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Suzuki–Miyaura Coupling of Halophenols and Phenol Boronic Acids: Systematic Investigation of Positional Isomer Effects and Conclusions for the Synthesis of Phytoalexins from Pyrinae

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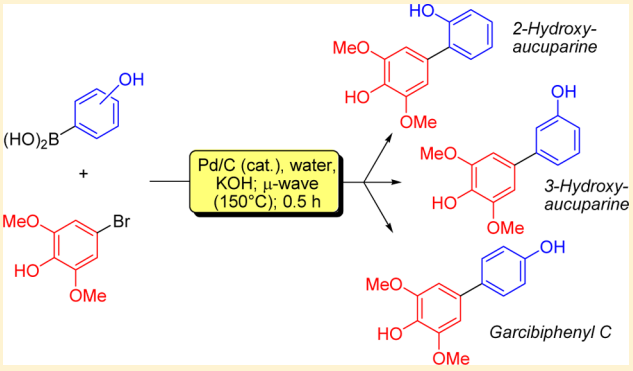
Supporting Information

ABSTRACT: The Suzuki–Miyaura couplings of *o*-, *m*-, and *p*-halophenols with *o*-, *m*-, and *p*-phenol boronic acids were investigated for all combinations under standardized conditions, using Pd/C as a heterogeneous catalyst and water as a solvent. In the case of iodophenols, conventional heating was used, while for bromophenols significantly better results could be obtained using microwave irradiation. This systematic study revealed that 2,4′-biphenol is particularly difficult to access, irrespective of the starting materials used, but that these difficulties can be overcome by using different additives. The conclusions drawn from this investigation allowed us to identify conditions for the protecting group-free or minimized total synthesis of biaryl-type phytoalexins. These compounds possess antibacterial activity and are produced by fruit trees as a response to microbial infection.



INTRODUCTION

Since its discovery in the late 1970s, the Suzuki–Miyaura coupling[1] has emerged as one of the most widely used C–C-bond forming reactions.[2] In particular, its potential for the synthesis of biaryls[3] has led to numerous applications, not only on laboratory scale but also in process chemistry.[4] In the latter field, the development of more active catalyst/ligand combinations has been an important topic because for large-scale applications low catalyst loadings and the use of the cheaper but less reactive aryl chlorides or bromides is required for economic reasons.[5] Other important developments include the search for alternative organoboron reagents,[6−8] the use of immobilized catalysts, in particular Pd/C,[9,10] heating by microwave irradiation,[11] and using water as an environmentally benign solvent.[12,13] It has also been reported that two or more of these special reaction conditions can be advantageously combined, e.g., by conducting Suzuki–Miyaura coupling reactions in water under microwave irradiation and with Pd/C as an easily recoverable catalyst.[14−20]

Based on this literature precedence, we have recently investigated the protecting group-free synthesis of 2,2′-biphenols via Suzuki–Miyaura coupling of 2-iodo- or 2-bromophenols with 2-boronophenols.[21] Essentially, we were able to establish user-friendly protocols for this cross-coupling using commercial Pd/C as a catalyst, water as a solvent, and heating by microwave irradiation for the less reactive bromophenols. Notably, we were able to show that the success of Suzuki–Miyaura couplings under these reaction conditions is largely independent of the source and manufacturing process of the Pd/C used, which is not necessarily the case for this catalyst.[22] Our main motivation for this study was the occurrence of the 2,2′-biphenol structural pattern in various plant-derived natural products, such as acerogenin E (**1**)[23] or magnolol (**2**).[24] However, 2,2′-biphenols are not the only common plant metabolites. Other examples are 2′-hydroxyaucuparin (*o*-**3**),[25] 3′-hydroxyaucuparin (*m*-**3**),[26] and garcibiphenyl C (*p*-**3**),[27] which are phytoalexins isolated from fruit trees of the subtribe Pyrinae. The plants produce these compounds in response to infection with bacterial diseases such as fire flight, which may cause severe economic damages in fruit tree plantations.[28] Apart from the biphenols, partially methylated derivatives (e.g., rhaphiolepsin (**4**),[29] 2′-methoxyaucuparin (*o*-**5**),[30,31] and 4′-methoxyaucuparin (*p*-**5**)[29,30]), a benzodioxol derivative **6**,[32,33] or partially deoxygenated derivatives (e.g., aucuparin (**7a**)[25,34] or its 3-*O*-demethylated derivative **7b**[34]) have also been isolated and identified as Pyrinae metabolites (Figure 1).

When we started to investigate protecting group-free syntheses of phytoalexins of the 4,*n*′-biphenol type using our previously established standard conditions,[21] we quickly discovered that some of these compounds were inaccessible in synthetically useful yields. This observation prompted us to systematically investigate all possible combinations of regioiso-

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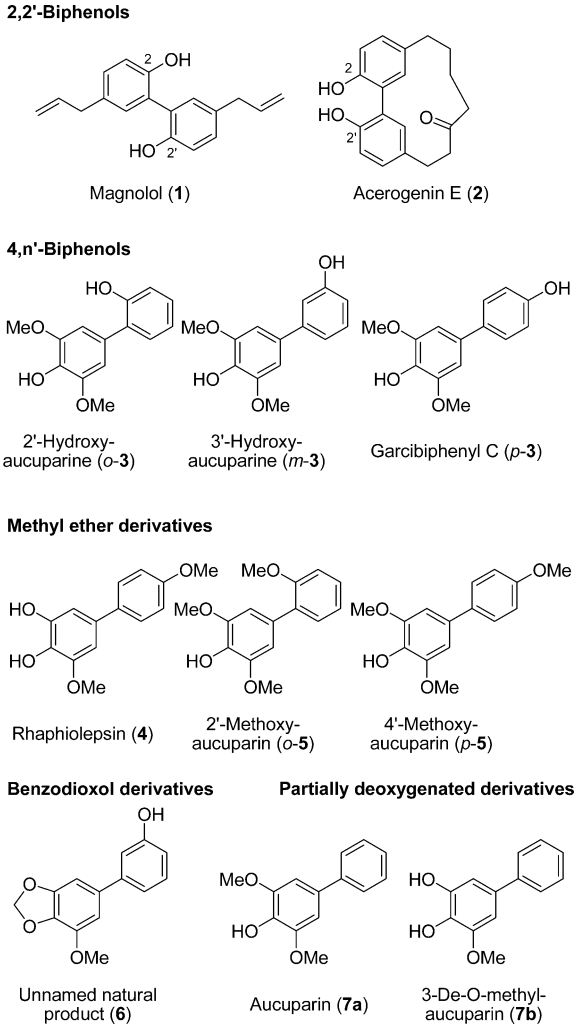

Figure 1. Naturally occurring biphenols.

meric halophenols **8** and boronophenols **9** in Pd/C-catalyzed aqueous Suzuki–Miyaura cross-coupling reactions, to identify regioisomers which are difficult to access, and to devise optimized protocols for these particular cases. In the next step, we wanted to check whether conclusions drawn from this study can assist in planning and executing the synthesis of various phytoalexins from Pyrinae, in particular, compounds **3**–**7** shown in Figure 1.

RESULTS AND DISCUSSION

Systematic Study of All Regioisomeric Iodophenol/Boronophenol Combinations. To study the effect of positional isomerism of the coupling partners on the reactivity in the Suzuki–Miyaura cross-coupling, *o*- (*o*-**8a**), *m*- (*m*-**8a**), and *p*-iodophenol (*p*-**8a**) were reacted with *o*- (*o*-**9**), *m*- (*m*-**9**), and *p*-boronophenol (*p*-**9**) in water in the presence of 4 equiv of K_2CO_3 and 2 mol % of commercial Pd/C as a precatalyst at 80 °C (Table 1). These are the optimized conditions for the protecting group-free synthesis of 2,2′-biphenols.[21]

For almost all combinations, the conversions to the expected biphenols **10** were reproducibly higher than 90%, corresponding to yields between 80% and 98%. Notable exceptions are both combinations leading to 2,4′-biphenol (**10c**), which proceed with conversions lower than 20%, and the cross coupling of *p*-**8a** and *p*-**9** to 4,4′-biphenol (**10f**), which was obtained only in mediocre conversion and yield. Obviously, combinations in which both coupling partners possess an electron-donating phenolate *ortho*- or *para*- to the reacting site are disfavored, with the exception of the *ortho*-,*ortho*-combination leading to **10a** in quantitative yield. Our search for an explanation for this remarkably different reactivity led us to investigate the cross-coupling of the three regioisomeric iodophenols (*o*-,*m*-,*p*-)-**8a** with the less electron-rich phenylboronic acid **11** under our standard conditions (Scheme 1). Electronic and steric effects have often been used to rationalize different reactivities of haloarenes in cross-coupling reactions, which is particularly important for regioselective transformations of polyhalogenated aromatic compounds.[35−37] In most cases, the oxidative addition step is believed to be rate-limiting, and a linear Hammett relationship has been found for the rate constants of the oxidative addition of various *para*-substituted iodobenzenes to a Pd(0)−phosphine complex.[38] The authors of this study drew an analogy between nucleophilic aromatic substitution and oxidative addition of haloarenes to transition metals, which means that the oxidative addition should be faster for electron-deficient haloarenes.[38] This is in line with an NMR-based model for predicting the order of reactivity in cross-coupling reactions of polyhalogenated hetarenes.[39] The higher rates of oxidative addition observed for haloarenes bearing electron-withdrawing substituents is also in line with DFT studies of the mechanism[40] that correlate the energy barriers of oxidative addition with the energy levels of the C−X σ^*- and π^*-orbitals.[41] Based on computational methods, Houk, Merlic, and co-workers proposed three crucial molecular orbital interactions for the site-selective oxidative addition of polyhalogenated hetarenes to a $Pd(0)L_2$ complex: $d_{xy}(Pd) \rightarrow \sigma^*(C-X)$, $\sigma(C-X) \rightarrow p_y(Pd)$, and $d_{xy}(Pd) \rightarrow \pi^*(C-X)$. They found that the ease of oxidative addition, and hence site selectivity, depends crucially on the HOMO–LUMO gap, which is obviously a function of the energy of the arene LUMO.[42]

From the results shown in Scheme 1, it can be seen that all three regioisomeric iodophenols **8a** react with phenylboronic acid (**11**) under standardized conditions in high yields and selectivities to give the expected *o*-, *m*-, and *p*-hydroxybiphenyls (*o*-,*m*-,*p*-**12**). In light of these results, it appears unlikely that different reactivities of the three iodophenols in the oxidative addition step are solely or predominantly responsible for the unsatisfactory yields of biphenols **10c** and **10f**, although this factor might well play a certain role for the overall outcome of the cross-coupling reactions.

We continued our investigation into the reasons for the low conversions to biphenols **10c**,**f** by reinvestigating the reaction of *p*-**8a** and *o*-**9** (Table 2). Testing various relative proportions of *o*-boronophenol and additives other than K_2CO_3 appeared to be most promising, and we therefore started with these parameters. In all of these optimization experiments, the conversion was quantified by ^{1}H NMR spectroscopy based on 1,3,5-trimethoxybenzene as an internal standard. For economic reasons and to simplify product isolation we had so far only used equimolar amounts of the coupling partners. In the first optimization experiments, the amount of *o*-boronophenol (*o*-**9**) was increased in steps of 0.25 equiv until 2.00 equiv of the boronic acid was present. All other parameters were maintained from the standard conditions (entries 1–5). We transcribed the results listed in Table 2, entries 1–5, into the graph shown in Figure 2. The conversion of 4-iodophenol (*p*-**8a**) to 2,4′-biphenol (**10c**) increases nearly linearly with the amount of o-

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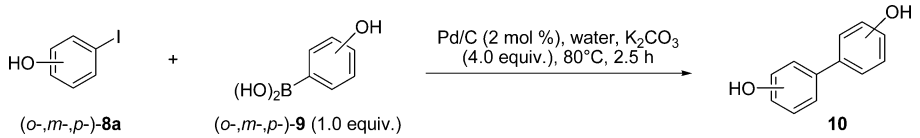
Table 1. Suzuki–Miyaura Cross-Coupling of Iodophenols 8 and Boronophenols 9

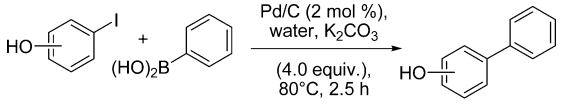


(*o*-,*m*-,*p*-)-**8a** (*o*-,*m*-,*p*-)-**9** (1.0 equiv.) **10**

Boronophenols → / Iodophenols ↓	*o*-**9**	*m*-**9**	*p*-**9**
o-**8a**	**10a** (quant./98%)[a]	**10b** (> 85%/91%)[a]	**10c** (< 20%/n. d.)[a]
m-**8a**	**10b** (quant./93%)[a]	**10d** (quant./95%)[a]	**10e** (> 90%/79%)[a]
p-**8a**	**10c** (<20%/n. d.)[a]	**10e** (> 90%/86%)[a]	**10f** (> 60%/39%)[a]

[a]Conversion/yield are reported in parentheses following the compound number. Conversion was determined on a 0.25 mmol scale by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethoxybenzene as internal standard.

