

# Lewis Acid-Promoted Reactions of Unsymmetrically Substituted Stilbenes with 2-Methoxy-1,4-benzoquinones: Stereoselective Synthesis of *trans*-2,3-Diaryl-2,3-dihydrobenzofurans

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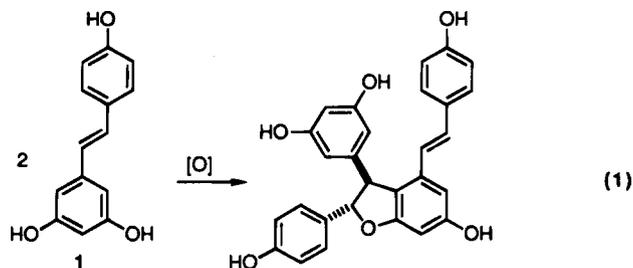
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Lewis acid (SnCl<sub>4</sub> or Ti(IV))-promoted reactions of 2-methoxy-1,4-benzoquinones with substituted (*E*)-4-methoxystilbenes stereoselectively yield *trans*-2-(4'-methoxyphenyl)-3-aryl-2,3-dihydrobenzofuran-5-ols in good yield.

## Introduction

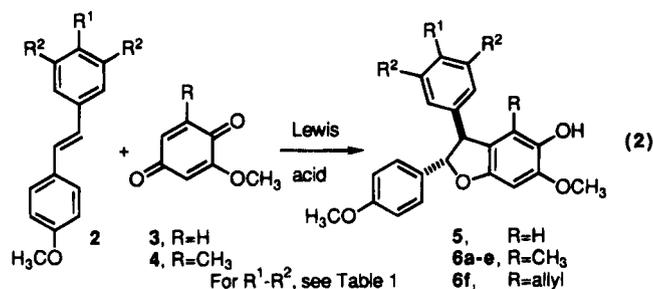
The 2,3-diaryl-2,3-dihydrobenzofuran moiety is found in a number of natural products, many of which display antifungal and/or antibacterial properties.<sup>1</sup> This moiety probably arises biogenetically through oxidative dimerization of resveratrol, **1**, and analogs, a postulate which is supported by studies on enzymatic oxidations (eq 1).<sup>2</sup> Because of their biological properties and possible roles in biological systems as phytoalexins or constitutive defense agents, there is considerable interest in resveratrol dimers, trimers, and higher oligomers.<sup>1–3</sup> A method for the efficient laboratory synthesis of 2,3-diaryl-2,3-dihydrobenzofurans would represent a potentially valuable starting point to access these classes of natural products and analogs. We recently reported a few examples of such a method based on Lewis acid-promoted reactions of stilbenes with 1,4-benzoquinones.<sup>4</sup> Herein, we report the details of an expanded study to define the scope and generality of this new method.



## Results and Discussion

Previous studies on Ti(IV)-promoted reactions of benzoquinones with styrenes established a general synthesis of *trans*-2-aryl-3-methyl-2,3-dihydrobenzofuran-5-ols.<sup>5</sup> Fol-

lowing similar procedures, reactions of stilbenes **2** with 2-methoxy-1,4-benzoquinones **3/4** promoted by either Ti(IV) or SnCl<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub> produced *trans*-2,3-diaryl-2,3-dihydrobenzofuran-5-ols **5/6**, respectively, generally in good yields (eq 2 and Table 1). In some cases, very low reaction temperatures gave the best results (entries 1, 2, 5, 6, and 8). The presence of a good electron-donating group on one ring of the stilbene is apparently required; attempted reactions of the quinones with (*E*)-stilbene and (*E*)-1-methyl-1,2-diphenylethene failed under a variety of conditions. However, with a *p*-methoxy group on one of the aryl rings of the stilbene, strong electron-withdrawing groups such as NO<sub>2</sub> are tolerated on the other. Polarized stilbenes are also apparently required; treatment of mixtures of **3** or **4** and (*E*)-4,4'-dimethoxystilbene with various Lewis acids at a number of different temperatures failed to give dihydrobenzofuran products.



Finally, reactions of 3,4,5-trimethoxystilbene (**2g**) with quinones **3/4** gave only low yields of dihydrobenzofuran products **5g/6g** under a variety of conditions (eq 3 and Table 2). The major products of these reactions were the biaryls **7/8**,<sup>6</sup> which apparently are formed via electrophilic aromatic substitution on the dimethoxyphenyl ring of the stilbene with the Lewis acid-bound quinone as the electrophile. Attempts to decrease the nucleophilicity of

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(1) (a) For a recent review, see: Sotheeswaran, S.; Pasupathy, V. *Phytochemistry* **1993**, *32*, 1083–1092. For additional examples, see the following: (b) Kitanaka, S.; Ikezawa, T.; Yasukawa, K.; Yamanouchi, S.; Takido, M.; Sung, H. K.; Kim, I. H. *Chem. Pharm. Bull.* **1990**, *38*, 432–435. (c) Lins, A. P.; Felicio, J. D.; Braggio, M. M.; Roque, L. C. *Phytochemistry* **1991**, *30*, 3144–3146. (d) Sultanbawa, M. U. S.; Surendrakumar, S.; Bladon, P. *Phytochemistry* **1987**, *26*, 799–801. (e) Oshima, Y.; Ueno, Y.; Hikino, H.; Yang, L.-L.; Yen, K.-Y. *Tetrahedron* **1990**, *46*, 5121–5126. (f) Powell, R. G.; Bajaj, R.; McLaughlin, J. L. *J. Nat. Prod.* **1987**, *50*, 293–296. (g) Nakajima, K.; Taguchi, H.; Endo, T.; Yoshioka, I. *Chem. Pharm. Bull.* **1978**, *26*, 3050–3057. (h) Kurihara, H.; Kawabata, J.; Ichikawa, S.; Mizutani, J. *Agric. Biol. Chem.* **1990**, *54*, 1097–1099.

(2) (a) Schultz, T. P.; Hubbard, T. F., Jr.; Jin, L.; Fisher, T. H.; Nicholas, D. D. *Phytochemistry* **1990**, *29*, 1501–1507. (b) Langcake, P.; Pryce, R. J. *J. Chem. Soc., Chem. Commun.* **1977**, 208–210. See also: (c) Donnelly, D. M. X.; Murphy, F. G.; Polonski, J.; Prangé, T. J. *Chem. Soc., Perkin Trans. I* **1987**, 2719–2722.

(3) For other examples, see the following: (a) Schultz, T. P.; Cheng, Q.; Boldin, W. D.; Hubbard, T. F., Jr.; Jin, L.; Fisher, T. H.; Nicholas, D. D. *Phytochemistry* **1991**, *30*, 2939–2945. (b) Hain, R.; Reif, H.-J.; Krause, E.; Langebartels, R.; Kindl, H.; Vornam, B.; Wiese, W.; Schmelzer, E.; Schreier, P. H.; Stöcker, R. H.; Stenzel, K. *Nature* **1993**, *361*, 153–156.

(4) Engler, T. A.; Draney, B. W.; Gfesser, G. A. *Tetrahedron Lett.* **1994**, *35*, 1661–1664.

(5) (a) Engler, T. A.; Combrink, K. D.; Letavic, M. A.; Lynch, K. O., Jr.; Ray, J. E. *J. Org. Chem.* **1994**, *59*, 6567–6587. (b) Engler, T. A.; Wei, D.; Letavic, M. A.; Combrink, K. D.; Reddy, J. P. *J. Org. Chem.* **1994**, *59*, 6588–6599.

(6) The structures of **7/8** were established by data from NMR experiments, including HMBC,<sup>4</sup> and other spectral data (IR, mass) and are further supported by subsequent chemical reactions. The latter experiments are included in the supplementary material.

