Palladium(0)-Catalyzed Allylation of 2,2’-Dihydroxybiphenyl by 1-Ethenylcyclopropyl Sulfonates: Preparation of 2,2’-Bis(cyclopropylideneethoxy) biphenyls

Giovanna Delogu,* a Jacques Salaün,* b Cristina de Candia, a,b Davide Fabbri, a,b Pier Paolo Piras, c Jean Ollivier* b

a Istituto di Chimica Biomolecolare, Sez: Sassari, CNR, Traversa La Crucca 3, reg. Baldinca, Li Punti, 07040 Sassari, Italy
b Laboratoire des Carbocycles, UMR 8615, Institut de Chimie Moléculaire d’Orsay, Bât. 420, Université de Paris-Sud, 91405 Orsay, France
Fax +33(1)69156278; E-mail: jasalaun@icmo.u-psud.fr
c Dipartimento di Scienze Chimiche, Cittadella Universitaria Monserrato, 9042 Monserrato, Italy

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Abstract: Dipotassium salts of 2,2’-dihydroxybiphenyl derivatives underwent palladium(0) catalyzed regioselective allylation by sulfonic esters (mesylates, tosylates) of 1-ethenylcyclopropanol to produce, in good yields, 2,2’-bis(cyclopropylideneethoxy)biphenyls, which are of biological interest. Whilst the tetrapotassium salt of 2,2’,6,6’-tetrahydroxybiphenyl, formed the triadduct 2,2’-tris(cyclopropylideneethoxy)hydroxybiphenyl as its main product. An unexpected palladium-induced rearrangement of the monoadducts 2-(2-cyclopropylideneethoxy)-2’-hydroxybiphenyl derivatives into the 2-[2-(1-ethenylcyclopropyloxy)]-2’-hydroxybiphenyl derivatives occurred; while the minor diastereomer of the monoadduct 2-[(2-cyclopropylidene-1-trimethylsilyl)ethoxy]-6,6-dimethoxy-2’-hydroxybiphenyl upon standing in CDCl3, underwent Claisen rearrangement into the 2,2’-dihydroxy-6,6’-dimethoxy-3-(2-trimethylsilyl)ethenyl)cyclopropylbiphenyl.

Key words: palladium(0), 1-ethenylcyclopropyl sulfonates, biphenyls, allylation, rearrangements

The growing number of isolated naturally occurring bioactive biphenyls led us to consider this moiety as a basic and valued framework for the synthesis of new pharmacologically and agrochemically active compounds. Additionally, the restricted rotation of the biphenyl backbone provides attractive building blocks, for example, to produce peptides with a frozen conformation entailing enhanced resistance to enzymatic degradation. Also worthy of note are cyclopropane containing compounds, these are of great general interest to synthetic organic chemists, especially bioorganic chemists, because they provide building blocks of unprecedented synthetic potential, due to their broad spectrum of biological properties. This led to the idea of preparing biphenyls linked to three-membered rings with the aim of developing new structures and prospective bioassays.

In fact, a few rare examples of natural cyclopropane containing biphenyls have been reported, for instance, a dimeric sesquiterpene of the cycloaurane type, lauribiphenyl-1 was isolated from the red alga Laurencia nidifica. Furthermore the bioactivity of several biphenyl-cyclopropane derivatives has been noted. Thus, the basic 2-biphenylcyclopropanecarboxylic acids 2 (R = H, Cl) were recognized for their activity in alleviating inflammation, pain, hypoglycemia and ketosis, while ovicidal activity against spider mites was found for the 2-biphenyl cyclopropanecarboxylate 3. The vinylogous hydroxamic acid 4, examined for its ability to inhibit various enzymes in the arachidonic acid cascade, was proved to be an active inhibitor of 5-lipoxygenase (rat basophilic leukemia cell line).2 and the oxime ether 5, tested for its activity at α- and β-adrenergic receptors, exhibited high efficiency in the inhibition of isoprenaline-induced tachycardia in anesthetized rats. (Figure 1).

In pursuit of the synthetic applications of the π,1,1-ethyleneallylmetal complexes, we report herein an efficient and selective method to prepare 2,2’-bis(2-cyclopropylideneethoxy)biphenyls. In fact, alkylidenecyclopropanes form a peculiar class of strained olefinic compounds with...
remarkable synthetic potential, \(^{13}\) and specific bioactivities. \(^{5}\) Allylation of 2,2''-dihydroxybiphenyl: the sulfonic esters (mesylate, tosylate) of the 1-ethenylcyclopropanol \(6a\) (\(R = H\)), (readily available from the cyclopropanone hemiacetal, \(^{14}\) 1-hydroxycyclopropanecarboxylic acid, \(^{15}\) or recently from titanium(IV)-mediated cyclopropanation of \(\beta\)-halo esters, \(^{16}\)) formed the 2,2''-1,1-ethyleneallylpalladium complex \(7\) upon treatment with palladium(0). Then, nucleophilic substitution of \(7\) by soft nucleophiles \(\text{Nu}_a\) (stabilized anions), provided the alkylidenecyclopropanes \(8\), while hard nucleophiles \(\text{Nu}_b\) (e.g., non stabilized organometallics), gave the 1-substituted vinylcyclopropanes \(9\), regioselectively (Scheme 1). \(^{11}\)