Scheme 1. Cross-Coupling of Regioisomeric Iodophenols 8a with Phenylboronic Acid (11)



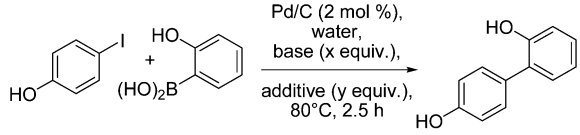
o-**8a**
m-**8a**
p-**8a**
11 (1.0 equiv.)
o-**12** (97%)
m-**12** (94%)
p-**12** (90%)

boronophenol (*o*-**9**) and reaches 88% when 2 equiv of *o*-**9** is used.

This observation might possibly be rationalized by assuming that *o*-boronophenol (*o*-**9**) is deprotonated under the reaction conditions to a phenolate *o*-**13**, which will be less electrophilic at the boron center than the protonated parent compound or an analogous alkyl ether. Similarly, deprotonation of the phenolic hydroxy group in *p*-**9** should also give a phenolate *p*-**13** with reduced Lewis acidity at the boron, whereas phenol deprotonation should affect the Lewis acidity only to a minor extent in the case of *m*-**9** (Scheme 2).

A certain degree of Lewis acidity, however, is essential for the transmetalation step, which is believed to proceed through a hydroxy-Pd species **C** formed via substitution of the halide in **B** by OH^- after the oxidative addition step.[7,43−45] This mechanistic scenario involves the attack of the Pd-bound OH group at the boron to form an intermediate **D**, which subsequently fragments in the actual transmetalation event to the Pd–diaryl complex **E**. The catalyst **A** is then regenerated by reductive elimination of the biaryl Ar–Ar′ (Scheme 3).

Table 2. Optimization of Reaction Conditions for the Combination *p*-8a/*o*-9



p-**8a** *o*-**9** (n equiv.) **10c**

entry	*n* (equiv of *o*-**9**)	base (equiv)	additive (equiv)	conv[a] (%)
1	1.00	K_2CO_3 (4.0)	none	25
2	1.25	K_2CO_3 (4.0)	none	38
3	1.50	K_2CO_3 (4.0)	none	52
4	1.75	K_2CO_3 (4.0)	none	75
5	2.00	K_2CO_3 (4.0)	none	88
6	1.00	K_2CO_3 (4.0)	$B(Oi\text{-}Pr)_3$ (2.00)	31
7	1.00	K_2CO_3 (4.0)	$B(Oi\text{-}Pr)_3$ (4.00)	37
8	1.00	K_2CO_3 (4.0)	$BF_3{\cdot}CH_3OH$ (2.00)	41
9	1.00	K_2CO_3 (4.0)	$BF_3{\cdot}CH_3OH$ (4.00)	75
10	1.00	none	KF (4.00)	>98

[a]Conversion was determined by ^{1}H NMR of the crude reaction mixture with 1,3,5-trimethoxybenzene as internal standard.

Under our reaction conditions, the formation of the crucial borate intermediate **D** might be disturbed by the reduced Lewis acidity of the phenolates *o*-**13** and *p*-**13**, which might account for the low yields of biphenols **10c** and **10f** reported in Table 1 when equimolar amounts of the coupling partners were used. The observation that the conversion to biphenol **10c** increases linearly with the amount of *o*-boronophenol (*o*-**9**) can be explained by assuming borate formation between phenolate *o*-

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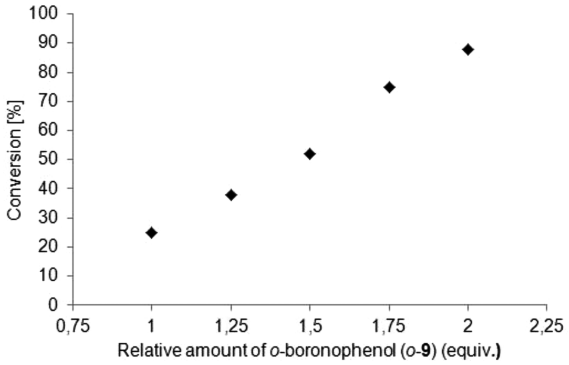
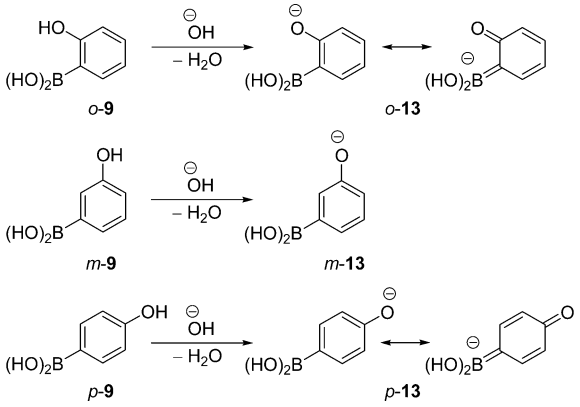
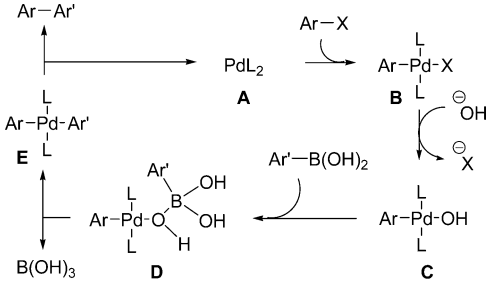


Figure 2. Influence of the molar ratio of *o*-**9** to *p*-**8a** on the conversion to **10c**. Reactions were run under standard conditions stated in Table 1. Conversions were determined by ^{1}H NMR spectroscopy of crude reaction mixtures with 1,3,5-trimethoxybenzene as internal standard.

Scheme 2. Influence of Boronophenolate Formation on Lewis Acidity of the Boronic Acid



Scheme 3. Mechanistic Scenario for the Transmetalation Step via Hydroxy-Pd Pathway[7]



13 and excess boronic acid. In such a dimeric structure **14**, the electrophilicity of one boronic acid should be maintained, whereas the other boron is present as a tetracoordinate boronate, which might react through a competing transmetalation pathway (Figure 3a).

A similar reasoning might be used to explain why equimolar amounts of *o*-**8a** and *o*-**9** react to 2,2′-biphenol (**10a**) quantitatively (see Table 1 and ref 21), although one would expect this combination to be disfavored as both coupling partners are present as phenolates under the reaction conditions and hence very electron rich: upon oxidative addition of the 2-iodophenol to the Pd (and possibly substitution of the iodide by hydroxide) we speculate that a borate **15a** is formed, from which the nucleophilic aryl substituent can be transferred to the Pd intramolecularly.

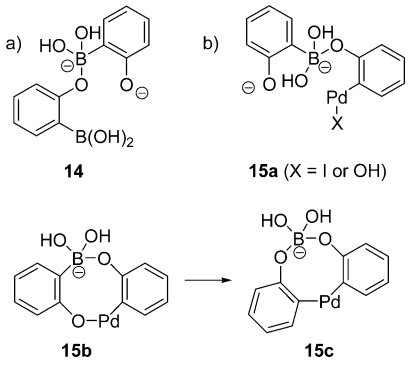


Figure 3. (a) Dimeric borate structure **14** with one capped phenolate that might explain the beneficial effect of excess boronic acid. (b) Proposed borate tethered transmetalation as a rationale for the high reactivity of *o*-**8a** and *o*-**9**.

One might even go one step further and propose the formation of a palladacycle **15b** through nucleophilic intramolecular attack of the boronophenolate at the Pd. From **15b**, the transmetalation would also be an intramolecular process and probably furnish the cyclic borate **15c**, which would eventually undergo reductive elimination as an intramolecular process, due to the boronate tether between the two phenolate oxygens (Figure 3b). Admittedly, these mechanistic rationales are at present purely speculative and we cannot provide any proof beyond the circumstantial experimental evidence discussed above. In particular, we could not yet observe borate structures using spectroscopical methods. In light of a recent report by Yu and Shi,[46] however, our mechanistic speculations appear plausible. These authors reported a Suzuki–Miyaura coupling of naphtholates and boronic acids through "mutual activation", that is by formation of a Lewis acid/Lewis base adduct between a phenolate and the boronic acid.

While improving the yield of **10c** by increasing the amount of *o*-boronophenol (*o*-**9**) as shown in Table 2, entries 1–5, and Figure 2 is quite effective, it is unfortunately expensive and complicates product isolation and purification. This led us to return to using equimolar ratios of the reactants *p*-**8a** and *o*-**9** and test a variety of additives for tuning this disfavored combination. Based on the assumption that excess boronic acid reacts with the *o*-boronophenolate to a boronate **14** (Figure 3a) which maintains the required degree of Lewis acidity at the boron, we reasoned that other Lewis acids should be similarly effective. To test this hypothesis, the comparatively mild Lewis acid tris-isopropoxy borate was added. With 2.00 (entry 6) and 4.00 (entry 7) equiv a small but noticeable improvement of the conversion was observed. The stronger Lewis acid boron trifluoride–methanol was significantly more effective, in particular when 4 equiv was used (entries 8 and 9). However, this is most likely not caused solely by the enhanced Lewis acidity and the more efficient capping of the phenolate, but at least to a certain extent by the hydrolysis of the Lewis acid and the liberation of fluoride. It should be noted in this context that potassium organotrifluoroborates, increasingly used nucleophilic coupling partners for Suzuki–Miyaura coupling reactions,[6,8] are also prone to hydrolysis[47−51] and that the fluoride ions liberated in the process coordinate to the catalytically active species. It has been proposed that palladium-bound fluoride promotes the transmetalation similar to a Pd-bound hydroxide through a Lewis acid/Lewis base interaction (analogous to structure **D** in Scheme 3). A second beneficial

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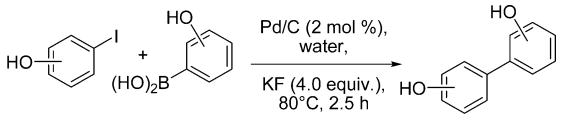
Table 3. Unfavorable Combinations under Fluoride-Promoted (Base-Free) Conditions



8a **9** (1.0 equiv.) **10**

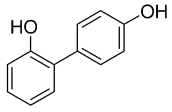
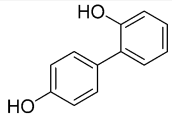
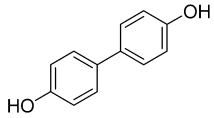
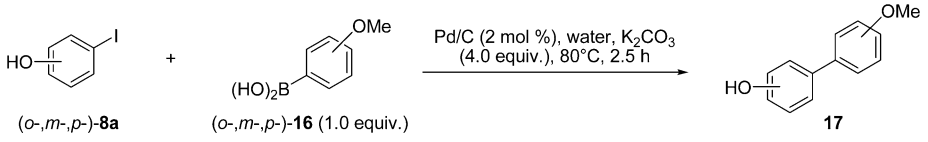
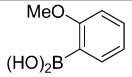
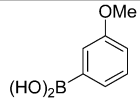
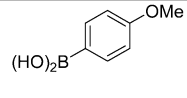
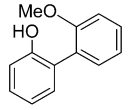
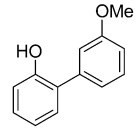
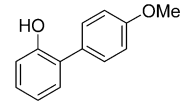
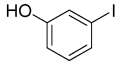
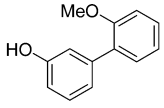
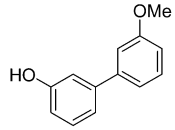
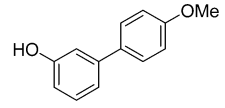
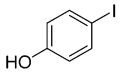
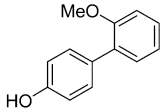
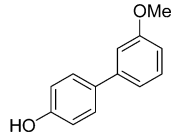
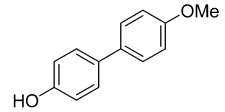
entry	Iodophenol	Boronophenol	Biphenol	Product (Yield)
1	*o*-**8a**	*p*-**9**		**10c** (87%)
2	*p*-**8a**	*o*-**9**		**10c** (76%)
3	*p*-**8a**	*p*-**9**		**10f** (42%)

Table 4. Suzuki–Miyaura Cross-Coupling of Iodophenols 8a and Methoxyphenylboronic Acids 16[a]