Table 1. Lewis Acid-Promoted Reactions of Stilbenes **2** with 1,4-Benzoquinones **3/4**

entry	stilbene			quinone R	Lewis acid (equiv) <sup>a</sup>	temp (°C)	product	yield (%)
	no.	R <sup>1</sup>	R <sup>2</sup>					
1	<b>2a</b>	CH <sub>3</sub>	H	H	SnCl <sub>4</sub> (1.0)	-100	<b>5a</b>	84
2	<b>2a</b>	CH <sub>3</sub>	H	CH <sub>3</sub>	SnCl <sub>4</sub> (1.9)	-100	<b>6a</b>	88
3	<b>2b</b>	H	H	H	SnCl <sub>4</sub> (2.0)	-78	<b>5b</b>	73
4	<b>2b</b>	H	H	CH <sub>3</sub>	SnCl <sub>4</sub> (2.0)	-78	<b>6b</b>	82
5	<b>2c</b>	Cl	H	H	SnCl <sub>4</sub> (1.0)	-100	<b>5c</b>	89
6	<b>2c</b>	Cl	H	CH <sub>3</sub>	SnCl <sub>4</sub> (2.0)	-100	<b>6c</b>	77
7	<b>2d</b>	H	Br	H	SnCl <sub>4</sub> (1.1)	-78	<b>5d</b>	58
8	<b>2d</b>	H	Br	H	SnCl <sub>4</sub> (1.0)	-100	<b>5d</b>	93
9	<b>2e</b>	H	NO <sub>2</sub>	H	3:1 TiCl <sub>4</sub> :Ti(OiPr) <sub>4</sub> (2.0)	-78	<b>5e</b>	83
10	<b>2e</b>	H	NO <sub>2</sub>	CH <sub>3</sub>	TiCl <sub>4</sub> (2.3)	-78	<b>6e</b>	66
11	<b>2f</b>	H	O <sub>2</sub> CAr <sup>b</sup>	H	3:1 TiCl <sub>4</sub> :Ti(OiPr) <sub>4</sub> (2.2)	-78	<b>5f</b>	92
12	<b>2f</b>	H	O <sub>2</sub> CAr <sup>b</sup>	allyl	3:1 TiCl <sub>4</sub> :Ti(OiPr) <sub>4</sub> (2.0)	-78	<b>6f</b>	68

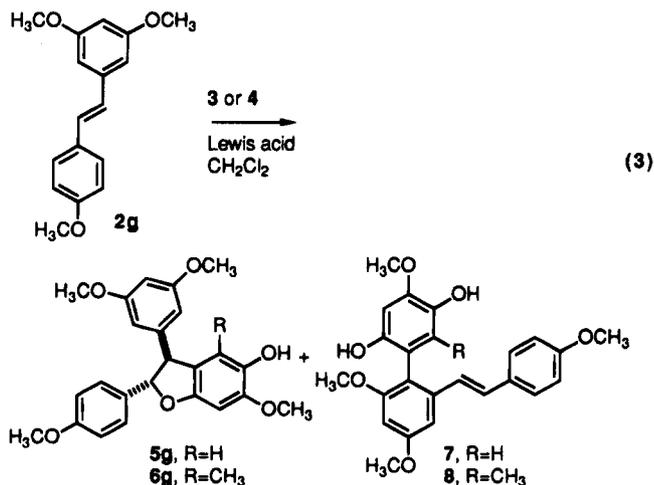
<sup>a</sup> With respect to quinone. <sup>b</sup> Ar = 2,6-C<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>.

Table 2. Lewis Acid-Promoted Reactions of Stilbene **2g** with Quinones **3/4**

entry	quinone	Lewis acid <sup>a</sup>	products (%)	
1	<b>3</b>	SnCl <sub>4</sub> (2.0)	<b>5g</b> (5)	<b>7</b> (52)
2	<b>3</b>	SnCl <sub>4</sub> (1.0)		<b>7</b> (52)
3	<b>3</b>	Ti(IV) (4) <sup>b</sup>	<b>5g</b> (5)	<b>7</b> (59)
4	<b>3</b>	SnCl <sub>4</sub> (22)	<b>5g</b> (13)	<b>7</b> (52)
5	<b>4</b>	SnCl <sub>4</sub> (2)	<b>6g</b> (3)	<b>8</b> (78)
6	<b>4</b>	SnCl <sub>4</sub> (15)	<b>6g</b> (9)	<b>8</b> (58)

<sup>a</sup> All reactions were done in CH<sub>2</sub>Cl<sub>2</sub> at -78 °C. <sup>b</sup> 2:1 TiCl<sub>4</sub>:Ti(OiPr)<sub>4</sub>.

this ring by coordination of the methoxy oxygens to excess Lewis acid failed (Table 2, entries 4 and 6).



The positions and stereochemistry of the substituents on the dihydrobenzofuran core of **5/6** are assigned on the basis of results from a combination of several NMR experiments. Three issues needed to be addressed in these experiments: (1) the position of the methoxy group and the methoxy/methyl groups in **5** and **6**, respectively; (2) the identity of the C-2 and C-3 aryl groups; and (3) the relative stereochemistry at C-2/C-3. Chemical shifts for H-4 and H-7 and chemical shifts and coupling constants for H-2 and H-3 in the series **5** and **6** were very similar and are summarized in Table 3.

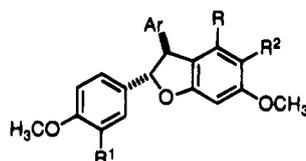
In the NMR spectra of compounds **5e-g**, H-4 and H-7 are well-resolved singlets, a fact which is consistent only with a C-6 methoxy substituent; for a 7-methoxydihydrobenzofuran,  $J_{H-4/H-6}$  would be expected to be ~2 Hz<sup>7</sup> and for a 4-methoxydihydrobenzofuran,  $J_{H-6/H-7}$  would be ~8 Hz. In addition, irradiation of H-3 in compound **5g** produced a weak NOE enhancement of the H-4 singlet (Figure 1). For the remaining compounds of the general

structure **5**, the singlets assigned to H-4 and H-7 were very close in chemical shift (~0.01 ppm), and there was concern that these two signals may be part of a partially visible AB quartet and thus indicative of a C-7 methoxy substitution pattern rather than a C-6. However, an HMBC experiment on **5a** confirmed the position of the C-6 methoxy group (Figure 2). In this experiment, the chemical shift of C-6 was identified by a <sup>3</sup>J with the C-6 methoxy hydrogens, and this carbon was further coupled to both H-4 (<sup>3</sup>J) and H-7 (<sup>2</sup>J). The assignment of the C-6 methoxy substituents in **5b-d** was made by analogy to **5a,e-g**.

In methyl-substituted dihydrobenzofurans **6b,g**, NOE enhancements of H-3 were observed on irradiation of the aryl methyl group, which indicated that this methyl group was located at C-4 (Figure 3). Further confirmation of the C-4 methyl group, and thus the C-6 methoxy group, came from an HMBC experiment on **6e** in which both H-3 and the C-4 methyl hydrogens were coupled to C-3a (Figure 4). The substitution pattern at C-4 through C-7 in **6a/c** was again assigned by analogy to **6b,e,g**.