Likewise reaction of the dipotassium salt \(10\) (formed upon treatment of commercially available 2,2''-dihydroxybiphenyl with 3 equiv of \(\text{K}_2\text{CO}_3\) in anhyd DMF at \(60 ^\circ\text{C}\) for 2 h) with mesylate \(6b\) (2.5 equiv, \(R = \text{OMs}\)) in the presence of palladium(0) \{from palladium dibenzylideneacetone \([\text{Pd(dba)}_2]\) and \(2\text{PPh}_3\)\} in DMF (r.t. for 3 h) gave 2,2''-bis(2-cyclopropylideneethoxy)biphenyl \([11]; 45\%\) Table 1, entry 1\}). Under the same conditions, but using a greater amount of the mesylate \(6b\) (4 equiv), improved the yield of \(11\) \((79\%)\) Table 1, entry 2\}). A longer reaction time (15 h) improved the yield of \(11\) further \((90\%)\) Table 1, entry 3\}). However, palladium(0) catalyzed nucleophilic substitution of the tosylate \(6c\) (\(R = \text{Ts}\)) by the dipotassium salt \(10\) (4 equiv, 15 h) led to the diadduct \(11\) \((70\%)\), revealing the leaving group effect of the sulfonate (Scheme 1, entry 4\}).

On the other hand, Pd(0)-catalyzed reaction under the same conditions of the monopotassium salt \(13\) (formed upon treatment of 2,2''-dihydroxybiphenyl with equiv of \(\text{K}_2\text{CO}_3\) with mesylate \(6b\) (2 equiv), gave 2-(2-cyclopropylideneethoxy)-2''-hydroxybiphenyl \((12\) as the major product \((79\%\)), as well as the diadduct \(11\) \((15\%)\) and the unexpected 2-(1-ethenylcyclopropoxy)-2''-hydroxybiphenyl \(\text{[(14); 4\%]}\) Table 1, entry 5\}).

A sample of the monoadduct-I \(12\) remained unaltered upon treatment with of \(\text{K}_2\text{CO}_3\) (1 equiv) in DMF (60 °C for 7 d), proving that the rearrangement \(12\) \((14\%\) Table 1, entry 5\}). On the other hand, reaction of the monoadduct-I \(12\) with palladium(0) \{from 5% \(\text{Pd(dba)}_2\) and 12% \(\text{PPhi}_3\)\} in DMF at (r.t. for 16 h) gave the isomeric monooadduct-II \(14\) in good yield \((81\%\)\). Seemingly coordination of the double bond of the alkylidenecyclopropane \(12\) with Pd(0) led to the formation of complex \(15\) and then to the \(\pi\)-1,1-etheneallylpalladium complex \((16\), probably favoured by a H-bond between the oxygen and the hydroxyl group. Therefore, the 2''-hydroxy-2-oxibiphenyl moiety must be regarded as a leaving group and a nucleophile simultaneously. However, the palladium(0) catalyzed reaction of the potassium salt of \(12\) (formed by reaction with 1 equiv of \(\text{K}_2\text{CO}_3\) in DMF at \(60 ^\circ\text{C}\) for 1 h) with the mesylate \(6b\) in DMF (r.t. for, 12 h, then \(60 ^\circ\text{C}\) for 30 h) did not lead to the monoadduct-II \(14\), but to the diadduct \(11\) in poor yield \((9\%)\). This is probably because in the presence of mesylate \(6b\) palladium(0) forms complex \(7\) more readily than the complexes \(15\) and \(16\) (Scheme 2), and therefore could not induce the rearrangement \(12\) \(\rightarrow\) \(14\), (Scheme 2).

