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Silver-Catalyzed Asymmetric Synthesis of 2,3-Dihydrobenzofurans: A New Chiral Synthesis of Pterocarpans

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Abstract: 2,3-Dihydrobenzofurans can be diastereoselectively prepared by condensation of aromatic aldehydes with 2,3-dihydrobenzoxasilepines under the catalysis of Ag^I complexes, and in the presence of a source of fluoride ion. The application of this strategy by using chiral catalysts leads to a new enantioselective total synthesis of natural *cis*-pterocarpans and their *trans* isomers. Through this method, the first enantioselective total synthesis of the antifungal agent (−)-pterocarpin was achieved. In addition, a new entry into the heteroaromatic system of 2,5-dihydrobenzoxepine is also presented.

Keywords: allylation · enantioselectivity · natural products · oxygen heterocycles · silanes

Introduction

2,3-Dihydrobenzofuran (coumaran) is a basic skeleton often found in natural products (pterocarpans, lignans) and other biologically active molecules. Therefore, efficient and enantioselective methods to construct such a moiety are strongly desirable. Many of the procedures used in the construction of this structure involve radical cyclizations that show low diastereoselectivity and no enantioselectivity.[1–5]

On the other hand, pterocarpans constitute numerous natural isoflavonoids[6] that have a benzofuranyl–benzopyran skeleton. These are produced by plants in response to phytopathogenic fungi infections[7] and are interesting due to their wide range of biological activities against, for example, tumors,[8] HIV,[9,10] malaria,[11] and snake venom.[12] Not many syntheses of enantiomerically pure pterocarpans have been reported so far, and most of these are based on racemic resolutions.[13–16]

Recently, we described a new strategy for a total synthesis of pterocarpans[17] in which one of the key reactions is the diastereoselective condensation of a 2,3-dihydrobenzoxasilepine with an aromatic aldehyde in the presence of a Lewis acid (Sakura—Hosomi modified reaction). In this paper, we investigated the possibility of using a chiral Lewis acid to perform an asymmetric condensation. In this way, 2,3-disubstituted-2,3-dihydrobenzofurans can be enantioselectively prepared, which is the crucial step in the asymmetric synthesis of pterocarpans by our methodology.

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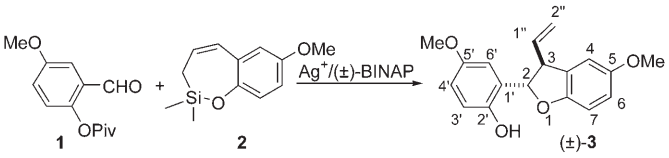
Results and Discussion

Synthesis of 2-aryl-3-vinyl-2,3-dihydrobenzofurans by using Ag^I complexes as Lewis acids: In a previous work we reported that the condensation between compounds **1** and **2** (Scheme 1) in the presence of $BF_3{\cdot}Et_2O$ yields the corresponding 2,3-dihydrobenzofuran with *cis* geometry.[17] The desirable enantioselection for this process could be derived from the use of Lewis acids that integrate chiral ligands into their structure. Firstly, we examined the TiF_4/BINOL system that had proved to be useful for the catalytic allylsilylation of aldehydes by using allyltrimethylsilane,[18] but in our case, we just recovered the starting materials. The same result was obtained with $Ti(i\text{PrO})_4$/BINOL.[19] Yamamoto and coworkers reported that the BINAP·AgF (BINAP = 2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl) complex in methanol[20] and the system KF/[18]crown-6 ether with the BINAP·AgOTf complex (TfO = trifluoro methanesulfonate) in polar aprotic solvents[21] are reactive chiral catalysts for asymmetric allylation with trimethoxysilanes. When we applied these methodologies to our substrates, the reaction was completely diastereoselective, but only the *trans* diastereoisomer

(±)-**3** was obtained (Scheme 1). The results are summarized in Table 1. The relative stereochemistry of (±)-**3** was assigned from NMR properties, the NOE effect observed between H-2 and H-1″ atoms being especially significant. The



Scheme 1. Formation of dihydrobenzofuran (±)-**3**.

Table 1. Reaction conditions for the synthesis of **3**.

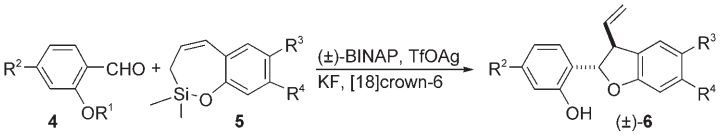
Entry	**2**[a]	**1**[a]	System[a,b]	Solvent	*T*	*t*[h]	Yield
I	1.5	1	0.1 (A)	MeOH	RT	22	s.m[e]
					reflux	2.5	
II	1	2	1 (A)	MeOH	reflux	1.5	s.m[d]
III	1	2	1 (A)	CH_2Cl_2[c]	RT	1.5	s.m
IV	1	2	0.2 (A)	THF[c]	RT	4	40%
					reflux	24	
V	1	2	1 (A)	THF[c]	reflux	1.5	55%
VI	1	1.5	0.2 (B)	THF	RT	0.5	15%
VII	1	1.5	0.2 (C)	THF	RT	0.5	70%

[a] Amounts of compounds refer to equivalents. [b] System A: AgF/(±)-BINAP (1:1); system B: AgOTf/(±)-BINAP/KF/[18]crown-6 (1:1:1:1); system C: AgOTf/(±)-BINAP/KF/[18]crown-6 (1:1:5:5). [c] System A was prepared in MeOH (5 min), then the MeOH was removed and the indicated solvent was added. [d] Compound **2** was recovered unaltered and compound **1** was recovered as its dimethylacetal derivative. [e] s.m. = starting material.

shielding of the signal of H-2 in the *trans* isomer compared to the *cis* isomer (formed in the BF_3·Et_2O-promoted reaction[17]) is also significant. This behavior was reported previously for similar compounds.[22,23]

From analysis of Table 1 it can be concluded that the choice of solvent is critical. Thus, the previously successful system A (AgF/(±)-BINAP in MeOH)[20] gave only the dimethylacetal derivative of the aldehyde (entry II). In CH_2Cl_2 and by using a separately prepared complex, no progress was observed (entry III). Moderate yields were obtained in THF (entries IV and V). To avoid this two-step procedure the source of fluoride was changed to KF, by using [18]crown-6 ether to solubilize it (system B). Although the conditions described [21,24] gave us a low yield, we could improve it by using a stoichiometric amount of KF/[18]crown-6 (system C), with the extra advantage of shorter reaction times and lower working temperatures.

As the diastereoselectivity of the reaction was the opposite to that observed upon using BF_3·Et_2O, a closer study of the reaction was needed. By using the optimized conditions (entry VII) several benzo[*f*][1,2]oxasilepines were condensed with a range of aromatic aldehydes. Only the *trans* diastereoisomers were obtained, with moderate to good yields (Scheme 2 and Table 2). The stereochemistry of **6a–g** was established in the same way as for compound **3**.



Scheme 2. Formation of 2,3-dihydrobenzofuran derivatives (±)-**6a–g**.

The 2,3-dihydrobenzofuran derivatives reported in entries 5–8 of the table can be transformed by following a previously reported methodology[17] into the natural pterocarpans pterocarpin, homopterocarpin, medicarpin, and maackianin, respectively. The behavior of benzo[*f*][1,2]oxasilepines **5b** and **5c** is remarkable and is in contrast with their low reactivity upon using BF_3·Et_2O as Lewis acid.[25]

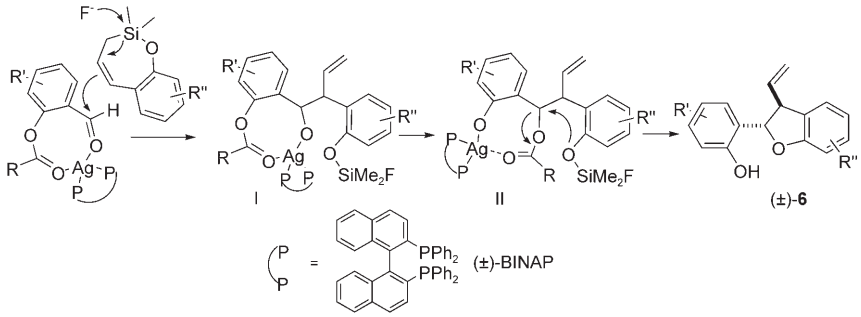
We initially chose all the aldehydes that have an esterified hydroxy group in the 2-position to allow a later cyclization of the B ring of the pterocarpan skeleton. As deprotection of the OH is observed in all the reactions, we can conceive that the protective group plays a role in the reaction mechanism (Scheme 3). The silver complex can coordinate both oxygen atoms of the aldehyde and the ester to form an eight-membered ring. The addition of the allylsiloxane to this complex gives the intermediate I that, after silver-catalyzed transesterification, leads to the intermediate II. Eventually cyclization takes place to form the 2,3-dihydrobenzofuran system.

