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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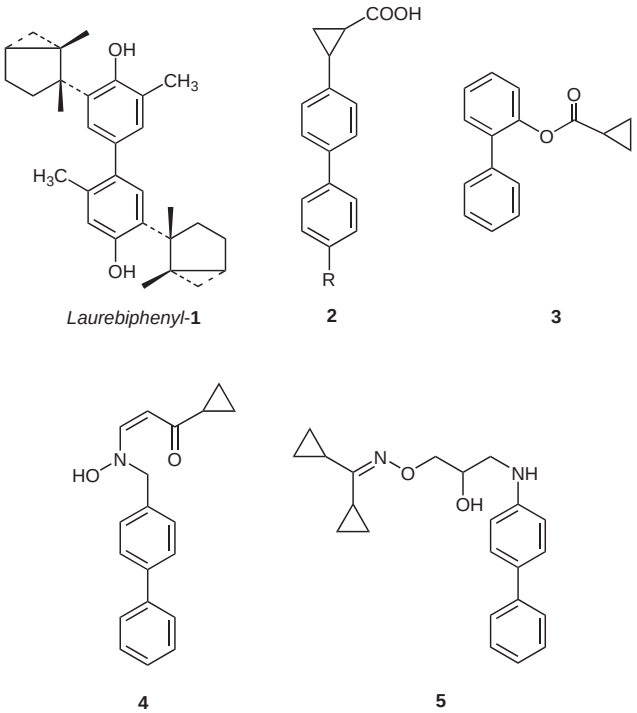
Abstract: Dipotassium salts of 2,2′-dihydroxybiphenyl derivatives underwent palladium(0) catalyzed regioselective allylation by sulfonic esters (mesylates, tosylates) of 1-ethenylcyclopropanol to produce, in good yields, 2,2′-bis(cyclopropylideneethoxy)biphenyls, which are of biological interest. Whilst 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 $CDCl_3$, underwent Claisen rearrangement into the 2,2′-dihydroxy-6,6′-dimethoxy-3-(2-trimethylsilylethenyl)cyclopropylbiphenyl.

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

The growing number of isolated naturally occurring bioactive biphenyls[1] led us to consider this moiety as a basic and valued framework for the synthesis of new pharmacologically[2] and agrochemically[3] 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.[4] 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,[5] due to their broad spectrum of biological properties.[6] 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 cyclolaurane type, laurebiphenyl-**1** was isolated from the red alga *Laurencia nidifica*.[7] Furthermore the bioactivity of several biphenylcyclopropane 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;[8a] while ovicidal activity against spider mites was found for the 2-biphenyl cyclopropanecarboxylate **3**.[8b] 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);[9] 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).[10]



Laurebiphenyl-**1** **2** **3**

4 **5**

Figure 1

In pursuit of the synthetic applications of the π-1,1-ethyleneallylmetal complexes,[11] we report herein an efficient and selective method[12] to prepare 2,2′-bis(2-cyclopropylideneethoxy)biphenyls. In fact, alkylidenecyclopropanes form a peculiar class of strained olefinic compounds with

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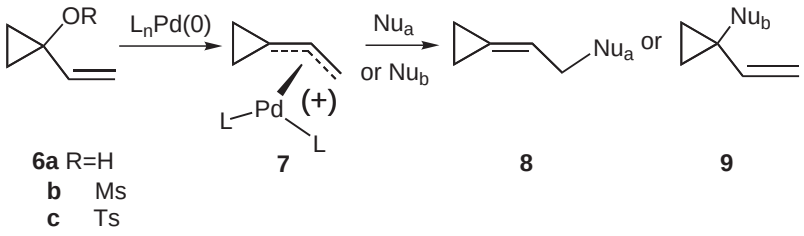


Scheme 1

remarkable synthetic potential,[13] and specific bioactivities.[6]