(*o*-,*m*-,*p*-)-**8a** (*o*-,*m*-,*p*-)-**16** (1.0 equiv.) **17**

			
	o-**16**	*m*-**16**	*p*-**16**
			
o-**8a**	**17a** (64%/95%[b])	**17b** (86%/95%[b])	**17c** (84%/93%[b])
			
m-**8a**	**17d** (88%)	**17e** (92%)	**17f** (92%)
			
p-**8a**	**17g** (84%)	**17h** (89%)	**17i** (79%)

[a]Yields in parentheses. [b]1.3 equiv of boronic acid used.

effect of fluoride can be a facilitated reductive elimination of the product by coordination of fluoride to the tetracoordinate Pd–diaryl complex resulting from transmetalation (structure **E** in Scheme 3).[52] The enhancement of the transmetalation step by bridging Pd and B via a fluoride ligand has, however, been questioned. Instead, it has been suggested that fluoride enhances the nucleophilicity of water through strong hydrogen bonding and thereby facilitates the formation of a Pd–hydroxy complex **C**, which is primarily responsible for catalytic turnover.[7,53] These considerations and previously reported protocols for Suzuki–Miyaura couplings using alkali fluorides as additives[54,55] prompted us to repeat the reaction without any

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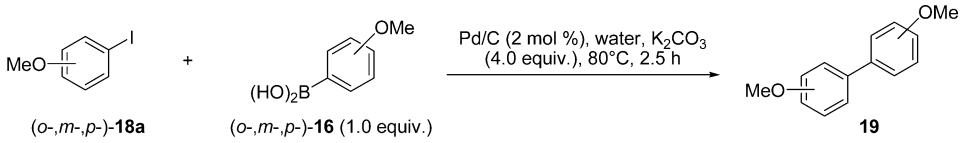
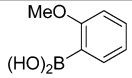
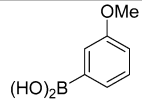
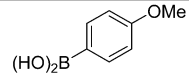
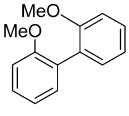
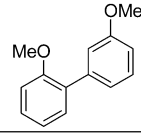
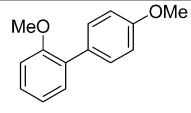
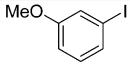
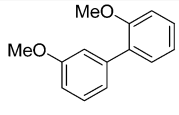
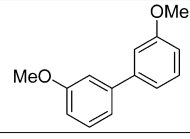
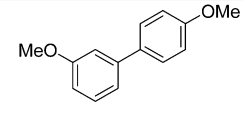
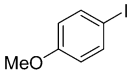
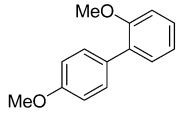
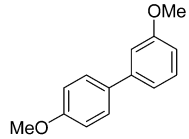
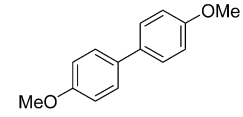
Table 5. Suzuki–Miyaura Cross-Coupling of Iodomethoxybenzenes 18a and Methoxyphenylboronic Acids 16[a]

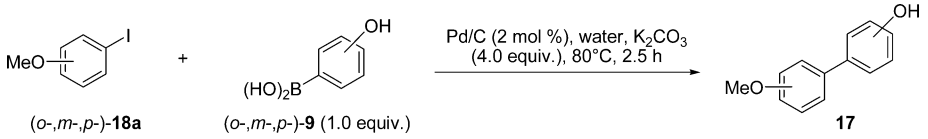


(*o*-,*m*-,*p*-)-**18a** (*o*-,*m*-,*p*-)-**16** (1.0 equiv.) **19**

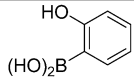
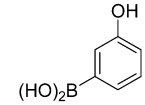
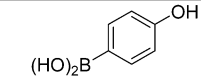
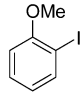
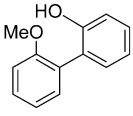
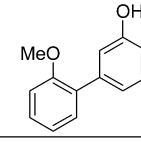
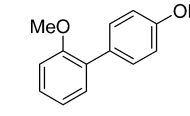
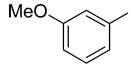
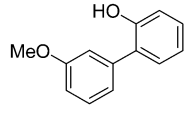
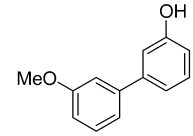
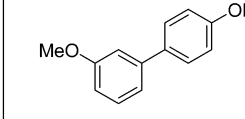
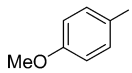
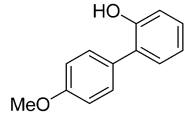
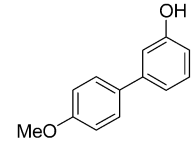
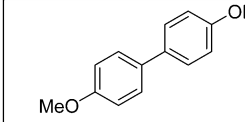
			
	***o*-16**	***m*-16**	***p*-16**
			
***o*-18a**	**19a** (81%)	**19b** (70%)	**19c** (70%)
			
***m*-18a**	**19b** (72%)	**19d** (76%)	**19e** (58%)
			
***p*-18a**	**19c** (82%)	**19e** (72%)	**19f** (93%)

[a]Yields in parentheses.

Table 6. Suzuki–Miyaura Cross-Coupling of Iodomethoxybenzenes 18a and Boronophenols 9[a]



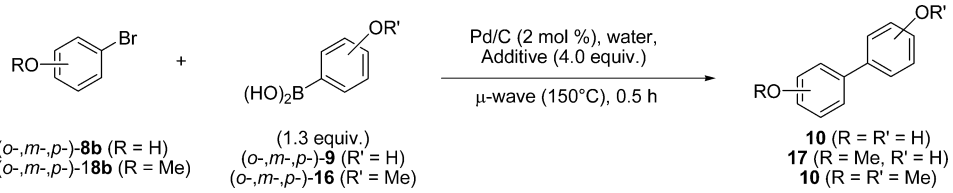
(*o*-,*m*-,*p*-)-**18a** (*o*-,*m*-,*p*-)-**9** (1.0 equiv.) **17**

			
	***o*-9**	***m*-9**	***p*-9**
			
***o*-18a**	**17a** (38%)	**17d** (39%)	**17g** (< 10%)
			
***m*-18a**	**17b** (47%)	**17e** (26%)	**17h** (< 10%)
			
***p*-18a**	**17c** (39%)	**17f** (25%)	**17i** (< 10%)

[a]Yields in parentheses.

dx.doi.org/10.1021/jo500675a | *J. Org. Chem.* 2014, 79, 4104–4118

Table 7. Cross-coupling of Bromoarenes under Microwave Irradiation[a]



(*o*-,*m*-,*p*-)-**8b** (R = H)
(*o*-,*m*-,*p*-)-**18b** (R = Me)

(1.3 equiv.)
(*o*-,*m*-,*p*-)-**9** (R' = H)
(*o*-,*m*-,*p*-)-**16** (R' = Me)

10 (R = R' = H)
17 (R = Me, R' = H)
10 (R = R' = Me)

entry	Ar-Br	Ar′-B(OH)$_2$	additive	R	R′	Ar-Ar′	yield (%)
1	*o*-**8b**	*o*-**9**	KOH	H	H	**10a**	83
2	*o*-**8b**	*m*-**9**	KOH	H	H	**10b**	87
3	*o*-**8b**	*p*-**9**	KOH	H	H	**10c**	33
4	*o*-**8b**	*p*-**9**	NBu$_4$F	H	H	**10c**	90
5	*m*-**8b**	*o*-**9**	KOH	H	H	**10b**	80
6	*m*-**8b**	*m*-**9**	KOH	H	H	**10d**	94
7	*m*-**8b**	*p*-**9**	KOH	H	H	**10e**	87
8	*p*-**8b**	*o*-**9**	KOH	H	H	**10c**	<20
9	*p*-**8b**	*o*-**9**	NBu$_4$F	H	H	**10c**	93
10	*p*-**8b**	*m*-**9**	KOH	H	H	**10e**	96
11	*p*-**8b**	*p*-**9**	KOH	H	H	**10f**	96
12	*o*-**8b**	*o*-**16**	KOH	H	Me	**17a**	<10
13	*o*-**8b**	*o*-**16**	NBu$_4$F	H	Me	**17a**	90
14	*o*-**8b**	*m*-**16**	KOH	H	Me	**17b**	46
15	*o*-**8b**	*m*-**16**	NBu$_4$F	H	Me	**17b**	89
16	*o*-**8b**	*p*-**16**	KOH	H	Me	**17c**	85
17	*m*-**8b**	*o*-**16**	NBu$_4$F	H	Me	**17d**	94
18	*m*-**8b**	*m*-**16**	NBu$_4$F	H	Me	**17e**	91
19	*m*-**8b**	*p*-**16**	NBu$_4$F	H	Me	**17f**	93
20	*p*-**8b**	*o*-**16**	NBu$_4$F	H	Me	**17g**	95
21	*p*-**8b**	*m*-**16**	NBu$_4$F	H	Me	**17h**	94
22	*p*-**8b**	*p*-**16**	NBu$_4$F	H	Me	**17i**	96
23	*o*-**18b**	*o*-**16**	NBu$_4$F	Me	Me	**19a**	62
24	*o*-**18b**	*m*-**16**	NBu$_4$F	Me	Me	**19b**	65
25	*o*-**18b**	*p*-**16**	NBu$_4$F	Me	Me	**19c**	81
26	*m*-**18b**	*o*-**16**	NBu$_4$F	Me	Me	**19b**	80
27	*m*-**18b**	*m*-**16**	NBu$_4$F	Me	Me	**19d**	71
28	*m*-**18b**	*p*-**16**	NBu$_4$F	Me	Me	**19e**	72
29	*p*-**18b**	*o*-**16**	NBu$_4$F	Me	Me	**19c**	87
30	*p*-**18b**	*m*-**16**	NBu$_4$F	Me	Me	**19e**	78
31	*p*-**18b**	*p*-**16**	NBu$_4$F	Me	Me	**19f**	63
32	*o*-**18b**	*o*-**9**	NBu$_4$F	Me	H	**17a**	61
33	*o*-**18b**	*m*-**9**	NBu$_4$F	Me	H	**17d**	64
34	*o*-**18b**	*p*-**9**	NBu$_4$F	Me	H	**17g**	62
35	*m*-**18b**	*o*-**9**	NBu$_4$F	Me	H	**17b**	86
36	*m*-**18b**	*m*-**9**	NBu$_4$F	Me	H	**17e**	71
37	*m*-**18b**	*p*-**9**	NBu$_4$F	Me	H	**17h**	52
38	*p*-**18b**	*o*-**9**	NBu$_4$F	Me	H	**17c**	76
39	*p*-**18b**	*m*-**9**	NBu$_4$F	Me	H	**17f**	69
40	*p*-**18b**	*p*-**9**	NBu$_4$F	Me	H	**17i**	67

[a]See Tables 1 and 4–6 for structural formulas of products **10**, **17**, and **19**.

base, but in the presence of potassium fluoride under otherwise identical conditions (Table 2, entry 10). Gratifyingly, the conversion to the desired 2,4′-biphenol (**10c**) was quantitative. We attribute this remarkable improvement not only to the "fluoride effect" discussed above but also to a smaller amount of *o*-boronophenolate *o*-**13** under these base-free (or at least less basic) conditions and, hence, a higher electrophilicity at the boron.

With these results in hand, we reinvestigated the three "unfavorable" combinations shown in Table 1. As can be seen from the results in Table 3, both *o*-,*p*-combinations work well under these conditions and furnish 2,4′-biphenol in synthetically useful yields of 87% and 76%, respectively. In contrast, the *p*-,*p*-combination remains problematic, as the yield of 4,4′-biphenol (**10f**) could not be improved compared to the standard conditions used to obtain the results shown in Table 1.

Systematic Study of All Regioisomeric Iodophenol/Methoxyphenyl Boronic Acid Combinations. As phenol deprotonation of the boronophenols under our aqueous basic standard conditions might possibly be a reason for the unsatisfactory results obtained in some experiments, we decided

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to repeat the systematic investigation of the various regioisomer combinations for iodophenols **8a** and the methoxy analogues **16** of the previously tested boronophenols **9**. As can be seen from the results in Table 4, almost all combinations give the expected biaryls in high yields with equimolar amounts of the coupling partners. A notable exception was the combination of *o*-**8a** and *o*-**16**, which furnished the *o*-,*o*-disubstituted biphenyl **17a** only in a moderate yield of 64%. Remarkably, for the analogous coupling reactions of boronophenols the *o*-,*o*-combination was among the most reactive (see Table 1 for comparison). The comparatively low yield of **17a** might result from steric hindrance and the inability of the reactants to form a dimeric borate, as discussed for the formation of 2,2′-biphenol (**10a**) in Figure 3. By increasing the amount of boronic acid *o*-**16** to 1.3 equiv a quantitative conversion to **17a** was achieved, which was isolated in 95% yield. By the same measure, the yields of **17b** and **17c** were improved by ca. 10%.

