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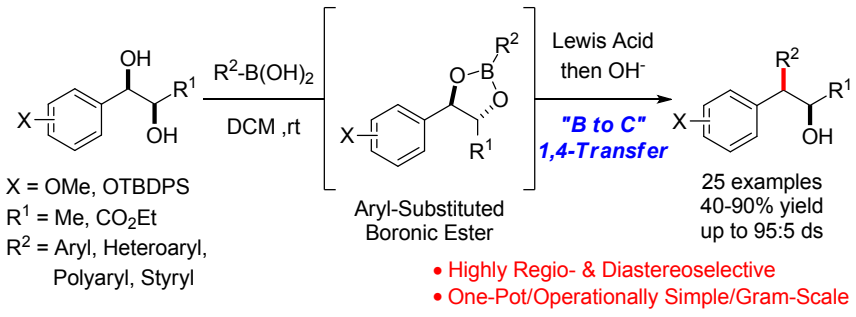
Lewis Acid-Promoted Regio- and Diastereoselective Cross-Coupling of Aryl-Substituted 1,2-Diols and Boronic Acids

Heesun Yu, Ryangha Lee, Hyoungsu Kim and Dongjoo Lee*

College of Pharmacy and Research Institute of Pharmaceutical Science and Technology (RIPST), Ajou University, 206 Worldcup-ro, Yeongtong-gu, Suwon 16499, Republic of Korea.

ABSTRACT

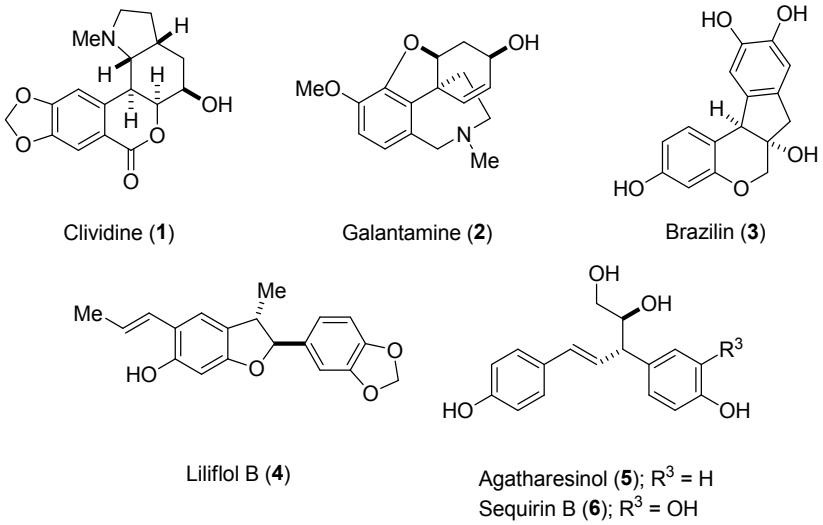
A Lewis acid-promoted highly regio- and diastereoselective C(sp^3)-C(sp^2) cross-coupling reaction between unprotected aryl-substituted 1,2-diols and styryl-, aryl-, heteroaryl-, and polyarylboronic acids has been developed in a one-pot procedure. The regioselective opening of aryl-substituted cyclic boronic esters promoted by a Lewis acid, followed by subsequent intramolecular 1,4-transfer of the carbon ligand from boron to a resonance-stabilized benzylic carbenium ion minimizing the allylic 1,3-strain in a stereoselective fashion led to the corresponding α-substituted *syn*-phenylethyl alcohols. The synthetic utility of the method was illustrated by a short and efficient enantioselective synthesis of cherylline diethyl ether (–)-**16**.



INTRODUCTION

The discovery of efficient and elegant methods to create stereogenic centers governed by acyclic stereocontrol elements is a continuing challenge to synthetic organic chemists.[1] The nucleophilic substitution reaction with chiral α-branched benzylic carbenium ions has emerged as a powerful tool for the highly diastereoselective construction of two contiguous stereogenic centers adjacent to an substituted benzene moiety.[2] The outcome of the highly diastereoselective substitution developed here can be predicted from conformational analysis on the basis of the allylic 1,3-strain concept (*vide infra*).[3]

Figure 1. Selected Natural Products Containing Phenylethyl Alcohol Moiety



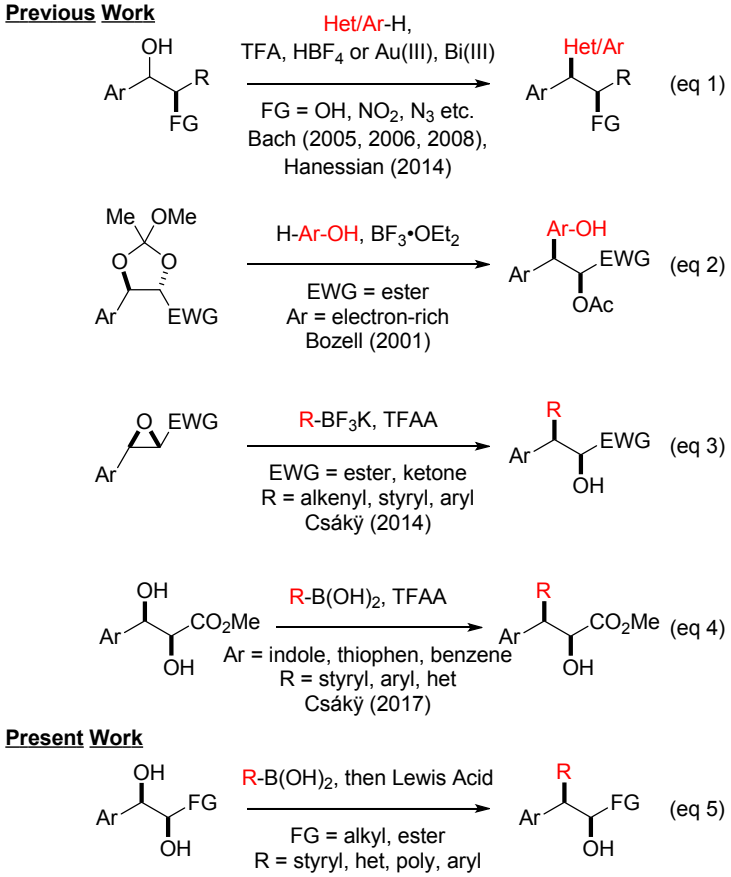
The phenylethyl alcohol moiety occurs in a myriad of biologically important natural products such as clividine (**1**), galantamine (**2**), brazilin (**3**), liliflol B (**4**), agatharesinol (**5**), sequirin B (**6**) and others (**Figure 1**). Consequently, highly diastereoselective carbon-carbon bond formation governed by the directing ability of an acyclic stereocontrol element (*i.e.*, substrate-controlled stereochemistry), especially at the benzylic carbon center, is an important strategy and a challenging current research topic.