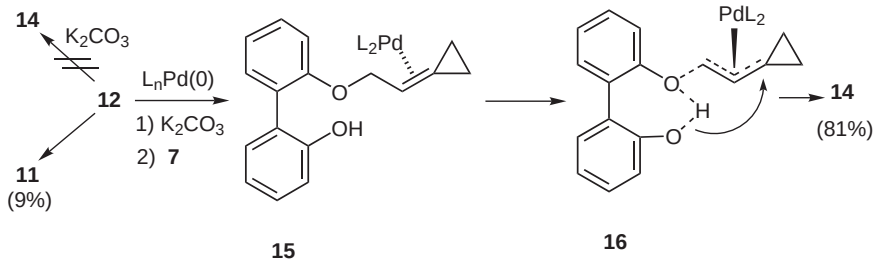
Allylation of 2,2′-dihydroxybiphenyl: the sulfonic esters (mesylate, tosylate) of the 1-ethenylcyclopropanol **6a** (R = H), (readily available from the cyclopropanone hemiacetal,[14] 1-hydroxycyclopropanecarboxylic acid,[15] or recently from titanium(IV)-mediated cyclopropanation of β-halo esters,[16]) formed the π-1,1-ethyleneallylpalladium complex **7**[11] upon treatment with palladium(0). Then, nucleophilic substitution of **7** by soft nucleophiles Nu_a^- (stabilized anions), provided the alkylidenecyclopropanes **8**, while hard nucleophiles 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 K_2CO_3 in anhyd DMF at 60 °C for 2 h) with mesylate **6b** (2.5 equiv, R = OMs) in the presence of palladium(0) {from palladium dibenzylideneacetone [$Pd(dba)_2$] and $2PPh_3$}, in DMF (r.t. for 3 h) gave 2,2′-bis(2-cyclopropylideneethoxy)biphenyl [**11**; 45%], and the monoadduct-I **12** [(16%) 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 = Ts) by the dipotassium salt **10** (4 equiv, 15 h) led to the diadduct **11** (70%), revealing the leaving group effect of the sulfonate (Table 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 K_2CO_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-ethenylcyclopropyloxy)-2'-hydroxybiphenyl [(**14**; 4%) Table 1, entry 5].

A sample of the monoadduct-I **12** remained unaltered upon treatment with of K_2CO_3 (1 equiv) in DMF (60 °C for 7 d), proving that the rearrangement **12**→**14**, was not simply base-induced. On the other hand, reaction of the monoadduct-I **12** with palladium(0) [from 5% $Pd(dba)_2$ and 12% PPh_3] in DMF at (r.t. for 16 h) gave the isomeric monoadduct-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 π-1,1-ethyleneallylpalladium complex (**16**), probably favoured by a H-bond between the oxygen and the hydroxyl group. Therefore, the 2′-hydroxy-2-oxybiphenyl 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 K_2CO_3 in DMF at 60 °C for 1 h) with the mesylate **6b**, in DMF (r.t. for, 12 h, then 60 °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**→**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).



Scheme 2

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

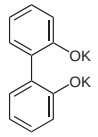
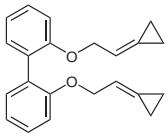
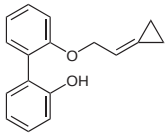
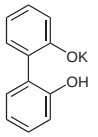
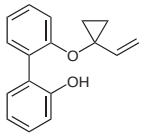
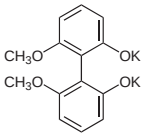
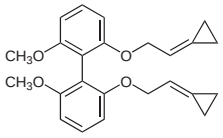
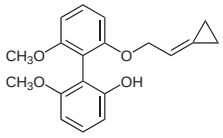
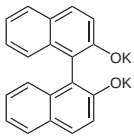
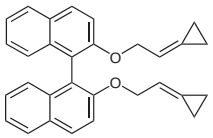
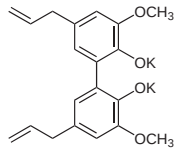
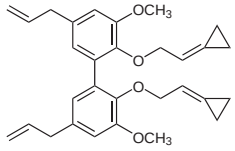
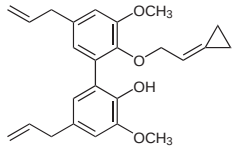
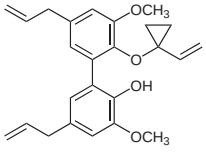
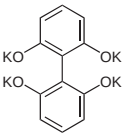
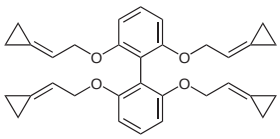
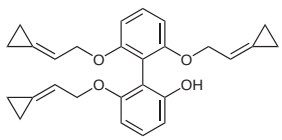
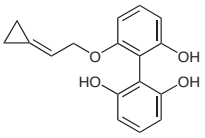
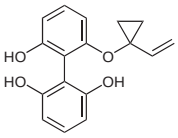
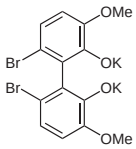
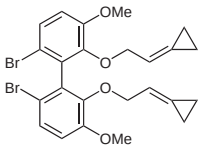
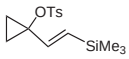
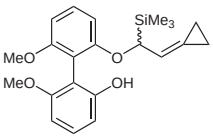
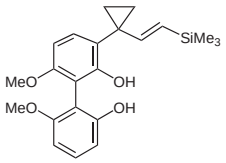
Entry	Nucleophile	Sulfonic ester (equiv)	T °C (reaction time)	Diadduct	Monoadduct-I (%)	Monoadduct-II (%)
						