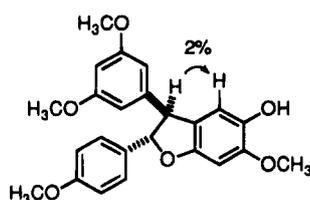
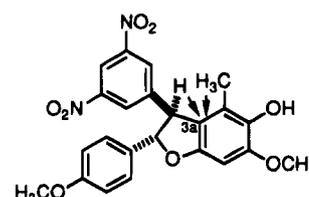
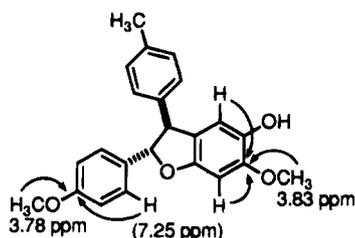
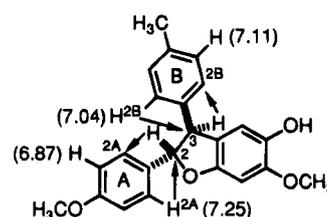
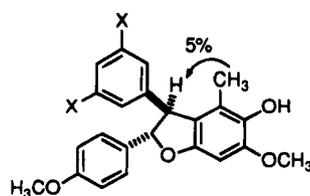
The identities of the aryl groups at C-2 and C-3 were established from HMBC and <sup>1</sup>H-<sup>1</sup>H NOE experiments. Compounds **5a,b,g** and **6b,e,g** were chosen as representative examples. In **5a**, all signals in the <sup>1</sup>H NMR spectrum, including the aryl-H signals, were well-resolved and assignments were made on the basis of chemical shift and coupling patterns as determined by decoupling or COSY experiments. Several key <sup>13</sup>C resonances were then identified through a HETCOR experiment, and the bond connectivity was confirmed through an HMBC experiment (Figure 5) in which H-2 was coupled to C-2A (<sup>3</sup>J) and H-3 was coupled to C-2B (<sup>3</sup>J). In addition, H-2A and H-2B were coupled (<sup>3</sup>J) to C-2 and C-3, respectively. Further evidence for the identity of the C-2 and C-3 aryl groups was provided by <sup>1</sup>H-<sup>1</sup>H NOE experiments. Thus, irradiation of H-2A in **5a** resulted in enhancements of both H-2 and H-3; however, the enhancement of H-2 was twice as great as that of H-3 (Figure 6). Irradiation of H-2B likewise produced enhancements of H-3 and H-2, with the former enhancement again being considerably larger than the latter. Similar results were found in HMBC and NOE experi-

(7) See refs 1h and 2b and the following: (a) Kurihara, H.; Kawabata, J.; Ichikawa, S.; Mishima, M.; Mizutani, J. *Phytochemistry* **1991**, *30*, 649-653. (b) Kawabata, J.; Ichikawa, S.; Kurihara, H.; Mizutani, J. *Tetrahedron Lett.* **1989**, *30*, 3785-3788. (c) Oshima, Y.; Kamijou, A.; Moritani, H.; Namao, K. i.; Ohizumi, Y. *J. Org. Chem.* **1993**, *58*, 850-853. (d) Sotheeswaran, S.; Sultanbawa, M. U. S.; Surendrakumar, S.; Balasubramaniam, S.; Bladon, P. *J. Chem. Soc., Perkin Trans. 1* **1985**, 159-162.

**Table 3.** Chemical Shifts ( $\delta$ , ppm) and Coupling Constants (Hz) of Selected Signals from 2,3-Diaryl-2,3-dihydrobenzofurans **5/6** and Related Compounds<sup>a</sup>

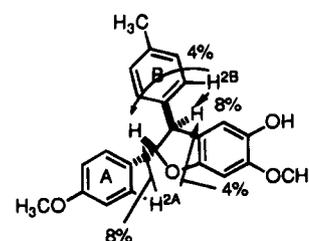
entry	compd	R	R <sup>1</sup>	R <sup>2</sup>	H-2	H-3	$J_{H-2/H-3}$	H-4	H-7	ref
1	<b>5a</b>	H	H	OH	5.40	4.47	8	6.57	6.55	this work
2	<b>5b</b>	H	H	OH	5.42	4.50	8	6.56	6.56	this work
3	<b>5c</b>	H	H	OH	5.33	4.46	8	6.54	6.53	this work
4	<b>5d</b>	H	H	OH	5.36	4.42	8	6.55	6.56	this work
5	<b>5e</b>	H	H	OH	5.39	4.74	7	6.61	6.51	this work
6	<b>5f</b>	H	H	OH	5.45	4.59	8	6.67	6.57	this work
7	<b>5g</b>	H	H	OH	5.42	4.41	8	6.59	6.54	this work
8	<i>b</i>	H	H	O-allyl	5.37	4.43	8	6.58	6.52	4
9	<b>6a</b>	CH <sub>3</sub>	H	OH	5.38	4.41	6		6.45	this work
10	<b>6b</b>	CH <sub>3</sub>	H	OH	5.41	4.44	6		6.47	this work
11	<b>6c</b>	CH <sub>3</sub>	H	OH	5.33	4.42	6		6.45	this work
12	<b>6e</b>	CH <sub>3</sub>	H	OH	5.37	4.69	5		6.52	this work
13	<b>6f</b>	allyl	H	OH	5.48	4.54	6		6.51	this work
14	<b>6g</b>	CH <sub>3</sub>	H	OH	5.40	4.36	6		6.44	this work
15	<i>b</i>	allyl	H	OH	5.34	4.38	5		6.50	4
16	<i>c</i>	CH <sub>3</sub>	OCH <sub>3</sub>	H	5.42	4.33	6		na <sup>e</sup>	1g
17	<b>12<sup>c</sup></b>	CH <sub>2</sub> R <sup>3</sup> <sup>d</sup>	H	H	5.44	4.26	6		~6.38	1h
18	<i>c</i>	CH <sub>2</sub> OH	OCH <sub>3</sub>	H	5.45	4.50	6		na <sup>e</sup>	1g
19	<i>c</i>	CH <sub>2</sub> OR <sup>4</sup> <sup>f</sup>	OCH <sub>3</sub>	H	5.46	4.45	6		na <sup>e</sup>	1g

<sup>a</sup> Solvent for all entries except 17 and 18 was CDCl<sub>3</sub>; solvent for entries 17 and 18 was acetone-*d*<sub>6</sub>. <sup>b</sup> Ar = C<sub>6</sub>H<sub>3</sub>-3,5-Br<sub>2</sub>. <sup>c</sup> Ar = C<sub>6</sub>H<sub>3</sub>-3,5-(OCH<sub>3</sub>)<sub>2</sub>. <sup>d</sup> R<sup>3</sup> = CH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>-4-OCH<sub>3</sub>. <sup>e</sup> na = not assigned. <sup>f</sup> R<sup>4</sup> = C(O)C<sub>6</sub>H<sub>4</sub>-4-Br.

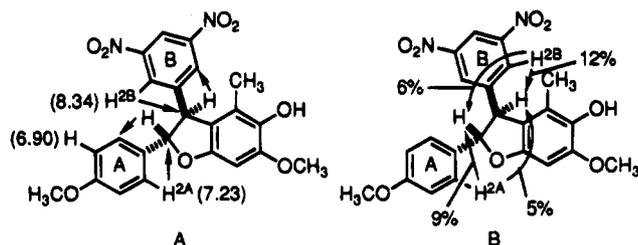
**Figure 1.** Selected <sup>1</sup>H-<sup>1</sup>H NOE data on **5g**.**Figure 4.** Selected data from an HMBC experiment on **6e**.**Figure 2.** Selected data from an HMBC experiment on **5a**.**Figure 5.** Selected data from an HMBC experiment on **5a** (chemical shifts are in ppm).**Figure 3.** Selected <sup>1</sup>H-<sup>1</sup>H NOE data on **6b** (X = H) and **6g** (X = OCH<sub>3</sub>).

ments on **6e** (Figure 7) and in NOE experiments on **5b,g** and **6b,g** (Figures summarizing these results are included in the supplementary material). We believe these results are indicative of the *p*-methoxyphenyl group in **5/6** at position 2.