Systematic Study of All Regioisomeric Iodomethoxybenzene/Methoxyphenylboronic Acid Combinations. In the next step, we tested the aqueous basic Suzuki−Miyaura coupling conditions for all regioisomeric combinations of iodophenol methyl ethers **18** and methoxyphenylboronic acids **16**. The results in Table 5 show that the yields of coupling products obtained with equimolar amounts of reactants are synthetically useful but in most cases lower than those reported for the iodophenol/boronophenol or the iodophenol/methoxy phenylboronic acid combinations. This is probably not exclusively caused by electronic effects of the substituents but more likely to a larger extent by the limited solubility of the aryl iodides **18a** under the aqueous basic reactions conditions.

Systematic Study of All Regioisomeric Iodomethoxybenzene/Boronophenol Combinations. To conclude this part of the study, we tested the standardized reaction conditions for all combinations of regioisomeric iodomethoxybenzenes **18a** and boronophenols **9** (Table 6). For all products **17a−i** the yields are significantly lower via this route than for the iodophenol/methoxyphenylboronic acid combination (see Table 4 for comparison). In particular, all reactions with *p*-boronophenol (*p*-**9**) give the desired coupling products only in trace amounts, which is partly in agreement with the results obtained for the synthesis of biphenols **10** (see Table 1 for comparison). As a possible explanation for these very low yields, we suggest a combination of two factors. The boronophenols will be deprotonated and therefore most likely deactivated under the aqueous basic conditions. Additionally, in contrast to the iodoarenes the boronophenolates will readily dissolve in the aqueous medium, resulting in a phase separation of the two reactants.

Synthesis of All Regioisomeric Biphenols and Their Mono- and Dimethyl Ethers from Bromoarenes. Bromoarenes are cheaper and normally more conveniently synthesized than the analogous iodoarenes, which can in part be attributed to the light-sensitivity of many organic iodo compounds. Unfortunately, bromoarenes are also generally less reactive in Pd-catalyzed coupling reactions. In our previous study,[21] we discovered for some examples with a 2,2′-biphenol substitution pattern that this drawback can be efficiently compensated or even overcompensated by heating the aqueous reaction mixture by microwave irradiation. In these experiments, KOH was used as a base or alternatively NBu_4F as a less basic rate accelerating additive. The very useful results obtained in these experiments prompted us to transfer the conditions for microwave accelerated aqueous Suzuki−Miyaura couplings to the synthesis of biphenols **10**, their monomethyl ethers **17**, and their dimethyl ethers **19**. In this study, the standardized conditions using microwave irradiation were applied to all possible combinations of bromoarenes **8b** or **18b** and boronic acids **9** or **16**. As can be seen from the results listed in Table 7, all 36 combinations give the desired biaryls in synthetically useful and sometimes even excellent yields. We comment only on some experiments specifically.

Out of all bromophenol/boronophenol combinations (entries 1−11), unsatisfactory results were only obtained for *o*-**8b**/*p*-**9** (entry 3) and *p*-**8b**/*o*-**9** (entry 8) using KOH as a base. Interestingly, low conversions to the expected product **10c** were also found with the corresponding iodophenols for both combinations under conventional heating conditions (see Table 1 for comparison). Replacing the base KOH by the fluoride source NBu_4F led to increased yields of ca. 90% (entries 4 and 9). 4,4′-Biphenol (**10f**) was isolated only in moderate yields of ca. 40% from *p*-iodophenol (*p*-**8a**) under thermal conditions with either K_2CO_3 as a base (Table 1) or KF as an additive (Table 3, entry 3). In contrast, **10f** was obtained from *p*-bromophenol (*p*-**8b**) under microwave irradiation in the presence of KOH in nearly quantitative yield (entry 11).

Out of the three reactions of *o*-**8b** with the regioisomeric methoxyphenylboronic acids **16** (entries 12−16), only the combination *o*-**8b**/*p*-**16** worked well under basic conditions (entry 16). The cross-couplings with *m*- and *p*-**16** could be significantly tuned by switching to NBu_4F as a rate-accelerating additive (entries 13 and 15), which resulted in yields of ca. 90% for **17a** and **17b**. From the experiments discussed so far, we came to the conclusion that the additive NBu_4F leads more reliably to good results than the base KOH for most combinations. For these reasons, only the fluoride was tested for the remaining combinations. All reactions of *m*- and *p*-**8b** with the three boronic acids **16** proceeded in yields higher than 90% for the expected monoethers **17** (entries 17−22). In general, the yields of coupling products **17a−i** are marginally higher for reactions with bromophenols **8b** under microwave irradiation compared to the use of the analogous iodophenols and conventional heating.

For the synthesis of dimethyl ethers **19** (entries 23−31), yields vary between 62% and 87% under microwave conditions, whereas the yields for conventional heating (see Table 5) range from 58% to 93%. For these examples, we cannot state that either one or the other method is clearly superior with respect to yields.

A group of cross-coupling reactions which worked significantly better with microwave irradiation than with conventional heating are the halomethoxyarene/boronophenol combinations (entries 32−40). Most yields of coupling products **17** vary between 61% and 76%. The lowest yield was observed for the reaction of *m*-**18b** and *p*-**9** to **17h** (52%, entry 37), whereas the combination *m*-**18b** and *o*-**9** furnished **17b** in a yield of 86%, which is significantly above average for this set of combinations. Particularly noteworthy is that *p*-boronophenol (*p*-**9**) undergoes a cross coupling reaction with all three regioisomers of **18b** to the expected biaryls **17g,h,i**, respectively, in acceptable yields (entries 34, 37, and 40). Under conventional heating and starting from the analogous iodoarenes **18a**, conversion to these cross-coupling products was lower than 10% (see Table 6 for comparison). All other combinations of regioisomers of **18a** and boronophenols **9** gave the products **17a−f** in yields ranging from 25% to 47%.

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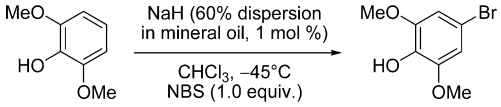
Notably, the *m*-**18**/*o*-**9** combination leading to **17b** is the most reactive one in this set of combinations under both conditions. Irrespective of the heating conditions and the halide present in the electrophilic coupling partner, it can be concluded that the monomethyl ethers **17** are advantageously synthesized from halophenols **8** (entries 12−22) rather than from the analogous methyl ethers **18** (entries 32−40).

Application of Microwave Accelerated Aqueous Suzuki−Miyaura Coupling in the Synthesis of Phytoalexins. With the results obtained from the systematic investigation of all haloarene/boronic acid cross-coupling combinations in hand, we set out to synthesize the phytoalexins **3**−**7** shown in Figure 1. For the synthesis of target molecules, the reactivity in cross-coupling reactions is only one criterion for deciding which coupling partner is assigned the electrophilic and which one the nucleophilic role. Equally important is the accessibility of the starting materials required for the envisaged combination. This led us to syntheses of the nine biaryl-type phytoalexins **3**−**7** in which the less substituted aryl moiety is introduced as a boronic acid and the more substituted one as an aryl bromide. For the synthesis of aucuparin (**7a**), the regioisomeric hydroxyaucuparins (**3**), and methoxyaucuparins (**5**), the bromoarene **21** was required, which was synthesized from 2,6-dimethoxyphenol (**20**) following a literature procedure (Scheme 4).[56,57]

Scheme 4. Synthesis of Bromoarene 21

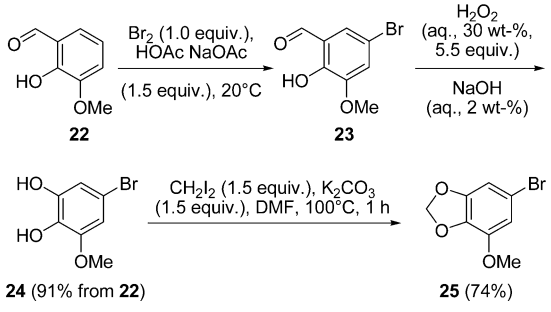


20 **21** (37%)

For rhaphiolepsin (**4**) and 3-de-*O*-methylaucuparin (**7b**), we needed 5-bromo-3-methoxycatechol (**24**), which was also synthesized according to a literature procedure in two steps from vanillin (**22**).[58] The intermediate bromovanillin **23** was used in the second step without purification. The same authors described the *O*-methylenation leading to the benzodioxole **25**, which is the starting material required for the synthesis of the remaining biaryl natural product **6**. We modified the literature procedure[58] by replacing bromochloromethane as the methylenating agent by diiodomethane (Scheme 5).

Phytoalexins with a 1-aryl-4-hydroxy-3,5-dimethoxy substitution pattern were synthesized from bromoarene **21** and boronic acids **9**, **11**, and **16**, respectively, using the standard conditions established in the optimization experiments. The results are summarized in Table 8. In contrast to the optimization experiments, better yields were obtained using the additive

Scheme 5. Synthesis of Bromoarenes 24 and 25



22 **23** **24** (91% from **22**) **25** (74%)

KOH rather than NBu_4F in most cases. The reactivity trend observed for the cross coupling of 4-halophenols *p*-**8a** or *p*-**8b** and the regioisomeric boronophenols **9** (see, e.g., Table 1 for comparison) correlates well with the results for the synthesis of the natural products hydroxyaucuparines *o*-**3** and *m*-**3** and garcibiphenyl C (*p*-**3**) (Table 8, entries 7−13). The *m*-boronophenol (*m*-**9**) was found to be most reactive, followed by the *p*-isomer *p*-**9**. As observed previously for the combination *p*-**8a** and *o*-**9** (or *o*-**8a** and *p*-**9**, see Table 1), the cross-coupling of **21** and *o*-boronophenol (*o*-**9**) failed even under the normally more effective microwave-accelerated standard conditions, regardless of the additive used. 2′-Hydroxyaucuparin (*o*-**3**) was eventually isolated in a moderate yield of 37% by increasing the amount of *o*-boronophenol (*o*-**9**) to 2.6 equiv (entry 13). All other phytoalexins synthesized from **21** were obtained in fair to good yields.

Next, the syntheses of rhaphiolepsin (**4**) and 3-de-*O*-methylaucuparin (**7b**) were addressed, which require the bromoarene **24** and the boronic acids *p*-**16** or **11** as starting materials. In a first experiment, **24** and *p*-**16** were coupled under standard conditions using the additive KOH (Table 9).

We could isolate the target molecule **4** only in a very low yield of 15% (entry 1). This is insofar surprising, as the cross coupling leading to the structurally closely related 4′-methoxyaucuparin (*p*-**5**) works well under identical conditions (see Table 8, entry 6). We suspected that the second acidic group of the bromoarene is responsible for the low yield and tested therefore the less basic additive NBu_4F, but to no avail (entry 2). Increasing the relative amount of additive to 6.0 equiv showed opposite effects for the two additives tested: while the yield of the cross coupling product **4** dropped below 10% with 6.0 equiv of KOH, a slightly better result was obtained with NBu_4F (entries 3 and 4). A significant improvement was eventually achieved by using a larger excess of boronic acid and KOH as an additive (entry 5). As for the cross-coupling reactions listed in Table 8, KOH appears to be the superior rate-accelerating additive. Further increasing the amount of boronic acid *p*-**16** gives only a marginally higher yield of rhaphiolepsin (**4**) (entry 7). Very similar results were also obtained for the cross coupling of **24** and **11**, which leads to the natural product 3-de-*O*-methylaucuparin (**7b**). Under standard conditions, both additives resulted in unsatisfactory yields of 28% and 20%, respectively (entries 8 and 9). With a relative amount of 2.6 equiv of boronic acid **11**, however, **7b** was isolated in significantly higher yields of 74% and 65%, respectively (entries 10, 11). As for the other cross-coupling reactions involving bromoarene **24**, KOH is the preferred additive.

For the synthesis of the unnamed natural product **6** we considered originally a two-step sequence comprising a cross coupling of **24** and *m*-boronophenol (*m*-**9**), followed by methylenation of the *vic*-diol moiety. However, the difficulties observed for the cross-coupling reactions involving diol **24** (see Table 9) prompted us to use bromoarene **25** (Scheme 5) and *m*-boronophenol (*m*-**9**) as cross-coupling partners. Gratifyingly, application of our standard conditions for the microwave-accelerated aqueous Suzuki−Miyaura coupling furnished the natural product **6** in good yield without any further optimization efforts (Scheme 6).

