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A Diastereoselective Route to *trans*-2-Aryl-2,3-dihydrobenzofurans through Sequential Cross-Metathesis/Isomerization/Allylboration Reactions: Synthesis of Bioactive Neolignans

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Keywords: Synthetic methods / Metathesis / Allylation / Natural products / Neolignans / Oxygen heterocycles

A new highly diastereoselective synthetic route to *trans*-2,3-dihydrobenzofuran systems, in particular those bearing an aryl substituent at the C2 position, is described. The cornerstone of our strategy is the implementation of a cross-metathesis/isomerization/allylboration sequence starting from 2-allyl-substituted phenols and aldehydes. After an intramolecular Mitsunobu cyclization step, the *anti*-homoallylic alcohols allow the synthesis of the desired skeleton in a stereoselective fashion. As an illustration, we used this strategy for the preparation of the dihydrodehydrodiconiferyl alcohol (**1a**), a natural dihydrobenzofuran neolignan, as well as for a formal synthesis of its *O*-demethylated derivative **1b**. An enantioselective version of this approach employing a chiral phosphoric acid in the allylboration step is also studied.

Introduction

Great interest is shown by the organic chemistry community in the 2,3-dihydrobenzofuran moiety because this scaffold is present in a large variety of natural bioactive products.[1] Of these, neolignans produced in plants as secondary metabolites derived from phenylpropanoids are of particular relevance, due to their many kinds of biological activities,[2] in particular as antioxidant,[3] neuritogenic,[4] antimicrobial,[5] and anti-HIV agents.[6] Thanks to its potential interest as an inhibitor of cell proliferation,[7] 3′,4-di-*O*-methylcedrusin (**1a**, also named dihydrodehydrodiconiferyl alcohol) has been often put forward as a lead compound in drug development (Figure 1).[8] A structure–activity relationship study based on this compound was carried out in order to investigate its potential antitumor activity.[9] It was thus established that some derivatives inhibit the growth of a variety of cancer cells by interaction with tubulin.[10] More recently, another report showed that a product containing a 2-aryl-2,3-dihydrobenzofuran scaffold strongly inspired by **1a** could be a promising anticancer drug though induction of apoptosis.[11] As a result, innovative strategies are required for building this kind of skeleton in order to offer the large structural diversity needed for the development of new therapeutic agents. The *trans* isomers being more prevalent in many members of this family of dihydrobenzofurans, particular attention is paid to the diastereoselectivity of the planned reactions.

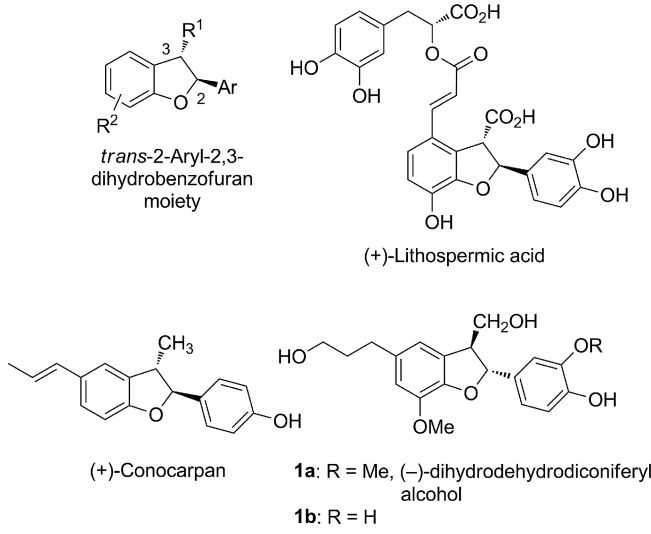

Figure 1. Selection of natural products containing *trans*-2-aryl-2,3-dihydrobenzofuran units.

Several synthetic approaches have been reported in the literature.[12] Among the predominant methods used for the stereoselective synthesis of the *trans*-2-aryl-2,3-dihydrobenzofuran motif, [3+2] cycloaddition between styrene derivatives and quinones catalyzed by various Lewis or Brønsted acids[13] and oxidative cross-coupling of phenols under different conditions[14] are well positioned, but suffer from a limited scope linked to the electronic nature of the substituents on olefins. Stereoselective construction in favor of *trans* isomers is also possible through intramolecular C–H insertion in the presence of a lactamide-type chiral auxiliary.[15] An alternative approach involving an inter-

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molecular C–H insertion followed by an intramolecular C–H oxidation[16] allows this drawback to be avoided. An efficient Pd-catalyzed oxyarylation from *o*-aminophenols was described, but only in the case of electron-rich styrene derivatives.[17] From recent years, we can also cite other strategies more rarely used, such as aldolization followed by cyclization,[18] rearrangement of chromanone,[19] radical cyclization onto a terminal double bond,[20] and Michael-type addition followed by an intramolecular nucleophic substitution.[21]

In line with our interest in the synthesis of natural products and analogues,[22] we recently outlined a highly diastereoselective synthesis of *anti*-homoallylic alcohols from allylbenzene derivatives and aldehydes including a sequential cross-metathesis/isomerization/allylboration (CMIA sequence) catalyzed by a ruthenium and iridium combination.[23] We envisioned that, by starting from suitably protected 2-allyl-substituted phenols, this three-component strategy could be useful for the construction of the five-membered oxygenated ring of 2,3-dihydrobenzofuran systems, through the addition of an intramolecular cyclization step in the synthetic pathway (Figure 2).

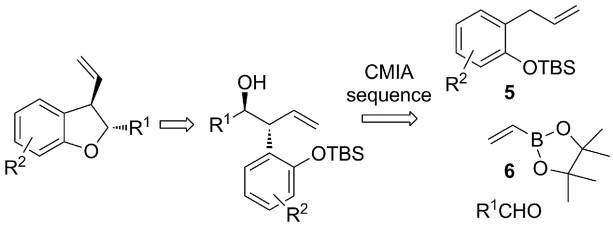
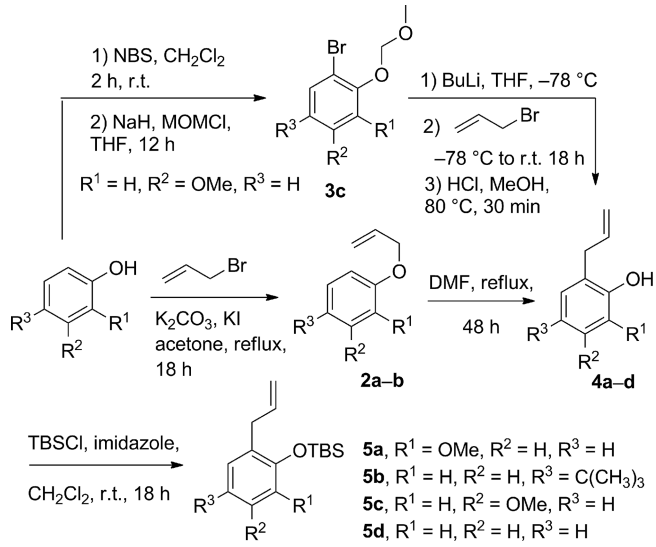


Figure 2. Retrosynthetic strategy for preparation of the *trans*-2,3-dihydrobenzofuran unit.

Here we report our efforts devoted to a new general route to this class of products, not limited to C2 aryl substituents. We then applied this approach to a diastereoselective preparation of **1a** and its *O*-demethylated derivative **1b**. An enantioselective version using a chiral phosphoric acid catalyst was also studied.

Results and Discussion

The synthesis of various protected 2-allyl-substituted phenols is the starting point for the implementation of our strategy. Compounds **5a** and **5b** were each obtained in three steps by means of a thermal aromatic Claisen rearrangement from the corresponding allyl aryl ether **2a** or **2b**, followed by protection of the phenol function with a TBS group. A mixture of products that was difficult to separate was obtained in the case of allyl 3-methoxyphenyl ether,[24] so we planned another route to **5c**. 3-Methoxyphenol was first brominated with NBS. After protection as a MOM ether, alkylation with allyl bromide, and treatment with HCl at 80 °C, the allylbenzene **4c** was isolated in a 37% unoptimized overall yield. With regard to **5d**, it was prepared from the commercially available 2-allylphenol (**4d**, Scheme 1).



Scheme 1. Synthesis of protected 2-allyl-substituted phenols.

These raw materials were then subjected to the cross-metathesis reaction conditions for coupling between allylbenzene derivatives and the pinacol vinyl boronate **6**, previously reported by us.[25] The corresponding alkenyl boronates **7a–d** were formed in all cases with excellent levels of conversion (>90% relative to compounds **5**) in favor of the *E* stereoisomers. Without any purification step except a simple filtration through a short pad of silica gel to eliminate the first-generation Grubbs catalyst (**G-I**),[26] the intermediates **7** were engaged in the "one-pot" process beginning with an iridium-catalyzed isomerization reaction followed by allylboration of an aldehyde. As expected, due to the highly stereoselective formation of transient allylboronates, the homoallylic alcohols **8** were obtained as single diastereoisomers (*anti*/*syn* ≥ 98:2) and in variable yields depending on the nature of the aldehyde used (Figure 3).