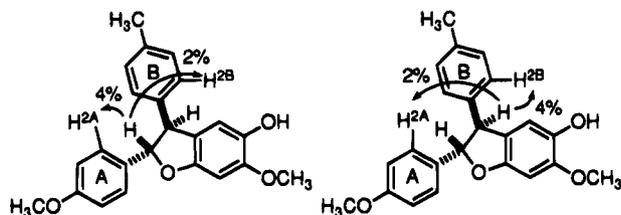
Results of additional <sup>1</sup>H-<sup>1</sup>H NOE experiments also support the assignment of a *trans* orientation between the C-2 and C-3 aryl groups. For example, irradiation of H-2

**Figure 6.** Selected <sup>1</sup>H-<sup>1</sup>H NOE data on **5a**.

in **5a** produced enhancements of the signals from H-2A (4%) and H-2B (2%), and irradiation of H-3 resulted in enhancements of the H-2B (4%) and H-2A (2%) signals (Figure 8). Experiments involving **5b,g** and **6b,e,g** gave similar results (figures summarizing these data are again included in the supplementary material). It has been shown previously that weak NOEs are occasionally



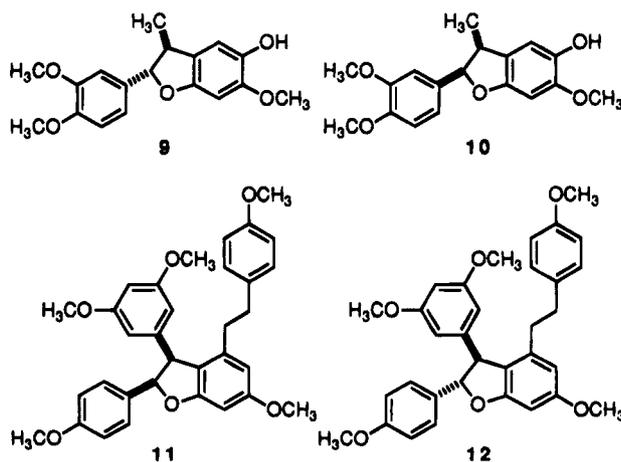
**Figure 7.** Selected data from HMBC (A) and  $^1\text{H}$ - $^1\text{H}$  NOE (B) experiments on **6e** (chemical shifts are in ppm).



**Figure 8.** Selected  $^1\text{H}$ - $^1\text{H}$  NOE data on **5e**.

observed between H-2 and H-3, in spite of their *trans* orientation.<sup>8</sup> Because of this, NOEs between H-2 and H-2B and between H-3 and H-2A,<sup>9</sup> as well as the relative magnitude of those shown in Figures 6 and 7, are more indicative of a *trans* C-2/C-3 stereochemistry; it is not likely that such NOE enhancements would be found in *cis*-2,3-diaryl-2,3-dihydrobenzofurans.

Finally, the magnitudes of  $J_{\text{H-2/H-3}}$  in 2,3-disubstituted-2,3-dihydrobenzofurans are not generally useful in assigning *cis/trans* stereochemistry.<sup>1g,5</sup> For example,  $J_{\text{H-2/H-3}}$  in **9** and **10** are both 9 Hz.<sup>10</sup> However, data collected on **5/6** were in agreement with data on similar compounds reported in the literature (Table 3, entries 16–19). Thus, in 2,3-diaryl-2,3-dihydrobenzofurans **5** (R = H),  $J_{\text{H-2/H-3}}$  were 7–8 Hz, whereas in 4-alkyl-2,3-diaryl-2,3-dihydrobenzofurans **6** (R = alkyl),  $J_{\text{H-2/H-3}}$  were 5–6 Hz. Unfortunately, data from *cis*-2,3-diaryl-2,3-dihydrobenzofurans are limited, preventing a complete pattern from emerging. The only reported (to our knowledge) *cis*-2,3-diaryl-2,3-dihydrobenzofuran is **11**, and  $J_{\text{H-2/H-3}}$  is 8 Hz, clearly different than that in the *trans* analog **12** ( $J_{\text{H-2/H-3}} = 6$  Hz).



The results are consistent with a mechanism involving a thermally allowed 5 + 2 cycloaddition of the pentadi-

enyl moiety of the Lewis acid–quinone complex with the stilbene to afford **13** (Scheme 1).<sup>4,5</sup> Fragmentation of the C-1/C-7 bond to give **14**, followed by C–O bond formation, loss of H<sup>+</sup>, and aqueous workup, produces **5/6**. The observed regioselectivity follows from the expected bidentate complexation of the quinone to the Lewis acid and an asynchronous cycloaddition transition state in which bond formation between the electrophilic C-5 of the Lewis acid–quinone complex and the nucleophilic C-β of the stilbene is more advanced than that between C-3 and C-α, resulting in a buildup of δ<sup>+</sup> charge at C-α that can be stabilized by Ar<sup>1</sup> (C<sub>6</sub>H<sub>4</sub>-4-OCH<sub>3</sub>). The formation of the *trans*-2,3-diaryl stereochemistry from **14** is as expected based on steric factors. This mechanism is similar to that postulated for the styrene/quinone reactions, for which there is considerable supporting evidence.<sup>5</sup> However, the results reported herein are also consistent with a mechanism involving nucleophilic addition of the stilbene to the Lewis acid-bound quinone to give **14** directly followed by ring closure; it is not possible at this stage to distinguish between the two possibilities (and others).<sup>11</sup>

In summary, Lewis acid-promoted reactions of 1,4-benzoquinones with unsymmetrically substituted stilbenes represent an efficient, regio- and stereoselective route to *trans*-2,3-diaryl-2,3-dihydrobenzofurans. We are currently exploring the application of this method to the synthesis of biologically relevant targets.<sup>1</sup> The results of these studies will be reported in due course.

## Experimental Section

All compounds were prepared as racemic mixtures. All reactions were done in flame-dried glassware under a nitrogen atmosphere with magnetic stirring. Solvents were distilled from appropriate drying agents under nitrogen when necessary.<sup>5a</sup> SnCl<sub>4</sub> and TiCl<sub>4</sub> were distilled under nitrogen from CaH<sub>2</sub> immediately before use. Brine refers to saturated aqueous sodium chloride. NMR spectra were recorded on samples dissolved in CDCl<sub>3</sub>, unless otherwise noted, and chemical shifts are reported in δ (ppm) relative to Me<sub>4</sub>Si or residual CHCl<sub>3</sub>. Coupling constants (*J*) are reported in hertz. Melting points are uncorrected. Reactions were monitored by thin-layer chromatography (TLC) on precoated 0.25 mm silica gel plates with a fluorescent indicator (Merck kieselgel 60 F<sub>254</sub>); visualization was effected with a UV lamp or by staining with *p*-anisaldehyde/H<sub>2</sub>SO<sub>4</sub> or phosphomolybdic acid. Chromatography refers to flash chromatography on silica gel [EM kieselgel 60 (0.04–0.063 mm mesh) or Selectro Scientific (0.032–0.063 mm mesh)] with the indicated eluent. 2-Allyl-6-methoxy-1,4-benzoquinone<sup>12</sup> was prepared *via* Fremy's salt oxidation of 2-allyl-6-methoxyphenol; for a representative procedure and for syntheses of the other quinones, see ref 5. Stilbenes **2** were prepared *via* Wittig reaction of the appropriate benzylidene phosphorane with a substituted benzaldehyde; full experimental details are included in the supplementary material.

**Lewis Acid-Promoted Reactions of Stilbenes with 1,4-Benzoquinones.** A similar workup procedure was used for all reactions. Thus, upon completion of the reactions (TLC), solid sodium bicarbonate and cold (–55 to –90 °C) 2-propanol were added, and the mixtures were filtered under vacuum through moist Celite. The aqueous layer was separated and extracted with CH<sub>2</sub>Cl<sub>2</sub> or CHCl<sub>3</sub> (one–three times), and the

(9) See refs 7a–c and 8 and Shirataki, Y.; Noguchi, M.; Yokoe, I.; Tomimori, T.; Komatsu, M. *Chem. Pharm. Bull.* **1991**, *39*, 1568–1572.