Table 2. 2,3-Dihydrobenzofuran synthesis.

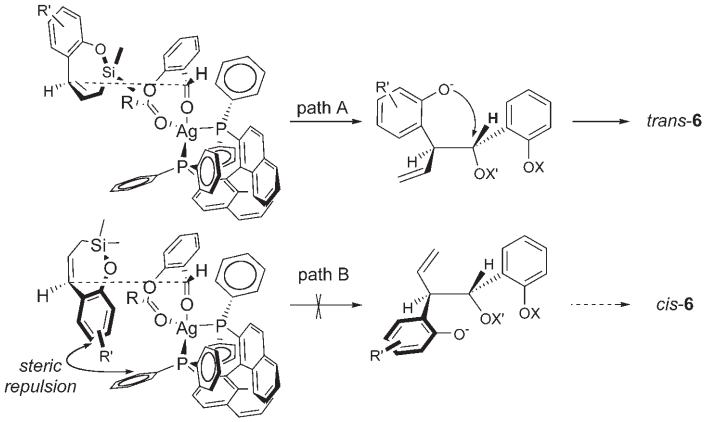
Entry	Substrates[a]	Product	Yield
1	**4a** R^1 = Piv, R^2 = H; **5a** R^3 = R_4 = H	**6a** R^2 = R^3 = R^4 = H	65
2	**4b** R^1 = Ac, R^2 = H; **2** R^3 = OCH_3, R^4 = H	**6b** R^2 = R^4 = H, R^3 = OCH_3	70
3	**4c** R^1 = Piv, R^2 = OPiv; **2** R^3 = OCH_3, R^4 = H	**6c** R^2 = OPiv, R^3 = OCH_3, R^4 = H	60
4	**4a** R^1 = Piv, R^2 = H; **2** R^3 = OCH_3, R^4 = H	**6b** R^2 = R_4 = H, R^3 = OCH_3	75
5	**4d** R^1 = Piv, R^2 = OCH_3; **5b** R^3 = R^4 = OCH_2O	**6d** R^2 = OCH_3, R^3 = R^4 = OCH_2O	70
6	**4d** R^1 = Piv, R^2 = OCH_3; **5c** R^3 = R^2 = H, R^4 = OCH_3	**6e** R^2 = R^4 = OCH_3, R^3 = H	65
7	**4c** R^1 = Piv, R^2 = OPiv; **5c** R^3 = H, R^4 = OCH_3	**6f** R^2 = OPiv, R^3 = H, R^4 = OCH_3	60
8	**4c** R^1 = Piv, R^2 = OPiv; **5b** R^3 = R^4 = OCH_2O	**6g** R^2 = OPiv, R^3 = R^4 = OCH_2O	70

[a] For the synthesis of the starting materials, see Supporting Information.

The most stable diastereoisomer (*trans*) is formed, and this can be easily understood by considering that the first step (Scheme 4) is under steric-approach control, path A being more feasible than path B. A Lewis acid-promoted isomerization could also take place through reversible ring-opening of the final benzofuran, as reported previously by Marsden and co-workers.[23] However, as there are no changes in diastereoselectivity in response to reaction temperature, we consider this last option less feasible.



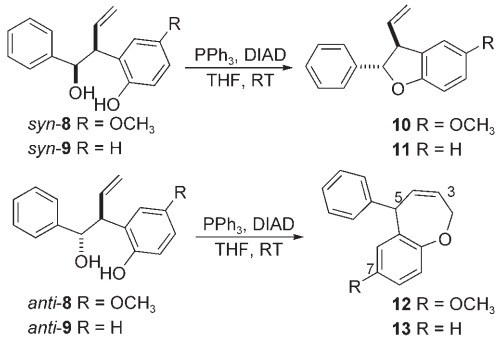
Scheme 3. Proposed mechanism for the formation of dihydrobenzofurans (±)-**6a–g**.



Scheme 4. Steric-approach control in the diastereospecific formation of dihydrobenzofurans (±)-**6a–g**. Path A depicts the most favored approach of one side of the allylsiloxane, path B shows how the attack from the other side is always disfavored.

To confirm this hypothesis we next tried the reaction with a series of aldehydes lacking *ortho* substituents, so we could check whether the ester was really involved in the process. Condensation of the same benzoxasilepines with several *para*-substituted benzaldehydes under the same reaction conditions gave a different result. The reaction was complete within a shorter time, but no cyclic products were obtained (Scheme 5). Furthermore, no diastereoselectivity was observed this time as 1:1 mixtures of both possible diastereoisomers were formed in all cases. In the reactions depicted in Scheme 5, silver would coordinate only the oxygen of the aldehyde, which would lead to the formation of both diastereoisomers through an open-chain intermediate. The lack of a leaving group would preclude the intramolecular cyclization that gives rise to the benzofuran ring closure.

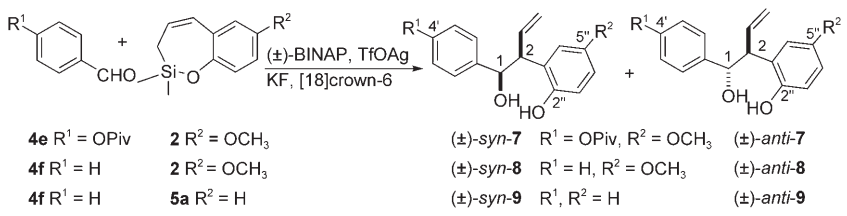
Careful column chromatography allowed the separation of both diastereoisomers in each of the reactions depicted in Scheme 5. Although their structures were confirmed by their NMR properties, the relative stereochemistry of the vinyl and hydroxy group could be only proposed, and was confirmed after the subsequent transformation. It was our intention to prepare the corresponding 2,3-dihydrobenzofuran systems from the isolated diastereoisomers of the homoallylic alcohols. Therefore, compounds **8** and **9** were subjected to Mitsunobu reaction conditions (diisopropyl diazodicarboxylate (DIAD)/PPh_3/THF, Scheme 6). In each case, one



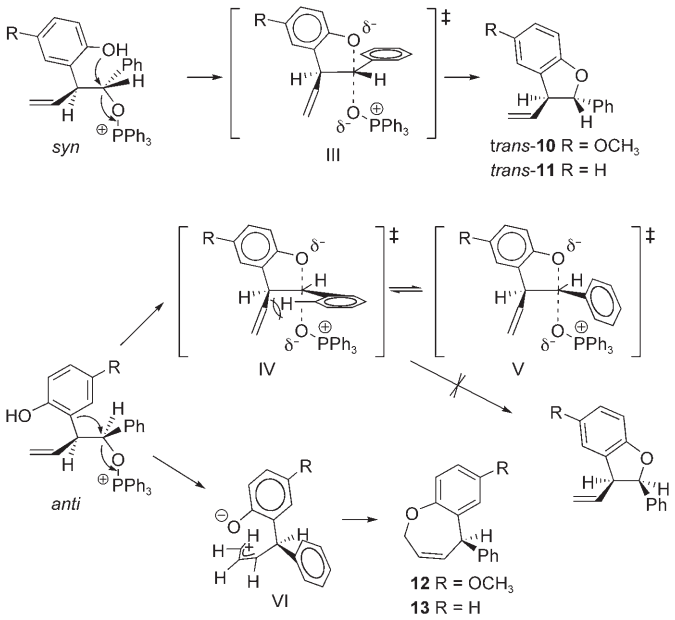
Scheme 6. Differences in behavior towards Mitsunobu cyclization of the *syn* and *anti* diastereoisomers of **8** and **9**.

of the diastereoisomers led to the desired product (**10** or **11**) that has a *trans* relative disposition of the substituents in the oxygenated ring, indicating a *syn* relative configuration of the initial homoallylic alcohol (**8** or **9**). To our surprise, each one of the *anti* diastereoisomers leads, under the same reaction conditions, to the 5-phenyl-2,5-dihydrobenzo[*b*]oxepines **12** and **13**, respectively. Possibly, the stereoelectronic requirements for the intramolecular S_N2 cyclization in the Mitsunobu reaction are not easily reached.

The transition state in a benzylic substitution is stabilized by the π-bond overlap that may arise if the nuclei and p orbitals are arranged in such a way that the (ideally straight) line joining the attacking atom of the nucleophile (Nu), the carbon atom being substituted (C), and the departing atom of the leaving group (LG) is *orthogonal* to the plane defined by the nuclei of the aromatic ring (Scheme 7).[26]



Scheme 5. Synthesis of compounds (±)-**7**–**9**.