■ CONCLUSIONS

In summary, we could demonstrate that all regioisomeric *n*,*n*′-biphenols and their mono- and dimethyl ethers are accessible

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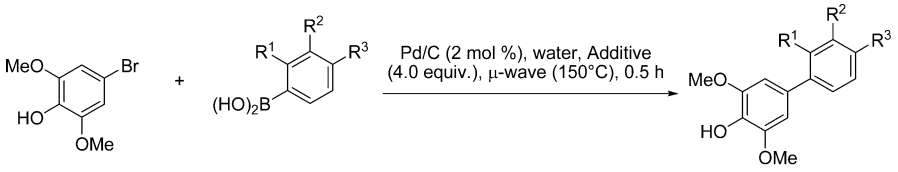
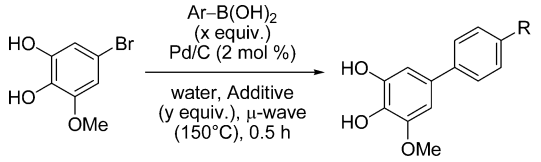
Table 8. Synthesis of Phytoalexins 3, 5, and 7a Derived from 21



21 (*o*-,*m*-,*p*-)-**9**; (*o*-,*m*-,*p*-)-**16**; **11** (*o*-,*m*-,*p*-)-**3**; (*o*-,*p*-)-**5**; **7a**

entry	$ArB(OH)_2$ (equiv)	R^1	R^2	R^3	additive	natural product (no.)	yield (%)
1	**11** (1.3)	H	H	H	NBu_4F	aucuparin (**7a**)	62
2	**11** (1.3)	H	H	H	KOH	aucuparin (**7a**)	75
3	*o*-**16** (1.3)	OMe	H	H	NBu_4F	2′-methoxyaucuparin (*o*-**5**)	49
4	*o*-**16** (1.3)	OMe	H	H	KOH	2′-methoxyaucuparin (*o*-**5**)	47
5	*p*-**16** (1.3)	H	H	OMe	NBu_4F	4′-methoxyaucuparin (*p*-**5**)	48
6	*p*-**16** (1.3)	H	H	OMe	KOH	4′-methoxyaucuparin (*p*-**5**)	67
7	*m*-**9** (1.3)	H	OH	H	NBu_4F	3′-hydroxyaucuparin (*m*-**3**)	34
8	*m*-**9** (1.3)	H	OH	H	KOH	3′-hydroxyaucuparin (*m*-**3**)	72
9	*p*-**9** (1.3)	H	H	OH	NBu_4F	harcibiphenyl C (*p*-**3**)	35
10	*p*-**9** (1.3)	H	H	OH	KOH	garcibiphenyl C (*p*-**3**)	52
11	*o*-**9** (1.3)	OH	H	H	NBu_4F	2′-hydroxyaucuparin (*o*-**3**)	<5
12	*o*-**9** (1.3)	OH	H	H	KOH	2′-hydroxyaucuparin (*o*-**3**)	<5
13	*o*-**9** (2.6)	OH	H	H	KOH	2′-hydroxyaucuparin (*o*-**3**)	37

Table 9. Optimization of Suzuki–Miyaura Couplings with Bromoarene 24

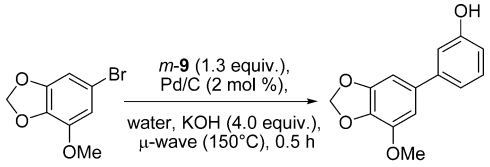


24

Rhaphiolepsin (**4**, R = OMe)
3-De-*O*-methylacucuparin (**7b**, R = H)

entry	Ar-$B(OH)_2$ (equiv)	additive (equiv)	R	product (yield, %)
1	*p*-**16** (1.3)	KOH (4.0)	OMe	**4** (15)
2	*p*-**16** (1.3)	$NBu_4F{\cdot}3H_2O$ (4.0)	OMe	**4** (15)
3	*p*-**16** (1.3)	KOH (6.0)	OMe	**4** (<10)
4	*p*-**16** (1.3)	$NBu_4F{\cdot}3H_2O$ (6.0)	OMe	**4** (24)
5	*p*-**16** (2.6)	KOH (4.0)	OMe	**4** (70)
6	*p*-**16** (2.6)	$NBu_4F{\cdot}3H_2O$ (4.0)	OMe	**4** (40)
7	*p*-**16** (3.0)	KOH (4.0)	OMe	**4** (72)
8	**11** (1.3)	KOH (4.0)	H	**7b** (28)
9	**11** (1.3)	$NBu_4F{\cdot}3H_2O$ (4.0)	H	**7b** (20)
10	**11** (2.6)	KOH (4.0)	H	**7b** (75)
11	**11** (2.6)	$NBu_4F{\cdot}3H_2O$ (4.0)	H	**7b** (65)

Scheme 6. Synthesis of Unnamed Natural Product 6



25 **6** (69%)

via Suzuki–Miyaura cross coupling of the regioisomeric haloarenes and the regioisomeric boronophenols or their respective methyl ethers in water, using commercial Pd/C as a catalyst. With iodophenols or their methyl ethers conventional heating conditions are in most cases sufficient to obtain the desired coupling products in good yields, whereas microwave heating was used advantageously for the corresponding bromophenols and their methyl ethers. Our study revealed that certain combinations of boronophenols and halophenols are disfavored, resulting in low yields of the biphenol coupling products, but that this problem can often be overcome by using fluorides as rate-accelerating additives. The optimized microwave-accelerated cross-coupling conditions were eventually applied to the synthesis of nine naturally occurring phytoalexins with biaryl structure. In further studies, we will investigate how these conditions can be applied to other natural or non-natural target molecules with biaryl moieties.

EXPERIMENTAL SECTION

General Methods. All experiments were conducted in dry reaction vessels under an atmosphere of dry nitrogen. Solvents were purified by standard procedures. Deionized water was used for the cross-coupling reactions. ^{1}H NMR spectra were obtained at 300 MHz in $CDCl_3$ with $CHCl_3$ (δ = 7.26 ppm) as an internal standard. Coupling constants are given in hertz. ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.0 ppm) as an internal standard. Whenever the solubility of the sample was insufficient in $CDCl_3$, one of the following solvents was used for NMR measurements: DMSO-d_6 (DMSO-d_5 as internal standard for ^{1}H NMR spectroscopy, δ = 2.50 ppm, DMSO-d_6 as internal standard for ^{13}C NMR spectroscopy, δ = 39.5 ppm); methanol-d_4 (CD_2HOD as internal standard for ^{1}H NMR spectroscopy, δ = 3.31 ppm, CD_3OD as internal standard for ^{13}C NMR spectroscopy, δ = 49.2 ppm; acetone-d_6 ($CD_2HC(O)CD_3$ as internal standard for ^{1}H NMR spectroscopy, δ = 2.05 ppm, $CD_3C(O)CD_3$ as internal standard for ^{13}C NMR spectroscopy, δ = 29.9 ppm). IR spectra were recorded as ATR-FTIR spectra. Wavenumbers (ν) are given in cm^{-1}. The peak intensities are defined as strong (s), medium (m), or weak (w). Low- and high-resolution mass spectra were obtained by EI/TOF. Microwave reactions were carried out in an Anton-Paar-monowave-300 reactor at 150 °C (monowave, maximum power 850 W, temperature control via IR-sensor, vial volume: 20 mL). Halophenols *o*-,*m*-,*p*-**8a**,**b** and *o*-,*m*-,*p*-**18a**,**b**, and boronic acids *o*-,*m*-,*p*-**9**, **11** and *o*-,*m*-,*p*-**16** were purchased and used without further purification. The Pd/C used for all experiments was purchased from Sigma-Aldrich (product no. 205699, 9.8–10.2% Pd on dry support,

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reduced, average particle size of the carbon is 15 μm, surface area of the carbon support is 750−1000 $m^2 \cdot g^{-1}$).[59]

General Procedure for the Synthesis of Biaryls 10, 12, 17, and 19 from Iodoarenes 8a or 18a under Thermal Conditions (Procedure A). The appropriate iodophenol **8a** (150 mg, 0.75 mmol or 100 mg, 0.50 mmol) or iodoanisol **18a** (176 mg, 0.75 mmol or 217 mg, 0.50 mmol) and the appropriate boronic acid **9** (104 mg, 0.75 mmol, 1.0 equiv or 69 mg, 0.50 mmol, 1.0 equiv or 97.5 mg, 0.65 mmol, 1.3 equiv, as indicated in the corresponding Tables 1 to 6), **11** (91.5 mg, 0.75 mmol, 1.0 equiv), or **16** (76 mg, 0.50 mmol, 1.0 equiv or 99 mg, 0.65 mmol, 1.3 equiv as indicated in the table) were suspended in water (10.0 mL/mmol). To the suspension was added either K_2CO_3 (4.0 equiv, 415 mg, 3.00 mmol or 276 mg, 2.00 mmol) or KF (4.0 equiv, 174 mg, 3.00 mmol or 116 mg, 2.00 mmol) as indicated in the corresponding Table 7, followed by Pd/C (10 wt %, 2 mol %; 15 mg for 0.75 mmol or 10 mg for 0.5 mmol scale). The mixture was immersed in an oil bath preheated to 80 °C for 2.5 h, cooled to ambient temperature, and carefully acidified by addition of aqueous HCl (1.0 M). It was extracted three times with MTBE (methyl *tert*-butyl ether, 50 mL each), and the organic layers were separated and dried with $MgSO_4$, filtered, and evaporated in vacuo. The residue was purified by column chromatography on silica using hexane/MTBE mixtures of increasing polarity as eluents.

General Procedure for the Synthesis of Biaryls 10, 17, and 19 from Bromoarenes 8b or 18b under Microwave Irradiation (Procedure B). The appropriate bromophenol **8b** (86.5 mg, 0.50 mmol) or bromoanisol **18b** (93.5 mg, 0.50 mmol) and the appropriate boronic acid **9** (97.5 mg, 0.65 mmol, 1.3 equiv) or **16** (99 mg, 0.65 mmol, 1.3 equiv) were suspended in water (10.0 mL/mmol) in a reaction vessel suited for microwave irradiation. To the suspension was added either KOH (4.0 equiv, 112 mg, 2.00 mmol) or $NBu_4F \cdot 3H_2O$ (4.0 equiv, 630 mg, 2.00 mmol) as indicated in the corresponding table, followed by Pd/C (10 wt %, 10.0 mg, 2 mol %). The closed vessel was placed in a microwave reactor, and irradiated at 150 °C for 0.5 h. The vessel was then cooled to ambient temperature, and the reaction mixture was carefully acidified by addition of aqueous HCl (1.0 M). It was extracted three times with MTBE (50 mL each), the organic layers were separated and dried with $MgSO_4$, filtered and evaporated in vacuo. The residue was purified by column chromatography on silica, using hexane/MTBE mixtures of increasing polarity as eluents.

*Biphenyl-2,2′-diol (**10a**).* General procedure A: obtained from *o*-**8a** (0.75 mmol) and *o*-**9** (0.75 mmol); yield 137 mg (0.74 mmol, 98%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 77 mg (0.42 mmol, 83%). Analytical data have been previously reported.[21]

*Biphenyl-2,3′-diol (**10b**).* General procedure A: obtained from *o*-**8a** (0.75 mmol) and *m*-**9** (0.75 mmol); yield 127 mg (0.68 mmol, 91%) or obtained from *m*-**8a** (0.75 mmol) and *o*-**9** (0.75 mmol); yield 130 mg (0.70 mmol, 93%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 81 mg (0.44 mmol, 87%) or obtained from *m*-**8b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 74 mg (0.40 mmol, 80%). Colorless solid: mp 96 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 7.8, 7.8 Hz, 1H), 7.30−7.21 (m, 2H), 7.05−6.95 (m, 3H), 6.92 (dd, J = 2.3, 1.6 Hz, 1H), 6.86 (dm, J = 8.1 Hz, 1H), 5.36 (s, 1H), 5.20 (s, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.4, 152.5, 138.9, 130.8, 130.2, 129.4, 127.8, 121.6, 121.0, 116.2, 116.0, 115.1; IR (ATR) ν 3370 (bm), 1592 (m), 1480 (m), 1436 (s), 1211 (s); HRMS (EI) calcd for $C_{12}H_{10}O_2^+$ [M^+] 186.0681, found 186.0693. Anal. Calcd for $C_{12}H_{10}O_2$ (186.21): C, 77.4; H, 5.4. Found: C, 77.6; H, 5.2.