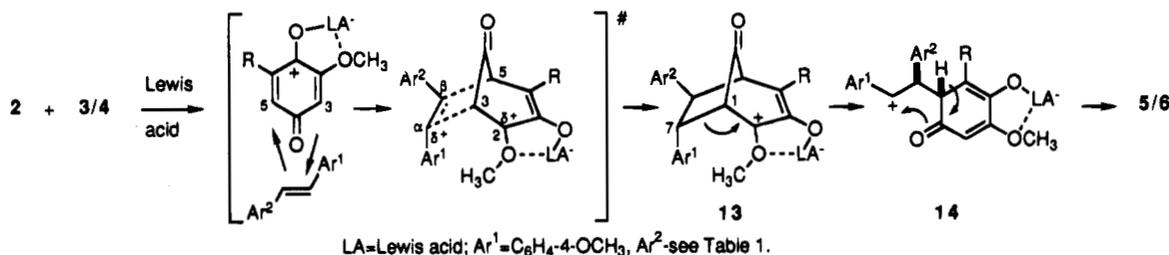
(10) Letavic, M. A. Ph.D. Dissertation, University of Kansas, Lawrence, KS, 1992.

(11) For a related discussion, see Gates, B. D.; Dalidowicz, P.; Tebben, A.; Wang, S.; Swenton, J. S. *J. Org. Chem.* **1992**, *57*, 2135–2143.

(12) Saa, J. M.; Morey, J.; Rubido, C. *J. Org. Chem.* **1986**, *51*, 4471–4473.

(8) Ref 7b and Tih, R. G.; Sondegam, B. L.; Martin, M. T.; Bodo, B. *Tetrahedron Lett.* **1989**, *30*, 1807–1810.

Scheme 1



combined organic solutions were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. The product was isolated by chromatography with the indicated solvents as eluents.

**trans-6-Methoxy-2-(4'-methoxyphenyl)-3-(4'-methylphenyl)-2,3-dihydrobenzofuran-5-ol (5a).** SnCl<sub>4</sub> (40 μL, 0.34 mmol) was added to a solution of stilbene **2a** (75 mg, 0.33 mmol) and quinone **3** (46 mg, 0.33 mmol) in a mixture of 15% pentane/CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -100 °C. After 1.5 h, the temperature was raised to -90 °C, and the solution was stirred for an additional 1 h. Workup and chromatography (10 and 20% EtOAc/hexanes) gave **5a** as an oil which dried under vacuum to a white foam (102 mg, 84%): <sup>1</sup>H NMR (300 MHz) 7.25 (d, *J* = 9, 2 H), 7.11 (d, *J* = 8, 2 H), 7.04 (d, *J* = 8, 2 H), 6.87 (d, *J* = 9, 2 H), 6.57 (s, 1 H), 6.55 (s, 1 H), 5.40 (d, *J* = 8, 1 H), 5.3 (bs, 1 H), 4.47 (d, *J* = 8, 1 H), 3.83 (s, 3 H), 3.78 (s, 3 H), 2.32 (s, 3 H); <sup>13</sup>C NMR (75 MHz) 159.5, 153.1, 146.7, 140.1, 138.8, 136.7, 132.8, 129.4, 128.1, 127.4, 121.2, 113.9, 110.8, 94.0, 93.3, 57.4, 56.1, 55.2, 21.1; HRMS *m/z* 363.1593 (calcd for C<sub>23</sub>H<sub>22</sub>O<sub>4</sub> + 1 363.1596).

**trans-6-Methoxy-2-(4'-methoxyphenyl)-4-methyl-3-(4'-methylphenyl)-2,3-dihydrobenzofuran-5-ol (6a).** SnCl<sub>4</sub> (100 μL, 0.85 mmol) was added to a solution of stilbene **2a** (90 mg, 0.40 mmol) and quinone **4** (67 mg, 0.44 mmol) in 15% pentane/CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -100 °C. After 10 min, the temperature was raised to -90 °C, and the solution was stirred for 1.7 h. Workup and chromatography (15% ether/hexanes) gave **6a** as an oil which dried under vacuum to an off-white foam (133 mg, 88%): <sup>1</sup>H NMR (300 MHz) 7.24 (d, *J* = 9, 2 H), 7.11 (d, *J* = 8, 2 H), 7.02 (d, *J* = 8, 2 H), 6.87 (d, *J* = 9, 2 H), 6.45 (s, 1 H), 5.38 (d, *J* = 6, 1 H), 5.30 (s, 1 H), 4.41 (d, *J* = 6, 1 H), 3.88 (s, 3 H), 3.79 (s, 3 H), 2.33 (s, 3 H), 1.81 (s, 3 H); <sup>13</sup>C NMR (126 MHz) 159.3, 152.5, 146.5, 140.0, 138.0, 136.3, 134.0, 129.4, 127.5, 126.8, 120.9, 119.8, 113.9, 92.7, 91.2, 57.1, 56.0, 55.1, 20.9, 12.0; HRMS *m/z* 376.1691 (calcd for C<sub>24</sub>H<sub>24</sub>O<sub>4</sub> 376.1675).

**6-Methoxy-2-(4-methoxyphenyl)-3-phenyl-2,3-dihydro-5-benzofuranol (5b).** SnCl<sub>4</sub> (0.090 mL, 0.77 mmol) was added dropwise to a solution of quinone **3** (53 mg, 0.38 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at -78 °C, and the mixture was stirred for 10 min. A solution of stilbene **2b** (97 mg, 0.46 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was added dropwise via cannula, and the mixture was stirred for 4.5 h. Workup and chromatography (20% EtOAc/hexanes) afforded **5b** as a viscous light yellow oil (97 mg, 73%): *R<sub>f</sub>* (30% EtOAc/hexanes) 0.33; <sup>1</sup>H NMR (500 MHz) 3.80 (s, 3H), 3.90 (s, 3H), 4.50 (d, *J* = 8, 1H), 5.22 (s, 1H), 5.42 (d, *J* = 8, 1H), 6.557 (s, 1H), 6.563 (s, 1H), 6.88 (d, *J* = 9, 2H), 7.15 (d, *J* = 7, 2H), 7.24-7.32 (m, 5H); <sup>13</sup>C NMR (126 MHz) 55.3 (CH<sub>3</sub>), 56.2 (CH<sub>3</sub>), 57.8 (CH), 93.2 (CH), 94.0 (CH), 110.8 (CH), 114.0 (CH), 121.0, 127.1 (CH), 127.4 (CH), 128.2 (CH), 128.8 (CH), 132.8, 140.1, 141.9, 146.8, 153.2, 159.6; HRMS *m/z* 348.1356 (Calcd for C<sub>22</sub>H<sub>20</sub>O<sub>4</sub> 348.1362).

**6-Methoxy-2-(4-methoxyphenyl)-4-methyl-3-phenyl-2,3-dihydro-5-benzofuranol (6b).** SnCl<sub>4</sub> (0.097 mL, 0.83 mmol) was added to a solution of quinone **4** (63 mg, 0.42 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) at -78 °C, and the mixture was stirred for 10 min. A solution of stilbene **2b** (105 mg, 0.50 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) was added dropwise via cannula, and the mixture was stirred for 4.5 h. Workup and chromatography (20% EtOAc/hexanes) gave **6b** as a light yellow solid (123 mg, 82%): mp 111-113 °C (EtOAc/hexanes); *R<sub>f</sub>* (30% EtOAc/hexanes) 0.43; <sup>1</sup>H NMR (500 MHz) 1.81 (s, 3H), 3.80 (s, 3H), 3.89 (s, 3H), 4.44 (d, *J* = 6, 1H), 5.28 (s, 1H), 5.41 (d, *J* = 6, 1H), 6.47 (s, 1H), 6.87 (d, *J* = 9, 2H), 7.14 (d, *J* = 9, 2H), 7.23-7.32 (m, 5H); <sup>13</sup>C NMR (126 MHz) 12.1 (CH<sub>3</sub>), 55.3 (CH<sub>3</sub>), 56.2

(CH<sub>3</sub>), 57.6 (CH), 91.3 (CH), 92.7 (CH), 114.0 (CH), 119.8, 120.9, 126.9 (2C, CH), 127.8 (CH), 128.8 (CH), 134.0, 138.1, 143.1, 146.6, 152.6, 159.4; signals at 126.9, 127.8, and 128.8 are resolved in C<sub>6</sub>D<sub>6</sub>; HRMS *m/z* 362.1509 (Calcd for C<sub>23</sub>H<sub>22</sub>O<sub>4</sub> 362.1518).