Scheme 7. Benzylic substitution leading to **10** and **11**, and proposed rearrangement for the formation of **12** and **13**.

Although for the *syn* diastereoisomers this requirement is easily achieved (III), a similar arrangement in the *anti* diastereoisomers would suffer from steric destabilization (IV), because one of the hydrogen atoms on the aromatic ring and one of the carbon atoms in the vinyl group would be too close. In the alternative arrangement shown in V, the Nu-C-LG line is *coplanar* with the aromatic carbons and, hence, any benzylic substitution would proceed much more slowly than in the unconstrained analogue. In this situation, a phenyl group migration would take place more readily, generating an allylic cation (VI) that will collapse into the 2,5-dihydrobenzo[*b*]oxepines **12** and **13**.

An alternative path leading to the formation of structures like **12** and **13** was described previously for similar compounds.[27] Departure of the leaving group ($Ph_3P{=}O$) would lead to formation of a cyclopropane intermediate that would form the seven-membered ring through a [3s,3s] pericyclic reaction. However, the reported temperature is so high that this would be very unlikely in our particular case.

2,5-Dihydrobenzo[*b*]oxepines are of pharmacological relevance and occur in a number of natural products, such as heliannuol B[28] and in the radulanins A, H, and L.[29,30] Nevertheless, there are very few methods of synthesis of this heterocyclic system, mainly ring-closing metathesis[31] and the Mitsunobu cyclization.[32] This system has also been formed as minor byproducts of radical homoallylation,[33] insertion of a triple bond into a C–H bond of an olefin in arene–chromium tricarbonyl complexes,[34] and Pd-catalyzed annulation of O-substituted 1,3-dienes.[35]

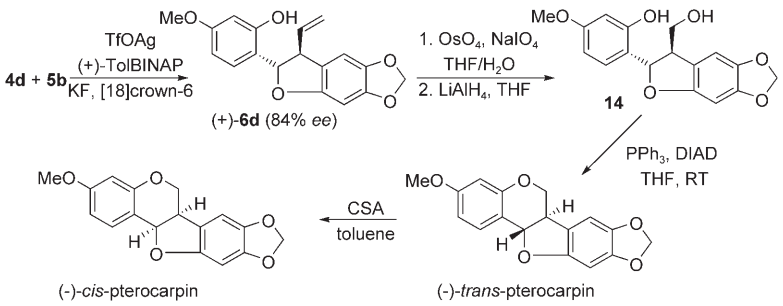
Asymmetric synthesis of *trans*-pterocarpin: The last stage was to check the applicability of the method to the asymmetric total synthesis of natural pterocarpans. Here, we describe the enantioselective total synthesis of (−)-*trans*-pterocarpin and its isomerization into the natural (−)-*cis*-pterocarpin. Compound (+)-**6d** was prepared by using the previously optimized reaction conditions and silver complexes with enantiomerically pure ligands. With (+)-(*R*)-BINAP at room temperature, the *ee* is low, however, it can be increased by decreasing the reaction temperature and by using (+)-TolBINAP (84% *ee* at −80°C). The results are summarized in Table 3. The optical purity was assessed by ^{1}H NMR spectroscopy by employing europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] ($Eu(hfc)_3$) as a chiral-shift reagent, followed by confirmation by conducting chiral HPLC.

Table 3. Effects of ligand and temperature on enantioselectivity in the preparation of (+)-**6d**.[a]

Entry	Ligand	*T*[°C]	*t*[h]	Yield[%]	*ee*[%]
1	(+)-(*R*)-BINAP	RT	0.5	70	29
2	(+)-(*R*)-BINAP	−20	0.5	74	39
3	(+)-(*R*)-BINAP	−45	1	69	54
4	(+)-(*R*)-BINAP	−80	3	70	69
5	(+)-(*R*)-TolBINAP	RT	0.5	71	39
6	(+)-(*R*)-TolBINAP	−20	0.5	72	57
7	(+)-(*R*)-TolBINAP	−45	1	70	63
8	(+)-(*R*)-TolBINAP	−80	3	75	84

[a] See entry VII in Table 1 for relative quantities.

The total synthesis of natural (−)-pterocarpin was completed as shown in Scheme 8 by the ring closure of the dihydrobenzopyran unit through the double-bond degradation (catalytic osmium tetroxide in excess of $NaIO_4$), aldehyde reduction ($LiAlH_4$), and Mitsunobu cyclization (DIAD/PPh_3) of the dihydroxy derivative. The *trans* pterocarpan was isomerized into the more stable natural *cis* structure through a high-yielding (97%) treatment with camphorsulfonic acid (CSA) in toluene at 110°C.[36]



Scheme 8. Synthesis of (−)-*cis*-pterocarpin.

Conclusion

We have described a convergent strategy for the silver-catalyzed diastereoselective synthesis of *trans*-2-aryl-3-vinyl-2,3-dihydrobenzofurans. This methodology can be applied to the asymmetric synthesis of natural and unnatural pterocarpans, such as pterocarpin. The presence of an ester group in the C-2 position of the benzaldehyde is required for the heterocyclization. The lack of this ester leads, under the same reaction conditions, to open-chain alcohols. Attempts to transform these alcohols into 2,3-dihydrobenzofurans under Mitsunobu cyclization conditions gives the desired product only if the *syn* diastereoisomers are used. A high-yielding rearrangement leading to 2,5-dihydrobenzoxepines is observed with the *anti* diastereoisomers.

Experimental Section

Infrared spectra were recorded in liquid film between NaCl plates by using an FTIR Mattson Genesis II spectrometer. NMR spectra were determined by using Bruker Avance DPX 300 and Bruker Avance-500 spectrometers. ^{1}H NMR and ^{13}C NMR spectra were recorded in deuterated solvents and are reported relative to tetramethylsilane. Degrees of carbon substitution were established by DEPT multipulse sequence, and ^{13}C NMR peak assignments were made with the aid of two-dimensional NMR (HMBC, HMQC, COSY, and NOESY). HRMS data was recorded by using an Autospec-Q VG Analytical (FISONS) mass spectrometer. Enantiomer ratios were determined by integration of significant signals observed in the ^{1}H NMR spectra after addition of an adequate quantity of a solution of europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] in $CDCl_3$ (7 mg mL^{-1}). Calculated *ee*'s were in agreement with the values obtained by chiral HPLC analysis relative to the authentic racemic products. A JASCO HPLC system with a Chiral Detector CD-2095 and a Chiracel OD-H column (25×0.46 cm, Daicel Chem.) was used. Gradients of hexane/*i*PrOH, from 100:0 to 70:30 in 20 min, flow rate 0.5 mL min^{-1}, were used. Optical rotations were measured by using a JASCO P-1030 polarimeter. All solvents were purified and dried by following standard procedures.

Condensation between benzoxasilepines and aldehydes by using Ag^I complexes as Lewis acid: A mixture of AgOTf, BINAP, KF, and [18]crown-6 ether was dissolved in dry THF under an argon atmosphere from which direct light was excluded. This solution was stirred at RT for 10–15 min. Next, the corresponding aldehyde and benzoxasilepine derivatives in THF were added dropwise. The mixture was stirred for 30 min at RT. Brine was added and the resulting suspension was extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residual crude product was purified by flash chromatography.

(2*R,3*R**)-2-(2-Hydroxy-5-methoxyphenyl)-5-methoxy-3-vinyl-2,3-dihydrobenzofuran (3)**: Reaction of **2** (67 mg, 0.30 mmol) and the aldehyde **1** (79 mg, 0.33 mmol) with the mixture of (±)-BINAP (37 mg, 0.06 mmol), [18]crown-6 (79 mg, 0.3 mmol), KF (17 mg, 0.3 mmol), and TfOAg (15 mg, 0.06 mmol) in dry THF (1.5 mL) yielded **3** (63 mg, 0.21 mmol, 70%) as a colorless oil; R_f=0.28 (hexane/Et$_2$O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.87 (d, J=8.8 Hz, 2H; H-7, H-3′), 6.84 (d, J=2.9 Hz, 1H; H-6′), 6.76 (dd, J=8.6, 3.0 Hz, 2H; H-6, H-4′), 6.72 (m, 1H; H-4), 6.46 (br s, 1H; OH), 5.96 (ddd, J=16.8, 10.0, 8.4 Hz, 1H; H-1″), 5.47 (d, J=10.0 Hz, 1H; H-2), 5.31 (dd, J=10.0, 1.4 Hz, 1H; H-2″a), 5.26 (dd, J=16.8, 0.9 Hz, 1H; H-2″b), 4.17 (t, J=9.2 Hz, 1H; H-3), 3.79 (s, 3H; OCH_3), 3.77 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.1* (C, C-5′), 153.1* (C, C-5), 151.8 (C, C-7a), 148.4 (C, C-2′), 136.0 (CH, C-1″), 130.6 (C, C-1′), 124.5 (C, C-3a), 119.1 (CH_2, C-2″), 117.8 (CH, C-3′), 114.5 (CH, C-7), 113.8[#] (CH, C-4), 112.9[#] (CH, C-4′), 110.7[##] (CH, C-6), 110.3[##] (CH, C-6′), 89.7 (CH, C-2), 55.9 (CH_3, OCH_3), 55.7 (CH_3, OCH_3), 54.7 ppm (CH, C-3) (*, [#] and [##] may be interchanged); IR (film): $\tilde{\nu}_{max}$=3396, 2999, 2932, 2833, 1486, 1432, 1270, 1202, 1034, 750 cm^{-1}; HRMS (EI): m/z: calcd for $C_{18}H_{18}O_4$: 298.1205 $[M]^+$; found: 298.1203.