*Biphenyl-2,4′-diol (**10c**).*[60] General procedure A: obtained from *o*-**8a** (0.75 mmol) and *p*-**9** (0.75 mmol); yield 121 mg (0.65 mmol, 87%) or obtained from *p*-**8a** (0.75 mmol) and *o*-**9** (0.75 mmol); yield 106 mg (0.57 mmol, 76%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 84 mg (0.45 mmol, 90%) or obtained from *p*-**8b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 87 mg (0.47 mmol, 93%). Colorless solid: mp 158 °C; ^{1}H NMR (300 MHz, methanol-d_4) δ 7.41 (dm, J = 8.7 Hz, 2H), 7.21 (dm, J = 7.7 Hz, 1H), 7.10 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.90−6.80 (m, 4H); ^{13}C{^{1}H} NMR (75 MHz, methanol-d_4) δ 157.1, 154.9, 131.4, 131.4, 129.8, 128.8, 128.4, 121.0, 116.8, 115.8; IR (ATR) ν 3331 (bm), 1608 (m), 1482 (s), 1218 (s), 1172 (s); HRMS (EI) calcd for $C_{12}H_{10}O_2^+$ [M^+]: 186.0681, found: 186.0682. Anal. Calcd for $C_{12}H_{10}O_2$ (186.21): C, 77.4; H, 5.4. Found: C, 77.4; H, 5.2.

*Biphenyl-3,3′-diol (**10d**).*[61] General procedure A: obtained from *m*-**8a** (0.75 mmol) and *m*-**9** (0.75 mmol); yield 133 mg (0.72 mmol, 95%). General procedure B: obtained from *m*-**8b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 87 mg (0.47 mmol, 94%). Colorless solid: mp 123 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.51 (s, 2H), 7.23 (dd, J = 8.0, 8.0 Hz, 2H), 7.01−6.99 (m, 4H), 6.77 (d, J = 8.0 Hz, 2H); ^{13}C{^{1}H} NMR (75 MHz, DMSO) δ 157.8, 141.8, 129.8, 117.4, 114.4, 113.4; IR (ATR) ν 3150 (bw), 1578 (m), 1233 (m), 1024 (s), 998 (s); HRMS (EI) calcd for $C_{12}H_{10}O_2^+$ [M^+] 186.0681, found 186.0684. Anal. Calcd for $C_{12}H_{10}O_2$ (186.21): C, 77.4; H, 5.4. Found: C, 77.3; H, 5.2%.

*Biphenyl-3,4′-diol (**10e**).*[62] General procedure A: obtained from *m*-**8a** (0.75 mmol) and *p*-**9** (0.75 mmol); yield 110 mg (0.59 mmol, 79%) or obtained from *p*-**8a** (0.75 mmol) and *m*-**9** (0.75 mmol); yield 120 mg (0.65 mmol, 86%). General procedure B: obtained from *m*-**8b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 81 mg (0.44 mmol, 87%) or obtained from *p*-**8b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 89 mg (0.48 mmol, 96%). Colorless solid: mp 192 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.54 (s, 1H), 9.43 (s, 1H), 7.43 (d, J = 8.5 Hz, 2H), 7.20 (dd, J = 8.1, 8.1 Hz, 1H), 7.00−6.98 (m, 2H), 6.86 (d, J = 8.5 Hz, 2H), 6.72 (dd, J = 8.0, 1.3 Hz, 1H); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6) δ 157.8, 157.1, 141.7, 131.2, 129.8, 127.7, 116.9, 115.7, 113.5, 112.9; IR (ATR) ν 3286 (bm), 1601 (m), 1424 (m), 1256 (s), 1201 (s); HRMS (EI) calcd for $C_{12}H_{10}O_2^+$ [M^+] 186.0681, found 186.0683. Anal. Calcd for $C_{12}H_{10}O_2$ (186.21): C, 77.4; H, 5.4. Found: C, 77.3; H, 5.2.

*Biphenyl-4,4′-diol (**10f**).*[63] General procedure A: obtained from *p*-**8a** (0.75 mmol) and *p*-**9** (0.75 mmol); yield 58 mg (0.31 mmol, 42%). General procedure B: obtained from *p*-**8b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 89 mg (0.48 mmol, 96%). Colorless solid: mp 280−282 °C; ^{1}H NMR (300 MHz, methanol-d_4) δ 7.35 (d, J = 8.5 Hz, 4H), 6.82 (d, J = 8.5 Hz, 4H); ^{13}C{^{1}H} NMR (75 MHz, methanol-d_4) δ 157.2, 134.0, 128.4, 116.5; IR (ATR) ν 3377 (bw), 1604 (m), 1494 (m), 1246 (s), 1003 (m); HRMS (EI) calcd for $C_{12}H_{10}O_2^+$ [M^+] 186.0681, found 186.0671. Anal. Calcd for $C_{12}H_{10}O_2$ (186.21): C, 77.4; H, 5.4. Found: C, 77.4; H, 5.2.

*Biphenyl-2-ol (**o-12**).* General procedure A: obtained from *m*-**8a** (0.75 mmol) and **11** (0.75 mmol); yield 124 mg (0.73 mmol, 97%). Analytical data have been previously reported.[21]

*Biphenyl-3-ol (**m-12**).*[64] General procedure A: obtained from *m*-**8a** (0.75 mmol) and **11** (0.75 mmol); yield 120 mg (0.71 mmol, 94%). Colorless solid: mp 74−75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.54 (m, 2H), 7.49−7.27 (m, 4H), 7.20 (dm, J = 7.7 Hz, 1H), 7.09 (dd, J = 2.3, 1.8 Hz, 1H), 6.84 (dm, J = 8.0, Hz, 1H), 5.05 (s, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.9, 143.2, 140.8, 130.1, 128.9, 127.6, 127.2, 120.0, 114.3, 114.3; IR (ATR) ν 3390 (bw), 1593 (m), 1475 (m), 1247 (m), 1197 (m); HRMS (EI) calcd for $C_{12}H_{10}O^+$ [M^+] 170.0732, found 170.0730. Anal. Calcd for $C_{12}H_{10}O$ (170.21): C, 84.7; H, 5.9. Found: C, 84.4; H, 6.0.

*Biphenyl-4-ol (**p-12**).*[65] General procedure A: obtained from *p*-**8a** (0.75 mmol) and **11** (0.75 mmol); yield 115 mg (0.68 mmol, 90%). Colorless solid: mp 162−170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90−7.20 (m, 7H), 6.91 (d, J = 8.2 Hz, 2H), 4.88 (s, 1H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.2, 140.9, 134.3, 128.9, 128.5, 126.9, 126.9, 115.8; IR (ATR) ν 3420 (bw), 1604 (m), 1489 (m), 1257 (s), 757 (s); HRMS (EI) calcd. for $C_{12}H_{10}O^+$ [M^+] 170.0732, found 170.0726. Anal. Calcd for $C_{12}H_{10}O$ (170.21): C, 84.7; H, 5.9. Found: C, 84.9; H, 5.7.

*2′-Methoxybiphenyl-2-ol (**17a**).*[66] General procedure A: obtained from *o*-**8a** (0.75 mmol) and *o*-**16** (0.98 mmol); yield 143 mg (0.71 mmol, 95%) or obtained from *o*-**18a** (0.50 mmol) and *o*-**9** (0.50 mmol); yield 38 mg (0.19 mmol, 38%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 90 mg (0.45 mmol, 90%) or obtained from *o*-**18b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 61 mg (0.31 mmol, 61%). Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.30 (m, 4H), 7.16 (dd, J = 7.5, 7.5 Hz, 1H),

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7.12−7.03 (m, 3H), 6.34 (s, 1H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.6, 153.8, 132.5, 131.4, 129.4, 129.3, 127.1, 126.3, 122.2, 121.1, 117.5, 111.7, 56.2; IR (ATR) ν 3388 (bw), 1577 (w), 1479 (s), 1228 (s), 1177 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0829.

*3′-Methoxybiphenyl-2-ol (**17b**).*[67] General procedure A: obtained from *o*-**8a** (0.75 mmol) and *m*-**16** (0.98 mmol); yield 143 mg (0.71 mmol, 95%) or obtained from *m*-**18a** (0.50 mmol) and *o*-**9** (0.50 mmol); yield 47 mg (0.24 mmol, 47%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 89 mg (0.45 mmol, 89%) or obtained from *m*-**18b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 86 mg (0.43 mmol, 86%). Colorless solid, mp 92 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41 (dd, J = 7.9, 7.9 Hz, 1H), 7.32−7.24 (m, 2H), 7.05 (dm, J = 7.5, Hz, 1H), 7.03−6.92 (m, 4H), 5.35 (s, 1H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.5, 152.6, 138.6, 130.5, 130.2, 129.4, 128.1, 121.3, 120.9, 115.9, 114.7, 113.8, 55.5; IR (ATR) ν 3419 (bw), 1582 (m), 1476 (s), 1421 (s), 1271 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0826.

*4′-Methoxybiphenyl-2-ol (**17c**).*[67] General procedure A: obtained from *o*-**8a** (0.75 mmol) and *p*-**16** (0.98 mmol); yield 140 mg (0.70 mmol, 93%) or obtained from *p*-**18a** (0.50 mmol) and *o*-**9** (0.50 mmol); yield 39 mg (0.20 mmol, 39%). General procedure B: obtained from *o*-**8b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 85 mg (0.43 mmol, 85%) or obtained from *p*-**18b** (0.50 mmol) and *o*-**9** (0.65 mmol); yield 76 mg (0.38 mmol, 76%). Colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, J = 8.8 Hz, 2H), 7.28−7.20 (m, 2H), 7.04 (d, J = 8.8 Hz, 2H), 7.01−6.94 (m, 2H), 5.18 (s, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.5, 152.7, 130.4, 130.4, 129.4, 128.9, 128.0, 120.9, 115.8, 114.9, 55.5; IR (ATR) ν 3378 (bw), 1517 (m), 1485 (s), 1234 (s), 1157 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0844.

*2′-Methoxybiphenyl-3-ol (**17d**).* General procedure A: obtained from *m*-**8a** (0.75 mmol) and *o*-**16** (0.98 mmol); yield 132 mg (0.66 mmol, 88%) or obtained from *o*-**18a** (0.50 mmol) and *m*-**9** (0.50 mmol); yield 39 mg (0.20 mmol, 39%). General procedure B: obtained from *m*-**8b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 94 mg (0.47 mmol, 94%) or obtained from *o*-**18b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 64 mg (0.32 mmol, 64%). Colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.27 (m, 3H), 7.11 (dm, J = 8.0, Hz, 1H), 7.07−6.97 (m, 3H), 6.81 (ddd, J = 8.1, 2.6, 0.9 Hz, 1H), 4.91 (s, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 156.6, 155.2, 140.3, 130.9, 130.4, 129.3, 128.9, 122.3, 121.0, 116.7, 114.1, 111.5, 55.7; IR (ATR) ν 3361 (bw), 1590 (m), 1429 (s), 1238 (s), 1183 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0831.

*3′-Methoxybiphenyl-3-ol (**17e**).*[64] General procedure A: obtained from *m*-**8a** (0.75 mmol) and *m*-**16** (0.98 mmol); yield 138 mg (0.69 mmol, 92%) or obtained from *m*-**18a** (0.50 mmol) and *m*-**9** (0.50 mmol); yield 26 mg (0.13 mmol, 26%). General procedure B: obtained from *m*-**8b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 91 mg (0.46 mmol, 91%) or obtained from *m*-**18b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 71 mg (0.36 mmol, 71%). Colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 7.9, 7.9 Hz, 1H), 7.30 (dd, J = 7.9, 7.9 Hz, 1H), 7.20−7.14 (m, 2H), 7.12 (dd, J = 2.3, 1.7 Hz, 1H), 7.07 (dd, J = 2.3, 1.7 Hz, 1H), 6.92 (ddd, J = 8.2, 2.5, 0.7 Hz, 1H), 6.84 (ddd, J = 8.0, 2.5, 0.8 Hz, 1H), 5.31 (s, 1H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.0, 156.0, 143.0, 142.4, 130.1, 129.9, 119.9, 119.8, 114.5, 114.3, 113.1, 113.0, 55.5; IR (ATR) ν 3375 (bw), 1599 (m), 1576 (s), 1477 (m), 1168 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0834.