**trans-3-(4'-Chlorophenyl)-6-methoxy-2-(4'-methoxyphenyl)-2,3-dihydrobenzofuran-5-ol (5c).** A portion (1.1 mL, ~0.55 mmol) of SnCl<sub>4</sub> of a solution of SnCl<sub>4</sub> (180 μL, 1.54 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added dropwise over 3 min to a solution of stilbene **2c** (122 mg, 0.50 mmol) and quinone **3** (76 mg, 0.55 mmol) in a mixture of 15% pentane/CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -95 °C, and the solution was stirred for 3.8 h at -90 °C. Workup and chromatography (15% ether/hexanes) gave the title compound as an oil, which dried under vacuum to a light yellow foam (170 mg, 89%): <sup>1</sup>H NMR (300 MHz) 7.26 (d, *J* = 8, 2 H), 7.22 (d, *J* = 9, 2 H), 7.06 (d, *J* = 8, 2 H), 6.86 (d, *J* = 9, 2 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.34 (s, 1 H), 5.33 (d, *J* = 8, 1 H), 4.46 (d, *J* = 8, 1 H), 3.84 (s, 3 H), 3.78 (s, 3 H); <sup>13</sup>C NMR (75 MHz) 159.5, 153.1, 146.9, 140.3, 140.2, 132.9, 132.3, 129.4, 128.8, 127.3, 120.4, 113.9, 110.5, 94.0, 93.1, 57.2, 56.1, 55.2; HRMS *m/z* 383.1044 (calcd for C<sub>22</sub>H<sub>19</sub><sup>35</sup>ClO<sub>4</sub> + 1 383.1051).

**trans-3-(4'-Chlorophenyl)-6-methoxy-2-(4'-methoxyphenyl)-4-methyl-2,3-dihydrobenzofuran-5-ol (6c).** SnCl<sub>4</sub> (100 μL, 0.85 mmol) was added to a solution of stilbene **2c** (98 mg, 0.40 mmol) and quinone **4** (67 mg, 0.44 mmol) in a mixture of 15% pentane/CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -100 °C. After 10 min, the temperature was raised to -90 °C, and the solution was stirred for an additional 2 h. Workup and chromatography (15% ether/hexanes) gave **6c** as an oil which dried under vacuum to a light yellow foam (122 mg, 77%): <sup>1</sup>H NMR (300 MHz) 7.26 (d, *J* = 8, 2 H), 7.21 (d, *J* = 9, 2 H), 7.06 (d, *J* = 8, 2 H), 6.86 (d, *J* = 9, 2 H), 6.45 (s, 1 H), 5.38 (s, 1 H), 5.33 (d, *J* = 6, 1 H), 4.42 (d, *J* = 6, 1 H), 3.84 (s, 3 H), 3.77 (s, 3 H), 1.80 (s, 3 H); <sup>13</sup>C NMR (126 MHz) 159.4, 152.5, 146.7, 141.5, 138.2, 133.5, 132.6, 129.0, 128.9, 126.8, 120.7, 119.1, 114.0, 92.6, 91.4, 56.9, 56.1, 55.2, 12.1; HRMS *m/z* 396.1135 (calcd for C<sub>23</sub>H<sub>21</sub><sup>35</sup>ClO<sub>4</sub> 396.1120).

**trans-3-(3',5'-Dibromophenyl)-2-(4'-methoxyphenyl)-6-methoxy-2,3-dihydrobenzofuran-5-ol (5d).** A solution of stilbene **2d** (2.21 g, 6.00 mmol) and quinone **3** (912 mg, 6.60 mmol) in a mixture of 15% pentane in CH<sub>2</sub>Cl<sub>2</sub> (160 mL) was cooled to -100 °C, and SnCl<sub>4</sub> (0.75 mL, 6.41 mmol) was added over 20 min. The orange-yellow solution turned green-black and was stirred for 1 h. The temperature was then raised to -90 °C until any frozen material thawed (~20 min). Workup and chromatography (15% EtOAc/hexanes) yielded **5d** as an oil, which dried under vacuum as a white foam (2.82 g, 93%): mp 118-120 °C (CH<sub>2</sub>Cl<sub>2</sub>/hexanes); <sup>1</sup>H NMR (300 MHz) 7.58 (t, *J* = 1.6, 1 H), 7.23 (d, *J* = 9, 2 H), 7.23 (d, *J* = 1.6, 2 H), 6.90 (d, *J* = 9, 2 H), 6.56 (s, 1 H), 6.55 (s, 1 H), 5.36 (d, *J* = 8, 1 H), 5.30 (s, 1 H), 4.42 (d, *J* = 8, 1 H), 3.91 (s, 3 H), 3.82 (s, 3 H); <sup>13</sup>C NMR (75 MHz) 159.7, 153.2, 147.2, 146.2, 140.3, 132.9, 132.1, 129.9, 127.3, 123.3, 119.4, 114.1, 110.4, 94.1, 92.2, 57.2, 56.2, 55.3; HRMS *m/z* 503.9548 (calcd for C<sub>22</sub>H<sub>18</sub>O<sub>4</sub><sup>79</sup>Br<sub>2</sub> 503.9572).

**trans-3-(3',5'-Dinitrophenyl)-6-methoxy-2-(4'-methoxyphenyl)-2,3-dihydrobenzofuran-5-ol (5e).** TiCl<sub>4</sub> (190 μL, 1.73 mmol) and Ti(OiPr)<sub>4</sub> (170 μL, 0.57 mmol) were added sequentially to CH<sub>2</sub>Cl<sub>2</sub> (5.65 mL) at -78 °C, and the solution was warmed to room temperature. A portion [1.57 mL, ~0.60 mmol of Ti(IV)] of this mixture was added in portions to a solution of (*E*)- and (*Z*)-stilbenes **2e** (7:1, 75 mg, 0.25 mmol) and quinone **3** (41 mg, 0.30 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (7 mL) at -78

°C. After 2–3 h, the solution had warmed to  $-50$  °C. Workup and chromatography (10 to 30% ether/hexanes) gave the title compound as an oil which dried under vacuum to an orange foam (91 mg, 83%):  $^1\text{H NMR}$  (300 MHz) 8.95 (t,  $J = 2.0$ , 1 H), 8.34 (d,  $J = 2.0$ , 2 H), 7.23 (d,  $J = 9$ , 2 H), 6.90 (d,  $J = 9$ , 2 H), 6.61 (s, 1 H), 6.51 (s, 1 H), 5.4 (bs, 1 H), 5.39 (d,  $J = 7$ , 1 H), 4.74 (d,  $J = 7$ , 1 H), 3.93 (s, 3 H), 3.82 (s, 3 H);  $^{13}\text{C NMR}$  (75 MHz) 160.1, 153.3, 148.8, 147.8, 147.1, 140.8, 131.2, 128.2, 127.2, 118.1, 117.8, 114.4, 110.0, 94.5, 92.5, 57.5, 56.2, 55.3; HRMS  $m/z$  438.1047 (calcd for  $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_8$  438.1063).