It must be also emphasized for comparison that the diadduct \(11\) did not undergo any rearrangement upon treatment with Pd(0) in DMF at (r.t. for 16 h).
Table 1  Palladium(0)-Catalyzed Nucleophilic Substitution of 1-Ethenylcyclopropyl Sulfonates by 2,2'-Dihydroxybiphenyls

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nucleophile</th>
<th>Sulfonic ester (equiv)</th>
<th>T °C (reaction time)</th>
<th>Diadduct</th>
<th>Monoadduct-I (%)</th>
<th>Monoadduct-II (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>6b (2.5)</td>
<td>r.t. (3 h)</td>
<td>11 (45)</td>
<td>12 (16)</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>6b (4)</td>
<td>r.t. (3 h)</td>
<td>11 (79)</td>
<td>12 (16)</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>6b (2.2)</td>
<td>r.t. (15 h)</td>
<td>11 (90)</td>
<td>12 (10)</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>6c (4)</td>
<td>r.t. (15 h)</td>
<td>11 (70)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>6b (2)</td>
<td>r.t. (3 h)</td>
<td>11 (15)</td>
<td>12 (79)</td>
<td>14 [4; 81 from 12 and Pd(0)]</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
<td>6b (4)</td>
<td>r.t. (12 h)</td>
<td>18 (60)</td>
<td>19 (0)</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>17</td>
<td>6c (2.2)</td>
<td>r.t. (24 h)</td>
<td>18 (70)</td>
<td>19 (30)</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>20</td>
<td>6b (4)</td>
<td>r.t. (12 h)</td>
<td>21 (84)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>6b (2.5)</td>
<td>r.t. (14 h)</td>
<td>23 (50)</td>
<td>24 (3)</td>
<td>25 (2)</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>6b (4)</td>
<td>r.t. (64 h)</td>
<td>23 (50)</td>
<td>24 (40)</td>
<td>25 (10)</td>
</tr>
<tr>
<td>11</td>
<td>22</td>
<td>6c (4)</td>
<td>r.t. (20 h)</td>
<td>23 (35)</td>
<td>24 (63)</td>
<td>25 (2)</td>
</tr>
</tbody>
</table>
Allylation of 2,2′-dihydroxy-6,6′-dimethoxybiphenyl: the reaction of the dipotassium salt 17 (formed upon treatment of 2,2′-dihydroxy-6,6′-dimethoxybiphenyl, 17 with 3 equiv of K₂CO₃ in anhyd DMF at 60 °C for 1 h), with mesylate 6b (4 equiv) in the presence of palladium(0) (r.t. for 14 h), underwent allylation to provide the 2-(2-cyclopropylideneethoxy)-6,6′-dimethoxybiphenyl 18 [(60%) Table 1, entry 6]. The dipotassium salt 17 when subjected to similar conditions, but using less tosylate 6c and with a longer reaction time (2.2 equiv at r.t. for 24 h), underwent mono- and dialkylation to produce the 2-(2-cyclopropylideneethoxy)-6,6′-dimethoxy-2′-hydroxybiphenyls 19 and 18 [(30% and 70%, respectively) Table 1, entry 7].

Allylation of 1,1′-bi-2-naphthol: palladium(0)-catalyzed reaction of the dipotassium salt 20 (prepared upon treatment of commercially available racemic 1,1′-bi-2-naphthol with 3 equiv of K₂CO₃ in anhyd DMF at 60 °C for 1 h) with mesylate 6b (4 equiv) in DMF (r.t. for 12 h) led to the 2,2′-bis(2-cyclopropylideneethoxy)-1,1′-binaphthalene (21) in good yield (84%), without noticeable formation of a monoadduct (Table 1, entry 8).

Allylation of 5,5′-bis(2-propenyl)-2,2′-dihydroxy-3,3′-dimethoxybiphenyl (dehydrodieugenol): this natural product can be isolated from various plants including the wood of an arborescent Lauraceae species from the Andes (Nectandra polita). 15 Dehydrodieugenol is an efficient hydroxyl radical scavenger, 19 able to inhibit UV-induced mutagenesis 20 and lipid peroxidation, which entail fatal damage to cells, in particular to skin, and provoke food deterioration. 21 Its dipotassium salt 22 (obtained upon treatment of dehydrodieugenol, 18 with 3 equiv of K₂CO₃ in anhyd DMF at 60 °C for 1 h), when reacted with mesylate 6b (2.5 equiv) in the presence of palladium(0) (r.t. for 14 h), underwent allylation to provide the 2,2′-bis(2-cyclopropylideneethoxy)-3,3′-dimethoxy-5,5′-di(2-propenyl)biphenyl (23, 50%), as well as the monoadducts 24 and 25 [(3% and 2%, respectively) Table 1, entry 9].

Palladium(0)-catalyzed reaction of 22 with mesylate 6b (4 equiv) for a longer reaction time (64 h) increased the yields of 24 and 25 [(40% and 10%, respectively) Table 1, entry 10]. Otherwise use of tosylate 6c (4 equiv for 20 h) gave the monoadduct-I 24 as major product [(63%) Table 1, entry 11].

Formation of the rearranged monoadduct-II 25 was observed after a longer reaction time (64 h at r.t.); whilst treatment of monoadduct-I 24 with palladium(0) [from 5% Pd(dba)₂ and 12% PPh₃] in DMF (r.t. for 16 h) generates a rearrangement to form the monoadduct-II 25 in good yield (60%).