The next stage of the strategy was the cleavage of the aryl silyl ether by treatment with tetrabutylammonium fluoride (TBAF) in THF, to liberate the phenol function needed for the intramolecular Mitsunobu reaction. This last step was performed with a slight excess of triphenyphosphine and diisopropyl azodicarboxylate (DIAD) relative to **9**. In the great majority of examples studied, the five-membered oxygenated heterocycles **10** were obtained in good overall yields from **8** (two steps) and with complete diastereoselectivity in favor of *trans* isomers, thus validating our approach (Figure 4).[27]

For compounds **9dd** and **9ed**, each of which also contains an allylic alcohol moiety in the carbon skeleton, the formation of the desired five-membered-ring compound was accompanied in an unforeseen manner by another product that was unfortunately inseparable by silica gel chromatography. Its structure was assigned in each case as a seven-membered-ring system, the formation of which could be the result of an intramolecular S_N2' substitution in an unconventional Mitsunobu reaction (Scheme 2).[28,29] The relative

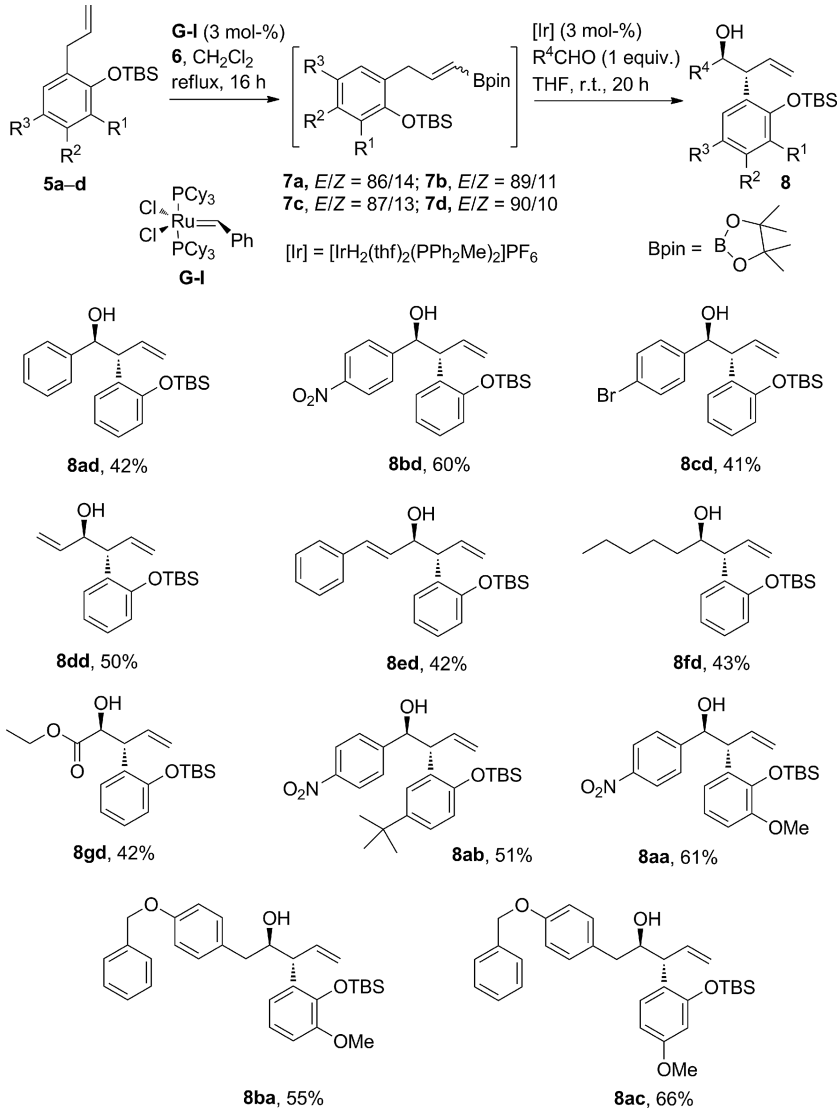
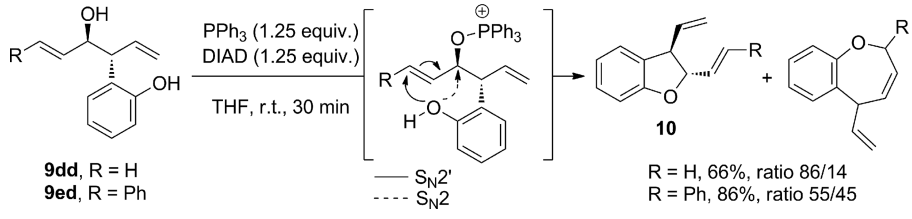


Figure 3. Synthesis of *anti*-homoallylic alcohols **8** by the cross-metathesis/isomerization/allylboration sequence.

configuration of the stereocenters in the 2,5-dihydrobenzo[*b*]oxepine derivative with R = Ph was not unambiguously assigned, although analysis of ^{1}H NMR spectrum seems to indicate the presence of only one diastereoisomer.

To illustrate the synthetic utility of the methodology for the construction of highly functionalized *trans*-2,3-dihydrobenzofurans, we then examined access to the bioactive 3′,4-di-*O*-methylcedrusin (**1a**). This natural product was isolated in low yield from the red latex (also called "sangre de drago") produced by various South American *Croton* species (Euphorbiaceae).[8,30] The retrosynthetic scheme developed for its synthesis involved the stereoselective preparation of a suitably protected *anti*-homoallylic alcohol **17**, which could be obtained through the three-component process with cheap commercially available starting materials such as eugenol and vanillin (Figure 5). A formal synthesis of 3-*O*-demethyldihydrodehydrodiconiferyl alcohol (**1b**),[31] which was isolated from the twigs of a species belonging to the genus *Taxus* present in Taiwan (*Taxus marei*),[32] by use of 4,5-dihydroxybenzaldehyde is also presented.



Scheme 2. Special cases in which the Mitsunobu reaction involves two pathways.

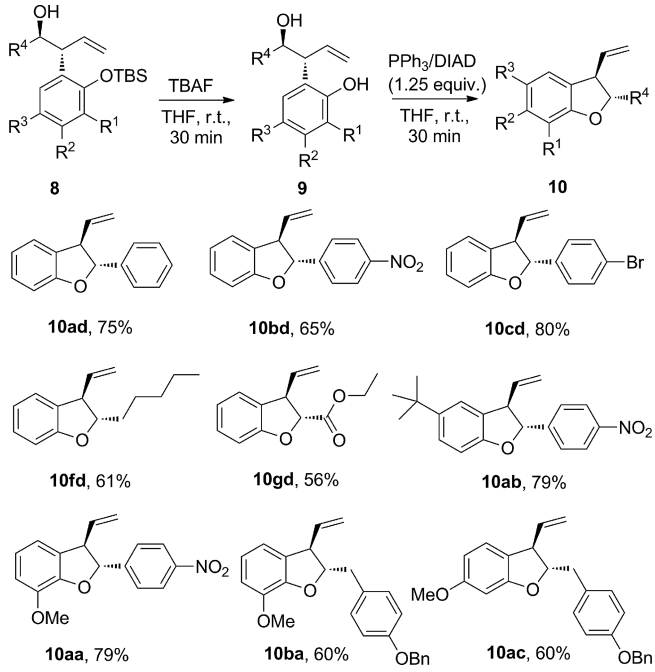


Figure 4. Synthesis of *trans*-2,3-dihydrobenzofurans from alcohols **8**.

The hydroboration/oxidation sequence starting from eugenol and initiated by use of a complexed borane reagent furnished **11** as a mixture of inseparable products in which the main regioisomer was the primary alcohol (ratio 9:1). Separation was achieved at the next stage after allylation of the phenol function. Compound **12** was obtained in pure form but in only moderate yield, as the result of a tedious chromatographic purification. The thermal Claisen rearrangement was performed in *N*,*N*-dimethylaniline as solvent at reflux, followed by selective protection of the aliphatic alcohol with pivaloyl chloride (PivCl) and silylation of the aromatic hydroxy group with *tert*-butyldimethylsilyl chloride (TBSCl). Eventually, the functionalized allylbenzene derivative **15** was produced from eugenol in a 21% overall yield (Scheme 3).

The cross-metathesis between compound **15** and pinacol vinyl boronate **6**, catalyzed by the first-generation Grubbs catalyst, led to the alkenyl boronate **16** with stereocontrolled formation of the double bond in favor of the *E* isomer. Although it could be isolated in a satisfying yield (75%), the use of the crude reaction mixture after removal of the ruthenium catalyst was preferred, in order to avoid the purification stage. The one-pot isomerization/allylboration process initiated by activated catalyst $[IrH_2(thf)_2(PPh_2Me)_2]PF_6$ furnished the *anti*-homoallylic alcohols **17a** and **17b** in moderate yields in a highly stereoselective manner (*anti*/*syn* ≥ 98:2). After removal of the silyl protecting group, compounds **18a** and **18b** were engaged in an intramolecular Mitsunobu reaction, thus providing the corresponding *trans*-2-aryl-3-vinyl-2,3-dihydrobenzofurans **19a** and **19b** (Scheme 4).

The oxidative cleavage of the double bond is one of last chemical transformations necessary to carry out to achieve the synthesis of set targets. Osmium tetroxide (OsO_4), in the presence of excess of sodium metaperiodate ($NaIO_4$) as co-oxidant, was chosen as system reagent for this step. The reaction, monitored by TLC, was complete after 4 h at 0 °C and without any detectable side products. After an aqueous workup, the aldehyde **20a** was purified by column chromatography without loss of stereochemical integrity, the low isolated yield being attributed to some level of aldehyde instability on silica gel. The magnitude of the coupling constant between H-2 and H-3 (J = 6.8 Hz) is consistent with a *trans* isomer. The reduction to the alcohol and cleavage of the pivaloyl protecting groups were performed in a concomitant manner by treatment with $LiAlH_4$ at low temperature, yielding the biologically active natural neolignan **1a**.[33] The advanced intermediate **19b** was synthesized under similar conditions; its conversion into the *O*-demethylated derivative **1b** had already been described in the literature (Scheme 5).[31]

In the hope of developing an enantioselective synthesis of (–)-dihydrodehydrodiconiferyl alcohol (**1a**), the sequence initiated by the isomerization reaction of the alkenyl boronate **16** was carried out in the presence of the commercially available chiral phosphoric acid catalyst (*S*)-TRIP-PA