1	**10**	**6b** (2.5)	r.t. (3 h)	**11** (45)	**12** (16)	–
2	**10**	**6b** (4)	r.t. (3 h)	**11** (79)	**12** (16)	–
3	**10**	**6b** (2.2)	r.t. (15 h)	**11** (90)	**12** (10)	
4	**10**	**6c** (4)	r.t. (15 h)	**11** (70)	–	
						
5	**13**	**6b** (2)	r.t. (3 h)	**11** (15)	**12** (79)	**14** [4; 81 from **12** and Pd(0)]
						
6	**17**	**6b** (4)	r.t. (12 h)	**18** (60)	**19** (0)	–
7	**17**	**6c** (2.2)	r.t. (24 h)	**18** (70)	**19** (30)	–
						
8	**20**	**6b** (4)	r.t. (12 h)	**21** (84)	–	–
						
9	**22**	**6b** (2.5)	r.t. (14 h)	**23** (50)	**24** (3)	**25** (2)
10	**22**	**6b** (4)	r.t. (64 h)	**23** (50)	**24** (40)	**25** (10)
11	**22**	**6c** (4)	r.t. (20 h)	**23** (35)	**24** (63)	**25** (2)
	 **26**					

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

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

[a] Tetraadduct .
[b] Triadduct.
[c] From $CDCl_3$ catalyzed Claisen rearrangement of **33**.

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 K_2CO_3 in anhyd DMF at 60 °C for 1 h), with mesylate **6b** (4 equiv) in the presence of palladium(0) in DMF (r.t. for 12 h), produced the 2,2′-bis(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 K_2CO_3 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 arboreous Lauracea species from the Andes *(Nectandra polita*).[18] D*ehydrodieugenol* 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 K_2CO_3 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% PPh_3] 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 K_2CO_3 (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**

as the principal product (60%), as well as 2,2′,6,6′-tetrakis(2-cyclopropylideneethoxy)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 K_2CO_3 (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-cyclopropylideneethoxy)-6,6-dibromo-3,3′-dimethoxy-biphenyl (**32**) in good yield [(75%) Table 1, entry 14].

Nucleophilic substitution of 1-tosyloxy-1-1(2-trimethylsilylethenyl)cyclopropane by 2,2′-dihydroxy-6,6′-dimethoxy-biphenyl, Claisen rearrangement: reaction of the dipotassium salt **17**, with the 1-(2-trimethylsilylethenyl)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-cyclopropylidene-1-trimethylsilyl)ethoxy]-6,6-dimethoxy-2′-hydroxybiphenyl (**33**; 25%). This resulted from hindered rotation along the main biphenyl axis. On standing in $CDCl_3$ for several weeks only the minor diastereomer of **33** underwent Claisen rearrangement[24] to provide the 2,2′-dihydroxy-6,6′-dimethoxy-3-[1-(2-trimethylsilylethenyl)cyclopropyl)]biphenyl [(**34**; 90%) Table 1, entry 15).