**trans-3-(3',5'-Dinitrophenyl)-6-methoxy-2-(4'-methoxyphenyl)-4-methyl-2,3-dihydrobenzofuran-5-ol (6e).**  $\text{TiCl}_4$  (100  $\mu\text{L}$ , 0.91 mmol) was added to a solution of (*E*)- and (*Z*)-stilbenes **2e** (7:1, 120 mg, 0.40 mmol) and quinone **4** (61 mg, 0.40 mmol) in  $\text{CH}_2\text{Cl}_2$  (15 mL) at  $-78$  °C, and the solution was stirred for 2.5 h. Workup and chromatography (10 to 30% ether/hexanes) gave the title compound as an oil which dried under vacuum to an orange foam (119 mg, 66%): mp 200–202 °C ( $\text{CH}_2\text{Cl}_2$ /hexanes);  $^1\text{H NMR}$  (300 MHz) 8.94 (t,  $J = 2.0$ , 1 H), 8.32 (d,  $J = 2.0$ , 2 H), 7.21 (d,  $J = 9$ , 2 H), 6.89 (d,  $J = 9$ , 2 H), 6.52 (s, 1 H), 5.37 (d,  $J = 5$ , 2 H), 5.2 (bs, 1 H), 4.69 (d,  $J = 5$ , 2 H), 3.93 (s, 3 H), 3.81 (s, 3 H), 1.81 (s, 3 H);  $^{13}\text{C NMR}$  (75 MHz) 159.9, 152.7, 148.9, 148.0, 147.6, 138.6, 132.4, 127.7, 126.8, 120.0, 117.6, 117.3, 114.3, 91.9, 91.8, 56.9, 56.2, 55.3, 12.5; HRMS  $m/z$  452.1226 (calcd for  $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_8$  452.1220). Anal. Calcd for  $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_8$ : C, 61.06; H, 4.46; N, 6.19. Found: C, 60.90; H, 4.07; N, 6.15.

**trans-3-[3',5'-Bis-(2'',6''-(Dichlorobenzoyl)oxy)phenyl]-6-methoxy-2-(4'-methoxyphenyl)-2,3-dihydrobenzofuran-5-ol (5f).**  $\text{TiCl}_4$  (105  $\mu\text{L}$ , 0.96 mmol) and  $\text{Ti}(\text{O}i\text{Pr})_4$  (85  $\mu\text{L}$ , 0.29 mmol) were added to  $\text{CH}_2\text{Cl}_2$  (2.8 mL) at  $-78$  °C, and the solution was warmed to room temperature. A portion [980  $\mu\text{L}$ , 0.44 mmol of  $\text{Ti}(\text{IV})$ ] of this mixture was slowly added to a solution of stilbene **2f** (100 mg, 0.17 mmol) and quinone **3** (28 mg, 0.20 mmol) in  $\text{CH}_2\text{Cl}_2$  (7 mL) at  $-78$  °C, and the solution was stirred for 5 h. Workup and chromatography (30 to 50% ether/hexanes) gave the title compound as an oil, which dried under vacuum to a white foam (114 mg, 92%): mp 179–180 °C ( $\text{CH}_2\text{Cl}_2$ /hexanes);  $^1\text{H NMR}$  (300 MHz) 7.42–7.33 (m, 6 H), 7.30 (d,  $J = 9$ , 2 H), 7.26 (t,  $J = 2$ , 1 H), 7.04 (d,  $J = 2$ , 2 H), 6.91 (d,  $J = 9$ , 2 H), 6.67 (s, 1 H), 6.57 (s, 1 H), 5.45 (d,  $J = 8$ , 1 H), 5.3 (bs, 1 H), 4.59 (d,  $J = 8$ , 1 H), 3.91 (s, 3 H), 3.82 (s, 3 H);  $^{13}\text{C NMR}$  (75 MHz) 162.5, 159.6, 153.2, 151.0, 147.1, 144.8, 140.3, 132.3, 132.1, 131.9, 131.5, 127.9, 127.4, 119.1, 119.0, 114.0, 113.9, 110.6, 94.1, 92.5, 57.4, 56.1, 55.2; HRMS  $m/z$  724.0245 (calcd for  $\text{C}_{36}\text{H}_{24}\text{O}_8^{35}\text{Cl}_4$  724.0225). Anal. Calcd for  $\text{C}_{36}\text{H}_{24}\text{O}_8\text{Cl}_4$ : C, 59.53; H, 3.33. Found: C, 59.48; H, 3.50.

**trans-3-[3',5'-Bis-(2'',6''-(dichlorobenzoyl)oxy)phenyl]-6-methoxy-2-(4'-methoxyphenyl)-4-(2-propenyl)-2,3-dihydrobenzofuran-5-ol (6f).**  $\text{TiCl}_4$  (100  $\mu\text{L}$ , 0.91 mmol) and  $\text{Ti}(\text{O}i\text{Pr})_4$  (90  $\mu\text{L}$ , 0.30 mmol) were added sequentially to  $\text{CH}_2\text{Cl}_2$  (3 mL) at  $-78$  °C, and the solution was warmed to room temperature. A portion [1.0 mL,  $\sim 0.40$  mmol of  $\text{Ti}(\text{IV})$ ] of this mixture was added to a solution of stilbene **2f** (118 mg, 0.20 mmol) and 2-allyl-6-methoxy-1,4-benzoquinone (36 mg, 0.20 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) at  $-78$  °C, and the solution was stirred for 26 h. Workup and chromatography (30% ether/hexanes) gave the title compound as an oil, which dried under vacuum to a white foam (105 mg, 68%):  $^1\text{H NMR}$  (500 MHz) 7.40–7.32 (m, 6 H), 7.27–7.24 (m, 3 H), 7.02 (d,  $J = 2.0$ , 2 H), 6.89 (d,  $J = 8.7$ , 2 H), 6.51 (s, 1 H), 5.70 (dddd,  $J = 17.0$ , 10.1, 6.6, 5.5, 1 H), 5.48 (d,  $J = 5.9$ , 1 H), 5.3 (bs, 1 H), 4.85 (dd,  $J = 10.1$ , 1.5, 1 H), 4.74 (dd, 17.0, 1.5, 1 H), 4.54 (d,  $J = 5.9$ , 1 H), 3.90 (s, 3 H), 3.81 (s, 3 H), 3.30 (dd,  $J = 15.2$ , 5.5, 1 H), 2.91 (dd,  $J = 15.2$ , 6.6, 1 H);  $^{13}\text{C NMR}$  (126 MHz) 162.6, 159.6, 152.9, 151.1, 147.3, 146.2, 138.2, 134.7, 133.4, 132.6, 132.1, 131.5, 128.0, 127.0, 122.4, 118.9, 118.5, 115.2, 114.1, 113.8, 92.2 (2 carbons), 56.9, 56.2, 55.3, 30.8; HRMS  $m/z$  764.0510 (calcd for  $\text{C}_{39}\text{H}_{28}\text{O}_8^{35}\text{Cl}_4$  764.0538).

**trans-6-Methoxy-2-(4'-methoxyphenyl)-3-(3',5'-dimethoxyphenyl)-2,3-dihydro-5-benzofuranol (5g) and (E)-2-(2',5'-dihydroxy-4'-methoxyphenyl)-3,4',5'-trimethoxystilbene (7).** Method A.  $\text{SnCl}_4$  (0.893 mL, 7.63 mmol) was added dropwise to a solution of quinone **3** (527 mg, 3.82 mmol) in  $\text{CH}_2\text{Cl}_2$  (25 mL) at  $-78$  °C. After 10 min, a solution

of stilbene **2g** (1.25 g, 4.61 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added dropwise via cannula, and the mixture was stirred for 4 h. Workup and chromatography (10, 20, and then 40% EtOAc/hexanes) gave dihydrobenzofuran **5g** (82 mg, 5%) as a viscous light yellow oil and biaryl **7** (817 mg, 52%) as a white solid after recrystallization from EtOAc/hexanes.