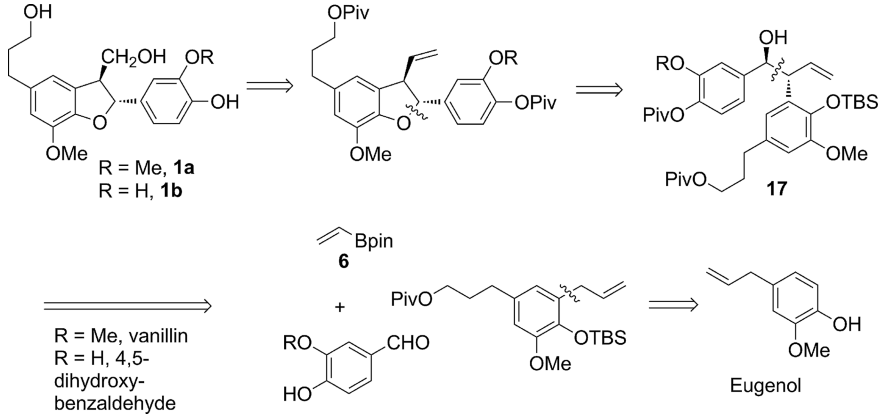
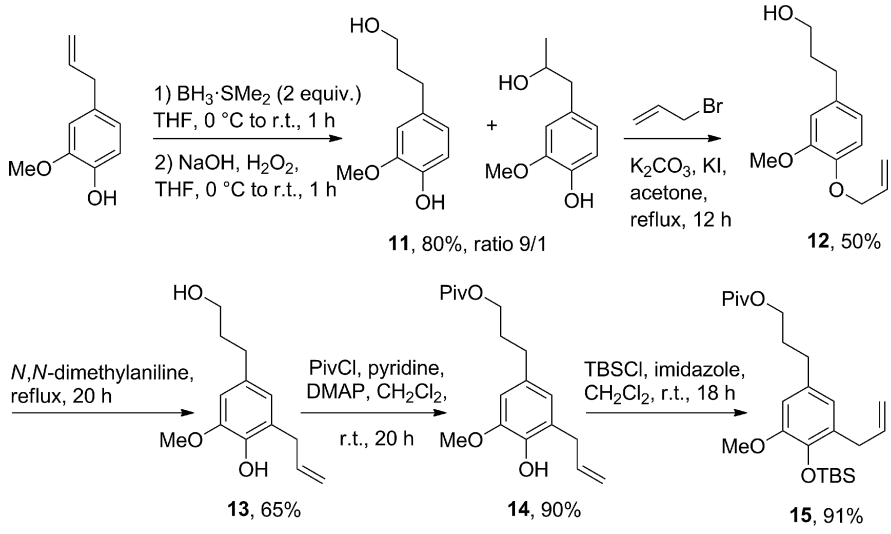
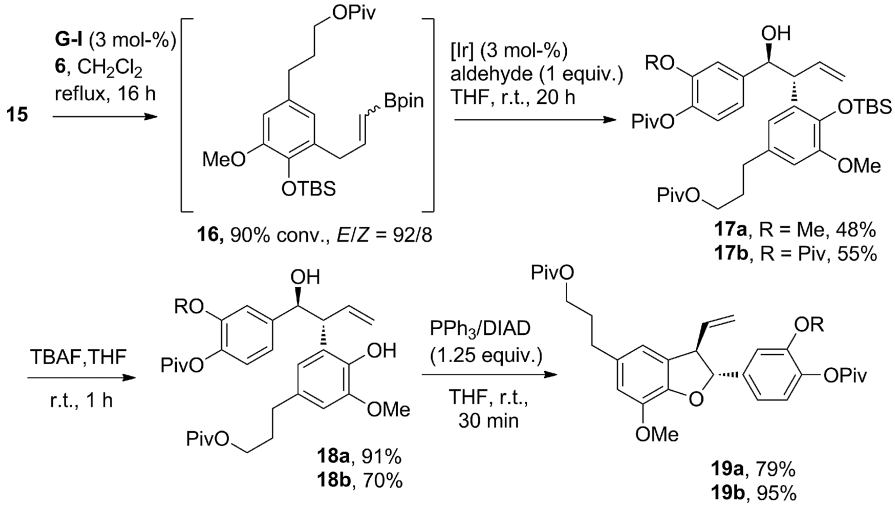


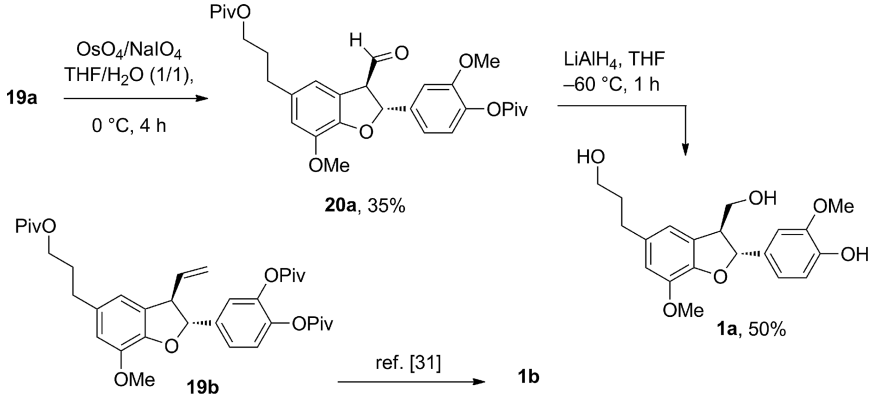
Figure 5. Retrosynthetic pathway for the synthesis of **1a** and **1b**.



Scheme 3. Preparation of **15** from eugenol.

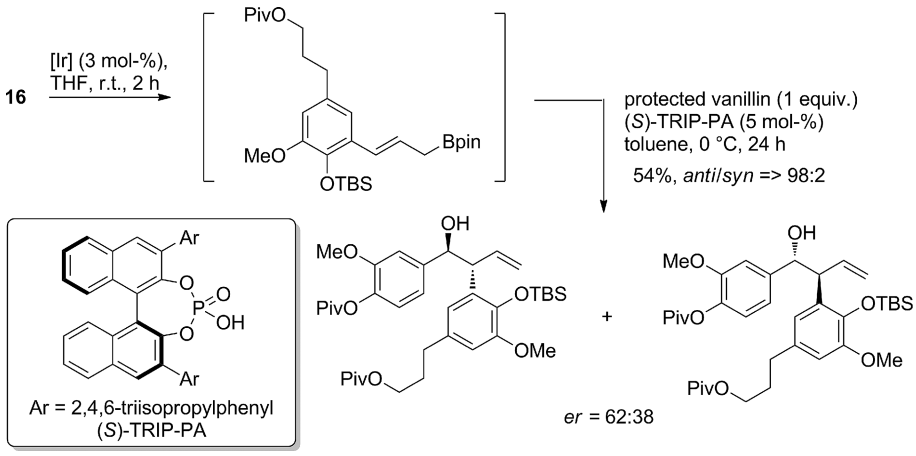


Scheme 4. Cross-metathesis/isomerization/allylboration sequence for the preparation of advanced intermediates of neolignans.



Scheme 5. Synthesis of (±)-dihydrodehydrodiconiferyl alcohol **1a**.

in the second step (Scheme 6). In some cases this Brønsted acid has demonstrated its efficiency in catalyzing allylboration of aldehydes in highly enantioselective manner.[34,35] After completion of the isomerization reaction of **16**, the solvent was evaporated and the crude mixture reaction was engaged in the allylboration of vanillin. Although the high diastereoselectivity in favor of the *anti* diastereoisomer was maintained under these conditions, and despite a satisfac-



Scheme 6. Toward an enantioselective synthesis of dihydrodehydrodiconiferyl (**1a**).

tory yield, the homoallylic alcohol was obtained with a rather low enantioselectivity (24% *ee*) measured by analysis of the ^{1}H NMR spectra of the corresponding Mosher's esters. In light of our previous work describing an enantioselective version of this sequential process starting from 3-aryl-substituted allylboronates and aldehydes, we assumed that this drop of enantioselectivity can mainly be attributed to steric hindrance by the *ortho* substituent in the transient allylboronate produced by isomerization of **16**. It is likely that the level of asymmetric induction of the reaction could be improved by increasing catalyst loading.[36] In our case, due to the low enantioselectivity obtained with use of 5 mol-% of catalyst, it appears likely that the amount of TRIP-PA required in order to achieve a high asymmetric induction would be significant, which is incompatible with the development of a low-catalyst-loading process.

Conclusions

We report a diastereoselective synthesis of *trans*-2,3-disubstituted dihydrobenzofurans, based on sequential cross-metathesis/isomerization/allylboration reactions, followed by an intramolecular Mitsunobu process as final step. This new strategy, complementary with those described previously, offers the advantage of providing access to five-membered ring systems with an aryl group in the C2 position, a scaffold widely observed throughout nature. In order to validate the approach for the synthesis of highly functionalized compounds, the natural neolignan **1a**, which had attracted our attention because of its biological activities, was prepared from eugenol, vanillin, and pinacol vinylboronate **6** in highly diastereoselective manner. Similarly, a formal synthesis of its *O*-demethylated derivative **1b** is also described. Unfortunately, our attempt to develop an enantioselective version in the presence of a chiral phosphoric acid catalyst was unsuccessful, likely due to the particular structure of the allylboronate generated in this strategy. Studies directed towards overcoming this impediment are underway in our laboratory.

Experimental Section

General: All air- and moisture-sensitive reactions were carried out in oven-dried glassware under argon. Anhydrous tetrahydrofuran (THF) and toluene were obtained after distillation over sodium/benzophenone under slightly positive argon pressure. Dichloromethane was distilled from P_2O_5. Cyclohexane and ethyl acetate (EtOAc) were distilled before utilization for column chromatography. Other chemicals were used as received. All the NMR spectra were recorded with a Bruker Advance I 300, a Bruker Advance I 400, or a Bruker Advance I 500 apparatus. Spectra were acquired at various field strengths as indicated (300 MHz, 400 MHz, or 500 MHz for ^{1}H NMR spectra, 75, 100, or 125 MHz for ^{13}C NMR spectra, 96 MHz for ^{11}B NMR spectra, 118 MHz or 376 MHz for ^{19}F NMR spectra). All products were analyzed in deuterated solvent solutions. ^{1}H and ^{13}C NMR chemicals shifts are referenced to Me_4Si as external reference, ^{19}F NMR chemical shifts to external $CFCl_3$ (δ =0.0 ppm), and ^{11}B NMR chemical shifts to external $BF_3{\cdot}OEt_2$ (δ =0.0 ppm). High-resolution mass spectra were recorded with a Bruker Micro-Tof-Q II or a Waters Q-Tof 2 instrument at the CRMPO (Centre régional de Mesures Physiques de l'Ouest, Rennes, France) with use of positive ion Electro-Spray Ionization (ESI). Purifications by column chromatography were all carried out on silica gel (Acros silica 0.060–0.200 mm, 60 Å). Thin-layer chromatography analyses were performed on Merck Silica Gel 60 F_{254} plates. Melting points were measured with a Kofler apparatus (Reichert–Jung heizbank). All catalysts used in this manuscript were purchased.

General Synthetic Procedure for Compounds 8: Compound **6** (0.5 mmol) and **G-I** catalyst (3 mol-%) were added successively to a solution of the appropriate compound **5** (0.25 mmol) in dry CH_2Cl_2 (0.2 M) under argon. The resulting mixture was heated at reflux for 18 h. After this time, the solution was filtered through a short pad of silica gel, and CH_2Cl_2 was removed under reduced pressure to afford the product **7**, which was used without further purification. A flask was charged with $[Ir(cod)(PPh_2Me_2)_2]PF_6$ (3 mol-%) and flushed with argon. Anhydrous THF (0.15 M) was added. Dihydrogen was gently bubbled into the solution through a needle for around 2 min to give a light yellow solution. The excess dihydrogen was then replaced with argon. A solution of the crude mixture **7** (0.25 mmol, 1.00 equiv.) in dry THF was added to the thus-obtained catalyst solution, immediately followed by aldehyde (0.25 mmol, 1.00 equiv.). The mixture was allowed to stir at room temperature for 20 h. THF was then removed under reduced pres-

sure, and the residue was purified by column chromatography with a suitable eluent to afford the desired homoallylic alcohol **8**.