Not surprisingly, extensive synthetic endeavors have been devoted to this approach. One of the

most notable methods involves the generation of resonance-stabilized benzylic carbenium ions derived from benzylic alcohols catalyzed by Brønsted or Lewis acids (eq 1, **Scheme 1**)[2,4,5,6] and aryl-substituted cyclic orthoesters in the presence of BF_3•OEt_2 (eq 2, **Scheme 1**),[7] followed by introduction of an arene nucleophile in an S_N1-type process. However, the scope reported for each method is notably limited to electron-rich arenes as nucleophiles, and their facial selectivity at the benzylic carbon center depends on the electron demand of the aromatic substituents. Nucleophilic opening of aryl-substituted epoxides by organometallics is the most common strategy. However, the requirement for strong nucleophiles such as organomagnesium,[8] organoaluminum,[9] and organocuprate[10] reagents restricts the scope of these reactions due to the functional group incompatibility. A recent approach to circumvent this limitation involved the use of a combination of potassium trifluoroborates[11] as mild nucleophiles and trifluoroacetic anhydride (TFAA) as the promoter (eq 3, **Scheme 1**). However, the substituents of the aryl-substituted epoxides were limited to electron-withdrawing groups such as carbonyls, presumably due to an increase in the stability of the epoxides through the inductive effect. While we were investigating Brønsted or Lewis acid-promoted regio- and diastereoselective cross-coupling reaction of aryl-substituted 1,2-diol and a diverse range of boronic acids and mechanism of the reaction, in late 2017 Csákÿ and co-workers[12] independently reported a cross-coupling reaction of aryl-substituted chiral 1,2-diol and boronic acids promoted by trifluoroacetic anhydride (TFAA) (eq 4, **Scheme 1**). However, the reported method suffers from low diastereoselectivity in some cases, which depends on aryl groups of substrates or boronic acid nucleophiles used. Despite substantial progress in this research field, there is still a need for general and mild methods for highly diastereoselective carbon-carbon bond formation at a benzylic carbon center. On the basis of the ready availability and stability of aryl-substituted 1,2-diols along with the advantages of using mild and functional group-tolerant organoboronic acids[13] as coupling partners, we sought to develop a diastereoselective

cross-coupling reaction at the benzylic carbon center employing these reagents (eq 5, **Scheme 1**).

Scheme 1. Diastereoselective Carbon-Carbon Bond Formation at the Benzylic Carbon Center

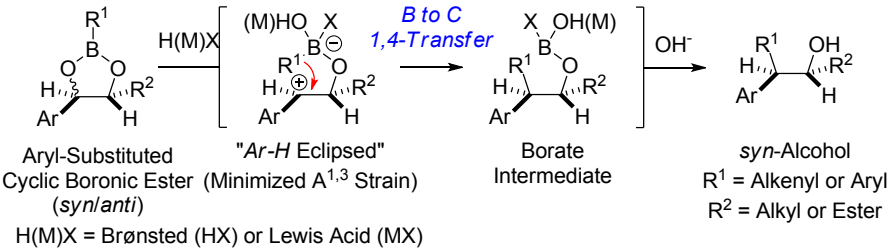


Boronic esters have played a pivotal role in rearrangement processes[14] wherein boron accepts an electron lone pair to form an anionic tetracoordinate organoborate complex. When a carbon electrophile is appropriately positioned, the resulting anionic organoborate complex undergoes an intramolecular ligand transfer from boron to carbon, leading to new carbon-carbon bond formation.

As depicted in **Scheme 2**, We postulated that a resonance-stabilized benzylic carbenium ion bearing a boronate ester substituent on the adjacent stereocenter, in which bond rotation is minimized due to the allylic 1,3-strain,[3] could be generated *via* cleavage of an aryl-substituted

cyclic boronic ester promoted by a Brønsted or Lewis acid. Then, subsequent stereoselective intramolecular 1,4-transfer of the carbon ligand from boron to the same face of the resonance-stabilized planar benzylic carbenium ion would lead to a highly stereocontrolled carbon-carbon bond formation at the benzylic carbon center.