**Physical and spectral data for 5g:**  $R_f$  (30% EtOAc/hexanes) 0.29;  $^1\text{H NMR}$  (500 MHz) 3.73 (s, 6H), 3.80 (s, 3H), 3.89 (s, 3H), 4.41 (d,  $J = 8$ , 1H), 5.23 (s, 1H), 5.42 (d,  $J = 8$ , 1H), 6.30 (d,  $J = 2$ , 2H), 6.36 (t,  $J = 2$ , 1H), 6.54 (s, 1H), 6.59 (d,  $J = 1$ , 1H), 6.87 (d,  $J = 9$ , 2H), 7.26 (d,  $J = 9$ , 2H);  $^{13}\text{C NMR}$  (126 MHz) 55.31 ( $\text{CH}_3$ ), 55.33 ( $\text{CH}_3$ ), 56.2 ( $\text{CH}_3$ ), 58.1 ( $\text{CH}$ ), 92.8 ( $\text{CH}$ ), 94.0 ( $\text{CH}$ ), 98.9 ( $\text{CH}$ ), 106.2 ( $\text{CH}$ ), 110.8 ( $\text{CH}$ ), 114.0 ( $\text{CH}$ ), 120.7, 127.4 ( $\text{CH}$ ), 133.0, 140.2, 144.4, 146.8, 153.2, 159.6, 161.0; HRMS  $m/z$  408.1584 (calcd for  $\text{C}_{24}\text{H}_{24}\text{O}_6$  408.1573).

**Physical and spectral data for 7:** mp 185.5–189 °C (EtOAc/hexanes);  $R_f$  (30% EtOAc/hexanes) 0.09.  $^1\text{H NMR}$  (500 MHz) 3.76 (s, 3H), 3.79 (s, 3H), 3.91 (s, 6H), 4.75 (s, 1H), 5.18 (s, 1H), 6.50 (d,  $J = 2$ , 1H), 6.60 (s, 1H), 6.66 (s, 1H), 6.71 (d,  $J = 16$ , 1H), 6.82 (d,  $J = 9$ , 2H), 6.91 (d,  $J = 2$ , 1H), 6.97 (d,  $J = 16$ , 1H), 7.26 (d,  $J = 9$ , 2H);  $^{13}\text{C NMR}$  (126 MHz) 55.3 ( $\text{CH}_3$ ), 55.4 ( $\text{CH}_3$ ), 55.9 ( $\text{CH}_3$ ), 56.0 ( $\text{CH}_3$ ), 98.1 ( $\text{CH}$ ), 99.5 ( $\text{CH}$ ), 101.5 ( $\text{CH}$ ), 114.0 ( $\text{CH}$ ), 114.1, 116.3, 117.3 ( $\text{CH}$ ), 124.6 ( $\text{CH}$ ), 128.0 ( $\text{CH}$ ), 129.9 ( $\text{CH}$ ), 130.0, 139.0, 139.7, 146.9, 147.2, 158.6, 159.4, 160.6; HRMS  $m/z$  408.1565 (calcd  $\text{C}_{24}\text{H}_{24}\text{O}_6$  408.1573).

**Method B.**  $\text{SnCl}_4$  (0.966 mL, 8.26 mmol) was added to a solution of stilbene **2g** (150 mg, 0.55 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at  $-78$  °C, and the solution was stirred for 10 min. A solution of quinone **3** (51 mg, 0.37 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) was then added dropwise via cannula, and the mixture was stirred for 30 min. Workup and chromatography (20 and 40% EtOAc/hexanes) afforded dihydrobenzofuranol **5g** (20 mg, 13%) as a light yellow oil and biaryl **7** (79 mg, 52%) as a white solid.

**trans-6-Methoxy-2-(4'-methoxyphenyl)-3-(3',5'-dimethoxyphenyl)-4-methyl-2,3-dihydro-5-benzofuranol (6g) and (E)-2-(3',6'-Dihydroxy-4'-methoxy-1'-methylphenyl)-3,4',5'-trimethoxystilbene (8).** Method A.  $\text{SnCl}_4$  (0.085 mL, 0.73 mmol) was added to a solution of quinone **4** (55 mg, 0.36 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at  $-78$  °C. After 10 min, a solution of stilbene **2g** (118 mg, 0.44 mmol) in  $\text{CH}_2\text{Cl}_2$  (1 mL) was added dropwise via cannula and the mixture was stirred for 15 min. Workup and chromatography (5, 10, 20, and then 40% EtOAc/hexanes) gave dihydrobenzofuranol **6g** (4.6 mg, 3%) as a light yellow oil and biaryl **8** (119.8 mg, 78%) as a white solid.

**Physical and spectral data for 6g:**  $R_f$  (30% EtOAc/hexanes) 0.30;  $^1\text{H NMR}$  (500 MHz) 1.86 (s, 3H), 3.73 (s, 6H), 3.79 (s, 3H), 3.87 (s, 3H), 4.36 (d,  $J = 6$ , 1H), 5.32 (s, 1H), 5.40 (d,  $J = 6$ , 1H), 6.29 (d,  $J = 2$ , 2H), 6.35–6.36 (t,  $J = 2$ , 1H), 6.44 (s, 1H), 6.87 (d,  $J = 9$ , 2H), 7.24 (d,  $J = 9$ , 2H);  $^{13}\text{C NMR}$  (126 MHz) 12.1 ( $\text{CH}_3$ ), 55.2 ( $\text{CH}_3$ ), 55.3 ( $\text{CH}_3$ ), 56.1 ( $\text{CH}_3$ ), 57.8 ( $\text{CH}$ ), 91.3 ( $\text{CH}$ ), 92.4 ( $\text{CH}$ ), 98.5 ( $\text{CH}$ ), 105.8 ( $\text{CH}$ ), 114.0 ( $\text{CH}$ ), 119.3, 121.0, 126.8 ( $\text{CH}$ ), 134.1, 138.1, 145.6, 146.6, 152.6, 159.4, 161.1; HRMS  $m/z$  422.1707 (calcd for  $\text{C}_{25}\text{H}_{26}\text{O}_6$  422.1729).

**Physical and spectral data for 8:** mp 224–227 °C dec (EtOAc/hexanes);  $R_f$  (30% EtOAc/hexanes) 0.12;  $^1\text{H NMR}$  (500 MHz) 1.88 (s, 3H), 3.72 (s, 3H), 3.78 (s, 3H), 3.89 (s, 3H), 3.92 (s, 3H), 4.40 (s, 1H), 5.34 (s, 1H), 6.48 (s, 1H), 6.50 (d,  $J = 2$ , 1H), 6.58 (d,  $J = 16$ , 1H), 6.80 (d,  $J = 9$ , 2H), 6.93 (d,  $J = 2$ , 1H), 7.00 (d,  $J = 16$ , 1H), 7.23 (d,  $J = 9$ , 2H);  $^{13}\text{C NMR}$  (126 MHz) 12.8, 55.3, 55.4, 55.8, 55.9, 96.1, 98.2, 101.1, 114.0, 114.4, 114.6, 123.7, 123.9, 128.0, 130.0, 130.1, 137.3, 139.9, 146.3, 146.4, 159.3, 159.4, 160.9; CIMS  $m/z$  (relative intensity) 423 ( $M + 1$ , 100), 422 ( $M +$ , 40), 301 (30), 121 (30); HRMS  $m/z$  423.1793 (calcd for  $\text{C}_{25}\text{H}_{27}\text{O}_6$  423.1807).

**Method B.**  $\text{SnCl}_4$  (0.65 mL, 5.58 mmol) was added to a solution of stilbene **2g** (152 mg, 0.56 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) at  $-78$  °C followed, after 10 min, by the dropwise addition of a solution of quinone **4** (51 mg, 0.37 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) via cannula. The mixture was stirred for 30 min, and workup and chromatography (10 and 20% EtOAc/hexanes) afforded dihydrobenzofuranol **6g** (17 mg, 9%) as a light yellow oil and biaryl **8** (106 mg, 58%) as a white solid.

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**Supplementary Material Available:** Procedures and data for experiments and products used to aid in identifying biaryl **7**; summaries of selected data from  $^1\text{H}$ - $^1\text{H}$  NOE experiments on **5b**, **5g**, **6b**, **6e**, and **6g**; full experimental

procedures for preparation of stilbenes **2**; IR and mass spectral data for dihydrobenzofurans **5/6**;  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of new compounds lacking combustion analysis (50 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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