(2*R,3*R**)-2-(2-Hydroxyphenyl)-5-methoxy-3-vinyl-2,3-dihydrobenzofuran (6b)**: Reaction of **2** (50 mg, 0.23 mmol) and the aldehyde **4a** (51 mg, 0.25 mmol) with the mixture of (±-BINAP (28 mg, 0.046 mmol), [18]crown-6 ether (61 mg, 0.23 mmol), KF (13 mg, 0.23 mmol), and TfOAg (12 mg, 0.046 mmol) in dry THF (1.5 mL) yielded **6b** (45 mg, 0.17 mmol, 75%) as a colorless oil; R_f=0.29 (hexane/Et$_2$O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.25 (dt, J=8.0, 1.6 Hz, 1H; H-4′), 7.14 (dd, J=7.6, 1.6 Hz, 1H; H-6′), 6.93 (m, 2H; H-3′, 5′), 6.87 (br d, J=8.6 Hz, 1H; H-7), 6.77 (dd, J=8.6, 2.6 Hz, 1H; H-6), 6.71 (dd, J=2.5, 1.0 Hz, 1H; H-4), 5.96 (ddd, J=17.0, 10.0, 8.5 Hz, 1H; H-1″), 5.50 (d, J=10.3 Hz, 1H; H-2), 5.32 (dd, J=10.0, 1.4 Hz, 1H; H-2″a), 5.24 (br d, J=17.2 Hz, 1H; H-2″b), 4.18 (dd, J=9.5, 9.2 Hz, 1H; H-3), 3.80 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.1 (C, C-5), 154.8 (C, C-2′), 151.7 (C, C-7a), 135.8 (CH, C-1″), 130.8 (C, C-3a), 129.5 (CH, C-4′), 127.5 (CH, C-6′), 123.4 (C, C-1′), 120.0* (CH, C-3′), 119.2 (CH_2, C-2″), 117.2* (CH, C-5′), 113.8 (CH, C-6), 110.7 (CH, C-4), 110.4 (CH, C-7), 90.2 (CH, C-2), 55.9 (CH_3, OCH_3), 54.6 ppm (CH, C-3) (* may be interchanged); IR (film): $\tilde{\nu}_{max}$=3393, 2958, 2921, 1660, 1638, 1596, 1483, 1454, 1429, 1255, 1199, 1027, 873, 800, 756 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{16}O_3$: 268.1099 $[M]^+$; found: 268.1097.

(2*R,3*R**)-2-(2-Hydroxy-4-pivaloyloxyphenyl)-5-methoxy-3-vinyl-2,3-dihydrobenzofuran (6c)**: Reaction of **2** (50 mg, 0.23 mmol) and the aldehyde **4c** (69 mg, 0.23 mmol) with the mixture of (±-BINAP (28 mg, 0.05 mmol), [18]crown-6 ether (61 mg, 0.23 mmol), KF (13 mg, 0.23 mmol), and TfOAg (12 mg, 0.05 mmol) in dry THF (1.5 mL) yielded **6c** (50 mg, 0.14 mmol, 60%) as a colorless oil; R_f=0.29 (hexane/Et$_2$O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.20 (s, 1H; OH), 7.11 (d, J=8.4 Hz, 1H; H-6′), 6.86 (d, J=8.6 Hz, 1H; H-7), 6.75 (dd, J=8.6, 2.8 Hz, 1H; H-6), 6.71 (d, J=2.1 Hz, 1H; H-4), 6.67 (d, J=2.1 Hz, 1H; H-3′), 6.62 (dd, J=8.2, 2.1 Hz, 1H; H-5′), 5.93 (ddd, J=17.0, 10.0, 8.8 Hz, 1H; H-1″), 5.48 (d, J=10.0 Hz, 1H; H-2), 5.30 (d, J=9.8 Hz, 1H; H-2″a), 5.24 (d, J=17.0 Hz, 1H; H-2″b), 4.14 (dd, J=10.0, 8.8 Hz, 1H; H-3), 3.79 (s, 3H; OCH_3), 2.18 ppm (s, 9H; $OCOC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=176.7 (C, $OCOC(CH_3)_3$), 155.6 (C, C-5), 155.2 (C, C-2′), 151.9 (C, C-4′), 151.7 (C, C-7a), 135.7 (CH, C-1″), 130.6 (C, C-3a), 127.9 (CH, C-6′), 121.0 (C, C-1′), 119.2 (CH_2, C-2″), 113.8 (CH, C-6), 113.0 (CH, C-5′), 110.7 (CH, C-4), 110.5 (CH, C-3′), 110.3 (CH, C-7), 89.7 (CH, C-2), 55.9 (CH_3, OCH_3), 54.7 (CH, C-3), 39.0 (C, $OCOC(CH_3)_3$), 30.8 ppm (CH_3, $OCOC(CH_3)_3$); HRMS (EI): m/z: calcd for $C_{22}H_{24}O_5$: 368.1624 $[M]^+$; found: 368.1626.

(2*R,3*R**)-2-(2-Hydroxy-4-methoxyphenyl)-5,6-methylenedioxy-3-vinyl-2,3-dihydrobenzofuran (6d)**: Reaction of **5b** (200 mg, 0.85 mmol) and the aldehyde **4d** (222 mg, 0.236 mmol) with the mixture of (±-BINAP (105 mg, 0.17 mmol), [18]crown-6 (224 mg, 0.85 mmol), KF (49 mg, 0.85 mmol), and TfOAg (44 mg, 0.17 mmol) in dry THF (3 mL) yielded **6d** (188 mg, 0.60 mmol, 70%) as a colorless oil; R_f=0.30 (hexane/Et$_2$O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.02 (d, J=8.5 Hz, 1H; H-6′), 6.80 (br s, 1H; OH), 6.60 (br s, 1H; H-4), 6.51* (s, 1H; H-7), 6.50* (s, 1H; H-3′), 6.47 (dd, J=8.5, 2.5 Hz, 1H; H-5′), 5.95 (d, J=1.4 Hz, 1H; OCH_2O), 5.94 (d, J=1.4 Hz, 1H; OCH_2O), 5.87 (ddd, J=16.9, 10.0, 8.6 Hz, 1H; H-1″), 5.43 (d, J=10.3 Hz, 1H; H-2), 5.27 (dd, J=10.0, 1.5 Hz, 1H; H-2″a), 5.21 (dd, J=16.9, 1.5 Hz, 1H; H-2″b), 4.09 (dd, J=10.3, 8.6 Hz, 1H; H-3), 3.80 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=160.9 (C, C-4′), 155.9 (C, C-2′), 152.2 (C, C-7a), 147.7 (C, C-6), 142.5 (C, C-5), 136.3 (CH, C-1″), 128.3 (CH, C-6′), 121.0 (C, C-3a), 118.8 (CH_2, C-2″), 115.9 (C, C-1′), 106.1 (CH, C-5′), 104.8 (CH, C-4), 102.7 (CH, C-3′), 101.3 (CH_2, OCH_2O), 93.7 (CH, C-7), 91.5 (CH, C-2), 55.2 (CH_3, OCH_3), 54.2 ppm (CH, C-3) (* may be interchanged); IR (film): $\tilde{\nu}_{max}$=3408, 3079, 2957, 2917, 2849, 1619, 1500, 1471, 1289, 1157, 112, 1036, 964, 936, 835 cm^{-1}; HRMS (EI): m/z: calcd for $C_{18}H_{16}O_5$: 312.0998 $[M]^+$; found: 312.0996.