Scheme 2. Concept: Bronsted or Lewis Acid Promoted Stereoselective Intramolecular 1,4-Ligand Transfer from Organoborate to the Resonance-Stabilized Benzylic Carbenium Ion

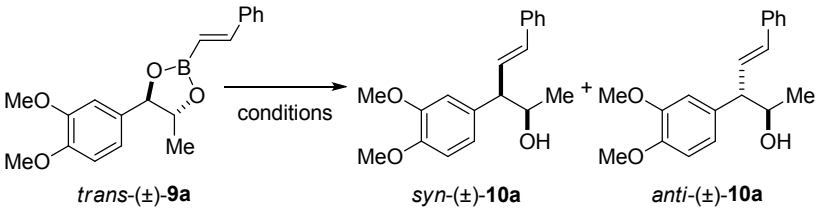


Herein is reported a highly regio- and diastereoselective boronic ester-mediated intramolecular ligand transfer strategy that involves the Lewis acid-promoted C(sp^3)-C(sp^2) cross-coupling reaction of unprotected aryl-substituted 1,2-diols with structurally diverse boronic acids at the benzylic carbon center.

RESULTS AND DISCUSSION

Optimization of the Reaction Conditions. To test the viability of the envisioned regio- and diastereoselective cross-coupling reaction at the outset of our studies, 3,4-dimethoxyphenyl substituted cyclic boronic ester *trans*-(±)-**9a** was employed as a model substrate, which was derived from known *syn*-1,2-diol (±)-**7a**[15] and commercially available (*E*)-styrylboronic acid **8a**. A variety of Brønsted acids as well as Lewis acids as promoters were examined in the model reaction in DCM (0.1 M) at room temperature, and the representative results are summarized in **Table 1**.

Table 1. Evaluation of Acid-Promoted Diastereoselective 1,4-Ligand Transfer of *trans*-(±)-**9a**[a]



trans-(±)-**9a** *syn*-(±)-**10a** *anti*-(±)-**10a**

entry	promoter	solvent	time [b] (h)	yield [c] (%)	*syn*/*anti*[d]
1[e]	AcOH	DCM	12	0	N.A.
2[f]	PTSA	DCM	12	0	N.A.[k]
3[g]	(+)-CSA	DCM	12	0	N.A.
4[h]	TFA	DCM	0.5	60	95:5
5[i]	TfOH	DCM	0.5	63	95:5
6[j]	$FeCl_3$	DCM	0.5	38	95:5
7	$BF_3{\cdot}OEt_2$	DCM	3.0	66	92:8
8	$Sc(OTf)_3$	DCM	4.5	78	95:5
9	$Bi(OTf)_3$	$MeNO_2$	0.5	80	95:5
10	$Yb(OTf)_3$	$MeNO_2$	6	80	95:5
11	$InCl_3$	DCM	1.5	82	95:5
12	$InBr_3$	DCM	1.5	82	95:5
13	$In(OTf)_3$	DCM	1.5	89	95:5
14	$In(OTf)_3$	MeCN	12	21	95:5
15	$In(OTf)_3$	THF	12	<5	95:5

[a]General conditions: *trans*-(±)-**9a** (0.3 mmol, 1.0 eq), promoter (0.36 mmol, 1.2 eq), solvent (3.0 mL, 0.1 M) at room temperature. [b]Time required for a complete conversion. [c)]Based on isolated product after purification by chromatography. [d]Diastereomeric ratio (*syn*/*anti*) of the crude product was determined by ^{1}H NMR spectroscopy. [e]AcOH (3.0 mmol, 10 eq). [f]PTSA (3.0 mmol, 10 eq). [g](+)-CSA (1.5 mmol, 5.0 eq). [h]TFA (1.5 mmol, 5.0 eq). [i]Reaction performed at -78 °C. [j]Reaction performed at 0 °C. [k]Not Available.

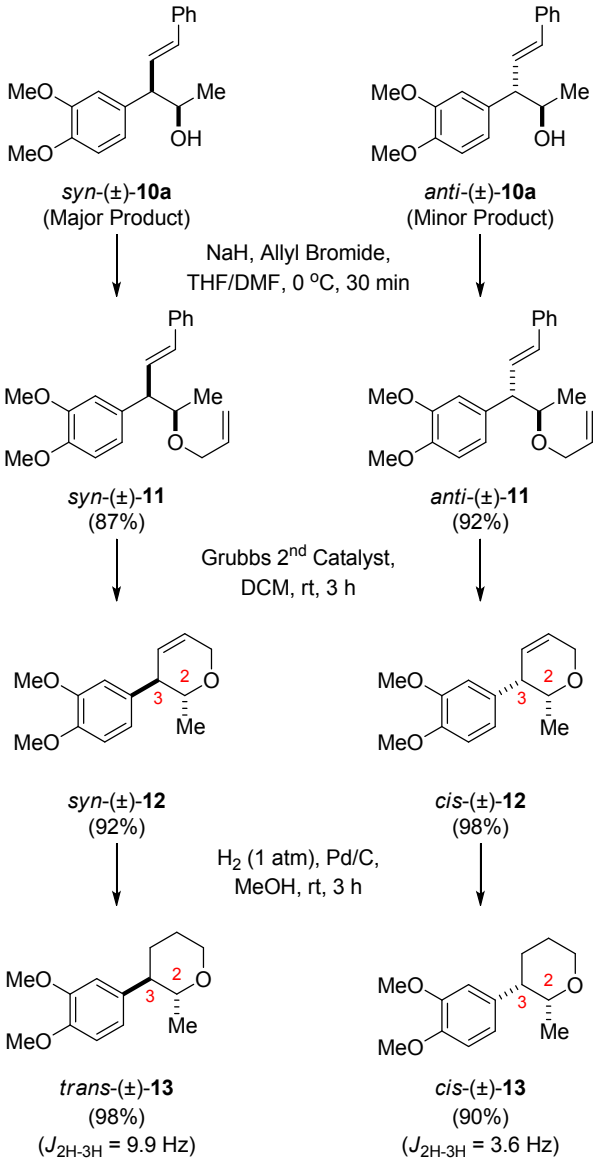
Initially, treatment of *trans*-(±)-**9a** with AcOH, PTSA or (+)-CSA failed to give the desired product, despite long exposure to such organic acids, and only unreacted starting *trans*-(±)-**9a** was recovered (entries 1-3, **Table 1**). Encouragingly, when a stronger Brønsted acid was employed such as TFA at room temperature or TfOH at −78 °C, *syn*-(±)-**10a** was formed as the