2-(1-Hydroxy-1-phenylbut-3-en-2-yl)phenol (8ad): This compound was prepared from **5d** and benzaldehyde and purified by column chromatography with cyclohexane/EtOAc (98:2, 95:5) as the eluent to afford **8ad** as a colorless oil (38 mg, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.21 (m, 6 H), 7.08–7.03 (m, 1 H), 6.93–6.88 (m, 1 H), 6.72 (dd, J = 8.0, 1.0 Hz, 1 H), 6.24 (ddd, J = 17.2, 10.2, 8.9 Hz, 1 H), 5.25–5.15 (m, 2 H), 4.95 (d, J = 7.2 Hz, 1 H), 4.19–4.14 (dd, J = 8.9, 7.2 Hz, 1 H), 2.45 (br. s, 1 H), 1.04 (s, 9 H), 0.23 (s, 3 H), 0.19 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 142.0, 137.8, 131.1, 129.3, 127.7, 127.3, 127.2, 126.7, 120.9, 118.2, 118.1, 76.2, 51.1, 26.0, 18.4, –4.06, –4.08 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{22}H_{30}O_2Si$ [M + Na]$^+$ 377.1912; found 377.1910.

2-[1-Hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]phenol (8bd): This compound was prepared from **5d** and 4-nitrobenzaldehyde and purified by column chromatography with cyclohexane/EtOAc (95:5, 90:10) as the eluent to afford **8bd** as a pale yellow powder (60 mg, 60%), m.p. 90–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.8 Hz, 2 H), 7.31 (d, J = 8.8 Hz, 2 H), 7.17 (dd, J = 7.6, 1.7 Hz, 1 H), 7.11–7.06 (m, 1 H), 6.95–6.89 (m, 1 H), 6.71 (dd, J = 8.1, 1.0 Hz, 1 H), 6.02 (ddd, J = 17.1, 10.0, 9.2 Hz, 1 H), 5.30–5.19 (m, 2 H), 4.98 (dd, J = 7.3, 1.9 Hz, 1 H), 4.11–4.06 (dd, J = 9.2, 7.3 Hz, 1 H), 2.71 (d, J = 1.9 Hz, 1 H), 1.00 (s, 9 H), 0.21 (s, 3 H), 0.16 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 149.4, 147.0, 136.8, 129.9, 129.1, 127.4, 122.8, 121.2, 119.2, 118.7, 75.5, 51.4, 25.6, 18.3, –4.1, –4.2 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{22}H_{29}NO_4Si$ [M + Na]$^+$ 422.1763; found 422.1760.

2-[1-(4-Bromophenyl)-1-hydroxybut-3-en-2-yl]phenol (8cd): This compound was prepared from **5d** and 4-bromobenzaldehyde and purified by column chromatography with cyclohexane/EtOAc (95:5) as the eluent to afford **8cd** as a colorless oil (45 mg, 41%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.4 Hz, 2 H), 7.17 (dd, J = 7.6, 1.7 Hz, 1 H), 7.10–7.04 (m, 3 H), 6.92–6.88 (m, 1 H), 6.72 (dd, J = 8.1, 0.9 Hz, 1 H), 6.19 (ddd, J = 17.1, 10.0, 9.2 Hz, 1 H), 5.27–5.17 (m, 2 H), 4.87 (d, J = 7.5 Hz, 1 H), 4.12–4.06 (dd, J = 9.2, 7.5 Hz, 1 H), 2.11 (br. s, 1 H), 1.02 (s, 9 H), 0.22 (s, 3 H), 0.19 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 140.9, 137.4, 130.8, 130.6, 129.2, 128.4, 127.5, 121.0, 121.0, 118.6, 118.5, 75.7, 51.1, 25.9, 18.3, –4.1 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{22}H_{29}BrO_2Si$ [M + Na]$^+$ 455.1018; found 455.1021.

2-(4-Hydroxyhexa-1,5-dien-3-yl)phenol (8dd): This compound was prepared from **5d** and acrolein and purified by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **8dd** as a colorless oil (38 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24 (dd, J = 7.5, 1.4 Hz, 1 H), 7.15–7.10 (m, 1 H), 6.98–6.93 (m, 1 H), 6.84 (dd, J = 8.0, 1.2 Hz, 1 H), 6.18 (ddd, J = 17.2, 9.9, 7.6 Hz, 1 H), 5.80 (ddd, J = 17.1, 10.2, 7.6 Hz, 1 H), 5.26–5.06 (m, 4 H), 4.36 (dd, J = 7.6, 7.6 Hz, 1 H), 3.94 (dd, J = 7.6, 7.6 Hz, 1 H), 2.06 (br. s, 1 H), 1.05 (s, 9 H), 0.30 (s, 3 H), 0.26 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0, 138.6, 137.5, 131.3, 129.2, 127.3, 121.1, 118.6, 117.9, 115.6, 74.8, 49.2, 25.9, 18.3, –3.9, –4.1 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{18}H_{28}O_2Si$ [M + Na]$^+$ 327.1756; found 327.1755.

2-(*E*)-(4-Hydroxy-6-phenylhexa-1,5-dien-3-yl)phenol (8ed): This compound was prepared from **5d** and *trans*-cinnamaldehyde and purified by column chromatography with cyclohexane/EtOAc (95:5) as the eluent to afford an inseparable mixture of **8ed** and the aldehyde (starting material). The yield (42%) was determined by use of an internal standard. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61–7.58 (m, 1 H), 7.48–7.45 (m, 2 H), 7.29–7.20 (m, 3 H), 7.15–7.09 (m, 1 H), 6.99–6.94 (m, 1 H), 6.83 (dd, J = 8.1, 1.1 Hz, 1 H), 6.52 (dd, J = 15.9, 1.1 Hz, 1 H), 6.25 (ddd, J = 17.1, 10.2, 8.9 Hz, 1 H), 6.14 (dd, J = 15.9, 6.2 Hz, 1 H), 5.29–5.21 (m, 2 H), 4.55–4.50 (m, 1 H), 4.07–4.02 (m, 1 H), 2.22 (br. s, 1 H), 1.02 (s, 9 H), 0.25 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0, 137.5, 137.1, 131.2, 130.8, 130.1, 129.1, 128.4, 127.4, 127.3, 126.5, 121.2, 118.7, 118.2, 74.8, 49.5, 25.9, 18.3, –3.98, –4.18 ppm.

2-(4-Hydroxynon-1-en-3-yl)phenol (8fd): This compound was prepared from **5d** and hexanal and purified by column chromatography with cyclohexane/EtOAc (95:5) as the eluent to afford **8ed** as a colorless oil (38 mg, 43%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (dd, J = 7.6, 1.7 Hz, 1 H), 7.14–7.08 (m, 1 H), 6.97–6.92 (m, 1 H), 6.84 (dd, J = 8.1, 1.1 Hz, 1 H), 6.23–6.09 (m, 1 H), 5.24–5.13 (m, 2 H), 3.85–3.78 (m, 2 H), 1.41–1.25 (m, 8 H), 1.05 (s, 9 H), 0.86 (t, J = 6.7 Hz, 3 H), 0.29 (s, 3 H), 0.26 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.0, 138.1, 132.3, 128.7, 127.1, 121.2, 118.6, 117.7, 73.5, 49.4, 34.4, 31.9, 25.9, 25.6, 22.6, 18.3, 14.0, –3.9, –4.1 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{21}H_{36}O_2Si$ [M + Na]$^+$ 371.2382; found 371.2384.

Ethyl 2-Hydroxy-3-(2-hydroxyphenyl)pent-4-enoate (8gd): This compound was prepared from **5d** and ethyl glyoxalate solution (50% in toluene) and purified by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **8gd** as a colorless oil (45 mg, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (dd, J = 7.6, 1.7 Hz, 1 H), 7.17–7.11 (m, 1 H), 6.99–6.94 (m, 1 H), 6.83 (dd, J = 8.1, 1.0 Hz, 1 H), 6.21 (ddd, J = 17.1, 10.0, 9.0 Hz, 1 H), 5.22–5.11 (m, 2 H), 4.48 (d, J = 3.1 Hz, 1 H), 4.32 (dd, J = 9.0, 3.1 Hz, 1 H), 4.22 (q, J = 7.1 Hz, 2 H), 2.85 (br. s, 1 H), 1.28 (t, J = 7.1 Hz, 3 H), 1.07 (s, 9 H), 0.32 (s, 3 H), 0.28 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 152.6, 134.9, 130.8, 129.7, 127.6, 121.1, 118.2, 118.1, 73.0, 61.7, 46.0, 25.8, 18.3, 14.2, –3.9, –4.3 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{19}H_{30}O_4Si$ [M + Na]$^+$ 373.1811; found 373.1809. $C_{19}H_{30}O_4Si$: calcd. C65.10, H 8.63, O 18.26; found C 65.12, H 8.61, O 18.27.

4-*tert*-Butyl-2-[1-hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]phenol (8ab): This compound was prepared from **5b** and 4-nitrobenzaldehyde and purified by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **8ab** as a colorless oil (58 mg, 51%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.8 Hz, 2 H), 7.28 (d, J = 8.8 Hz, 2 H), 7.10–7.06 (m, 2 H), 6.65 (d, J = 8.5 Hz, 1 H), 6.23 (ddd, J = 17.0, 10.1, 9.2 Hz, 1 H), 5.31–5.22 (m, 2 H), 5.01 (d, J = 7.3 Hz, 1 H), 4.10–4.04 (dd, J = 9.2, 7.3 Hz, 1 H), 2.76 (br. s, 1 H), 1.26 (s, 9 H), 1.02 (s, 9 H), 0.22 (s, 3 H), 0.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.5, 149.4, 147.0, 143.7, 136.9, 128.7, 127.4, 126.1, 124.5, 122.8, 119.1, 117.9, 75.7, 52.0, 34.1, 31.4, 25.9, 18.3, –4.1, –4.2 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{26}H_{37}NO_4Si$ [M + Na]$^+$ 478.2389; found 478.2388.

2-[1-Hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]-6-methoxyphenol (8aa): This compound was prepared from **5a** and 4-nitrobenzaldehyde and purified by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford an inseparable mixture of **8aa** and the aldehyde (starting material). The yield (61%) was determined by use of an internal standard. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.8 Hz, 2 H), 7.31 (d, J = 8.8 Hz, 2 H), 6.93–6.72 (m, 3 H), 6.16 (ddd, J = 17.1, 10.1, 8.8 Hz, 1 H), 5.29–5.18 (m, 2 H), 4.92 (d, J = 7.0 Hz, 1 H), 4.24 (dd, J = 8.8, 7.0 Hz, 1 H), 3.73 (s, 3 H), 2.68 (br. s, 1 H), 0.98 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0, 149.2, 147.0, 142.5, 136.6, 130.6, 127.5, 122.7, 121.0, 120.3, 119.1, 110.1, 75.8, 54.7, 50.1, 26.2, 18.9, –3.6, –3.7 ppm.