(2*R,3*R**)-2-(2-Hydroxy-4-methoxyphenyl)-6-methoxy-3-vinyl-2,3-dihydrobenzofuran (6e)**: Reaction of **5c** (65 mg, 0.29 mmol) and the aldehyde

4d (70 mg, 0.29 mmol) with the mixture of (±-BINAP (36 mg, 0.06 mmol), [18]crown-6 (76 mg, 0.29 mmol), KF (17 mg, 0.29 mmol), and TfOAg (15 mg, 0.06 mmol) in dry THF (1.5 mL) yielded **6e** (56 mg, 0.19 mmol, 65%) as a colorless oil; R_f=0.27 (hexane/Et_2O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.06 (d, J=8.4 Hz, 1H; H-6′), 7.03 (br d, J=9.0 Hz, 1H; H-4), 6.80 (br s, 1H; OH), 6.54 (dd, J=9.0, 2.3 Hz, 1H; H-5), 6.53 (d, J=2.1 Hz, 1H; H-7), 6.50 (d, J=2.4 Hz, 1H; H-3′), 6.47 (dd, J=8.3, 2.4 Hz, 1H; H-5′), 5.92 (ddd, J=16.9, 10.2, 8.4 Hz, 1H; H-1″), 5.48 (d, J=9.9 Hz, 1H; H-2), 5.26 (d, J=10.2 Hz, 1H; H-2″a), 5.22 (d, J=16.9 Hz, 1H; H-2″b), 4.12 (t, J=9.2 Hz, 1H; H-3), 3.82 (s, 3H; OCH_3), 3.79 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=160.8* (C, C-6), 160.8* (C, C-4′), 159.0 (C, C-7a), 155.9 (C, C-2′), 136.4 (CH, C-1″), 128.3 (CH, C-6′), 124.9 (CH, C-4), 121.7 (C, C-3a), 118.5 (CH_2, C-2″), 116.0 (C, C-1′), 107.3 (CH, C-5), 106.1 (CH, C-5′), 102.7 (CH, C-3′), 96.8 (CH, C-7), 90.4 (CH, C-2), 55.5 (CH_3, OCH_3), 55.2 (CH_3, OCH_3), 53.5 ppm (CH, C-3) (* may be interchanged); HRMS (EI): m/z: calcd for $C_{18}H_{18}O_4$: 298.1205 $[M]^+$; found: 298.1204.

(2*R,3*R**)-2-(2-Hydroxy-4-pivaloyloxyphenyl)-6-methoxy-3-vinyl-2,3-dihydrobenzofuran (6f)**: Reaction of **5c** (50 mg, 0.23 mmol) and the aldehyde **4c** (69 mg, 0.23 mmol) with the mixture of (±-BINAP (28 mg, 0.05 mmol), [18]crown-6 ether (61 mg, 0.23 mmol), KF (13 mg, 0.23 mmol), and TfOAg (11 mg, 0.05 mmol) in dry THF (1.5 mL) yielded **6f** (50 mg, 0.13 mmol, 60%) as a colorless oil; R_f=0.29 (hexane/Et_2O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.15 (d, J=8.1 Hz, 1H; H-6′), 7.02 (dd, J=8.9, 1.2 Hz, 1H; H-4), 6.67 (d, J=2.4 Hz, 1H; H-3′), 6.63 (dd, J=8.1, 2.4 Hz, 1H; H-5′), 6.55 (dd, J=8.9, 2.4 Hz, 1H; H-5), 6.54 (d, J=2.4 Hz, 1H; H-7), 5.94 (ddd, J=16.9, 10.1, 8.5 Hz, 1H; H-1″), 5.53 (d, J=9.7 Hz, 1H; H-2), 5.27 (dd, J=10.1, 1.6 Hz, 1H; H-2″a), 5.22 (dd, J=16.9, 1.6 Hz, 1H; H-2″b), 4.10 (dd, J=9.7, 8.5 Hz, 1H; H-3), 3.82 (s, 3H; OCH_3), 1.37 ppm (s, 9H; $OCOC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=160.8 (C, C-6, $OCOC(CH_3)_3$), 159.0 (C, C-7a), 155.3 (C, C-2′), 151.9 (C, C-4′), 136.4 (CH, C-1″), 127.8 (CH, C-6′), 125.0 (CH, C-4), 121.5* (C, C-1′), 121.4* (C, C-3a), 118.5 (CH_2, C-2″), 113.2 (CH, C-5′), 110.5 (CH, C-3′), 107.4 (CH, C-5), 96.8 (CH, C-7), 89.8 (CH, C-2), 55.5 (CH_3, OCH_3), 53.7 (CH, C-3), 39.0 (C, $OCOC(CH_3)_3$), 27.0 ppm (CH_3, $OCOC(CH_3)_3$) (* may be interchanged): HRMS (EI): m/z: calcd for $C_{22}H_{24}O_5$: 368.1624 $[M]^+$; found: 368.1622.

(2*R,3*R**)-2-(2-Hydroxy-4-pivaloyloxyphenyl)-5,6-methylenedioxy-3-vinyl-2,3-dihydrobenzofuran (6g)**: Reaction of **5b** (50 mg, 0.23 mmol) and the aldehyde **4c** (73 mg, 0.23 mmol) with the mixture of (±)-BINAP (30 mg, 0.05 mmol), [18]crown-6 (63 mg, 0.23 mmol), KF (14 mg, 0.23 mmol), and TfOAg (11 mg, 0.05 mmol) in dry THF (1.5 mL) yielded **6g** (57 mg, 0.15 mmol, 70%) as a colorless oil; R_f=0.30 (hexane/Et_2O 85:15); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.12 (d, J=8.2 Hz, 1H; H-6′), 6.64 (d, J=2.2 Hz, 1H; H-3′), 6.62 (dd, J=8.2, 2.3 Hz, 1H; H-5′), 6.59 (d, J=0.9 Hz, 1H; H-4), 6.52 (br s, 1H; H-7), 5.95 (d, J=1.4 Hz, 1H; OCH_2O), 5.94 (d, J=1.4 Hz, 1H; OCH_2O), 5.91 (ddd, J=16.9, 10.2, 8.5 Hz, 1H; H-1″), 5.50 (d, J=9.7 Hz, 1H; H-2), 5.26 (dd, J=10.2, 1.1 Hz, 1H; H-2″a), 5.20 (dd, J=16.9, 1.1 Hz, 1H; H-2″b), 4.06 (dd, J=9.7, 8.5 Hz, 1H; H-3), 1.36 ppm (s, 9H; $OCOC(CH_3)_3$; ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.4 (C, C-2′, $OCOC(CH_3)_3$), 152.3 (C, C-7a), 151.9 (C, C-4′), 147.8 (C, C-6), 142.5 (C, C-5), 136.3 (CH, C-1″), 127.8 (CH, C-6′), 121.4 (C, C-1′), 120.7 (C, C-3a), 118.7 (CH_2, C-2″), 113.0 (CH, C-5′), 110.4 (CH, C-3′), 104.8 (CH, C-4), 101.3 (CH_2, OCH_2O), 93.6 (CH, C-7), 89.9 (CH, C-2), 54.3 (CH, C-3), 39.0 (C, $OCOC(CH_3)_3$), 27.0 ppm (CH_3, $OCOC(CH_3)_3$; IR (film): $\tilde{\nu}_{max}$=3415, 2972, 2934, 2904, 2875, 1751, 1726, 1608, 1501, 1474, 1285, 1271, 1155, 1119, 1036, 975 cm^{-1}; HRMS (EI): m/z: calcd for $C_{22}H_{22}O_6$: 382.1416 $[M]^+$; found: 382.1418.

(1*R,2*S**)-2-(2-Hydroxy-5-methoxyphenyl)-1-(4-pivaloyloxyphenyl)-3-buten-1-ol (*syn*-7) and (1*R**,2*R**)-2-(2-Hydroxy-5-methoxyphenyl)-1-(4-pivaloyloxyphenyl)-3-buten-1-ol (*anti*-7)**: Reaction of **2** (50 mg, 0.23 mmol) and **4e** (51 mg, 0.25 mmol) with the mixture of (±)-BINAP (28 mg, 0.04 mmol), [18]crown-6 (60 mg, 0.23 mmol), KF (13 mg, 0.23 mmol), and TfOAg (11 mg, 0.04 mmol) in dry THF (2 mL) yielded **7** (*syn*/*anti* 1:1) with an overall yield of 83%.