major product in good yield, exhibiting excellent diastereoselectivity (dr = 95:5) at the benzylic carbon center in a highly efficient manner (entries 4 and 5, **Table 1**). Also, a diverse range of Lewis acids were surveyed, and $FeCl_3$, BF_3•OEt_2, $Sc(OTf)_3$, $Bi(OTf)_3$, or $Yb(OTf)_3$ proved to be effective for the desired cross-coupling reaction (entries 6-10, **Table 1**). Among the Lewis acids tested, In(III) salts most efficiently induced the cleavage and subsequent intramolecular ligand transfer in *trans*-(±)-**9a**. The reactions with $InCl_3$, $InBr_3$ and $In(OTf)_3$ resulted in rapid, efficient (1.5 hours at room temperature), and extremely regio- and diastereoselective transformations that resulted in *syn*-(±)-**10a** in high yields (entries 11-13, respectively, **Table 1**). However, upon changing the solvent to THF or MeCN, the chemical yield of the cross-coupling reaction was substantially diminished, however, with no effect on the diastereoselectivity (entries 14 and 15, **Table 1**).

Confirmation of the Configuration at the Newly Generated Benzylic Stereocenter. As depicted in **Scheme 3**, the relative configuration of the newly generated benzylic stereocenter was unambiguously established by transformation[16] of the major and minor products *syn*- and *anti*-(±)-**10a** into respectively known cyclic derivatives reported by Kawahara and co-workers.[17] The coupling constants of hydrogen atoms between C(2) and C(3) were compared in the 2,3-substituted tetrahydropyrans *trans*- and *cis*-(±)-**13**, which were derived from the major and minor diastereomers *syn*- and *anti*-(±)-**10a** in a parallel route through *O*-allylation [*syn*- and *anti*-(±)-**11**], ring-closing metathesis of the resultant olefins [*trans*- and *cis*-(±)-**12**] utilizing Grubbs' second-generation catalyst (Grubbs II),[17] and Pd-mediated catalytic hydrogenation. The large coupling constant value ($J_{2H\text{-}3H}$ = 9.9 Hz) between C(2) and C(3) in *trans*-(±)-**13** indicates that the relative configuration of the major diastereomer must be *syn*, whereas the small constant value ($J_{2H\text{-}3H}$ = 3.6 Hz) between C(2) and C(3) in *cis*-(±)-**13** indicates that the relative configuration of the minor diastereomer must be *anti*. In addition, by comparison of the spectral data of *syn*-(±)-**10r** (**Scheme 6**) with those reported by

Bozell and co-workers,[7] we confirmed the relative configuration of the major and minor products *syn*- and *anti*-(±)-**10a**, demonstrating that this reaction occurs with overall retention of configuration at the benzylic stereocenter. The relative configurations of the other major products were assigned by analogy.

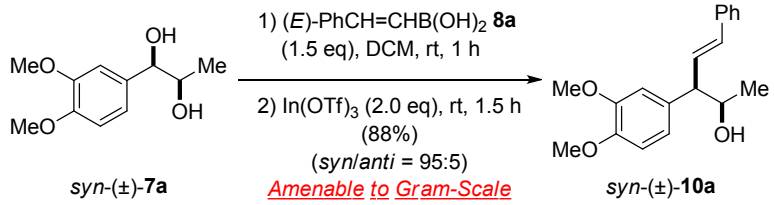
Scheme 3. Confirmation of the Relative Configuration of Major and Minor Diastereomers



One-Pot and Gram-Scale Approach. To increase the synthetic utility of this method, we next focused on a sequential one-pot process involving *in situ* formation of the transient aryl-substituted cyclic boronic ester *trans*-(±)-**9a**, followed by intramolecular transfer of the styryl

group promoted by $In(OTf)_3$ (**Scheme 4**). We were pleased to find that the sequential treatment of *syn*-(±)-**7a** with (*E*)-styrylboronic acid **8a** (1.5 eq) in DCM for 1 hour and $In(OTf)_3$ (2.0 eq) for 1.5 hour at room temperature led to the desired *syn*-(±)-**10a** in 88% overall yield while retaining excellent diastereoselectivity (dr = 95:5) at the benzylic stereocenter from *syn*-(±)-**7a** without purifying the cyclic boronic ester *trans*-(±)-**9a**. This process was also found to be amenable to gram-scale synthesis without notable erosion of yield and diastereoselectivity.