2-{5-[4-(Benzyloxy)phenyl]-4-hydroxypent-1-en-3-yl}-6-methoxyphenol (8ba): This compound was prepared from **5a** and 2-[4-(benzyloxy)phenyl]acetaldehyde and purified by column chromatography

with cyclohexane/EtOAc (90:10) as the eluent to afford **8ba** as a colorless oil (69 mg, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.33 (m, 5 H), 7.09 (d, J = 8.5 Hz, 2 H), 6.93–6.87 (m, 4 H), 6.76 (dd, J = 7.5, 1.9 Hz, 1 H), 6.22 (ddd, J = 17.2, 10.2, 8.7 Hz, 1 H), 5.27–5.18 (m, 2 H), 5.05 (s, 2 H), 4.08–4.03 (m, 1 H), 3.94 (ddd, J = 9.6, 6.7, 3.1 Hz, 1 H), 3.81 (s, 3 H), 2.71–2.53 (m, 2 H), 1.72 (br. s, 1 H), 1.05 (s, 9 H), 0.24 (s, 3 H), 0.19 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.3, 150.0, 142.5, 137.9, 137.2, 132.8, 131.6, 130.2, 128.5, 127.9, 127.4, 121.0, 120.2, 117.6, 114.8, 109.5, 75.1, 70.0, 54.6, 48.1, 40.2, 26.3, 19.0, –3.5, –3.7 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{31}H_{40}O_4Si$ [M + Na]$^+$ 527.2594; found 527.2596.

2-{5-[4-(Benzyloxy)phenyl]-4-hydroxypent-1-en-3-yl}-5-methoxyphenol (8ac): This compound was prepared from **5c** and 2-[4-(benzyloxy)phenyl]acetaldehyde and purified by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **8ac** as a colorless oil (83 mg, 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.34 (m, 5 H), 7.18 (d, J = 8.5 Hz, 1 H), 7.12 (d, J = 8.6 Hz, 2 H), 6.92 (d, J = 8.6 Hz, 2 H), 6.57 (dd, J = 8.5, 2.5 Hz, 1 H), 6.46 (d, J = 2.5 Hz, 1 H), 6.22 (ddd, J = 17.1, 10.1, 8.5 Hz, 1 H), 5.25 (ddd, J = 10.1, 1.6, 0.8 Hz, 1 H), 5.19 (ddd, J = 17.1, 1.6, 0.8 Hz, 1 H), 5.07 (s, 2 H), 4.01–3.96 (m, 1 H), 3.83 (dd, J = 8.5, 7.1 Hz, 1 H), 3.81 (s, 3 H), 2.73–2.56 (m, 2 H), 1.89 (d, J = 2.7 Hz, 1 H), 1.07 (s, 9 H), 0.32 (s, 3 H), 0.28 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.8, 157.4, 153.9, 138.2, 131.6, 130.3, 129.2, 128.6, 127.9, 127.5, 124.6, 117.4, 114.8, 106.1, 105.2, 74.9, 70.0, 55.2, 48.4, 40.3, 26.0, 18.4, –3.8, –4.1 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{31}H_{40}O_4Si$ [M + Na]$^+$ 527.2594; found 527.2594.

General Synthetic Procedure for Compounds 9: A solution of TBAF (1 M, 0.12 mmol, 1.20 equiv.) was added dropwise to a solution of the appropriate protected homoallylic alcohol **8** (0.10 mmol, 1.00 equiv.) in anhydrous THF (0.05 M). The resulting mixture was stirred at room temperature for 30 min, and the reaction was then quenched with water. The mixture was then extracted with Et_2O, and the combined organic phases were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography with a suitable eluent.

2-(1-Hydroxy-1-phenylbut-3-en-2-yl)phenol (9ad): Purification by column chromatography with cyclohexane/EtOAc (80:20) as the eluent afforded **9ad** as a colorless oil (21 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (br. s, 1 H), 7.33–7.25 (m, 5 H), 7.19–7.13 (m, 1 H), 6.95–6.80 (m, 3 H), 6.22 (ddd, J = 17.1, 10.3, 7.8 Hz, 1 H), 5.21–5.18 (m, 2 H), 5.04 (ddd, J = 17.1, 1.5, 1.2 Hz, 1 H), 3.86 (dd, J = 7.8, 3.6 Hz, 1 H), 2.68 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.5, 141.5, 133.9, 130.6, 128.4, 128.1, 127.9, 127.4, 126.4, 120.5, 118.6, 117.5, 78.0, 54.7 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{16}H_{16}O_2$ [M + Na]$^+$ 263.1048; found 263.1049.

2-[1-Hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]phenol (9bd): Purification by column chromatography with cyclohexane/EtOAc (80:20, 70:30) as the eluent afforded **9bd** as a colorless oil (26 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.8 Hz, 2 H), 7.40 (d, J = 8.8 Hz, 2 H), 7.15–7.10 (m, 1 H), 6.96–6.94 (m, 1 H), 6.86–6.79 (m, 2 H), 6.46 (br. s, 1 H), 6.23 (ddd, J = 17.1, 10.2, 8.4 Hz, 1 H), 5.25–5.22 (m, 2 H), 5.12 (dd, J = 17.1, 1.0 Hz, 1 H), 3.86 (dd, J = 8.4, 5.1 Hz, 1 H), 3.03 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.7, 149.2, 147.3, 134.3, 130.1, 128.5, 127.3, 126.5, 123.1, 120.9, 119.4, 116.8, 76.3, 54.3 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{16}H_{15}NO_4$ [M + Na]$^+$ 308.0898; found 308.0898.

2-[1-(4-Bromophenyl)-1-hydroxybut-3-en-2-yl]phenol (9cd): Purification by column chromatography with cyclohexane/EtOAc (90:10, 80:20) as the eluent afforded **9cd** as a colorless oil (31 mg, 97%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.39 (m, 2 H), 7.17–7.09 (m, 3 H), 6.93–6.80 (m, 3 H), 6.18 (ddd, J = 17.1, 10.2, 8.2 Hz, 1 H), 5.12 (ddd, J = 10.2, 1.4, 0.9 Hz, 1 H), 5.11–5.04 (m, 2 H), 3.82 (dd, J = 8.2, 4.3 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1, 140.5, 134.1, 131.1, 130.4, 128.4, 128.2, 127.0, 121.6, 120.7, 118.9, 117.2, 77.2, 54.4 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{16}H_{15}BrO_2$ [M + Na]$^+$ 341.0153; found 341.0152.

2-(4-Hydroxyhexa-1,5-dien-3-yl)phenol (9dd): Purification by column chromatography with cyclohexane/EtOAc (90:10, 80:20) as the eluent afforded **9dd** as a colorless oil (15 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (br. s, 1 H), 7.20–7.14 (m, 1 H), 7.07 (dd, J = 7.6, 1.6 Hz, 1 H), 6.94–6.86 (m, 2 H), 6.20 (ddd, J = 17.2, 10.4, 7.7 Hz, 1 H), 5.90 (ddd, J = 17.3, 10.5, 6.6 Hz, 1 H), 5.31 (ddd, J = 17.3, 1.4, 1.3 Hz, 1 H), 5.25 (ddd, J = 10.5, 1.4, 1.3 Hz, 1 H), 5.23 (ddd, J = 10.4, 1.4, 1.4 ,Hz, 1 H), 5.16 (ddd, J = 17.2, 1.4, 1.4 Hz, 1 H), 4.59 (dd, J = 6.6, 3.3 Hz, 1 H), 3.74 (dd, J = 7.7, 3.3 Hz, 1 H), 2.68 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6, 137.8, 134.5, 130.4, 128.4, 127.1, 120.4, 118.3, 117.6, 117.2, 77.0, 52.0 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{12}H_{14}O_2$ [M + Na]$^+$ 213.0891; found 213.0889.

2-(*E*)-(4-Hydroxy-6-phenylhexa-1,5-dien-3-yl)phenol (9ed): Purification by column chromatography with cyclohexane/EtOAc (90:10, 80:20) as the eluent afforded **9ed** as a colorless oil (26 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87 (br. s, 1 H), 7.35–7.28 (m, 5 H), 7.22–7.16 (m, 1 H), 7.09 (dd, J = 7.6, 1.5 Hz, 1 H), 6.95 (dd, J = 8.0, 1.1 Hz, 1 H), 6.93–6.87 (m, 1 H), 6.63 (dd, J = 15.9, 0.6 Hz, 1 H), 6.32–6.18 (m, 2 H), 5.27 (ddd, J = 10.2, 1.4, 1.1 Hz, 1 H), 5.21 (ddd, J = 17.2, 1.4, 1.1 Hz, 1 H), 4.75 (m, 1 H), 3.85 (dd, J = 7.9, 3.1 Hz, 1 H), 2.71 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7, 136.2, 134.7, 132.7, 130.3, 128.6, 128.4, 128.1, 127.7, 126.7, 120.5, 118.4, 117.7, 77.2, 52.1 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{18}H_{18}O_2$ [M + Na]$^+$ 289.1204; found 289.1204.

2-(4-Hydroxynon-1-en-3-yl)phenol (9fd): Purification by column chromatography with cyclohexane/EtOAc (80:20) as the eluent afforded **9fd** as a colorless oil (15 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (br. s, 1 H), 7.19–7.17 (m, 1 H), 7.06 (dd, J = 7.6, 1.6 Hz, 1 H), 6.91 (dd, J = 8.2, 1.2 Hz, 1 H), 6.89–6.84 (m, 1 H), 6.26 (ddd, J = 17.1, 10.3, 8.0 Hz, 1 H), 5.25 (ddd, J = 10.3, 1.6, 1.0 Hz, 1 H), 5.16 (ddd, J = 17.1, 1.6, 1.6 Hz, 1 H), 4.11–4.05 (m, 1 H), 3.58 (dd, J = 8.0, 2.6 Hz, 1 H), 1.83 (br. s, 1 H), 1.59–1.23 (m, 8 H), 0.90 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6, 134.7, 130.4, 128.3, 128.0, 120.3, 118.3, 117.6, 75.8, 53.0, 34.9, 31.6, 25.6, 22.6, 14.0 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{15}H_{22}O_2$ [M + Na]$^+$ 257.1517; found 257.1518.

