H18 +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.
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
CV carried out in MeOH/CH2Cl2 as the working electrodes, with Pt as the counter electrode and Ag/AgNO3 (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 LiClO4 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/AgNO3 (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 CH2Cl2 (10 mL) was then added. The mixture was then poured into H2O and extracted with CH2Cl2 (3 × 20 mL). The combined organic layer was then washed with H2O, dried (Na2SO4), 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 CH2Cl2 and eluted through a short SiO2 column with CH2Cl2 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 LiClO4.** Controlled potential electrolysis of 1 (0.084 V, 1 F mol\(^{-1}\)) yielded a mixture, which on centrifugal preparative TLC (SiO2, 2:1 hexanes/CH2Cl2 to 100% CH2Cl2) gave two fractions. HPLC of the first fraction (Chiralpak IA column, 10% i-PrOH/n-hexane, 1.0 mL/min) gave 1b (0.5 mg, 1%) and 1d (2.3 mg, 5%), while HPLC of the second fraction (Luna Phenyl-Hexyl column, 18% H2O/MeCN, 15 mL/min) gave 1a (29.0 mg, 56%), 1b (11.5 mg, 22%), 1c (3.0 mg, 5%). See Table 2 and Table 3, entry 1.

\[(25,3R,8R,5S)-2,3,4,5-Tetakis(4-methoxyphenyl)tetrahydrofuran (1a)\]

Light yellow oil, and subsequently, colorless block crystals from hexanes/EtO; mp 118–122 °C; 1H NMR (CDCl3, 400 MHz) δ 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 C32H32O5 + H, 497.2323)

\[(25,3R,8R,5S)-2,3,4,5-Tetakis(4-methoxyphenyl)tetrahydrofuran (1b)\]

Light yellow oil, and subsequently, colorless block crystals from hexanes/CH2Cl2; mp 100–102 °C; 1H NMR (CDCl3, 400 MHz) δ 3.66 (2H, dd, J = 4.6, 1.6 Hz), 3.71 (6H, s), 5.77 (6H, s), 5.47 (2H, dd, J = 4.6, 1.6 Hz), 6.63 (4H, d, J = 8.6 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 C32H32O5 + H, 497.2323)

\[(1R,2R)-7-Methoxy-1-(4-methoxyphenyl)-2,3-bis(4-fluoromethyl)tetrahydrofuran (10a)\]

Yellowish oil, 1F NMR (CDCl3, 400 MHz) δ 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), 6.92 (1H, d, J = 8.7 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 555.1761 [M + H]+ (calcd for C36H34F2O2 + H, 555.1753)

\[(1R,2R)-6-Methoxy-1-(4-methoxyphenyl)-2,3-bis(4-fluoromethyl)tetrahydrofuran (10b)\]

Yellowish oil, 1F NMR (CDCl3, 400 MHz) δ 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), 6.92 (1H, d, J = 8.7 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 555.1760 [M + H]+ (calcd for C36H34F2O2 + H, 555.1753)

**Anodic Oxidation of 10 in MeCN/0.2 M LiClO4.** Controlled potential electrolysis of 10 (+0.33 V, in MeCN) yielded a mixture, which on centrifugal preparative TLC (SiO2, 1:1 hexanes/CH2Cl2, NH3-saturated to 100% CH2Cl2, NH3-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%), 14b (0.5 mg, 1%), and 14k (15.9 mg, 27%). Controlled potential electrolysis of 14 (+0.37 V, in 5% H2O/MeCN) gave after similar fractionation 14a (15.7 mg, 30%), 14b (6.3 mg, 12%), 14d (10.7 mg, 20%), and 14k (11.3 mg, 22%). See Table 3, entries 15 and 16.

\[(25,3R,8R,5S)-3,4-Bis(4-methoxyphenyl)tetrahydrofuran-2,5-diyldibis(N,N-dimethyline) (14a)\]