Scheme 4. One-Pot and Gram-Scale Approach for the Lewis Acid-Promoted Cross-Coupling Reaction of Aryl-Substituted 1,2-Diol *syn*-(±)-**7a** and Styrylboronic Acid **8a**

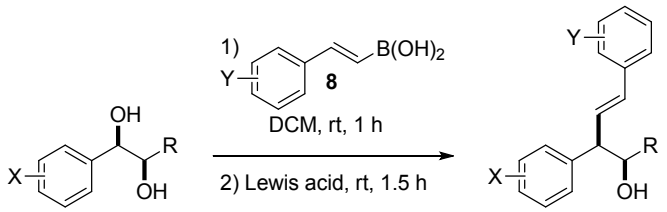


syn-(±)-**7a** *syn*-(±)-**10a**

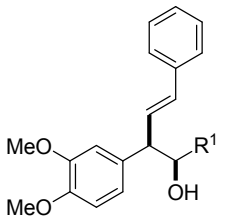
Scope and Limitations of Substrates. Having optimized reaction conditions in hand, the scope of this Lewis acid-promoted regio- and diastereoselective cross-coupling reaction was examined by investigating a diverse range of aryl-substituted 1,2-diols and (*E*)-styrylboronic acids as coupling partners. As shown in **Scheme 5**, the scope was limited to electron-rich aryl-substituted 1,2-diols, which provided the desired products in high yield with excellent diastereoselectivities (**Scheme 5**, *syn*-(±)-**10a-m**). Unfortunately, the application of phenyl-substituted 1,2-diol did not provide the desired product. These results are consistent with the postulated resonance-stabilized carbenium ion intermediate (*vide infra*). An ester group was highly compatible with the present reaction conditions, which enhance the synthetic utility of the current protocol (**Scheme 5**, *syn*-(±)-**10b**, *syn*-(±)-**10d**, *syn*-(±)-**10f**). We also explored a series of (*E*)-styrylboronic acids with *para*-substituents having various degrees of electron

demand. Notably, substituents with an electron-withdrawing effect led to the desired products with high yields (**Scheme 5**, *syn*-(±)-**10h-j**), whereas electron-donating substituents provided the products in moderate yields (**Scheme 5**, *syn*-(±)-**10k-m**).

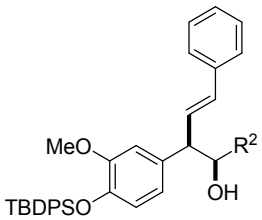
Scheme 5. Scope of Aryl-Substituted 1,2-Diols and (*E*)-Styrylboronic Acids[a, b, c]



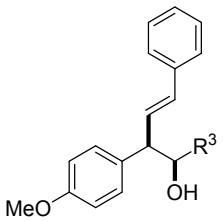
syn-(±)-**7** *syn*-(±)-**10**



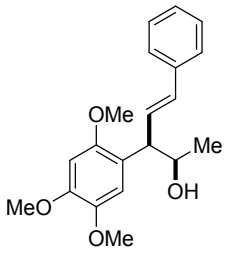
(±)-**10a**; R^1 = Me
(88%, dr = 95:5, $In(OTf)_3$)
(±)-**10b**; R^1 = CO_2Et
(67%, dr = 95:5, $In(OTf)_3$)



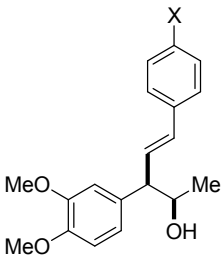
(±)-**10c**; R^2 = Me
(65%, dr = 95:5, $In(OTf)_3$)
(±)-**10d**; R^2 = CO_2Et
(78%, dr = 95:5, $InBr_3$)



(±)-**10e**; R^3 = Me
(66%, dr = 95:5, $InBr_3$)
(±)-**10f**; R^3 = CO_2Et
(60%, dr = 95:5, $InBr_3$)



(±)-**10g**
(88%, dr = 95:5, $In(OTf)_3$)



(±)-**10h**; X = CF_3
(86%, dr = 95:5, $InBr_3$)
(±)-**10i**; X = F
(79%, dr = 95:5, $InBr_3$)
(±)-**10j**; X = Cl
(82%, dr = 95:5, $InBr_3$)
(±)-**10k**; X = Ph
(69%, dr = 95:5, $InBr_3$)
(±)-**10l**; X = Me
(50%, dr = 95:5, $InBr_3$)
(±)-**10m**; X = OMe
(40%, dr = 95:5, BF_3•OEt_2)

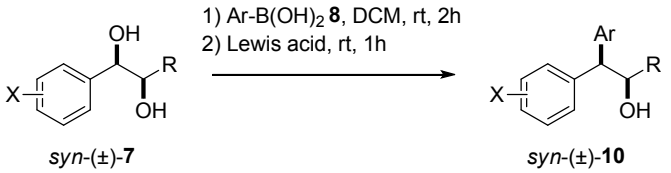
[a]General conditions: *syn*-(±)-**7a-g** (0.3 mmol, 1.0 eq), boronic acid **8a-g** (1.5 eq), DCM (3.0 mL, 0.1 M) at room temperature, 1 h, then promoter (in parentheses) (2.0 eq), at room temperature, 1.5 h. [b]Based on isolated product after purification by chromatography. [c]Diastereomeric ratio (*syn*/*anti*) of the crude product was determined by ^{1}H NMR spectroscopy.