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

^{1}H NMR spectra were recorded on Brücker AM 250 (250 MHz), AC 250 (250 MHz) and AC 200 (200 MHz) spectrometers; δ = 0 for TMS, 7.27 for $CHCl_3$. ^{13}C NMR spectra were also recorded on Brüker AM 250, AC 250 (63 MHz), AC 200 (50 MHz): δ = 77 for $CDCl_3$, 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 chromatographer. 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 Microanalyse, 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-Ethenyl-1-mesyloxycyclopropane (6b)
Compound **6b** was prepared from vinylation of cyclopropanone hemiacetal, followed by mesylation according to known procedures.[11a,14]

1-Ethenyl-1-tosyloxycyclopropane (6c)
Compound **6c** was prepared from titanium(IV)-mediated cyclopropanation of ethyl β–chloropropionate and one-pot tosylation, according to known procedures.[16]

1-Tosyloxy-1-1(2-trimethylsilylethenyl)cyclopropane (6d)
Compound **6d** was prepared from cyclopropanone hemiacetal, followed by tosylation according to known procedures.[11d]

Palladium(0)-Catalyzed Substitution of 1-Ethenyl-1-mesyloxycyclopropane (6b) by the Dipotassium Salt of 2,2′-dihydroxybiphenyl (10); Typical Procedure
A solution of $Pd(dba)_2$ (32mg, 0.055 mmol) and of PPh_3 (35 mg, 0.13 mmol) was degassed under vacuum for 1 h and stirred in a N_2 atmosphere, to this 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 K_2CO_3 (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, Et_2O (20 mL) and sat. NH_4Cl (20 mL) were added. The organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 9:1) of the residue gave 2,2′-bis-(2-cyclopropylideneethoxy)biphenyl (**11**; 143 mg 90%), and 2′-(2-cyclopropylidene ethoxy)-2′-hydroxybiphenyl (**12**; 13 mg 10%).

2,2′-Bis-(2-cyclopropylideneethoxy)biphenyl (11)
Colorless oil.

IR ($CDCl_3$): 3100–2800, 1593, 1480, 1261 cm^{-1}.

^{1}H NMR ($CDCl_3$): 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).

^{13}C NMR ($CDCl_3$): 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* (%) = 318 (50) [M$^+$], 289 (100), 247 (57), 233 (79), 219 (57), 181 (62), 165 (65).

HRMS: *m*/*z* calcd for $C_{22}H_{22}O_2$: 318.1619; found: 318.1616.

2′-(2-Cyclopropylideneethoxy)-2′-hydroxybiphenyl (12)
Colorless oil.

IR ($CDCl_3$): 3800–3200, 3100, 2800, 1593, 1480, 1261 cm^{-1}.

^{1}H NMR ($CDCl_3$): 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).

^{13}C NMR ($CDCl_3$): δ = 1.01, 1.9, 69.6, 112.6, 113.6, 117.7, 121, 122.4, 126.7, 128, 128.8, 129, 129.1, 131.3, 132.6, 153.9, 154.5.

MS (EI) *m*/*z* (%) = 252 (100) [M$^+$], 237 (56), 223 (38), 165 (17), 181 (15), 115 (10).

HRMS: *m*/*z* calcd for $C_{17}H_{16}O_2$: 252.1150; found: 252.1153.

Palladium(0)-Catalyzed Allylic Substitution of 1-Ethenyl-1-tosyloxycyclopropane (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 PPh_3 (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 Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 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 K_2CO_3 (110 mg, 0.8 mmol) was stirred for 7 d in anhyd DMF (5 mL) at 60 °C. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried on Na_2SO_4. 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 PPh_3 (23.2 mg, 0.088 mmol) was stirred overnight in anhyd DMF (15 mL) at r.t.. After addition of Et_2O (20 mL) and of sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. 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 ($CDCl_3$): 3600–3100, 3060–2900, 1594, 1483, 1440, 1266 cm^{-1}.