Allylation of 2,2′,6,6′-tetrahydroxybiphenyl: the tetrapotassium salt 26 (prepared by treatment of 2,2′,6,6′-tetrahydroxybiphenyl, 22 with K₂CO₃ (5 equiv) in anhyd DMF at 60 °C for 1 h) similarly underwent palladium(0)-catalyzed allylation upon treatment with an excess (8 equiv) of mesylate 6b in DMF (r.t. for 12 h) to produce the triadduct 28.

### Table 1: Palladium(0)-Catalyzed Nucleophilic Substitution of 1-Ethenylcyclopropyl Sulfonates by 2,2′-Dihydroxybiphenyls (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Nucleophile</th>
<th>Sulfonic ester (equiv)</th>
<th>T °C (reaction time)</th>
<th>Diadduct</th>
<th>Monoadduct-I (%)</th>
<th>Monoadduct-II (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>26</td>
<td>6b (8)</td>
<td>r.t. (12 h)</td>
<td>27 (15)</td>
<td>28* (60)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>26</td>
<td>6b (4)</td>
<td>r.t. (3 d)</td>
<td>29 (60)</td>
<td></td>
<td>30 (40)</td>
</tr>
<tr>
<td>14</td>
<td>31</td>
<td>6c (2.3)</td>
<td>r.t. (3 h)</td>
<td>32 (75)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>17</td>
<td>6d (2.4)</td>
<td>r.t. (3 h)</td>
<td>33 (25; de: 20%)</td>
<td>34* (90%)</td>
<td></td>
</tr>
</tbody>
</table>

* Tetraadduct .
* Triadduct.
* From CDCl₃ catalyzed Claisen rearrangement of 33.
as the principal product (60%), as well as 2,2',6,6'-tetraakis(2-cyclopropyldieneethoxy)biphenyl 27 [(15%) Table 1, entry 12]. Curiously, in this case, the formation of mono- or diadducts was not observed in the crude reaction mixture. However, palladium(0) catalyzed reaction of 26 with less mesylate 6b (4.4 equiv) was slower but after stirring the reaction mixture for a long period of time (r.t. for 3 d) produced the monoadduct I 29 (60%), and the isomeric monoadduct II 30 [(40%) Table 1, entry 13]. This probably arises from a palladium(0)-catalyzed rearrangement analogous to 12-14 (Scheme 2).

Allylation of 6,6-dibromo-2,2'-dihydroxy-3,3'-dimethoxybiphenyl: the dipotassium salt 31 (formed upon treatment of 6,6-dibromo-2,2'-dihydroxy-3,3'-dimethoxybiphenyl,23 with K₂CO₃ (4 equiv) in anhyd DMF at 60 °C for 1 h) readily underwent reaction with the tosylate 6c (2.3 equiv) in the presence of 5% of palladium(0) (at r.t. for 3 h). This produced the 2,2'-bis(2-cyclopropyldieneethoxy)-6,6-dibromo-3,3'-dimethoxy-biphenyl (32) in good yield [(75%) Table 1, entry 14].

Nucleophilic substitution of 1-tosyloxy-1-(2-trimethylsilyl)ethoxy)cyclopropane by 2,2'-dihydroxy-6,6'-dimethoxybiphenyl, Ciasen rearrangement: reaction of the dipotassium salt 17, with the 1-(2-trimethylsilyl)ethoxy)cyclopropyl tosylate 6d in the presence of 5% of palladium(0) in DMF (r.t. for 3 h) led to a 60:40 diastereomeric mixture of 2-[(2-cyclopropyldiene-1-trimethylsilyl)ethoxy]-6,6-dimethoxy-2'-hydroxybiphenyl (33; 25%). This resulted from hindered rotation along the main biphenyl axis. On standing in CDCl₃ for several weeks only the minor diastereomer of 33 underwent Ciasen rearrangement24 to provide the 2,2'-dihydroxy-6,6'-dimethoxy-3-[1-(2-trimethylsilyl)ethoxy)cyclopropyl]biphenyl [(34; 90%) Table 1, entry 15].

A sample of the dihydroegenol derivative 23, is currently under investigation in order to test its eventual bioactivity on plants.

1H NMR spectra were recorded on Brucker AM 250 (250 MHz), AC 250 (250 MHz) and AC 200 (200 MHz) spectrometers; δ = 0 for TMS. 7.27 for CHCl₃. 13C NMR spectra were also recorded on Brucker AM 250, AC 250 (63 MHz), AC 200 (50 MHz); δ = 77 for CDCl₃, the NMR data are reported in δ (ppm) from TMS. The DEPT-135 pulse was used for the determination of signal types. IR spectra were run on a FT-IR Perkin Elmer spectrophotometer. Mass spectra were measured with a Nermag R-10 coupled with a OKI DP 125 gas chromatograph. Relative percentages are shown in brackets; high resolution mass spectra were recorded with a Finningan MAT 95S. Elemental analyses were performed with a Perkin-Elmer 240 C analyzer by the Service of Microanalysis, Institut de Chimie des Substances Naturelles, Gif-sur-Yvette (France). Preparative column chromatography was performed on SDS normal silica gel (70–230 mesh), on SDS flash silica gel (35–70 mesh) or on Fluka neutral alumina 507c (100–200 mesh). All reactions requiring anhydrous conditions were performed under argon.