Compound syn-**7**: R_f=0.29 (hexane/Et_2O 8:2); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.22 (d, J=8.5 Hz, 2H; H-2′, 6′), 6.97 (d, J=8.5 Hz, 2H; H-3′, 5′), 6.80 (d, J=8.7 Hz, 1H; H-3″), 6.68 (dd, J=8.7, 3.0 Hz, 1H; H-4″), 6.47 (d, J=3.0 Hz, 1H; H-6″), 6.17 (ddd, J=16.9, 10.4, 8.5 Hz, 1H; H-3), 5.20 (dt, J=10.4, 1.7 Hz, 1H; H-4a), 5.11 (d, J=3.2 Hz, 1H; H-1), 5.09 (dt, J=16.9, 1.7 Hz, 1H; H-4b), 3.81 (br dd, J=8.5, 3.2 Hz, 1H; H-2), 3.70 (s, 3H; OCH_3), 1.36 ppm (s, 9H; $OCOC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.7 (C, $OCOC(CH_3)_3$), 153.2 (C, C-5″), 150.4 (C, C-4′), 148.3 (C, C-2″), 138.8 (C, C-1′), 134.2 (CH, C-3), 128.2 (C, C-1″), 127.5 (CH, C-2′, C-6′), 120.9 (CH, C-3′, C-5′), 118.6 (CH_2, C-4), 117.8 (CH, C-3″), 115.8 (CH, C-6″), 113.1 (CH, C-4″), 77.4 (CH, C-1), 55.6 (CH_3, OCH_3), 54.1 (CH, C-2), 39.0 (C, $OCOC(CH_3)_3$), 27.0 ppm (CH_3, $OCOC(CH_3)_3$); HRMS (EI): m/z: calcd for $C_{22}H_{26}O_5$: 370.1780 $[M]^+$; found: 370.1776.

Compound anti-**7**: R_f=0.28 (hexane/Et_2O 8:2); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.22 (d, J=8.6 Hz, 2H; H-2′, 6′), 6.96 (d, J=8.6 Hz, 2H; H-3′, 5′), 6.84 (d, J=8.7 Hz, 1H; H-3″), 6.68 (dd, J=8.7, 3.0 Hz, 1H; H-4″), 6.37 (d, J=3.0 Hz, 1H; H-6″), 6.17 (ddd, J=17.5, 10.5, 7.3 Hz, 1H; H-3), 5.14 (dt, J=10.5, 1.4 Hz, 1H; H-4a), 5.10 (d, J=5.6 Hz, 1H; H-1), 5.06 (dt, J=17.5, 1.4 Hz, 1H; H-4b), 3.70 (m, 1H; H-2), 3.67 (s, 3H; OCH_3), 1.35 ppm (s, 9H; $OCOC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=177.1 (C, $OCOC(CH_3)_3$), 153.3 (C, C-5″), 150.4 (C, C-4′), 148.7 (C, C-2″), 139.2 (C, C-1′), 136.3 (CH, C-3), 127.3 (CH, C-2′, C-6′), 126.9 (C, C-1″), 121.2 (CH, C-3′, C-5′), 118.0 (CH, C-3″), 117.3 (CH_2, C-4), 116.5 (CH, C-6″), 113.2 (CH, C-4″), 78.1 (CH, C-1), 55.6 (CH_3, OCH_3), 54.8 (CH, C-2), 39.0 (C, $OCOC(CH_3)_3$), 27.0 ppm (CH_3, $OCOC(CH_3)_3$); IR (film): $\tilde{\nu}_{max}$=3385, 2970, 2934, 2906, 2873, 1747, 1636, 1604, 1495, 1395, 1366, 1276, 1200, 1164, 1125, 1039, 811 cm^{-1}; HRMS (EI): m/z: calcd for $C_{22}H_{26}O_5$: 370.1780 $[M]^+$; found: 370.1781.

(1*R,2*S**)-2-(2-Hydroxy-5-methoxyphenyl)-1-phenyl-3-buten-1-ol (*syn*-8) and (1*R**,2*R**)-2-(2-Hydroxy-5-methoxyphenyl)-1-phenyl-3-buten-1-ol (*anti*-8)**: Reaction of **2** (85 mg, 0.38 mmol) and benzaldehyde **4f** (45 mg, 0.42 mmol) with the mixture of (±)-BINAP (47 mg, 0.07 mmol), [18]crown-6 (100 mg, 0.38 mmol), KF (22 mg, 0.38 mmol), and TfOAg (19 mg, 0.07 mmol) in dry THF (2 mL) yielded **8** (*syn*/*anti* 1:1) with an overall yield of 85%.

Compound syn-**8**: R_f=0.29 (hexane/Et_2O 8:2); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.32 (m, 3H; H-3′, 4′, 5′), 7.25 (m, 2H; H-2′, 6′), 6.83 (d, J=8.6 Hz, 1H; H-3″), 6.71 (dd, J=8.6, 3.1 Hz, 1H; H-4″), 6.49 (d, J=3.1 Hz, 1H; H-6″), 6.20 (ddd, J=17.0, 10.1, 8.0 Hz, 1H; H-3), 5.22 (ddd, J=10.1, 1.6, 1.0 Hz, 1H; H-4a), 5.18 (d, J=4.0 Hz, 1H; H-1), 5.09 (dt, J=17.0, 1.6 Hz, 1H; H-4b), 3.86 (br dd, J=8.0, 4.0 Hz, 1H; H-2), 3.70 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.3 (C, C-5″), 148.3 (C, C-2″), 141.3 (C, C-1′), 134.0 (CH, C-3), 128.3 (C, C-1″), 128.0 (CH, C-3′, C-5′), 127.8 (CH, C-4′), 126.3 (CH, C-2′, C-6′), 118.6 (CH_2, C-4), 118.0 (CH, C-3″), 116.0 (CH, C-6″), 113.1 (CH, C-4″), 78.0 (CH, C-1), 55.6 (CH_3, OCH_3), 54.2 ppm (CH, C-2); IR (film): $\tilde{\nu}_{max}$=3371, 3077, 3030, 2956, 2906, 1715, 1699, 1635, 1603, 1496, 1258, 1205, 1038, 920, 749, 700 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{18}O_3$: 270.1255 $[M+H]^+$; found: 271.1256.

Compound anti-**8**: R_f=0.30 (hexane/Et_2O 8:2); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.39 (br s, 1H; OH), 7.27 (m, 5H; H-2′, 3′, 4′, 5′, 6′), 6.85 (d, J=8.9 Hz, 1H; H-3″), 6.69 (dd, J=8.9, 3.2 Hz, 1H; H-4″), 6.39 (d, J=3.2 Hz, 1H; H-6″), 6.18 (ddd, J=17.4, 10.5, 7.3 Hz, 1H; H-3), 5.14 (dt, J=10.5, 1.2 Hz, 1H; H-4a), 5.11 (d, J=5.6 Hz, 1H; H-1), 5.07 (dt, J=17.4, 1.2 Hz, 1H; H-4b), 3.78 (br dd, J=7.3, 5.6 Hz, 1H; H-2), 3.66 (s, 3H; OCH_3), 2.91 ppm (br s, 1H; OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.2 (C, C-5″), 148.7 (C, C-2″), 141.6 (C, C-1′), 136.3 (CH, C-3), 128.2 (CH, C-3′, C-5′), 127.9 (CH, C-4′), 127.2 (C, C-1″), 126.2 (CH, C-2′, C-6′), 118.1 (CH, C-3″), 117.3 (CH_2, C-4), 116.4 (CH, C-6″), 113.1 (CH, C-4″), 78.8 (CH, C-1), 55.6 (CH_3, OCH_3), 54.6 ppm (CH, C-2): IR (film): $\tilde{\nu}_{max}$=3354, 2955, 2924, 2853, 1717, 1634, 1600, 1496, 1452, 1432, 1244, 1205, 1153, 1040, 918, 810, 699 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{18}O_3$: 270.1255 $[M+H]^+$: found; 271.1248.

(1*R,2*S**)-2-(2-Hydroxyphenyl)-1-phenyl-3-buten-1-ol (*syn*-9) and (1*R**,2*R**)-2-(2-hydroxyphenyl)-1-phenyl-3-buten-1-ol (*anti*-9)**: Reaction of **5a** (54 mg, 0.28 mmol) and benzaldehyde **4f** (33 mg, 0.31 mmol) with the mixture of (±)-BINAP (38 mg, 0.06 mmol), [18]crown-6 (74 mg, 0.28 mmol), KF (16 mg, 0.28 mmol), and TfOAg (16 mg, 0.06 mmol) in dry THF (1.5 mL) yielded **9** (*syn*/*anti* 1:1) with an overall yield of 82%.