^1H NMR ($CDCl_3$): 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, 4 H).

^{13}C NMR ($CDCl_3$): 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, 153.38, 153.52.

MS (EI) *m*/*z* (%) = 252 (54) [M^+], 234 (100), 186 (86), 179 (86), 131 (55), 129 (55), 103 (47).

HRMS: *m*/*z* calcd for $C_{17}H_{16}O_2$: 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 PPh_3 (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 K_2CO_3 (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 Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 1:1) of the residue gave the pure product **18** (116 mg, 60%).

2,2′-Bis-(2-cyclopropylideneethoxy)-6,6′-dimethoxybiphenyl (18)
Colorless oil.

IR ($CDCl_3$): 3100–2800, 1593, 1480, 1261 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.02 (s, 8 H), 3.74 (s, 6 H), 4.64 (d, 4 H, *J* = 5.3 Hz), 5.8–5.9 (m, 2 H), 6.64 – 6.68 (d, 2 H, *J* = 8.3 Hz), 6.66–6.71 (d, 2 H, *J* = 5.3 Hz), 7.42–7.33 (t, 2 H, *J* = 8.3).

^{13}C NMR ($CDCl_3$): δ = 1.74, 1.87, 55.83, 68.89, 104.09, 105.96, 113.18, 114.46, 125.36, 128.21, 157.45, 158.33.

MS (EI) *m*/*z* (%) = 379 (27) [M^+], 378 (100)

HRMS: *m*/*z* calcd for $C_{24}H_{26}NaO_2$ (M + Na): 401.1728; found: 401.1729.

A mixture of tosylate **6c** (547 mg, 2.4 mmol), $Pd(dba)_2$ (17.25 mg, 0.03 mmol), and PPh_3 (18.86 mg, 0.072 mmol) in anhyd DMF (20 mL) was stirred at r.t. for 15 min, then the potassium salt **17**, (0.6 mmol; generated as above) was added and the reaction mixture stirred at r.t. for 24 h. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 1:1) of the residue gave the pure products **18** and **19** (70% and 30% respectively).

2-(2-Cyclopropylideneethoxy)-6,6′-dimethoxy-2′-hydroxybiphenyl (19)
Colorless oil.

IR ($CDCl_3$): 3800–3200, 3100–2800, 1593, 1480, 1261 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.03 (s, 4 H), 3.73 (s, 3 H), 3.76 (s, 3 H), 4.75 (d, 2 H, *J* = 4,4 17, 11 Hz), 5.11 (s, 1 H), 5.81–6.02 (m, 1 H), 6.52–6.63 (m, 1 H), 6.63–6.82 (m, 3 H), 7.21–7.42 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 1.86, 2.03, 55.86, 55.98, 68.94, 103.22, 104.3, 106.26, 108.57, 110.02, 110.05, 113.64, 126.66, 128.95, 129.83, 154.27, 157.66, 158.58, 159.22.

MS (EI) *m*/*z* (%) = 313 (21) [MH^+], (M) 312 (100).

HRMS: *m*/*z* calcd for $C_{19}H_{20}NaO_4$ (M + Na): 335.1259; found: 335.1259.

Palladium(0)-Catalyzed Allylic Substitution of 1,1′-Bi-2-naphthol
A mixture of mesylate **6b** (648 mg, 4 mmol), $Pd(dba)_2$ (28.75 mg, 0.05 mmol), and PPh_3 (1.44 mg, 0.120 mmol) in anhyd DMF (20 mL) was stirred at r.t. for 15 min, then a solution of the dipotassium salt **20** [1 mmol; generated from 1,1′-bi-2-naphthol (286 mg, 1 mmol) and K_2CO_3 (414 mg, 3 mmol) in anhyd DMF (5 mL) heated for 1 h at 60 °C] was added and stirring continued for 12 h at r.t., After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography of the residue, (C_5H_{12}–Et_2O, 9:1) gave the pure compound **21** (368 mg, 84%).

2,2′-Bis-(2-cyclopropylideneethoxy)-1,1′-binaphthalene (21)
Colorless oil.