1-Ethyl-1-tosyloxy cyclopropane (6c)

Compound 6c was prepared from vinylation of cyclopropane hemiacetal, followed by mesylation according to known procedures.14

1-Tosyloxy-1-(2-trimethylsilyl)ethoxy cyclopropane (6d)

Compound 6d was prepared from cyclopropane hemiacetal, followed by tosylation according to known procedures.14

Palladium(0)-Catalyzed Substitution of 1-Ethynyl-1-mesyloxy-cyclopropane (6b) by the Dipotassium Salt of 2,2'-dihydroxybiphenyl (10); Typical Procedure

A solution of Pd(dba)₂ (32mg, 0.055 mmol) and of PPh₃ (35 mg, 0.13 mmol) was degassed under vacuum for 1 h and stirred in a N₂ atmosphere, to which was added a solution of mesylate 6b (178 mg, 1.1 mmol) in anhyd DMF (20 mL). The mixture was stirred at r.t. for 15 min, then a solution of the dipotassium salt 10 [0.5 mmol; generated from the reaction of 2,2'-dihydroxybiphenyl (93 mg, 0.5 mmol) with K₂CO₃ (207 mg, 1.5 mmol) in anhyd DMF (5 mL) for 2 h at 60 °C] was added. Stirring was continued at r.t. for 15 h; then, Et₂O (20 mL) and sat. NH₄Cl (20 mL) were added. The organic phase was extracted with Et₂O (2×20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography (C₆H₆–Et₂O, 9:1) of the residue gave 2,2'-bis-(2-cyclopropyldieneethoxy)biphenyl (11; 143 mg 90%), and 2'-[(2-cyclopropyldieneethoxy)-2'-hydroxybiphenyl (12; 13 mg 10%).

2,2'-Bis-(2-cyclopropyldieneethoxy)biphenyl (11)

Colorless oil.

IR (CDCl₃): 3100–2800, 1593, 1480, 1261 cm⁻¹.

1H NMR (CDCl₃): δ = 1.03 (s, 8 H), 4.65 (d, 4 H, J = 5.8 Hz), 5.8 (m, 2 H), 6.9 (t, 4 H, J = 6.8 Hz), 7.3 (m, 4 H).

13C NMR (CDCl₃): δ = 1.8, 1.9, 68.6, 112.8, 114.3, 120.2, 125.9, 128.1, 128.5, 131.5, 156.2.

MS (EI) m/z (δ%) = 318 (50) [M⁺], 289 (100), 247 (57), 233 (79), 219 (57), 181 (62), 165 (65).

HRMS: m/z calc for C₂₃H₂₀O₂: 318.1619; found: 318.1612.

2'-[(2-Cyclopropyldieneethoxy)-2'-hydroxybiphenyl (12)

Colorless oil.

IR (CDCl₃): 3800–3200, 3100, 2800, 1593, 1480, 1261 cm⁻¹.

1H NMR (CDCl₃): δ = 1.2 (s, 4 H), 4.8 (d, 2 H, J = 6.3 Hz), 5.9–6.1 (m, 1 H), 6.9–7.2 (m, 4 H), 7.3–7.5 (m, 4 H).

13C NMR (CDCl₃): δ = 1.01, 1.9, 69.6, 112.6, 113.6, 117.7, 121, 122.4, 126.7, 128.8, 129, 129.1, 131.3, 132.6, 153.9, 154.5.

MS (EI) m/z (δ%) = 252 (100) [M⁺], 237 (56), 232 (38), 165 (17), 181 (15), 115 (10).

HRMS: m/z calc for C₂₃H₁₈O₂: 252.1150; found: 252.1153.

Palladium(0)-Catalyzed Allylic Substitution of 1-Ethynyl-1-mesyloxy-cyclopropane (6c) by the Dipotassium Salt 10 of 2,2'-Dihydroxybiphenyl

A mixture of tosylate 6c (952 mg, 4 mmol), Pd(dba)₂ (120 mg, 0.2 mmol), and PPh₃ (105 mg, 0.4 mmol) was stirred at r.t. in anhyd DMF (20 mL) for 15 min. A solution of the dipotassium salt 10 (1 mmol; generated as above) was added and stirring continued at r.t. for 15 h, then the reaction was heated at 60 °C for 4 d. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2×20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography (C₆H₆–Et₂O, 9:1) of the residue gave 11 as a colorless oil (220 mg, 70%).
Palladium(0)-Induced Rearrangement of 12

Method A

Attempted base-induced rearrangement: A solution of 2-(2-cyclopropylideneethoxy)-2'-hydroxybiphenyl 12 (202 mg, 0.8 mmol) and K₂CO₃ (110 mg, 0.8 mmol) was stirred for 7 d in anhyd DMF (5 mL) at 60 °C. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 x 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo recovered the unreacted 12 (200 mg, 0.8 mmol).