Compound syn-**9**: R_f=0.27 (hexane/Et_2O 8:2); white solid; m.p. 90–92 °C; ^1H NMR (300 MHz, $CDCl_3$): δ=7.30 (m, 5H; H-2′, 3′, 4′, 5′,6′), 7.16 (ddd, J=8.1, 7.4, 1.8 Hz, 1H; H-4″), 6.94 (dd, J=7.6, 1.8 Hz, 1H; H-6″), 6.90 (br d, J=8.1 Hz, 1H; H-3″), 6.83 (dt, J=7.4, 1.2 Hz, 1H; H-5″), 6.23 (ddd, J=17.3, 10.5, 8.1 Hz, 1H; H-3), 5.22 (d, J=4.0 Hz, 1H; H-1), 5.20 (dt, J=10.5, 1.6 Hz, 1H; H-4a), 5.05 (dt, J=17.3, 1.6 Hz, 1H; H-4b), 3.87 (br dd, J=8.1, 4.0 Hz, 1H; H-2), 2.85 ppm (br s, 1H; OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.4 (C, C-2″), 141.5 (C, C-1′), 134.0 (CH, C-3), 130.5 (CH, C-6″), 128.2 (CH, C-4″), 128.0 (CH, C-3′, C-5′), 127.7 (CH, C-4′), 127.3 (C, C-1″), 126.3 (CH, C-2′, C-6′), 120.4 (CH, C-5″), 118.4 (CH_2, C-4), 117.4 (CH, C-3″), 77.9 (CH, C-1), 54.5 ppm (CH, C-2); IR(film): $\tilde{\nu}_{max}$=3366, 2920, 2852, 1647, 1633, 1581, 1486, 1453, 1416, 1246, 1024, 875, 752, 698, 667 cm^{-1}; HRMS (EI): m/z: calcd for $C_{16}H_{16}O_2$: 222.1044 $[M-H_2O]^+$; found: 222.1048.

Compound anti-**9**: R_f=0.26 (hexane/Et_2O 8:2); colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ=7.83 (br s, 1H; OH), 7.27 (m, 5H; H-2′, 3′, 4′, 5′, 6′), 7.14 (ddd, J=8.1, 6.5, 2.4 Hz, 1H; H-4″), 6.93 (br d, J=7.7 Hz, 1H; H-6″), 6.76 (m, 2H; H-3″, 5″), 6.24 (ddd, J=17.4, 10.5, 6.9 Hz, 1H; H-3), 5.20 (d, J=6.5 Hz, 1H; H-1), 5.16 (dt, J=10.5, 1.6 Hz, 1H; H-4a), 5.09 (dt, J=17.4, 1.6 Hz, 1H; H-4b), 3.79 (br dd, J=6.9, 6.5 Hz, 1H; H-2), 2.83 ppm (br s, 1H; OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.9 (C, C-2″), 141.5 (C, C-1′), 136.4 (CH, C-3), 131.2 (CH, C-6″), 128.4 (CH, C-4″), 128.2 (CH, C-3′, C-5′), 127.9 (CH, C-4′), 126.1 (CH, C-2′, 6′), 125.7 (C, C-1″), 120.3 (CH, C-5″), 117.5 (CH_2, C-4), 117.2 (CH, C-3″), 78.7 (CH, C-1), 55.1 ppm (CH, C-2): HRMS (EI): m/z: calcd for $C_{16}H_{16}O_2$: 222.1044 $[M-H_2O]^+$; found: 222.1041.

Mitsunobu cyclization of the *syn* and *anti* diastereoisomers of 8 and 9: Synthesis of 10–13

(2*R,3*R**)-5-Methoxy-2-phenyl-3-vinyl-2,3-dihydrobenzofuran (10)**: PPh_3 (12 mg, 0.045 mmol) and DIAD (0.008 mL, 0.04 mmol) were added to a solution of *syn*-**8** (10 mg, 0.037 mmol) in anhyd THF (1 mL). After 30 min the solvent was removed in vacuo. Flash chromatography of the residue afforded **10** (7 mg, 0.03 mmol, 72%); R_f=0.29 (hexane/Et_2O 9:1); colorless oil; ^1H NMR ($CDCl_3$, 300 MHz): δ=7.40 (m, 5H; H-2′, 3′, 4′, 5′,6′), 6.83 (d, J=8.6 Hz, 1H; H-7), 6.77 (dd, J=8.6, 0.8 Hz, 1H; H-6), 6.70 (d, J=0.8 Hz, 1H; H-4), 5.99 (ddd, J=16.9, 10.0, 8.5 Hz, 1H; H-1″), 5.39 (d, J=9.0 Hz, 1H; H-2), 5.26 (dd, J=10.0, 1.5 Hz, 1H; H-2a), 5.23 (dd, J=16.9, 1.5 Hz, 1H; H-2b), 4.01 (t, J=8.5 Hz, 1H; H-3), 3.79 ppm (s, 3H; OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=153.3 (C, C-5, C-7a), 140.4 (C, C-1′), 136.8 (CH, C-1″), 130.1 (C, C-3a), 128.4 (3CH), 128.0 (CH), 125.8 (CH), 117.9 (CH_2, C-2″), 113.8 (CH, C-6), 110.7 (CH, C-4), 109.5 (CH, C-7), 90.0 (CH, C-2), 56.5 (CH_3, OCH_3), 56.0 ppm (CH, C-3); IR (film): $\tilde{\nu}_{max}$=2937, 2830, 1603, 1490, 1452, 1263, 1200, 1030, 985, 920, 750 cm^{-1}: HRMS (EI): m/z: calcd for $C_{17}H_{16}O_2$: 252.1150 $[M]^+$; found: 252.1154.

(2*R,3*R**)-2-Phenyl-3-vinyl-2,3-dihydrobenzofuran (11)**: PPh_3 (25 mg, 0.096 mmol) and DIAD (0.018 mL, 0.096 mmol) were added to a solution of *syn*-**9** (20 mg, 0.08 mmol) in anhyd THF (2 mL). After 30 min the solvent was removed in vacuo. Flash chromatography of the residue afforded **11** (14 mg, 0.063 mmol, 75%); R_f=0.29 (hexane/Et_2O 95:5); colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ=7.47–7.33 (m, 5H; H-2′, H-3′, H-4′, H-5′, H-6′), 7.23 (dd, J=7.9, 7.3 Hz, 1H; H-6), 7.12 (d, J=7.3 Hz, 1H; H-4), 6.94 (t, J=7.3 Hz, 1H; H-5), 6.92 (d, J=7.9 Hz, 1H; H-7), 6.00 (ddd, J=18.5, 10.2, 8.8 Hz, 1H; H-1″), 5.42 (d, J=8.8 Hz, 1H; H-2), 5.25 (br d, J=10.2 Hz, 1H; H-2″a), 5.20 (br d, J=18.5 Hz, 1H; H-2″b), 4.04 ppm (t, J=8.8 Hz, 1H; H-3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.2 (C, C-7a), 140.4 (C, C-1′), 137.0 (CH, C-1″), 129.1 (C, C-3a), 128.7 (CH, C-6), 128.5 (CH, C-3′, C-5′), 128.0 (CH, C-4′), 125.8 (CH, C-2′, C-6′), 124.7 (CH, C-4), 120.8 (CH, C-5), 117.8 (CH_2, C-2″), 109.5 (CH, C-7), 89.7 (CH, C-2), 56.2 ppm (CH, C-3); IR (film): $\tilde{\nu}_{max}$=3064, 3031, 2959, 2922, 2885, 1638, 1596, 1476, 1262, 1228, 1099, 1014, 982, 922, 865, 750, 697 cm^{-1}; HRMS (EI): m/z: calcd for $C_{16}H_{15}O$: 223.1123 $[M+H]^+$; found: 223.1128.

7-Methoxy-5-phenyl-2,5-dihydrobenzo[*b*]oxepine (12): PPh_3 (14 mg, 0.05 mmol) and DIAD (0.010 mL, 0.05 mmol) were added to a solution of *anti*-**8** (12 mg, 0.04 mmol) in anhyd THF (1 mL). After 30 min the solvent was removed in vacuo. Flash chromatography of the residue afforded **12** (10 mg, 0.04 mmol, 90%); R_f=0.29 (hexane/Et_2O 9:1); colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ=7.41 (d, J=7.4 Hz, 2H; H-2′, 6′), 7.33 (dd, J=7.4, 7.1 Hz, 2H; H-3′, 5′), 7.23 (t, J=7.1 Hz, 1H; H-4′), 7.01 (d, J=8.5 Hz, 1H; H-9), 6.71 (dd, J=8.1, 3.1 Hz, 1H; H-8), 6.54 (d, J=3.1 Hz, 1H; H-6), 6.06 (dddd, J=6.0, 4.6, 3.3, 2.2 Hz, 1H; H-3), 5.68 (m, 1H; H-4), 4.82 (m, 1H; H-5), 4.69 (dddd, J=17.0, 3.3, 1.8, 1.8 Hz, 1H; H-2b), 4.56 (ddd, J=17.0, 4.6, 2.4 Hz, 1H; H-2a), 3.73 ppm (s, 3H; OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.8 (C, C-7), 151.6 (C, C-9a), 142.6 (C, C-1′), 140.6 (C, C-5a), 129.4 (CH, C-3), 128.4* (CH, C-3′, C-5′), 128.2* (CH, C-2′, C-6′), 127.9 (CH, C-4), 126.4 (CH, C-4′), 122.5 (CH, C-9), 114.8 (CH, C-6), 112.1 (CH, C-8), 71.0 (CH_2, C-2), 55.4 (CH_3, OCH_3), 49.0 ppm (CH, C-5) (* may be interchanged); IR (film): $\tilde{\nu}_{max}$=3023, 2941, 2882, 2834, 1726, 1659, 1600, 1487, 1265, 1202, 1066, 1037, 827, 749, 700 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{16}O_2$: 252.1150 $[M]^+$; found: 252.1149.