Subsequently, we further investigated the substrate scope with respect to a variety of aromatic,

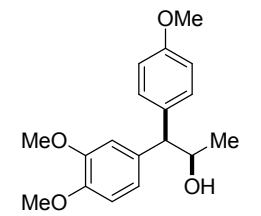
heteroaromatic, and polyaromatic boronic acid nucleophiles as coupling partners. As depicted in **Scheme 6**, the scope was limited to electron-rich aromatic and heteroaromatic boronic acids, which yielded the desired products in moderate to high yield with excellent diastereoselectivities (**Scheme 6**, *syn*-(±)-**10n-v**). In contrast to (*E*)-styrylboronic acids with an electron-withdrawing substituents, however, the reaction did not perform well with phenyl boronic acid or electron-poor aromatic boronic acids. There are still more research which needs to be done to understand the electronic effect of substituents of styryl and aryl ligands upon the 1,4-ligand transfer process from boron to benzylic carbenium ion. However, based on the results we observed, we postulated that styryl and aryl ligand on boronic ester would undergo an intramolecular nucleophilic addition to the benzylic carbenium ion, leading to the resulting electron-deficient benzylic carbenium and arenium ion, respectively. Subsequent elimination of the borate group would then reveal 1,4-ligand transfer from boron to benzylic carbon center. Compared with the stability of the benzylic carbenium ion, that of the high energy-transition state and dearomatized arenium ion is more susceptible to the electronic effect of substituents. Therefore, the ability of the electron-donating substituents to stabilize an electron-deficient arenium ion should promote the desired 1,4-ligand transfer process. Unlike (*E*)-styrylboronic acids, aromatic and heteroaromatic nucleophiles required BF_3•OEt_2 or $InBr_3$ as a promoter for the best results rather than $In(OTf)_3$. Notably, both high yields and excellent diastereoselectivity were also observed with polyaromatic boronic acids, including 1-naphthyl (**Scheme 6**, *syn*-(±)-**10w**), 9-phenanthrenyl (**Scheme 6**, *syn*-(±)-**10x**), 1-pyrenyl (**Scheme 6**, *syn*-(±)-**10y**) groups. However, the more sterically hindered 8-anthracenyl boronic acid was not compatible with the reaction conditions thus far developed.

Scheme 6. Scope of Aryl-Substituted 1,2-Diols and Aromatic, Heteroaromatic and

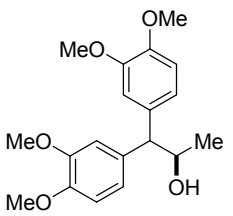
Polyaromatic Boronic Acids[a, b, c]



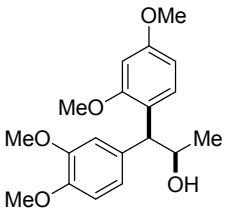
syn-(±)-**7** *syn*-(±)-**10**



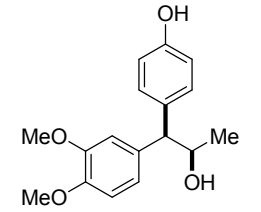
(±)-**10n**
(73%, dr = 92:8, BF_3•OEt_2)



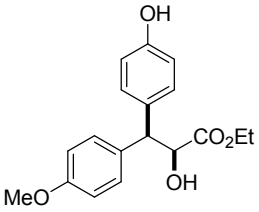
(±)-**10o**
(71%, BF_3•OEt_2)



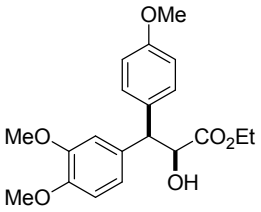
(±)-**10p**
(66%, dr = 92:8, BF_3•OEt_2)



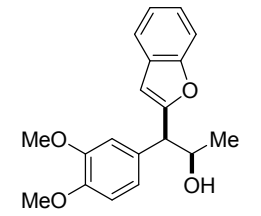
(±)-**10q**
(70%, dr = 92:8, BF_3•OEt_2)



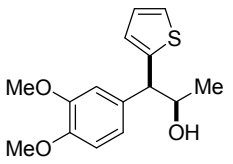
(±)-**10r**
(72%, dr = 92:8, BF_3•OEt_2)



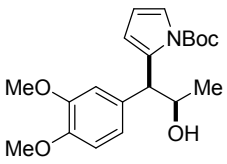
(±)-**10s**
(85%, dr = 92:8, BF_3•OEt_2)



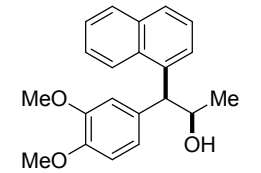
(±)-**10t**
(85%, dr = 92:8, $InBr_3$)



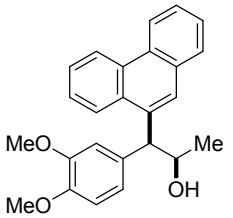
(±)-**10u**
(63%, dr = 92:8, $InBr_3$)



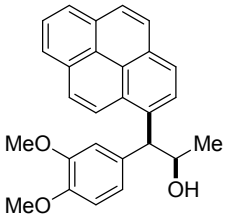
(±)-**10v**
(60%, dr = 92:8, BF_3•OEt_2)



(±)-**10w**
(90%, dr = 95:5, BF_3•OEt_2)



(±)-**10x**
(76%, dr = 95:5, BF_3•OEt_2)

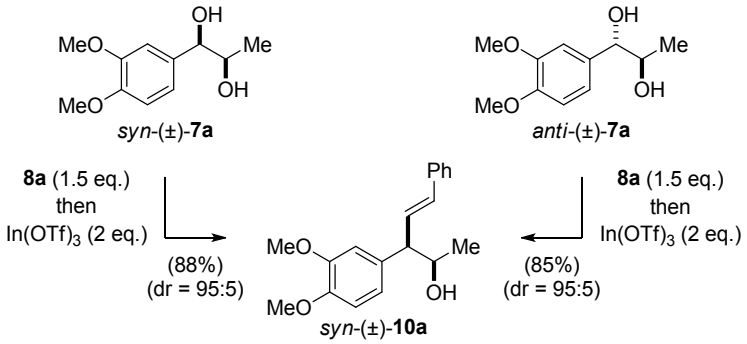


(±)-**10y**
(68%, dr = 95:5, BF_3•OEt_2)

[a]General conditions: *syn*-(±)-**7a-b**, **7f** (0.3 mmol, 1.0 eq), boronic acid **8h-q** (1.5 eq), DCM (3.0 mL, 0.1 M) at room temperature, 1 h, then promoter (in parentheses) (2.0 eq), at room temperature, 1.5 h. [b]Based on isolated product after purification by chromatography. [c]Diastereomeric ratio (*syn*/*anti*) of the crude product was determined by ^{1}H NMR spectroscopy.