Method B

Palladium(0)-induced rearrangement: A mixture of 12 (186 mg, 0.73 mmol), Pd(dba)₂ (21.21 mg, 0.037 mmol) and PPh₃ (23.2 mg, 0.088 mmol) was stirred overnight in anhyd DMF (15 mL) at r.t. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 x 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo produced 2-(1-ethenylcyclopropyloxy)-2'-hydroxybiphenyl 14 (150 mg, 81%); the lack of 12 in the crude product proved that the conversion was complete.

2-(1-Ethenylcyclopropyloxy)-2'-hydroxybiphenyl (14)

Colorless oil.

IR (CDCl₃): 3100–2800, 1593, 1480, 1261 cm⁻¹. 1H NMR (CDCl₃): δ = 1.09 (m, 2 H), 1.325 (m, 2 H), 5.13 (dd, 1 H, J = 17, 11 Hz), 5.75 (dd, 1 H, J = 17, 11 Hz), 6.26 (s, 1 H), 6.95–7.21 (m, 4 H), 7.26–7.42 (m, 2 H). 13C NMR (CDCl₃): δ = 15.88, 61.07, 113.12, 115.55, 117.23, 120.83, 122.02, 126.27, 126.92, 128.65, 129.06, 131.25, 132.36, 137.50, 138.53, 153.52. MS (EI) m/z (%): 252 (54) [M⁺], 230 (100), 179 (86), 131 (55), 129 (55), 103 (47).

HRMS: m/z calcd for C₁₇H₁₆O₂: 252.1150; found: 252.1150.

Palladium(0)-Catalyzed Allylic Substitution of 2,2'-Dihydroxy-6,6'-dimethoxybiphenyl

To a mixture of mesylate 6b (324 mg, 2 mmol), Pd(dba)₂ (58 mg, 0.1 mmol) and PPh₃ (53 mg, 0.2 mmol) in anhyd DMF (20 mL) was added a solution of the dipotassium salt 17 (0.5 mmol; generated from the reaction of 2,2'-dihydroxy-6,6'-dimethoxybiphenyl (17) (123 mg, 0.5 mmol) with K₂CO₃ (207 mg, 1.5 mmol) in anhyd DMF (5 mL) for 1 h at 60 °C) This reaction mixture was stirred at r.t. for 12 h. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 x 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography (C₅H₁₂–Et₂O, 4:1) of the residue gave the pure product 25 (116 mg, 69%).

2,2'-Bis-(2-cyclopropylideneethoxy)-6,6'-dimethoxybiphenyl (18)

Colorless oil.

IR (CDCl₃): 3000–3100, 2900–2950, 1591, 1440, 1266 cm⁻¹. 1H NMR (CDCl₃): δ = 0.81 (s, 4 H), 0.96 (s, 4 H), 4.65 (d, 4 H, J = 5.3 Hz), 5.68–5.80 (m, 2 H), 6.64–6.66 (d, 2 H, J = 8.3 Hz), 7.09–7.16 (d, 2 H, J = 8.3 Hz), 7.28–7.42 (m, 2 H, J = 8.3 Hz). 13C NMR (CDCl₃): δ = 17.99, 195.69, 144.30, 116.14, 120.69, 123.44, 125.53, 126.00 126.25, 127.75, 128.91, 129.26, 134.13, 154.20.

MS (EI) m/z (%): 418 (54) [M⁺], 268 (100), 284 (72), 351 (68), 255 (62), 239 (53).

HRMS: m/z calcd for C₃₀H₂₆O₄: 418.1933; found: 418.1939.

Palladium(0)-Catalyzed Allylic Substitution of 5,5'-Bis-(2-propeny)-2,2'-dihydroxy-3,3'-dimethoxybiphenyl (Dehydrodieu-Dehydrogenol)

A mixture of mesylate 6b (586.5 mg, 3.62 mmol), Pd(dbaz)₂ (41.68 mg, 0.072 mmol) and PPh₃ (45.6 mg, 0.174 mmol) in anhyd DMF (40 mL) was stirred for 14 h at r.t. With the diplatassium salt 12 (1.45 mmol; generated from dehydrodieu-dehydrogenol, 13 (473, mg 1.45 mmol) and K₂CO₃ (301 mg, 2.18 mmol) in anhyd DMF (5 mL) for 1 h at 60 °C) After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 x 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography (C₅H₁₂–Et₂O, 4:1) of the residue, gave the pure product 25 (332 mg, 50%). 24 and 25.
2.2'- Bis(2-cyclopropylidenenoxy)-3,3',-dimethoxy-5,5'-di(2-propenyl)biphenyl (23)

Colorless oil.