5-Phenyl-2,5-dihydrobenzo[*b*]oxepine (13): PPh_3 (17 mg, 0.06 mmol) and DIAD (0.013 mL, 0.06 mmol) were added to a solution of *anti*-**9** (13 mg, 0.05 mmol) in anhyd THF (1 mL). After 30 min the solvent was removed in vacuo. Flash chromatography of the residue afforded **13** (10 mg, 0.045 mmol, 88%); R_f=0.29 (hexane/Et_2O 9:1); colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ=7.47–7.33 (m, 5H; H-2′–6′), 6.92–6.70 (m, 4H; H-6–9), 6.15 (dddd, J=6.1, 4.3, 3.3, 2.2 Hz, 1H; H-3), 5.60 (m, 1H; H-4), 4.76 (m, 1H; H-5), 4.62 (dddd, J=16.8, 3.3, 1.7, 1.7 Hz, 1H; H-2a), 4.59 ppm (ddd, J=16.8, 4.3, 2.2 Hz, 1H; H-2b); ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.4 (C, C-9a), 143.0 (C, C-1′), 140.2 (C, C-5a), 133.1 (CH), 129.2 (CH), 128.9* (CH, C-3′, C-5′), 128.2* (CH, C-2′, C-6′), 127.2 (CH), 126.2 (CH), 124.3 (CH), 123.6 (CH), 114.7 (CH), 69.8 (CH_2, C-2), 47.1 ppm (CH, C-5) (* may be interchanged); HRMS (EI): m/z: calcd for $C_{16}H_{14}O$: 222.1045 $[M]^+$; found: 222.1049.

Asymmetric synthesis of *trans*-pterocarpin: (+)-(2*S*,3*S*)-2-(2-hydroxy-4-methoxyphenyl)-3,4-methylenedioxy-3-vinyl-2,3-dihydrobenzofuran (6d): Reaction of **5b** (50 mg, 0.21 mmol) and the aldehyde **4d** (50 mg, 0.21 mmol) with (+)-(*R*)-TolBINAP (27 mg, 0.042 mmol) at −80 °C, by using the procedure described for the racemic version, yielded (+)-**6d** (46 mg, 0.16 mmol, 75%) with an *ee* of 84%; $[\alpha]_D^{20}$=+3.4° (c=0.1, CH_2Cl_2).

(−)-(2*S*,3*R*)-3-Hydroxymethyl-5,6-methylenedioxy-2-(4-methoxy-2-hydroxyphenyl)-2,3-dihydrobenzofuran (14): Compound **6d** (84% *ee*) (16 mg, 0.051 mmol) was dissolved in THF/H_2O (1 mL, 1:1 v/v) and cooled at 0 °C. The flask was protected from the light. OsO_4 (44 μL, 0.01 mmol, 2.5% in isopropanol) and $NaIO_4$ (43 mg, 0.2 mmol) were added. The mixture was stirred at 0 °C for 5 h, then water was added and the mixture was extracted with CH_2Cl_2. The dried (Na_2SO_4) extract was concentrated in vacuo. The residue was dissolved in THF (2 mL) and was cooled at −40 °C. Then, $LiAlH_4$ (5 mg, 0.13 mmol) was added and the suspension was stirred for 1 h. Next, a saturated solution of NH_4Cl/H_2O was added and the mixture was extracted with CH_2Cl_2. The organic layer was dried over anhyd Na_2SO_4 and the solvent was removed in vacuo. Flash chromatography of the residue (hexane/Et_2O 6:4) gave **14** (14 mg, 0.044 mmol, 86%) as a solid foam; $[\alpha]_D^{20}$=−44.0° (c=0.3, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): δ=7.18 (d, J=9.0 Hz, 1H; H-6′), 6.60 (s, 1H; H-4), 6.55 (s, 1H; H-7), 6.49 (d, J=2.5 Hz, 1H; H-3′), 6.48 (dd, J=6.2, 2.5 Hz, 1H; H-5′), 5.93 (s, 2H; OCH_2O), 5.81 (d, J=11.6 Hz, 1H; H-2), 4.01 (dd, J=10.1, 4.6 Hz, 1H; H-1″a), 3.89 (t, J=10.1 Hz, 1H; H-1″b), 3.78 (s, 3H; OCH_3), 3.51 ppm (m, 1H; H-3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=160.4 (C, C-4′), 154.0 (C, C-7a), 153.7 (C, C-2′), 148.2 (C, C-6), 141.9 (C, C-5), 126.2 (CH, C-6′), 119.7 (C, C-1′), 116.2 (C, C-3a), 106.2 (CH, C-5′), 104.4 (CH, C-4), 102.8 (CH, C-3′), 101.3 (CH_2, OCH_2O), 93.3 (CH, C-7), 84.4 (CH, C-2), 65.3 (CH_2, C-1″), 55.2 (CH_3, OCH_3), 52.8 ppm (CH, C-3); IR (film): $\tilde{\nu}_{max}$=3397, 2932, 2895, 1709, 1618, 1500, 1474, 1458, 1294, 1200, 1150, 1036, 936, 828, 736 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{16}O_6$: 316.0947 $[M]^+$; found; 316.0949.

(−)-*trans*-Pterocarpin: PPh_3 (16 mg, 0.04 mmol) and DIAD (0.012 mL, 0.06 mmol) were added to a solution of **14** (12 mg, 0.038 mmol) in anhyd THF (1 mL). After 30 min the solvent was removed in vacuo. Flash chromatography of the residue afforded *trans*-pterocarpin (11 mg, 0.037 mmol, 97%); R_f=0.289 (hexane/Et_2O 9:1); white solid; m.p. 160–162 °C; $[\alpha]_D^{20}$=−35.0° (c=0.1, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): δ=7.30 (m, 1H; H-1), 6.67 (d, J=1.2 Hz, 1H; H-7), 6.64 (s, 1H; H-10), 6.54

(dd, $J=8.1$, 2.4 Hz, 1H; H-2), 6.47 (d, $J=2.4$ Hz, 1H; H-4), 5.96 (d, $J=$ 1.2 Hz, 1H; OCH_2O), 5.95 (d, $J=1.2$ Hz, 1H; OCH_2O), 5.13 (dd, $J=$ 13.3, 0.8 Hz, 1H; H-11a), 4.85 (dd, $J=9.7$, 4.4 Hz, 1H; H-6′), 4.44 (dd, $J=11.9$, 9.7 Hz, 1H; H-6), 3.80 (s, 3H; OCH_3), 3.53 ppm (ddd, $J=13.3$, 11.9, 4.4 Hz, 1H; H-6a); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=160.4$ (C, C-3), 156.3 (C, C-10a), 153.8 (C, C-4a), 147.5 (C, C-9), 142.0 (C, C-8), 123.6 (CH, C-1), 118.7 (C, C-6b), 116.8 (C, C-11b), 106.2 (CH, C-2), 103.7 (CH, C-7), 102.0 (CH, C-4), 101.2 (CH_2, OCH_2O), 94.9 (CH, C-10), 84.5 (CH, C-11a), 69.0 (CH_2, C-6), 55.3 (CH_3, OCH_3), 45.4 ppm (CH, C-6a); IR (film): $\tilde{\nu}_{max}=2959$, 2923, 2852, 1740, 1619, 1585, 1505, 1460, 1441, 1384, 1260, 1159, 1112, 1094, 1034, 800 cm^{-1}; HRMS (EI): m/z: calcd for $C_{17}H_{14}O_5$: 298.0841 $[M]^+$; found: 298.0838.

(−)-*cis*-Pterocarpin: A solution of (−)-*trans*-pterocarpin (11 mg, 0.037 mmol) in toluene (1.5 mL) was stirred in the presence of (±)-10-camphorsulfonic acid (4 mg, 0.017 mmol) for 6 h. The cooled mixture was washed with saturated $NaHCO_3$ solution, the organic layer was dried, concentrated, and then purified over silica gel (hexane/Et_2O 9:1) yielding *cis*-pterocarpin (10 mg, 0.034 mmol, 92%). Spectral data were in agreement with those reported previously [15] and with those of an authentic sample,[37] except for the optical rotation value: $[\alpha]_D^{20}=-181°$ ($c=1.0$, CH_2Cl_2) (previously reported $[\alpha]_D^{20}=-223.0°$ ($c=0.11$, $CHCl_3$)[15]).

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