Stereoconvergent Reaction of Diastereomeric 1,2-Diols and Proposed Reaction Mechanism. To demonstrate the stereoselective nature of this reaction and gain some insight into the reaction mechanism, each of the diastereomeric aryl-substituted 1,2-diols *syn*- and *anti*-(±)-**7a** was treated separately with (*E*)-styrylboronic acid **8a** (1.5 eq) and $In(OTf)_3$ (2.0 eq) in DCM under one-pot conditions (**Scheme 7**). In both cases, *syn*-(±)-**10a** was formed preferentially.

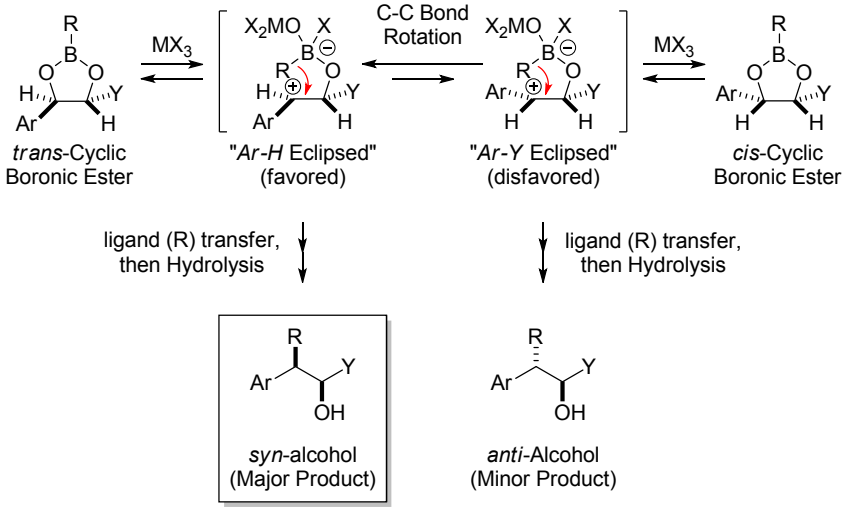
Scheme 7. Stereoconvergent Reaction of Each of *syn*- and *anti*-(±)-**7a** with **8a** under the One-Pot Condition



Csákÿ and co-workers[12] proposed the 1,4-transfer of the carbon ligand (R) from boron to the benzylic carbon center *via* a borderline S_Ni-type mechanism when a cyclic boronic ester was treated with trifluoroacetic anhydride (TFAA) as the promoter, which would lead to the coupling product with retention of the original configuration at the benzylic carbon center. However, based on the results from our stereoconvergent reactions, we demonstrated a reaction mechanism that involves an S_N1-type process (**Scheme 8**). The favorable stereochemical outcome observed in this transformation can be rationalized on the basis that the most stable "*Ar-H* eclipsed" geometry predominates over the "*Ar-Me* or *Ar-*CO_2Et eclipsed" geometry, in which the aryl substituent eclipses the hydrogen in the transition state to minimize the allylic 1,3-strain[3] in the resonance-stabilized benzylic carbenium ion. Then, the intramolecular 1,4-

transfer of the sp^2-hybridized carbon ligand from boron to the same face of the resonance-stabilized planar benzylic carbenium ion and subsequent basic hydrolysis would generate *syn*-alcohol as the major diastereomer.

Scheme 8. Proposed Reaction Mechanism[a]

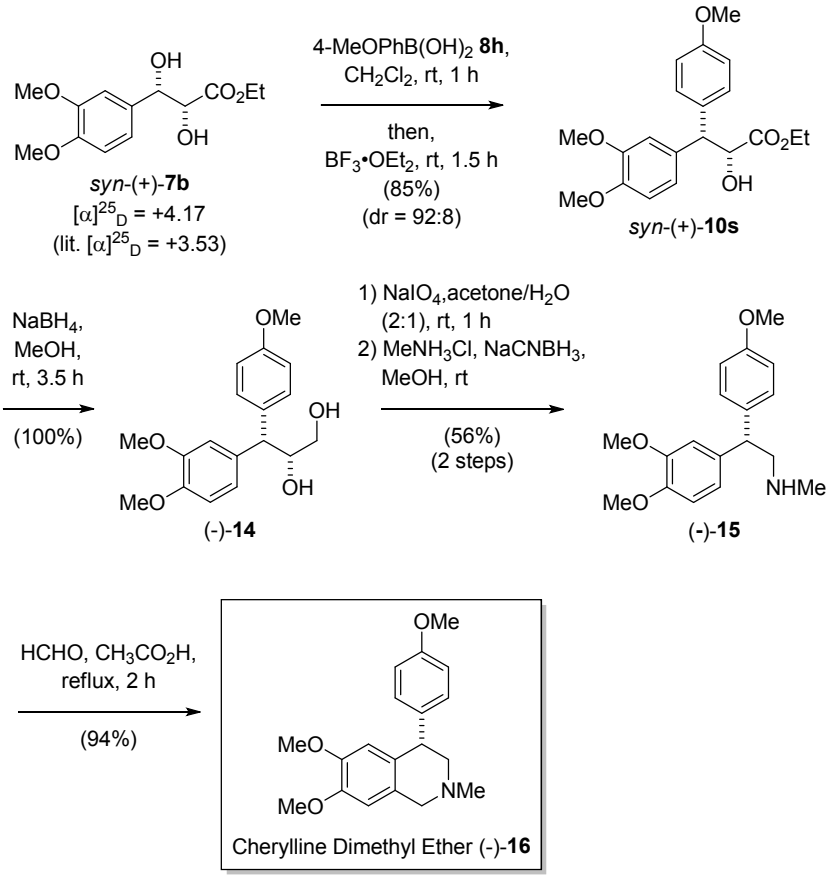


[a]M =metal, X = ligand (OTf, Br, F), R = aryl, heteroaryl, or polyaryl, Y = Me or CO_2Et