IR ($CDCl_3$): 3300–2700, 1591, 1507, 1261 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.81 (s, 4 H), 0.96 (s, 4 H), 4.65 (d, 4 H, *J* = 6.3 Hz), 5.68–5.8 (m, 2 H), 7.12–7.16 (d, 2 H), 7.28–7.24 (dd, 2 H, *J* = 7.5, 0.9 Hz), 7.28–7.36 (dd, 2 H, *J* = 6.4, 1.4 Hz), 7.41–7.46 (d, 2 H, *J* = 9.0 Hz), 7.84 (d, 2 H, *J* = 8.3 Hz), 7.92 (d, 2 H, *J* = 8.8 Hz).

^{13}C NMR ($CDCl_3$): δ = 1.79, 1.95, 69.72, 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 $C_{30}H_{26}O_2$: 418.1933; found: 418.1939.

Palladium(0)-Catalyzed Allylic Substitution of 5,5′-Bis(2-propenyl)-2,2′-dihydroxy-3,3′-dimethoxybiphenyl (*Dehydrodieugenol*)
A mixture of mesylate **6b** (586.5 mg, 3.62 mmol), $Pd(dba)_2$, (41.68 mg, 0.072 mmol) and PPh_3 (45.6 mg, 0.174 mmol) in anhyd DMF (40 mL) was stirred for 14 h at r.t with the dipotassium salt **22** [1.45 mmol; generated from dehydrodieugenol,[18] (473, mg 1.45 mmol) and K_2CO_3 (301 mg, 2.18 mmol) in anhyd DMF (5 mL) for 1 h at 60 °C]. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 4:1) of the residue, gave the pure products **23** (332 mg, 50%), **24** and **25**.

2,2′-Bis(2-cyclopropylideneethoxy)-3,3′-dimethoxy-5,5′-di(2-propenyl)biphenyl (23)
Colorless oil.

IR ($CDCl_3$): 3000–2700, 1581, 1462, 1268 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.92 (m, 4 H), 1.02 (m, 4 H), 3.35 (d, 4 H, *J* = 7.9 Hz), 3.92 (s, 6 H), 4.41 (d, 4 H, *J* = 7.9 Hz), (5.10 m, 4 H), 5.81–5.92 (m, 2 H), 5.92–6.11 (m, 2 H), 6.72 (d, 2 H, *J* = 1.8 Hz), 6.77 (d, 2 H, *J* = 1.8 Hz).

^{13}C NMR ($CDCl_3$): δ = 1.37, 2.10, 40.02, 55.81, 73.11, 111.63, 114.89, 115.62, 123.50, 126.31, 132.94, 134.68, 137.44, 144.01, 152.73.

MS (EI) *m*/*z* (%) = 458 (7) [M^+], 391 (26), 350 (100), 321 (88), 281 (31), 240 (17), 214 (40), 165 (15), 40 (23).

HRMS: *m*/*z* calcd for $C_{30}H_{34}O_4$: 458.2461; found 458.2454.

2-(2-Cyclopropylideneethoxy)-3,3′-dimethoxy-5,5′-di(2-propenyl)biphenyl-2′-hydroxybiphenyl (24)
As above a mixture of mesylate **6b** (648 mg, 4 mmol), $Pd(dba)_2$ (46.3 mg, 0.08 mmol), and PPh_3 (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 dehydrodieugenol[18] (326.2 mg, 1 mmol) and K_2CO_3 (207 mg, 1.5 mmol)]. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 4:1) of the residue, gave the pure products **24** (156 mg, 40%) and **25** (39 mg, 10%).

Colorless oil.

IR ($CDCl_3$): 3800–3200, 3100–2800, 1582, 1452, 1268 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.92 (m, 2 H), 1.02 (m, 2 H), 3.35 (d, 4 H, *J* = 5.8 Hz), 3.8 (s, 3 H), 3.89 (s, 3 H), 4.87 (d, 2 H, *J* = 7.9 Hz), 5.11 (m, 4 H), 5.81–5.92 (m, 1 H), 5.92–6.09(m, 2 H), 6.65–6.81 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ =1.47, 2.13, 40.03, 55.65, 55.85, 73.14, 109.59, 111.61, 111.76, 114.98, 115.66, 123.41, 123.66, 126.156, 133.387, 133.855, 134.67, 134.85, 137.39, 137.48, 140.56, 152.76, 152.91.