*4′-Methoxybiphenyl-3-ol (**17f**).*[64] General procedure A: obtained from *m*-**8a** (0.75 mmol) and *p*-**16** (0.98 mmol); yield 138 mg (0.69 mmol, 92%) or obtained from *p*-**18a** (0.50 mmol) and *m*-**9** (0.50 mmol); yield 25 mg (0.13 mmol, 25%). General procedure B: obtained from *m*-**8b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 93 mg (0.47 mmol, 93%) or obtained from *p*-**18b** (0.50 mmol) and *m*-**9** (0.65 mmol); yield 69 mg (0.35 mmol, 69%). Colorless solid: mp 117 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J = 8.9 Hz, 2H), 7.29 (dd, J = 7.9, 7.9 Hz, 1H), 7.14 (dm, J = 7.7, 1.6, 1.0 Hz, 1H), 7.03 (dd, J = 2.3, 1.7 Hz, 1H), 6.97 (d, J = 8.9 Hz, 2H), 6.79 (ddd, J = 8.0, 2.5, 0.9 Hz, 1H), 5.13 (s, 1H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.4, 156.0, 142.7, 133.4, 130.1, 128.3, 119.5, 114.4, 113.8, 113.8, 55.5; IR (ATR) ν 3420 (bm), 1597 (s), 1449 (s), 1205 (s), 1014 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+]: 200.0837, found: 200.0827. Anal. Calcd for $C_{13}H_{12}O_2$ (200.23): C, 78.0; H, 6.0. Found: C, 77.5; H, 5.7.

*2′-Methoxybiphenyl-4-ol (**17g**).*[68] General procedure A: obtained from *p*-**8a** (0.75 mmol) and *o*-**16** (0.98 mmol); yield 126 mg (0.63 mmol, 84%) or obtained from *o*-**18a** (0.50 mmol) and *p*-**9** (0.50 mmol); yield 10 mg (0.05 mmol, 10%). General procedure B: obtained from *p*-**8b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 95 mg (0.48 mmol, 95%) or obtained from *o*-**18b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 62 mg (0.31 mmol, 62%). Colorless solid: mp 117−119 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.36 (d, J = 8.6 Hz, 2H), 7.31−7.22 (m, 2H), 7.04 (dd, J = 8.7, 0.9 Hz, 1H), 6.98 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.88 (d, J = 8.6 Hz, 2H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, acetone-d_6) δ 157.5, 157.4, 131.5, 131.3, 131.1, 130.6, 128.8, 121.6, 115.6, 112.5, 55.8; IR (ATR) ν 3380 (bw), 1595 (m), 1485 (s), 1236 (s), 1175 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0841. Anal. Calcd for $C_{13}H_{10}O_2$ (200.08): C, 78.0; H, 6.0. Found: C, 77.4; H, 6.2.

*3′-Methoxybiphenyl-4-ol (**17h**).*[69] General procedure A: obtained from *p*-**8a** (0.75 mmol) and *m*-**16** (0.98 mmol); yield 134 mg (0.67 mmol, 89%) or obtained from *m*-**18a** (0.50 mmol) and *p*-**9** (0.50 mmol); yield 10 mg (0.05 mmol, 10%). General procedure B: obtained from *p*-**8b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 94 mg (0.47 mmol, 94%) or obtained from *m*-**18b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 52 mg (0.26 mmol, 52%). Colorless solid: mp 91 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.7 Hz, 2H), 7.34 (dd, J = 8.0, 8.0 Hz, 1H), 7.15 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.09 (dd, J = 2.0, 1.8 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 6.87 (ddd, J = 8.0, 2.5, 0.8 Hz, 1H), 5.10 (s(br), 1H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.0, 155.4, 142.5, 134.0, 129.9, 128.6, 119.5, 115.8, 112.7, 112.3, 55.5; IR (ATR) ν 3421 (bw), 1597 (s), 1484 (s), 1172 (s), 1025 (s); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0840.

*4′-Methoxybiphenyl-4-ol (**17i**).*[70] General procedure A: obtained from *p*-**8a** (0.75 mmol) and *p*-**16** (0.98 mmol); yield 118 mg (0.59 mmol, 79%) or obtained from *p*-**18a** (0.50 mmol) and *p*-**9** (0.50 mmol); yield 10 mg (0.05 mmol, 10%). General procedure B: obtained from *p*-**8b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 96 mg (0.48 mmol, 96%) or obtained from *p*-**18b** (0.50 mmol) and *p*-**9** (0.65 mmol); yield 67 mg (0.34 mmol, 67%). Colorless solid: mp 181−182 °C; ^1H NMR (300 MHz, acetone-d_6) δ 7.48 (d, J = 8.9 Hz, 2H), 7.41 (d, J = 8.7 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, acetone-d_6) δ 159.6, 157.5, 134.4, 132.9, 128.3, 128.1, 116.5, 115.0, 55.6; IR (ATR) ν 3413 (bw), 1502 (m), 1248 (m), 1178 (w), 1038 (m); HRMS (EI) calcd for $C_{13}H_{12}O_2^+$ [M^+] 200.0837, found 200.0838. Anal. Calcd for $C_{13}H_{10}O_2$ (200.08): C, 78.0; H, 6.0. Found: C, 77.8; H, 6.1.

*2,2′-Dimethoxy-1,1′-biphenyl (**19a**).*[71] General procedure A: obtained from *o*-**18a** (0.50 mmol) and *o*-**16** (0.50 mmol); yield 87 mg (0.41 mmol, 81%). General procedure B: obtained from *o*-**18b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 66 mg (0.31 mmol, 62%). Colorless solid: mp 156−157 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (ddd, J = 8.2, 7.5, 1.8 Hz, 2H), 7.32 (dd, J = 7.5, 1.8 Hz, 2H), 7.07 (ddd, J = 7.5, 7.5, 1.1 Hz, 2H), 7.03 (dm, J = 8.2 Hz, 2H), 3.83 (s, 6H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 157.2, 131.6, 128.7, 128.0, 120.5, 111.3, 55.8; IR (ATR) ν 2928 (bw), 1723 (w), 1590 (w), 1456 (m), 1111 (m); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.0976. Anal. Calcd for $C_{14}H_{14}O_2$ (214.10): C, 78.5; H, 6.6. Found: C, 78.3; H, 6.6.

*2,3′-Dimethoxy-1,1′-biphenyl (**19b**).*[71] General procedure A: obtained from *o*-**18a** (0.50 mmol) and *m*-**16** (0.50 mmol); yield 75 mg (0.35 mmol, 70%) or obtained from *m*-**18a** (0.50 mmol) and *o*-**16** (0.50 mmol); yield 77 mg (0.36 mmol, 72%). General procedure B: obtained from *o*-**18b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 70 mg (0.33 mmol, 65%) or obtained from *m*-**18b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 86 mg (0.40 mmol, 80%). Colorless solid: mp 41 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46−7.36 (m, 3H), 7.24−7.18 (m, 2H), 7.11 (dd, J = 7.5, 7.5 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 6.97 (ddd, J = 8.1, 2.5, 0.8, 1H), 3.91 (s, 3H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR

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(75 MHz, $CDCl_3$) δ 159.4, 156.6, 140.1, 130.9, 130.7, 129.0, 128.8, 122.2, 120.9, 115.5, 112.6, 111.5, 55.6, 55.3; IR (ATR) ν 1592 (s), 1477 (s), 1215 (s), 1025 (s), 697 (s); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.0998. Anal. Calcd for $C_{14}H_{14}O_2$ (214.10): C, 78.5; H, 6.6. Found: C, 78.0; H, 6.4.

*2,4′-Dimethoxy-1,1′-biphenyl (**19c**).*[71] General procedure A: obtained from *o*-**18a** (0.50 mmol) and *p*-**16** (0.50 mmol); yield 75 mg (0.35 mmol, 70%) or obtained from *p*-**18a** (0.50 mmol) and *o*-**16** (0.50 mmol); yield 88 mg (0.41 mmol, 82%). General procedure B: obtained from *o*-**18b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 87 mg (0.40 mmol, 81%) or obtained from *p*-**18b** (0.50 mmol) and *o*-**16** (0.65 mmol); yield 93 mg (0.47 mmol, 87%). Colorless solid: mp 67−68 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−7.54 (m, 2H), 7.44−7.34 (m, 2H), 7.11 (ddm, J = 7.5, 7.5 Hz, 1H), 7.08−7.01 (m, 3H), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.8, 156.6, 131.0, 130.7, 130.7, 130.5, 128.2, 120.9, 113.6, 111.4, 55.6, 55.3; IR (ATR) ν 1596 (w), 1464 (m), 1239 (s), 1022 (m), 547 (m); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.0993. Anal. Calcd for $C_{14}H_{14}O_2$ (214.10): C, 78.5; H, 6.6. Found: C, 78.4; H, 6.6.

*3,3′-Dimethoxy-1,1′-biphenyl (**19d**).*[72] General procedure A: obtained from *m*-**18a** (0.50 mmol) and *m*-**16** (0.50 mmol); yield 81 mg (0.38 mmol, 76%). General procedure B: obtained from *m*-**18b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 76 mg (0.36 mmol, 71%). Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, J = 7.9, 7.9 Hz, 2H), 7.24 (dm, J = 7.9, Hz, 2H), 7.19 (dd, J = 2.5, 1.7 Hz, 2H), 6.96 (ddd, J = 7.9, 2.5, 0.8 Hz, 2H), 3.90 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 160.1, 142.7, 129.8, 119.8, 113.1, 112.9, 55.3; IR (ATR) ν 1574 (s), 1475 (m), 1231 (s), 1029 (s), 693 (s); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.0983.

*3,4′-Dimethoxy-1,1′-biphenyl (**19e**).*[71] General procedure A: obtained from *m*-**18a** (0.50 mmol) and *p*-**16** (0.50 mmol); yield 62 mg (0.29 mmol, 58%) or obtained from *p*-**18a** (0.50 mmol) and *m*-**16** (0.50 mmol); yield 77 mg (0.36 mmol, 72%). General procedure B: obtained from *m*-**18b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 77 mg (0.36 mmol, 72%) or obtained from *p*-**18b** (0.50 mmol) and *m*-**16** (0.65 mmol); yield 83 mg (0.39 mmol, 78%). Colorless solid: mp 59 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.8 Hz, 2H), 7.38 (dd, J = 7.9, 7.9 Hz, 1H), 7.19 (dd, J = 7.9, 0.8 Hz, 1H), 7.17−7.09 (m, 1H), 7.02 (d, J = 8.8 Hz, 2H), 6.90 (dd, J = 7.9, 2.5 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 160.1, 159.4, 142.5, 133.7, 129.8, 128.3, 119.4, 114.3, 112.7, 112.2, 55.4, 55.3; IR (ATR) ν 1598 (m), 1473 (m), 1241 (m), 1219 (s), 1032 (s); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.1013.

*4,4′-Dimethoxy-1,1′-biphenyl (**19f**).*[71] General procedure A: obtained from *p*-**18a** (0.50 mmol) and *p*-**16** (0.50 mmol); yield 99 mg (0.46 mmol, 93%). General procedure B: obtained from *p*-**18b** (0.50 mmol) and *p*-**16** (0.65 mmol); yield 67 mg (0.32 mmol, 63%). Colorless solid: mp 175−178 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.9 Hz, 4H), 7.00 (d, J = 8.9 Hz, 4H), 3.88 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.9, 133.7, 127.9, 114.3, 55.5; IR (ATR) ν 1604 (m), 1495 (m), 1183 (s), 1242 (s), 1040 (s); HRMS (EI) calcd for $C_{14}H_{14}O_2^+$ [M^+] 214.0994, found 214.1001. Anal. Calcd for $C_{14}H_{14}O_2$ (214.10): C, 78.5; H, 6.6. Found: C, 78.4; H, 6.6.

*4-Bromo-2,6-dimethoxyphenol (**21**).*[56,57] To a solution of **20** (6.16 g, 40.0 mmol) in $CHCl_3$ (120 mL) was added NaH (60 wt % dispersion in mineral oil, 16 mg, 1 mol %) at ambient temperature. The solution was cooled to −45 °C, and *N*-bromosuccinimide (7.12 g, 40.0 mmol) was added in one portion. Stirring was continued at a temperature of ca. −35 °C for 0.5 h, and the mixture was then allowed to warm to ambient temperature within 0.5 h. After reaching ambient temperature, the solution was heated to reflux for another 0.5 h. The mixture was then cooled to ambient temperature, and all volatiles were evaporated in vacuo until dryness. The resulting solid was thoroughly extracted with diethyl ether (200 mL) and removed by filtration. The filter cake was again extracted with diethyl ether, and the combined ethereal extracts were evaporated. The residue was purified by column chromatography on silica, using hexane/MTBE mixtures as eluent, to furnish **21** (3.40 g, 14.6 mmol, 37%) as a colorless solid: mp 95−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (s, 2H), 3.86 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147. 8, 134.3, 111.2, 108.8, 56.6; IR (ATR) ν 3505 (bm), 1610 (m), 1504 (s), 1208 (s), 1111 (s); HRMS (EI) calcd for $C_8H_9O_3{}^{79}Br^+$ [M^+] 232.9735, found 231.9742.