Ethyl 2-Hydroxy-3-(2-hydroxyphenyl)pent-4-enoate (9gd): Purification by column chromatography with cyclohexane/EtOAc (80:20) as the eluent afforded **9gd** as a colorless oil (15 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (br. s, 1 H), 7.23–7.17 (m, 1 H), 7.15 (dd, J = 7.6, 1.6 Hz, 1 H), 6.94 (dd, J = 8.0, 1.1 Hz, 1 H), 6.86–6.81 (m, 1 H), 6.22 (ddd, J = 17.1, 10.2, 7.8 Hz, 1 H), 5.23 (ddd, J = 10.2, 1.3, 1.1 Hz, 1 H), 5.15 (ddd, J = 17.1, 1.3, 1.3 Hz, 1 H), 4.60 (d, J = 2.3 Hz, 1 H), 4.32 (q, J = 7.1 Hz, 2 H), 3.95 (m, 2 H), 1.35 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.1, 154.8, 132.8, 130.7, 129.0, 126.1, 120.5, 118.9, 118.0, 74.7, 62.6, 51.8, 14.2 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{13}H_{16}O_4$ [M + Na]$^+$ 259.0946; found 259.0943.

4-*tert*-Butyl-2-[1-hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]phenol (9ab): Purification by column chromatography with cyclohexane/EtOAc (90:10, 80:20) as the eluent afforded **9ab** as a colorless oil

(33 mg, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.8 Hz, 2 H), 7.38 (d, J = 8.8 Hz, 2 H), 7.13 (dd, J = 8.4, 2.3 Hz, 1 H), 6.85 (d, J = 2.3 Hz, 1 H), 6.74 (d, J = 8.4 Hz, 1 H), 6.41 (br. s, 1 H), 6.28 (ddd, J = 17.1, 10.2, 8.4 Hz, 1 H), 5.27–5.23 (m, 2 H), 5.14 (dd, J = 17.1, 1.0 Hz, 1 H), 3.84 (dd, J = 8.4, 5.2 Hz, 1 H), 3.12 (br. s, 1 H), 1.21 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.3, 149.2, 147.2, 143.7, 134.5, 127.3, 127.2, 125.5, 125.2, 123.0, 119.3, 116.3, 76.3, 54.8, 34.0, 31.4 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{20}H_{23}NO_4$ [M + Na]$^+$ 364.1524; found 364.1526.

2-[1-Hydroxy-1-(4-nitrophenyl)but-3-en-2-yl]-6-methoxyphenol (9aa): Purification by column chromatography with cyclohexane/EtOAc (85:15, 80:20, 75:25) as the eluent afforded **9aa** as a colorless oil (28 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.7 Hz, 2 H), 7.42 (d, J = 8.7 Hz, 2 H), 6.77–6.73 (m, 2 H), 6.63 (dd, J = 6.0, 3.2 Hz, 1 H), 6.32 (ddd, J = 17.2, 9.7, 9.7 Hz, 1 H), 5.84 (br. s, 1 H), 5.28–5.17 (m, 3 H), 3.92–3.89 (m, 1 H), 3.88 (s, 3 H), 2.29 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.7, 147.1, 146.6, 142.9, 135.6, 127.4, 125.7, 123.0, 121.3, 119.9, 119.3, 109.3, 74.8, 56.0, 53.8 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{17}H_{17}NO_5$ [M + Na]$^+$ 338.1004; found 338.1003.

2-{5-[4-(Benzyloxy)phenyl]-4-hydroxypent-1-en-3-yl}-6-methoxyphenol (9ba): Purification by column chromatography with cyclohexane/EtOAc (85:15, 80:20) as the eluent afforded **9ba** as a colorless oil (30 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.34 (m, 5 H), 7.15–7.12 (m, 2 H), 6.93–6.78 (m, 5 H), 6.31 (ddd, J = 17.2, 10.2, 8.6 Hz, 1 H), 6.15 (br. s, 1 H), 5.27–5.21 (m, 2 H), 5.06 (s, 2 H), 4.21 (ddd, J = 9.2, 6.5, 3.5 Hz, 1 H), 3.91 (s, 3 H), 3.75 (dd, J = 8.6, 6.5 Hz, 1 H), 2.78–2.56 (m, 2 H), 2.03 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.4, 146.9, 143.2, 137.2, 137.1, 131.3, 130.3, 128.6, 127.9, 127.6, 127.5, 121.4, 119.8, 117.7, 114.8, 109.1, 74.4, 70.0, 56.0, 51.0, 40.2 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{25}H_{26}O_4$ [M + Na]$^+$ 413.1729; found 413.1729.

2-{5-[4-(Benzyloxy)phenyl]-4-hydroxypent-1-en-3-yl}-5-methoxyphenol (9ac): Purification by column chromatography with cyclohexane/EtOAc (70:30) as the eluent afforded **9ac** as a colorless oil (27 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.47 (br. s, 1 H), 7.46–7.34 (m, 5 H), 7.12 (d, J = 8.6 Hz, 2 H), 6.96–6.93 (m, 3 H), 6.50 (d, J = 2.6 Hz, 1 H), 6.44 (dd, J = 8.4, 2.6 Hz, 1 H), 6.33 (ddd, J = 17.1, 10.2, 7.9 Hz, 1 H), 5.29 (ddd, J = 10.2, 1.4, 1.0 Hz, 1 H), 5.20 (ddd, J = 17.1, 1.4, 1.2 Hz, 1 H), 5.07 (s, 2 H), 4.25–4.22 (m, 1 H), 3.78 (s, 3 H), 3.61 (d, J = 7.9 Hz, 1 H), 2.90–2.61 (m, 2 H), 2.57 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0, 157.8, 155.9, 136.9, 134.8, 131.0, 130.4, 129.7, 128.6, 128.0, 127.5, 120.2, 118.0, 115.3, 106.2, 103.3, 76.8, 70.1, 55.3, 51.8, 40.2 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{25}H_{26}O_4$ [M + Na]$^+$ 413.1729; found 413.1729.

General Synthetic Procedure for Compounds 10: PPh_3 (0.125 mmol, 1.25 equiv.) and DIAD (0.125 mmol, 1.25 equiv.) were successively added to a solution of the appropriate homoallylic alcohol **9** (0.10 mmol, 1.00 equiv.) in anhydrous THF (0.03 M). The resulting mixture was stirred at room temperature for 30 min and then concentrated in vacuo. The crude product was purified by column chromatography with a suitable eluent.

2-Phenyl-3-vinyl-2,3-dihydrobenzofuran (10ad): Purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent afforded **10ad** as a colorless oil (19 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.35 (m, 5 H), 7.26–7.21 (m, 1 H), 7.14–7.12 (m, 1 H), 6.98–6.91 (m, 2 H), 6.00 (ddd, J = 16.9, 10.0, 8.6 Hz, 1 H), 5.42 (d, J = 8.6 Hz, 1 H), 5.27–5.18 (m, 2 H), 4.07 (dd, J = 8.6, 8.6 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 140.5, 137.1, 129.2, 128.8, 128.6, 128.1, 125.9, 124.8, 120.9, 117.9, 109.6, 89.8, 56.3 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{16}H_{14}O$ [M + Na]$^+$ 245.0942; found 245.0943.

2-(4-Nitrophenyl)-3-vinyl-2,3-dihydrobenzofuran (10bd): Purification by column chromatography with cyclohexane/EtOAc (95:5) as the eluent afforded **10bd** as a pale yellow powder (19 mg, 70%), m.p. 56–58 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (d, J = 8.8 Hz, 2 H), 7.62 (d, J = 8.8 Hz, 2 H), 7.26–7.21 (m, 1 H), 7.14–7.11 (m, 1 H), 7.00–6.94 (m, 2 H), 6.02 (ddd, J = 17.0, 10.0, 8.7 Hz, 1 H), 5.50 (d, J = 8.7 Hz, 1 H), 5.32 (dd, J = 10.0, 0.6 Hz, 1 H), 5.23 (dd, J = 17.0, 0.6 Hz, 1 H), 3.96 (dd, J = 8.7, 8.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 147.9, 147.7, 136.5, 129.1, 128.5, 126.3, 124.9, 123.9, 121.5, 118.8, 109.8, 88.3, 56.7 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{16}H_{13}NO_3$ [M + Na]$^+$ 290.0793; found 290.0791.

2-(4-Bromophenyl)-3-vinyl-2,3-dihydrobenzofuran (10cd): Purification by column chromatography with cyclohexane/EtOAc (95:5) as the eluent afforded **10cd** as a colorless oil (26 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (d, J = 8.5 Hz, 2 H), 7.33 (d, J = 8.5 Hz, 2 H), 7.26–7.21 (m, 1 H), 7.13–7.11 (m, 1 H), 6.98–6.91 (m, 2 H), 5.98 (ddd, J = 17.0, 10.0, 8.7 Hz, 1 H), 5.37 (d, J = 8.7 Hz, 1 H), 5.27 (dd, J = 10.0, 0.7 Hz, 1 H), 5.20 (ddd, J = 17.0, 1.2, 0.7 Hz, 1 H), 3.97 (dd, J = 8.7, 8.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 139.6, 136.8, 131.7, 129.0, 128.9, 127.5, 124.8, 122.0, 121.1, 118.3, 109.7, 89.0, 56.4 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{16}H_{13}BrO$ [M + Na]$^+$ 323.0047; found 323.0048.

2-Pentyl-3-vinyl-2,3-dihydrobenzofuran (10fd): Purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent afforded **10fd** as a colorless oil (19 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.13 (m, 1 H), 7.09–7.07 (m, 1 H), 6.90–6.84 (m, 1 H), 6.81–6.78 (m, 1 H), 5.86 (ddd, J = 17.0, 10.0, 8.5 Hz, 1 H), 5.27–5.17 (m, 2 H), 4.47–4.40 (m, 1 H), 3.72 (dd, J = 8.5, 8.5 Hz, 1 H), 1.89–1.71 (m, 2 H), 1.38–1.28 (m, 6 H), 0.92 (t, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 138.0, 129.7, 128.5, 124.8, 120.3, 117.0, 109.4, 88.9, 53.3, 34.7, 31.8, 25.3, 22.6, 14.0 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{15}H_{20}O$ [M + Na]$^+$ 239.1412; found 239.1413.