MS (EI) *m*/*z* (%) = 392 (4) [M^+], 350 (13), 321 (100), 280 (10), 281 (15), 280 (10), 268 (7), 214 (5), 55 (30).

HRMS: *m*/*z* calcd for $C_{25}H_{28}O_4$: 392.1990; found 392.1990.

3,3′-Dimethoxy-5,5′-di(2-propenyl)-2-(1-ethenylcyclopropyloxy)-2′-hydroxybiphenyl (25)
Colorless oil.

IR ($CDCl_3$): 3600–3150, 3100–2850, 1583, 1453, 1267 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.93 (m, 2 H), 1.04 (m, 2 H), 3.32 (d, 4 H, *J* = 6 Hz), 3.80 (s, 3 H), 3.87 (s, 3 H), 4.72 (dd, 1 H, *J* = 10.8, 1.5 Hz), 4.83 (dd, 1 H, *J* = 17.7, 1.5 Hz), 5.03–5.12 (m, 4 H), 5.30 (s, 1 H), 5.82–5.87 (m, 1 H), 5.88–6.03 (m, 2 H), 6.69 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 14.46, 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^+], 350 (13), 321 (100), 280 (10), 281 (15), 280 (10), 268 (7), 214 (5), 55 (30).

HRMS: *m*/*z* calcd for $C_{25}H_{28}O_4$: 392.1990; found 392.1990.

Palladium(0)-Catalyzed Allylic Substitution of 2,2′,6,6′-Tetrahydroxybiphenyl (26)
A mixture of mesylate **6b** (1296 mg, 8 mmol), $Pd(dba)_2$ (28.75 mg, 0.048 mmol) and PPh_3 (31.44 mg, 0.120 mmol) in anhyd DMF (40 mL) was stirred for for 12 h at r.t. with the tetrapotassium salt **26** [1 mmol; generated from 2,2′,6,6′-tetrahydroxybiphenyl (**26**)[22] (218 mg, 1 mmol) and K_2CO_3 (345 mg, 2.5 mmol) in anhyd DMF (5 mL) for 1 h at 60 °C]. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography of the residue (C_5H_{12}–Et_2O, 6:4), gave the pure products **27** (75 mg, 15%) and **28** (75 mg, 60%).

2,2′,6,6′-Tetra-(2-cyclopropylideneethoxy)biphenyl (27)
Colorless oil.

IR ($CDCl_3$): 3100–2800, 1593, 1480, 1261 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.99 (s, 8 H), 4.55–4.65 (d, 8 H, *J* = 5.8 Hz), 5.85–5.95 (m, 4 H), 6.60–6.64 (d, 4 H, *J* = 8.3 Hz), 7.14–7.23 (t, 2 H, *J* = 8.3 Hz).

^{13}C NMR ($CDCl_3$): δ = 1.70, 1.81, 68.78, 105.71, 114.46, 114.57, 125.16, 127.83, 157.57

MS (EI) *m*/*z* (%) = 483 (36) [M^+], 482 (100).

HRMS: *m*/*z* calcd for $C_{32}H_{34}NaO_4$ (M + Na): 505.2355; found 505.2355.

2′-Hydroxy-2,6,6′-tris-(2-cyclopropylideneethoxy)biphenyl (28)
Colorless oil.

IR ($CDCl_3$): 3800–3200, 3100–2800, 1561, 1480, 1259 cm^{-1}.

^1H NMR ($CDCl_3$): 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).

^{13}C NMR ($CDCl_3$): 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).

A mixture of mesylate **6b** (712.8 mg, 4.4 mmol), $Pd(dba)_2$ (126.5 mg, 0.22 mmol) and PPh_3 (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 d. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography of the residue (C_5H_{12}–Et_2O, 1:1), gave the pure products **29** (170 mg, 60%) and **30** (114 mg, 40%).