IR (CDCl₃): 3000–2700, 1581, 1462, 1268 cm⁻¹.

¹H NMR (CDCl₃): δ = 5.92 (m, 4 H), 1.02 (m, 4 H), 3.35 (d, 4 H, J = 5.8 Hz), 3.80 (s, 3 H), 3.87 (s, 3 H), 4.72 (dd, 1 H, J = 10.8, 1.5 Hz), 4.33 (dd, 1 H, J = 17.7, 1.5 Hz), 5.03–5.12 (m, 4 H), 3.50 (s, 1 H), 5.82–5.97 (m, 1 H), 5.88–6.03 (m, 2 H), 6.69 (m, 4 H).

¹C NMR (CDCl₃): δ = 4.16, 19.42, 40.02, 55.83, 56.026, 73.29, 109.67, 111.62, 111.75, 114.98, 115.75, 123.41, 123.65, 128.79, 129.57, 129.70, 130.88, 132.47, 140.49, 152.73.

MS (EI) m/z (%) = 392 (4) [M⁺], 391 (100), 280 (10), 281 (15), 280 (10), 268 (7), 214 (5), 55 (30).


2-(2-Cyclopropylidenenoxy)-3,3'-dimethoxy-5,5'-di(2-propenyl)biphenyl-2'-hydroxybiphenyl (24)

As a mixture of mesylate 6b (468 mg, 4 mmol), Pd(dbach₂)₂ (46.3 mg, 0.08 mmol), and PPh₃ (49.8 mg, 0.19 mmol) was stirred for 64 h at r.t. with the dipotassium salt 22 [1 mmol; generated as above from dehydrodegeninol (326 mg, 1 mmol) and K₂CO₃ (207 mg, 1.5 mmol)]. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 × 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography (C₅H₁₂–Et₂O, 1:1), gave the pure products 24 (156 mg, 40%) and 25 (39 mg, 10%).

Colorless oil.

IR (CDCl₃): 3800–3200, 3100–2800, 1582, 1452, 1268 cm⁻¹.

¹H NMR (CDCl₃): δ = 1.02 (m, 2 H), 3.35 (d, 4 H, J = 5.8 Hz), 3.83 (s, 3 H), 3.87 (s, 3 H), 4.73 (dd, 1 H, J = 10.8, 1.5 Hz), 4.33 (dd, 1 H, J = 17.7, 1.5 Hz), 5.03–5.12 (m, 4 H), 3.50 (s, 1 H), 5.82–5.97 (m, 1 H), 5.88–6.03 (m, 2 H), 6.65–6.81 (m, 4 H).

¹C NMR (CDCl₃): δ = 144.6, 19.42, 40.02, 55.83, 56.026, 73.29, 109.67, 111.62, 111.75, 114.98, 115.75, 123.41, 123.65, 128.79, 129.57, 129.70, 130.88, 132.47, 140.49, 152.73.

MS (EI) m/z (%) = 392 (4) [M⁺], 391 (100), 280 (10), 281 (15), 280 (10), 268 (7), 214 (5), 55 (30).

HRMS: m/z calc'd for C₂₂H₂₀NaO₄ (M + Na): 505.2355; found 505.2355.

1-Hydroxy-2,2'-6,6'-tris-(2-cyclopropylidenenoxy)biphenyl (28)

Colorless oil.

IR (CDCl₃): 3000–2700, 1581, 1462 cm⁻¹.

¹H NMR (CDCl₃): δ = 1.11 (s, 4 H), 4.25 (m, 2 H), 5.95–6.08 (m, 1 H), 7.36–7.57 (m, 6 H).

¹C NMR (CDCl₃): δ = 1.84, 19.0, 20.9, 65.85, 68.94, 104.89, 106.15, 108.67, 113.82, 114.50, 125.49, 126.50, 128.67, 128.82, 129.46, 157.62, 157.81.

MS (EI) m/z (%) = 416 (53) [M⁺], 349 (76), 91 (86), 77 (85), 67 (100).

A mixture of mesylate 6b (712.8 mg, 4.4 mmol), Pd(dbach₂)₂ (126.5 mg, 0.22 mmol) and PPh₃ (138.3 mg, 0.53 mmol) in anhyd DMF (20 mL) was stirred for 15 min; then the potassium salt 26 (1 mmol, generated as above) was added and the reaction mixture stirred at r.t. for 3 h. After addition of Et₂O (20 mL) and sat. NH₄Cl (20 mL), the organic phase was extracted with Et₂O (2 × 20 mL) and dried over Na₂SO₄. Removal of the solvent in vacuo and flash chromatography of the residue (C₅H₁₂–Et₂O, 1:1), gave the pure products 29 (170 mg, 60%) and 30 (114 mg, 40%).