Ethyl 3-Vinyl-2,3-dihydrobenzofuran-2-carboxylate (10gd): Purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent afforded **10gd** as a colorless oil (18 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23–7.18 (m, 1 H), 7.14–7.11 (m, 1 H), 6.97–6.92 (m, 2 H), 5.96 (ddd, J = 17.0, 10.0, 7.5 Hz, 1 H), 5.33–5.24 (m, 2 H), 4.89 (d, J = 7.5 Hz, 1 H), 4.32 (q, J = 7.1 Hz, 2 H), 4.23 (dd, J = 7.5, 7.5 Hz, 1 H), 1.34 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 158.8, 137.0, 129.0, 127.4, 124.8, 121.4, 117.7, 110.1, 84.5, 61.6, 51.3, 14.2 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{13}H_{14}O_3$ [M + Na]$^+$ 241.0840; found 241.0838.

5-*tert*-Butyl-2-(4-nitrophenyl)-3-vinyl-2,3-dihydrobenzofuran (10ab): Purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent afforded **10ab** as a white powder (26 mg, 80%), m.p. 90–92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (d, J = 8.8 Hz, 2 H), 7.62 (d, J = 8.9 Hz, 2 H), 7.30–7.27 (m, 1 H), 7.12 (d, J = 1.1 Hz, 1 H), 6.88 (d, J = 8.4 Hz, 1 H), 6.03 (ddd, J = 17.0, 10.0, 8.9 Hz, 1 H), 5.48 (d, J = 8.9 Hz, 1 H), 5.33 (dd, J = 10.0, 0.6 Hz, 1 H), 5.23 (dd, J = 17.0, 0.6 Hz, 1 H), 3.94 (dd, J = 8.9, 8.9 Hz, 1 H), 1.33 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.7, 148.1, 147.7, 144.7, 136.6, 128.1, 126.4, 125.9, 123.8, 121.7, 118.9, 109.0, 88.4, 57.0, 34.5, 31.7 ppm. HRMS (ESI$^+$): *m*/*z* calcd. for $C_{20}H_{21}NO_3$ [M + Na]$^+$ 346.1419; found 346.1418.

7-Methoxy-2-(4-nitrophenyl)-3-vinyl-2,3-dihydrobenzofuran (10aa): Purification by column chromatography with cyclohexane/EtOAc

(90:10) as the eluent afforded **10aa** as a white powder (25 mg, 84%), m.p. 80–82 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.8 Hz, 2 H), 7.64 (d, J = 8.8 Hz, 2 H), 6.98–6.93 (m, 1 H), 6.89–6.86 (m, 1 H), 6.75 (dd, J = 7.2, 1.0 Hz, 1 H), 6.00 (ddd, J = 17.0, 10.0, 8.9 Hz, 1 H), 5.54 (d, J = 8.9 Hz, 1 H), 5.30 (dd, J = 10.0, 0.7 Hz, 1 H), 5.22 (dd, J = 17.0, 0.7 Hz, 1 H), 4.00 (dd, J = 8.9, 8.9 Hz, 1 H), 3.96 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 147.6, 147.1, 144.6, 136.3, 129.6, 126.5, 123.8, 122.2, 118.9, 116.8, 112.1, 89.0, 57.1, 56.1 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{17}H_{15}NO_4$ [M + Na]$^+$ 320.0898; found 320.0898.

2-[4-(Benzyloxy)benzyl]-7-methoxy-3-vinyl-2,3-dihydrobenzofuran (10ba): Purification by column chromatography with cyclohexane/EtOAc (95:5) as the eluent afforded **10ba** as a white powder (28 mg, 75%), m.p. = 62–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.32 (m, 5 H), 7.23 (d, J = 8.2 Hz, 2 H), 6.94 (d, J = 8.2 Hz, 2 H), 6.87–6.82 (m, 1 H), 6.80–6.77 (m, 1 H), 6.71–6.69 (m, 1 H), 5.73 (ddd, J = 17.0, 10.2, 8.3 Hz, 1 H), 5.10–5.06 (m, 3 H), 5.03 (d, J = 10.2 Hz, 1 H), 4.77–4.70 (m, 1 H), 3.91 (s, 3 H), 3.84 (dd, J = 8.3, 8.3 Hz, 1 H), 3.25–3.03 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 147.5, 144.5, 137.5, 137.1, 130.7, 130.6, 129.2, 128.6, 127.9, 127.5, 121.0, 117.1, 117.0, 114.9, 111.7, 89.8, 70.0, 56.1, 52.2, 39.3 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{25}H_{24}O_3$ [M + Na]$^+$ 395.1623; found 395.1624. $C_{25}H_{24}O_3$: calcd. C80.62, H 6.50, O 12.89; found C 80.60, H 6.51, O 12.92.

2-[4-(Benzyloxy)benzyl]-6-methoxy-3-vinyl-2,3-dihydrobenzofuran (10ac): Purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent afforded **10ac** as a colorless oil (24 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.33 (m, 5 H), 7.23 (d, J = 8.5 Hz, 2 H), 6.98–6.95 (m, 3 H), 6.46–6.42 (m, 2 H), 5.78 (ddd, J = 17.0, 10.3, 8.3 Hz, 1 H), 5.14–5.08 (m, 4 H), 4.66 (ddd, J = 8.3, 7.3, 5.2 Hz, 1 H), 3.79 (s, 3 H), 3.73 (dd, J = 8.3, 8.3 Hz, 1 H), 3.10 (dd, J = 14.3, 7.3 Hz, 1 H), 3.01 (dd, J = 14.3, 5.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.8, 160.5, 157.6, 137.9, 137.2, 130.5, 129.7, 128.6, 127.9, 127.5, 125.0, 121.4, 116.8, 114.9, 106.1, 96.3, 90.1, 70.0, 55.5, 51.7, 39.6 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{25}H_{24}O_3$ [M + Na]$^+$ 395.1623; found 395.1623.

3-(4-(*tert*-Butyldimethylsilyloxy)-3-{1-hydroxy-1-[3-methoxy-4-(pivaloyloxy)phenyl]but-3-en-2-yl}-5-methoxyphenyl)propyl Pivalate (17a): The procedure was the same as described for the synthesis of compounds **8**, with use of **15** (0.50 mmol) and 4-formyl-2-methoxyphenyl pivalate (0.50 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **17a** as a white powder (0.15 g, 48%), m.p. = 127–129 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.89–6.83 (m, 3 H), 6.61 (d, J = 1.8 Hz, 1 H), 6.53 (d, J = 1.8 Hz, 1 H), 6.17 (ddd, J = 17.2, 10.2, 8.2 Hz, 1 H), 5.19 (d, J = 10.2 Hz, 1 H), 5.08 (d, J = 17.2 Hz, 1 H), 4.92 (d, J = 6.0 Hz, 1 H), 4.28 (dd, J = 8.2, 6.0 Hz, 1 H), 4.07 (t, J = 6.4 Hz, 2 H), 3.76 (s, 3 H), 3.72 (s, 3 H), 2.60 (t, J = 7.6 Hz, 2 H), 1.94–1.88 (m, 2 H), 1.37 (s, 9 H), 1.25 (s, 9 H), 1.02 (s, 9 H), 0.20 (s, 3 H), 0.15 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 176.6, 150.6, 149.7, 140.7, 140.6, 139.2, 137.1, 133.6, 131.4, 121.8, 120.7, 119.0, 118.0, 110.9, 109.9, 76.1, 63.5, 55.8, 54.7, 49.5, 39.0, 38.8, 31.9, 30.4, 27.3, 27.2, 26.3, 19.0, –3.5, –3.7 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{37}H_{56}O_8Si$ [M + Na]$^+$ 679.3642; found 679.3640. $C_{37}H_{56}O_8Si$: calcd. C67.65, H 8.59, O 19.48; found C 67.66, H 8.57, O 19.47.

4-(2-{2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-5-[3-(pivaloyloxy)-propyl]phenyl}-1-hydroxybut-3-enyl)-1,2-phenylene Bis(2,2-dimethylpropanoate) (17b): The procedure was the same as described for the synthesis of compounds **8**, with use of **15** (0.50 mmol) and 4-formyl-1,2-phenylene bis(2,2-dimethylpropanoate) (0.50 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (95:5, 90:10) as the eluent to afford **17b** as a colorless oil (0.20 g, 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.09–6.99 (m, 3 H), 6.63 (d, J = 1.8 Hz, 1 H), 6.54 (d, J = 1.8 Hz, 1 H), 6.13 (ddd, J = 17.1, 10.2, 8.5 Hz, 1 H), 5.18 (d, J = 10.2, 0.8 Hz, 1 H), 5.06 (dd, J = 17.1, 0.8 Hz, 1 H), 4.92 (d, J = 5.6 Hz, 1 H), 4.26 (dd, J = 8.5, 5.6 Hz, 1 H), 4.07 (t, J = 6.5 Hz, 2 H), 3.75 (s, 3 H), 2.60 (t, J = 7.6 Hz, 2 H), 2.49 (br. s, 1 H), 1.96–1.89 (m, 2 H), 1.34 (s, 9 H), 1.33 (s, 9 H), 1.24 (s, 9 H), 1.01 (s, 9 H), 0.19 (s, 3 H), 0.16 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 175.7, 175.5, 149.8, 141.9, 141.5, 140.7, 140.6, 136.4, 133.6, 131.3, 124.3, 122.4, 121.4, 120.6, 118.3, 110.1, 75.5, 63.6, 54.7, 49.5, 39.1, 39.0, 38.8, 31.9, 30.4, 27.3, 27.2, 26.3, 19.0, –3.5, –3.6 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{41}H_{62}O_9Si$ [M + Na]$^+$ 749.4061; found 749.4063.

4-(1-Hydroxy-2-{2-hydroxy-3-methoxy-5-[3-(pivaloyloxy)propyl]phenyl}but-3-enyl)-2-methoxyphenyl Pivalate (18a): The procedure was the same as described for the synthesis of compounds **9**, with use of **17a** (0.20 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (70:30) as the eluent to afford **18a** as a colorless oil (99 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.90–6.80 (m, 3 H), 6.53 (d, J = 1.6 Hz, 1 H), 6.46 (d, J = 1.6 Hz, 1 H), 6.31 (ddd, J = 17.0, 10.1, 8.6 Hz, 1 H), 5.83 (br. s, 1 H), 5.23–5.15 (m, 2 H), 5.05 (d, J = 6.5 Hz, 1 H), 4.03 (t, J = 6.5 Hz, 2 H), 3.91 (dd, J = 8.6, 6.5 Hz, 1 H), 3.86 (s, 3 H), 3.73 (s, 3 H), 2.55 (t, J = 7.6 Hz, 2 H), 1.91–1.82 (m, 2 H), 1.35 (s, 9 H), 1.24 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.5, 176.6, 150.6, 146.5, 141.2, 140.9, 139.2, 136.4, 132.5, 126.5, 121.8, 121.4, 118.9, 118.3, 110.8, 109.3, 75.7, 63.4, 56.0, 55.8, 53.4, 39.0, 38.8, 31.8, 30.5, 27.3, 27.2 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{31}H_{42}O_8$ [M + Na]$^+$ 565.2777; found 565.2781.