2-(2-Cyclopropylideneethoxy)-2′,6,6′-trihydroxybiphenyl (29)
Colorless oil.

^1H NMR ($CDCl_3$): 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).

^{13}C NMR ($CDCl_3$): 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.

2-(1-Ethenylcyclopropyloxy)-2′,6,6′-trihydroxybiphenyl (30)
Colorless oil.

^1H NMR ($CDCl_3$): δ = 0.83 (m, 2 H), 0.95 (m, 2 H), 4.98–5.08 (m), 5.60–5.75 (m, 1 H), 6.60–6.84 (m, 4 H), 7.19–7.33 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 15.96, 60.93, 108.23, 108.32, 112.99, 130.89, 131.20, 137.76, 154.68.

MS (EI) *m*/*z* (%) = 284 (3) [M^+], 262 (64), 183 (100), 108 (72), 77 (7), 57 (8), 51 (27), 39 (11).

HRMS: *m*/*z* calcd for $C_{17}H_{16}NaO_4$ (M + Na): 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, 0.0765mmol) and PPh_3 (49 mg, 0.184 mmol) was degassed under vacuum for 1 h and stirred in a N_2 atmosphere, then 1-ethenyl-1-tosyloxycyclopropane **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[23] (260 mg, 0.66 mmol), and K_2CO_3 (0.180 mg, 1.35 mmol) in DMF (10 mL, for 1 h at 60 °C)] was added, and the mixture stirred at r.t. for 3 h. After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 8:2) of the residue gave the 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, 1436, 1368 cm^{-1}.

^1H 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).

^{13}C NMR ($CDCl_3$): δ = 1.53, 2.11, 55.87, 73.33, 113.05, 114.62, 114.84, 126.51, 127.03, 133.97, 147.25, 152.31.

MS (EI) *m*/*z* (%) = 534 (5) [M^+], 322 (41), 309 (100), 214(95), 133 (41), 44 (82).

Palladium(0)-Catalyzed Substitution of 1-Tosyloxy-1-1(2-trimethylsilylethenyl)cyclopropane by the Dipotassium Salt 17 of 2,2′-Dihydroxy-6,6′-dimethoxybiphenyl

A solution of $Pd(dba)_2$ (37 mg, 0.0645 mmol) and PPh_3 (40 mg, 0.15 mmol) was degassed under vacuum for 1 h and stirred in a N_2 atmosphere, then 1-tosyloxy-1-1(2-trimethylsilylethenyl)cyclopropane **6d** (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 dipotassium salt **17** (generated as above) was added, and the mixture stirred at r.t. for 3 h; After addition of Et_2O (20 mL) and sat. NH_4Cl (20 mL), the organic phase was extracted with Et_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo and flash chromatography (C_5H_{12}–Et_2O, 6:4) of the residue gave a 60:40 diastereomeric mixture of **33** (50 mg, 25%).

2-[(2-Cyclopropylidene-1-trimethylsilyl)ethoxy]-6,6-dimethoxy-2′-hydroxybiphenyl (33)

Colorless oil.

IR ($CDCl_3$): 3541, 2958, 2928, 2855, 1589, 1465, 1247, 1090 cm^{-1}.

^1H NMR ($CDCl_3$): δ = –0.15 (s, 9H), 0.92–1.04 (m, 4 H), 3.72 (s, 3 H), 3.74 (s, 3 H), 4.93 (s, 1 H), 5.70 (m, 1 H), 6.50–6.65 (m, 4 H), 7.17–7.27 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = –3.76, 0.46, 2.37, 2.92, 56.02, 56.35, 103.09, 103.79, 104.78, 106.42, 108.31, 109.74, 113.90, 116.98, 118.58, 121.65, 123.65, 128.94, 129.75, 138.79.

MS (EI) *m*/*z* (%) = 384.2 (7) [M^+], 369 (71), 311(100), 263(95), 187(22), 73(10).

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_5H_{12}–Et_2O, 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}.

^1H 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, 1 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, 128.97, 129.92, 131.99, 150.65, 154.66, 154.76, 157.37, 158.17.

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

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