*5-Bromo-3-methoxybenzene-1,2-diol (**24**).*[58] *5-Bromo-2-hydroxy-3-methoxybenzaldehyde (**23**).* Vanillin (**22**, 7.37 g, 48.0 mmol) and sodium acetate (6.00 g, 73.0 mmol) were dissolved in acetic acid (200 mL). A solution of bromine (2.50 mL, 48.0 mmol) in acetic acid (20 mL) was added dropwise over a period of 0.5 h at ambient temperature. All volatiles were then evaporated in vacuo, and the residue was redissolved in CH_2Cl_2 (100 mL). The solution was extracted with water (100 mL), and the organic layer was separated and washed twice with water (100 mL each), and finally dried with $MgSO_4$. The solution was filtered, and all volatiles were evaporated in vacuo to furnish crude aldehyde **23**, which was sufficiently pure to be used in the next step without further purification. Analytical data of **23**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.98 (s, 1H), 9.84 (s, 1H), 7.29 (d, J = 2.1 Hz, 1H), 7.16 (d, J = 2.1 Hz, 1H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 195.5, 151.0, 149.4, 126.2, 121.5, 120.9, 111.2, 56.7.

*5-Bromo-3-methoxybenzene-1,2-diol (**24**).* The crude **23** (ca. 11 g) obtained from the previous step was dissolved in a solution of NaOH (1.90 g) in water (200 mL). An aqueous solution of H_2O_2 (30 wt %, 30.00 g, 265.0 mmol) was diluted with water (200 mL) and then slowly added at ambient temperature to the first solution. The mixture was stirred for 0.5 h at this temperature and then carefully acidified by addition of aqueous HCl (2 M, 30 mL). The resulting solution was extracted thoroughly with CH_2Cl_2, and the combined organic extracts were washed with a saturated aqueous solution of Na_2SO_3. The organic layer was separated, dried with $MgSO_4$, filtered, and evaporated in vacuo. The residue was purified by chromatography on silica using hexane/MTBE mixtures as eluent to furnish **24** (9.60 g, 43.8 mmol, 91% based on **22**) as a colorless solid: mp 76 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (d, J = 2.1 Hz, 1H), 6.61 (d, J = 2.1 Hz, 1H), 5.36 (s, 2H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147.5, 144.8, 131.8, 112.4, 111.9, 107.0, 56.6; IR (ATR) ν 3432 (bm), 1615 (m), 1501 (s), 1198 (s), 1093 (s); HRMS (EI) calcd for $C_7H_7O_3{}^{79}Br^+$ [M^+]: 217.9579, found 217.9562.

*6-Bromo-4-methoxybenzo[d][1,3]dioxole (**25**).* Diol **24** (1.10 g, 5.0 mmol), K_2CO_3 (1.04 g, 7.5 mmol), and CH_2I_2 (0.58 mL, 7.5 mmol) were suspended in dry DMF (20 mL). The mixture was heated for 1 h in an oil bath preheated to 100 °C. After the mixture was cooled to ambient temperature, brine (10 mL) was added and the aqueous layer was extracted three times with ethyl acetate (50 mL each). The combined organic extracts were dried with $MgSO_4$, filtered, and evaporated in vacuo. The residue was purified by column chromatography on silica to yield **25** (0.85 g, 3.7 mmol, 74%) as a colorless solid: mp 80−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67−6.65 (m, 2H), 5.96 (s, 2H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 149.6, 144.3, 135.0, 113.4, 111.3, 106.29, 102.0, 56.9; IR (ATR) ν 2913 (w), 1625 (m), 1420 (m), 1182 (s), 1102 (s); HRMS (EI) calcd for $C_8H_7O_3{}^{79}Br^+$ [M^+] 230.9657, found 230.9675.

*Aucuparin (**7a**).* General procedure B: obtained from **21** (175 mg, 0.75 mmol) and **11** (119 mg, 0.98 mmol) with KOH (168 mg, 3.00 mmol) as additive; yield 130 mg (0.57 mmol, 75%). ^{1}H and ^{13}C NMR spectroscopical data match those reported for the natural product.[25] Colorless solid: mp 80−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dm, J = 8.1 Hz, 2H), 7.42 (ddm, J = 8.1, 7.2 Hz, 2H), 7.32 (tt, J = 7.2, 1.3 Hz, 1H), 6.81 (s, 2H), 5.56 (s, 1H), 3.96 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147.5, 141.6, 134.7, 133.1, 128.9, 127.1, 127.1, 104.4, 56.6; IR (ATR) ν 3423 (bm), 1609 (m), 1222 (m), 1112 (s), 762 (m); HRMS (EI) calcd for $C_{14}H_{14}O_3^+$ [M^+] 230.0943, found 230.0947. Anal. Calcd for $C_{14}H_{14}O_3$ (230.26): C, 73.0; H, 6.1. Found: C, 72.5; H, 6.1.

*2′-Methoxyaucuparin (*o*-**5**).* General procedure B: obtained from **21** (117 mg, 0.50 mmol) and *o*-**16** (99 mg, 0.65 mmol) with $NBu_4F\cdot 3H_2O$ (630 mg, 2.00 mmol) as additive; yield 64 mg (0.25 mmol, 49%). ^{1}H NMR spectroscopical data match those reported for the natural product.[30] Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.28 (m, 2H), 7.08−6.97 (m, 2H), 6.81 (s, 2H), 5.60 (s(br), 1H), 3.92 (s, 6H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.5, 146.7, 134.2, 130.9, 130.7, 129.7, 128.4, 120.9, 111.5, 106.8, 56.4, 55.7;

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IR (ATR) ν 3502 (bm), 2938 (m), 1605 (m), 1241 (s), 1106 (s); HRMS (EI) calcd for $C_{15}H_{16}O_4^+$ [M^+] 260.1049, found 260.1048.

4′-Methoxyaucuparin (p-5). General procedure B: obtained from **21** (117 mg, 0.50 mmol) and *p*-**16** (99 mg, 0.65 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 87 mg (0.34 mmol, 67%). ^{1}H and ^{13}C NMR spectroscopical data match those reported for the natural product.[30] Colorless solid: mp 97−99 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.77 (s, 2H), 5.56 (s, 1H), 3.96 (s, 6H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.0, 147.4, 134.2, 132.7, 128.0, 114.3, 104.0, 56.5, 55.5; IR (ATR) ν 3440 (bm), 1608 (m), 1502 (s), 1242 (s), 1110 (s); HRMS (EI) calcd for $C_{15}H_{16}O_4^+$ [M^+] 260.1049, found 260.1032.

2′-Hydroxyaucuparin (o-3). General procedure B: obtained from **21** (117 mg, 0.50 mmol) and *o*-**9** (179 mg, 1.30 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 45 mg (0.18 mmol, 37%). ^{1}H and ^{13}C NMR spectroscopical data match those reported for the natural product.[25] Colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.15 (m, 2H), 7.05−6.93 (m, 2H), 6.67 (s, 2H), 5.64 (s (br), 1H), 5.45 (s (br), 1H), 3.90 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.6, 147.8, 134.7, 130.1, 129.1, 128.4, 128.1, 120.8, 115.8, 106.0, 56.5; IR (ATR) ν 3336 (bm), 1612 (m), 1342 (m), 1212 (s), 1111 (s); HRMS (EI) calcd for $C_{14}H_{14}O_4^+$ [M^+] 246.0892, found 246.0894.

3′-Hydroxyaucuparin (m-3). General procedure B: obtained from **21** (117 mg, 0.50 mmol) and *m*-**9** (90 mg, 0.65 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 88 mg (0.36 mmol, 72%). ^{1}H and ^{13}C NMR spectroscopical data match those reported previously.[26] Colorless solid: mp 153−155 °C; ^{1}H NMR (300 MHz, methanol-d_4) δ 7.19 (dd, J = 8.0, 7.7 Hz, 1H), 7.01 (dm, J = 7.7 Hz, 1H), 6.99 (m, 1H), 6.80 (s, 2H), 6.73 (ddd, J = 8.0, 2.3, 1.0 Hz, 1H), 3.86 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, methanol-d_4) δ 158.6, 149.4, 144.1, 136.3, 133.6, 130.7, 119.1, 114.7, 114.5, 105.4, 56.9; IR (ATR) ν 3403 (bm), 1585 (s), 1485 (s), 1215 (s), 1111 (s); HRMS (EI) calcd for $C_{14}H_{14}O_4^+$ [M^+] 246.0892, found 246.0883.

Garcibiphenyl C (p-3). General procedure B: obtained from **21** (117 mg, 0.50 mmol) and *p*-**9** (90 mg, 0.65 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 64 mg (0.27 mmol, 52%). ^{1}H NMR spectroscopical data match those reported for the natural product.[27] Colorless solid: mp 204−205 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 8.33 (s, 1H), 7.45 (d, J = 8.7 Hz, 2H), 7.16 (s, 1H), 6.88 (d, J = 8.7 Hz, 2H), 6.84 (s, 2H), 3.89 (s, 6H); ^{13}C{^{1}H} NMR (75 MHz, acetone-d_6) δ 157.5, 149.1, 133.8, 132.8, 128.5, 116.4, 105.1, 56.8; IR (ATR) ν 3344 (bm), 1609 (m), 1504 (m), 1232 (s), 1122 (s); HRMS (EI) calcd for $C_{14}H_{14}O_4^+$ [M^+] 246.0892, found 246.0883. Anal. Calcd for $C_{14}H_{14}O_4$ (246.26): C, 68.3; H, 5.7. Found: 68.3; H, 5.6.

Rhaphiolepsin (4). General procedure B: obtained from **24** (110 mg, 0.50 mmol) and *p*-**16** (198 mg, 1.30 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 86 mg (0.35 mmol, 70%). ^{1}H NMR spectroscopical data match those reported for the natural product.[29] Colorless solid: mp 93−95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.84 (s, 1H), 6.67 (s, 1H), 5.73 (s (br), 1H), 5.69 (s (br), 1H), 3.92 (s, 3H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.0, 147.4, 144.3, 133.9, 133.4, 131.8, 128.0, 114.3, 107.5, 102.2, 56.4, 55.5; IR (ATR) ν 3404 (bm), 1607 (m), 1502 (s), 1241 (s), 906 (s); HRMS (EI) calcd for $C_{14}H_{14}O_4^+$ [M^+] 246.0892, found 246.0888.

3-De-O-methylaucuparin (7b). General procedure B: obtained from **24** (110 mg, 0.50 mmol) and **11** (159 mg, 1.30 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 81 mg (0.38 mmol, 75%). ^{1}H and ^{13}C NMR spectroscopical data match those reported previously.[34] Colorless solid: mp 107−109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 7.3 Hz, 2H), 7.44 (dd, J = 7.3, 7.3 Hz, 2H), 7.36 (m, 1H), 6.93 (s, 1H), 6.75 (s, 1H), 5.79 (s, 2H), 3.94 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 147.3, 144.2, 141.1, 133.7, 132.2, 128.8, 127.0 126.9, 108.0, 102.6, 56.4; IR (ATR) ν 3295 (bm), 1616 (m), 1491 (s), 1197 (s), 1093 (s); HRMS (EI) calcd for $C_{13}H_{12}O_3^+$ [M^+] 216.0779, found 216.0786. Anal. Calcd for $C_{14}H_{12}O_4$ (246.26): C, 68.3; H, 5.7. Found: C, 68.3; H, 5.6.

3-(7-Methoxybenzo[d][1,3]dioxol-5-yl)phenol (6). General procedure B: obtained from **25** (116 mg, 0.50 mmol) and *m*-**9** (90 mg, 0.65 mmol) with KOH (112 mg, 2.00 mmol) as additive; yield 84 mg (0.35 mmol, 69%). All analytical data match those reported for the natural product.[33] Colorless solid: mp 93−95 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, J = 8.0, 7.7 Hz, 1H), 7.08 (ddd, J = 7.7, 1.5, 0.9 Hz, 1H), 6.99 (dd, J = 2.5, 1.5 Hz, 1H), 6.81 (dd, J = 8.0, 2.5 Hz, 1H), 6.74−6.72 (m, 2H), 5.99 (s, 2H), 5.50 (s (br), 1H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.9, 149.3, 143.7, 142.8, 135.9, 135.1, 130.0, 119.6, 114.2, 114.1, 107.2, 101.7, 101.6, 56.8; IR (ATR) ν 3401 (w), 1630 (m), 1583 (m), 1482 (s), 1422 (s); HRMS (EI) calcd for $C_{14}H_{13}O_4^+$ [M+H$^+$] 245.0814, found 245.0798. Anal. Calcd for $C_{14}H_{12}O_4$ (246.26): C, 68.5; H, 5.0. Found: C, 68.9; H, 5.0.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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