4-(1-Hydroxy-2-{2-hydroxy-3-methoxy-5-[3-(pivaloyloxy)propyl-phenyl]but-3-enyl})-1,2-phenylene Bis(2,2-dimethylpropanoate) (18b): The procedure was the same as described for the synthesis of compounds **9**, with use of **17b** (0.20 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (70:30) as the eluent to afford **18b** as a colorless oil (85 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08–7.04 (m, 2 H), 6.98–6.95 (m, 1 H), 6.55 (d, J = 1.8 Hz, 1 H), 6.48 (d, J = 1.8 Hz, 1 H), 6.30 (ddd, J = 17.1, 10.2, 9.0 Hz, 1 H), 5.89 (br. s, 1 H), 5.22 (d, J = 10.2, 1.5 Hz, 1 H), 5.16 (d, J = 17.1, 1.5 Hz, 1 H), 5.06 (d, J = 6.5 Hz, 1 H), 4.04 (t, J = 6.5 Hz, 2 H), 3.89 (dd, J = 9.0, 6.5 Hz, 1 H), 3.86 (s, 3 H), 2.67 (br. s, 1 H), 2.60 (t, J = 7.6 Hz, 2 H), 1.92–1.83 (m, 2 H), 1.34 (s, 9 H), 1.33 (s, 9 H), 1.24 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 175.8, 175.7, 146.6, 142.0, 141.5, 141.3, 140.9, 135.8, 132.6, 126.3, 124.3, 122.4, 121.4, 118.6, 109.5, 75.1, 63.5, 56.0, 53.3, 39.1, 39.0, 38.8, 31.8, 30.5, 27.3, 27.2 ppm. HRMS (ESI$^+$): m/z calcd. for $C_{35}H_{48}O_9$ [M + Na]$^+$ 635.3196; found 635.3188.

3-{7-Methoxy-2-[3-methoxy-4-(pivaloyloxy)phenyl]-3-vinyl-2,3-dihydrobenzofuran-5-yl}propyl Pivalate (19a): The procedure was the same as described for the synthesis of compounds **10**, with use of **18a** (0.10 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (80:20) as the eluent to afford **19a** as a pale yellow powder (41 mg, 79%), m.p. 84–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.06 (m, 1 H), 7.02–6.97 (m, 2 H), 6.66 (br. s, 1 H), 6.55 (br. s, 1 H), 5.94 (ddd, J = 17.0, 10.2, 9.2 Hz, 1 H), 5.39 (d, J = 9.2 Hz, 1 H), 5.24 (dd, J = 10.2, 1.4 Hz, 1 H), 5.19 (dd, J = 17.0, 1.4 Hz, 1 H), 4.09 (t, J = 6.5 Hz, 2 H), 4.02 (dd, J = 9.2, 9.2 Hz, 1 H), 3.92 (s, 3 H), 3.82 (s, 3 H), 2.66 (t, J = 7.6 Hz, 2 H), 2.01–1.91 (m, 2 H), 1.38 (s, 9 H), 1.24 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 176.7, 151.3, 145.8, 144.1, 140.0, 138.6, 136.8, 135.0, 130.4, 122.6, 118.4, 118.3, 116.5, 112.4,

110.1, 90.4, 63.5, 56.8, 56.1, 56.0, 39.1, 38.8, 32.0, 30.6, 27.3, 27.2 ppm. HRMS (ESI$^+$): *m/z* calcd. for $C_{31}H_{40}O_7$ [M + Na]$^+$ 547.2672; found 547.2673. $C_{31}H_{40}O_7$: calcd. C70.97, H 7.69, O 21.35; found C 70.89, H 7.71, O 21.39.

4-{7-Methoxy-5-[3-(pivaloyloxy)propyl]-3-vinyl-2,3-dihydrobenzofuran-2-yl}-1,2-phenylene Bis(2,2-dimethylpropanoate) (19b): The procedure was the same as described for the synthesis of compounds **10**, with use of **18b** (0.10 mmol), followed by purification by column chromatography with cyclohexane/EtOAc (90:10) as the eluent to afford **19b** as a colorless oil (57 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.26 (m, 2 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 6.65 (br. s, 1 H), 6.54 (br. s, 1 H), 5.93 (ddd, *J* = 16.9, 9.9, 9.0 Hz, 1 H), 5.40 (d, *J* = 9.0 Hz, 1 H), 5.28–5.18 (m, 2 H), 4.09 (t, *J* = 6.4 Hz, 2 H), 4.01 (dd, *J* = 9.0, 9.0 Hz, 1 H), 3.92 (s, 3 H), 2.68–2.63 (m, 2 H), 2.00–1.90 (m, 2 H), 1.35 (s, 18 H), 1.27 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 175.8, 175.6, 145.7, 144.1, 142.6, 142.3, 138.6, 136.5, 135.2, 130.3, 123.8, 123.3, 121.0, 118.6, 116.5, 112.4, 89.6, 63.5, 56.7, 56.2, 39.2, 39.1, 38.8, 32.0, 30.7, 27.3, 27.2 ppm. HRMS (ESI$^+$): *m/z* calcd. for $C_{35}H_{46}O_8$ [M + Na]$^+$ 617.3090; found 617.3090.

3-{3-Formyl-7-methoxy-2-[3-methoxy-4-(pivaloyloxy)phenyl]-2,3-dihydrobenzofuran-5-yl}propyl Pivalate (20a): A *tert*-butanol solution of OsO_4 (2.5%, 87.60 μL, 10.00 μmol, 0.20 equiv.) and $NaIO_4$ (85 mg, 0.20 mmol, 4.0 equiv.) were added to a solution of **19a** (52 mg, 0.10 mmol, 1.00 equiv.) in a THF/H_2O mixture (1:1, 0.025 M) with exclusion of light. The resulting mixture was stirred for 4 h at 0 °C. Water was then added, and the mixture was extracted with dichloromethane. Organic phases were washed with brine, dried with $MgSO_4$, and concentrated under vacuum. The crude product was purified by column chromatography with cyclohexane/EtOAc (70:30) as the eluent to afford **20a** as a colorless oil (18 mg, 30%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.88 (s, 1 H), 7.01–6.92 (m, 3 H), 6.75 (br. s, 1 H), 6.73 (br. s, 1 H), 6.15 (d, *J* = 6.8 Hz, 1 H), 4.25 (d, *J* = 6.8 Hz, 1 H), 4.11 (t, *J* = 6.4 Hz, 2 H), 3.93 (s, 3 H), 3.81 (s, 3 H), 2.68 (t, *J* = 7.6 Hz, 2 H), 2.00–1.95 (m, 2 H), 1.38 (s, 9 H), 1.24 (s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.5, 178.6, 176.6, 151.1, 146.4, 144.6, 140.2, 138.6, 135.7, 123.0, 122.8, 117.8, 116.3, 113.5, 109.9, 83.2, 63.6, 63.4, 56.2, 56.0, 39.1, 38.8, 32.0, 30.6, 27.3, 27.2 ppm. HRMS (ESI$^+$): *m/z* calcd. for $C_{30}H_{38}O_8$ [M + Na]$^+$ 549.2464; found 549.2465.

4-[3-(Hydroxymethyl)-5-(3-hydroxypropyl)-7-methoxy-2,3-dihydrobenzofuran-2-yl]-2-methoxyphenol or Dihydrodehydrodiconiferyl Alcohol (1a): $LiAlH_4$ (72 mg, 1.90 mmol, 20.00 equiv.). was added at –60 °C to a solution of **20a** (50 mg, 95.30 μmol, 1.00 equiv.) in anhydrous THF (2 mL). The resulting mixture was stirred for 1 h. After this time, water was added at the same temperature until bubbling stopped. HCl (1 N) was added, and the resulting mixture was extracted with Et_2O. Organic phases were washed with brine, dried with $MgSO_4$, and concentrated under vacuum. Crude product was purified by column chromatography with EtOAc as the eluent to afford **1a** as a colorless oil (11 mg, 32%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.96 (d, *J* = 1.8 Hz, 1 H), 6.93 (dd, *J* = 8.2, 1.8 Hz, 1 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 6.71 (br. s, 1 H), 6.70 (br. s, 1 H), 5.64 (br. s, 1 H), 5.57 (d, *J* = 7.4 Hz, 1 H), 4.00 (dd, *J* = 10.9, 5.9 Hz, 1 H), 3.93 (dd, *J* = 10.9, 4.8 Hz, 1 H), 3.91 (s, 3 H), 3.89 (s, 3 H), 3.72 (t, *J* = 6.3 Hz, 2 H), 3.65–3.62 (m, 1 H), 2.72–2.69 (m, 2 H), 1.94–1.89 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.7, 146.6, 145.6, 144.2, 135.4, 133.1, 127.7, 119.4, 115.9, 114.3, 112.5, 108.8, 87.9, 63.9, 62.3, 56.1, 56.0, 53.8, 34.6, 32.0 ppm. HRMS (ESI$^+$): *m/z* calcd. for $C_{20}H_{24}O_6$ [M + Na]$^+$ 383.1471; found 383.1471. $C_{20}H_{24}O_6$: calcd. C66.65, H 6.71, O 26.63; found C 66.57, H 6.73, O 26.71. Physical and spectra data were found to be consistent with those reported.[30c]

Supporting Information (see footnote on the first page of this article): Description of experimental procedures unreported in the experimental section, analytical and spectroscopic data for **5**, **7**, **11**, **12**, **13**, **14**, **15**, and **16** and copies of ^{1}H and ^{13}C NMR spectra of all compounds.

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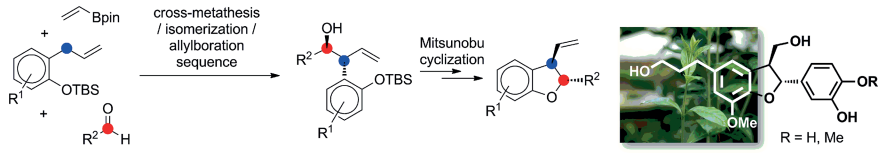

The development of a highly diastereoselective synthesis of *trans*-2,3-dihydrobenzofurans based on a cross-metathesis/isomerization/allylboration sequence is reported. This new approach was efficiently employed for the preparation of natural neolignans.

Keywords: Synthetic methods / Metathesis / Allylation / Natural products / Neolignans / Oxygen heterocycles