Colorless oil.

IR (CDCl₃): 3100–2800, 1593, 1480, 1261 cm⁻¹.

¹H NMR (CDCl₃): δ = 1.01 (s, 12 H), 4.52–4.71 (m, 6 H), 5.81–5.92 (m, 3 H), 6.52–6.73 (m, 4 H), 7.15–7.31 (m, 2 H).

¹C NMR (CDCl₃): δ = 1.84, 1.90, 2.09, 65.85, 68.94, 104.89, 106.15, 108.67, 113.82, 114.50, 125.49, 126.50, 128.67, 128.82, 129.46, 157.62, 157.81.

MS (EI) m/z (%) = 416 (53) [M⁺], 349 (76), 91 (86), 77 (85), 67 (100).

HRMS: m/z calc'd for C₁₇H₁₆NaO₄: 307.0946; found 307.0943.
Palladium(0)-Catalyzed Allylic Substitution of 6,6'-Dibromo-2,2'-dihydroxy-3,3'-dimethoxybiphenyl

A solution of Pd(dba)$_2$ (44 mg, 0.0765 mmol) and PPh$_3$ (49 mg, 0.184 mmol) was degassed under vacuum for 1 h and stirred in a N$_2$ atmosphere, then 1-ethynyl-1-oxoxydiphenyl cyclopropane 6c (360 mg, 1.53 mmol) in anhyd DMF (15 mL) was added. After 10 min this mixture had turned green and a solution of the potassium salt 31 (0.66 mmol, generated from 6,6'-dibromo-2,2'-dihydroxy-3,3'-dimethoxybiphenyl) was degassed under vacuum for 1 h and stirred in a N$_2$ atmosphere, then 1-tosyloxy-1-1(2-trimethylsilylethenyl)cyclopropane (380 mg, 1.29 mmol) in 15 ml of anhyd DMF was added. After 10 min this mixture had turned green and a solution of the potassium salt (41), 44 (82).

Removal of the solvent in vacuo and flash chromatography (CH$_2$Cl$_2$-Et$_2$O, 6:4) of the residue gave pure product 32 (260 mg, 75%).

2,2'-Bis(2-cyclopropylideneethoxy)-6,6'-dibromo-3,3'-dimethoxybiphenyl (32)

Colorless oil.

IR (CDCl$_3$): 3060, 3008, 2938, 2839, 1571, 1460, 1346, 1368 cm$^{-1}$.

$^1$H NMR (CDCl$_3$) δ = 0.82–0.94 (m, 8 H), 3.88 (s, 6 H), 4.55 (m, 4 H), 5.75 (m, 2 H), 6.86 (d, 2 H, $J$ = 8.4 Hz), 7.48 (d, 2 H, $J$ = 8.4 Hz).


MS (EI) m/z (%) = 384 (4) [M$^+$], 370 (11), 311 (52), 167 (70), 149 (100).

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References


Claisen Rearrangement of 33

A solution of 10 mg of the minor diastereomer 34 was kept at r.t. for several weeks in CDCl$_3$. After removal of the solvent in vacuo, flash chromatography (C$_6$H$_6$-Et$_2$O, 6:4) of the residue gave pure 34.

2,2'-Dihydroxy-6,6'-dimethoxy-3-[1-(2-trimethylsilylethenyl)]cyclopropyl)biphenyl (34)

Colorless oil (9 mg, 90%).

IR (CDCl$_3$): 3546, 2957, 2928, 2855, 1721, 1607, 1587, 1467 cm$^{-1}$.

$^1$H NMR (CDCl$_3$): δ = 0.10 (s, 9 H), 0.80–1.10 (m, 4 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 5.07 (s, 1 H), 5.31 (d, 1 H, $J$ = 18.1 Hz), 5.37 (s, 1 H), 5.59 (d, 1 H, $J$ = 18.1 Hz), 6.59 (d, 2 H, $J$ = 8.4 Hz), 6.68 (d, 1 H, $J$ = 8.4 Hz), 7.18 (d, 1 H, $J$ = 8.4 Hz), 7.27 (d, 2 H, $J$ = 8.4 Hz).

$^{13}$C NMR (CDCl$_3$): δ = –0.64, 15.52, 15.71, 30.09, 56.25, 56.38, 103.24, 103.76, 107.31, 109.14, 120.99, 127.09, 129.92, 131.99, 150.65, 154.66, 157.37, 158.17.

MS (EI) m/z (%) = 384 (4) [M$^+$], 370 (11), 311 (52), 167 (70), 149 (100).