Yellow oil, and subsequently, yellowish block crystals from MeOH/CH2Cl2; mp 177–179 °C; 1H NMR (CDCl3, 400 MHz) δ 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 C32H30N2O2 + H, 523.2959)

\[(25,3R,8R,5S)-3,4-Bis(4-methoxyphenyl)tetrahydrofuran-2,5-diyldibis(N,N-dimethyline) (14b)\]

Yellowish oil; 1H NMR (CDCl3, 400 MHz) δ 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 C32H30N2O2 + H, 523.2961)

\[(25,3R,8R,5S)-3,4-Bis(4-dimethylamino)phenyl)benzal (14e)\]

Yellow oil; 1H NMR (CDCl3, 400 MHz) δ 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, d, 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 = 8.5 Hz)
8.7 Hz), 9.55 (1H, s); HRESIMS m/z 523.3978 [M + H]^+ (calcd for C_{24}H_{26}N_2O_5 + H, 523.3961).

(44′-((2R,3R,4R,5S)-3,4-Bis(4-methoxyphenyl)tetrathyrofuoran-2,5-diyldibis(N,N-dimethylaniline) (14k)). Yellowish oil, and subsequently, yellowish needles from hexanes/CH_2Cl_2 mp 175–178 °C; ^1H NMR (CDCl_3, 400 MHz) δ 2.87 (6H, s), 2.96 (6H, s), 3.53 (1H, t, J = 8.2 Hz), 3.74 (1H, s), 1.74 (3H, s), 1.88 (3H, s), 2.20 (1H, s), 2.28 (3H, s), 3.15 (1H, t, J = 8.2 Hz), 3.68 (1H, t, J = 8.2 Hz), 4.34 (1H, q, J = 6.2 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 = 7.8 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_{24}H_{26}NO_3 + H, 586.4049).

Anodic Oxidation of 17 in MeCN/0.2 M LiClO_4. Controlled potential electrolysis of 17 (+0.76 V) yielded a mixture, which on centrifugal preparative TLC (SiO_2; 4:1 hexanes/CH_2Cl_2 to 100% CH_2Cl_2) gave a semisolid fraction. This fraction was loaded onto a Sephadex LH20 column and eluted with 20% MeCN/MeOH to give 21p (14.9 mg, 30%) and 21s (25.4 mg, 5%). See Table S, entry 1.

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 semisolid fraction. This fraction was loaded onto a Sephadex LH20 column and eluted with 20% MeCN/MeOH to give 21p (14.9 mg, 30%) and 21s (25.4 mg, 5%). See Table S, entry 1.
graphic data in CIF format for compounds 1a, 1b, 1c, 29, 1h, 1i, 2a, 2b, 2d, 4b, 6d, 7c, 9a, 10a, 10b, 1oc, 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**
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**REFERENCES**

(30) If the reaction mixture was evaporated to complete dryness before passing through SiO2, no THF products were detected; only the regioisomeric dehydrotetralins were obtained in slightly increased yields. The reaction was also characterized by overall lower yields of products and the concomitant observation of significant polar polymeric side products.
(34) Several naturally occurring tetrahydrofurans (restrytisols A and B), in addition to a naturally occurring dehydrotetralin (restrytisol C) and pallidol, have been obtained via microbial oxidation of resveratrol.12k
(35) Dehydrotetralins and tetralins have been obtained from oxidation of certain stilbenes with FeCl3.12d,i
(37) The indane acetamides obtained from the anodic oxidation of stilbenes 17–19 incorporate a core carbon skeleton reminiscent of that in quadrangularin A (or ampelopsin D) and related polyphenols (see also ref 40). These compounds have also been obtained from the reaction of resveratrol with peroxidases12b or from stilbenes with one-electron oxidants.12k
(39) Pallidol- and ampelopsin F-type products have also been produced by the reaction of various stilbenes with peroxidases12b and with various one-electron oxidants such as FeCl3, MnO2, and K3[Fe(CN)6].12b,a,b