A Short and Efficient Enantioselective Synthesis of Cherylline Dimethyl Ether (–)-16. We next turned our attention to a short and efficient enantioselective synthesis of cherylline dimethyl ether (–)-**16** to prove the synthetic utility of this method (**Scheme 9**). Sequential treatment of chiral diol *syn*-(+)-**7b**[18] with 4-methoxyphenyl boronic acid **8h** in DCM for 1 hour and BF_3•OEt_2 for 1.5 hours at room temperature afforded *syn*-(+)-**10s** in 85% yield, exhibiting excellent diastereoselectivity (dr = 92:8). Reduction[19] of α-hydroxy ester *syn*-(+)-**10s** with an excess amount of $NaBH_4$ afforded the resulting diol (–)-**14**, which was transformed into the corresponding methyl amine (–)-**15** through oxidative cleavage, followed by subsequent reductive amination[20] in 56% yield over 2 steps. Finally, Pictet-Spengler cyclization according to Soundararajan and co-workers[21] generated cherylline dimethyl ether

(–)-**16**. The spectral characteristics[22] and optical rotation of our synthetic material (–)-**16** were in good agreement with those reported for cherylline dimethyl ether synthesized by an alternative route: $[\alpha]_D$ = –12.44 (*c* = 0.50, MeOH) [synthetic: lit.[23] $[\alpha]_D$ = –21.65 (c = 0.965, MeOH)].

Scheme 9. A Short and Efficient Enantioselective Synthesis of Cherylline Dimethyl Ether (–)-**16**



CONCLUSIONS

In conclusion, we have developed a highly regio- and diastereoselective C(sp^3)-C(sp^2) cross-

coupling reaction of unprotected aryl-substituted 1,2-diols with styryl, aryl, heteroaryl, and polyaryl boronic acids as nucleophiles in a one-pot procedure under mild reaction conditions. The Lewis acid-promoted regioselective cleavage of an aryl-substituted cyclic boronic ester, followed by the stereoselective intramolecular 1,4-transfer of the carbon ligand from boron to the same face of the resulting resonance-stabilized planar benzylic carbenium ion resulted in the highly diastereoselective carbon-carbon bond formation at the benzylic carbon center. The synthetic utility of the method was illustrated by a short asymmetric synthesis of cherylline dimethyl ether (–)-**16** in 5 steps from known chiral diol.

EXPERIMENTAL SECTION

General Information

Except as otherwise indicated, reactions were carried out under a nitrogen (N_2) atmosphere in flame- or oven-dried glassware. In aqueous work-up, all organic solutions were dried over sodium sulfate or magnesium sulfate, and filtered prior to rotary evaporation at water aspirator pressure. Reactions were monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck pre-coated silica gel plates (Kieselgel $60F_{254}$, Merck). Spots were detected by viewing under a UV light, colorizing with charring after dipping in *p*-anisaldehyde solution with acetic acid and sulfuric acid and MeOH or ceric ammonium molybdate solution with sulfuric acid and ethanol. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by E. Merck. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. Commercial reagents and solvents were used as received with the following exceptions. All solvents were freshly purified and dried by standard techniques just before use. Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Dichloromethane (DCM) and acetonitrile (MeCN) were distilled from calcium hydride (CaH_2). Methanol (MeOH) was

distilled from magnesium sulfate ($MgSO_4$). ^1H and ^{13}C spectra were recorded on a 400 MHz or 600 MHz spectrometer. Chemical shifts are reported as δ value relative to internal chloroform (δ 7.26 for ^1H and δ 77.0 for ^{13}C). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant in Hz, and assignment. Infrared (IR) spectra were measured on a FT-IR spectrometer referenced to a polystyrene standard. Data are represented as follows: frequency of the absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad), and assignment (where appropriate). High resolution mass spectra (HRMS) were recorded with FAB (fast atom bombardment) or EI (electron impact) method. High resolution values are calculated to four decimal places from the molecular formula, all found values being within a tolerance of 5 ppm.

General Procedure for the Synthesis of (*E*)-Styrenes

To a stirred solution of phenol (1.0 equiv.) in DCM (10.0 mL/mmol) was added imidazole (3.0 equiv.), DMAP (0.1 equiv.), and TBDPSCl (1.2 equiv.) at 0 °C. The reaction mixture was stirred at room temperature for 2 hours under N_2 atmosphere and then poured onto water (10.0 mL/mmol) and the layers were separated. The aqueous layer was extracted with DCM (2×10.0 mL/mmol), and the combined organic layer was washed with brine (5.0 mL/mmol), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using the appropriate mixture of eluents, provided the corresponding (*E*)-styrenes.

*(E)-tert-Butyl-(2-methoxy-4-(prop-1-en-1-yl)phenoxy)diphenylsilane [(E)-**SI-1c**].* From isoeugenol (206.0 mg, 1.26 mmol), imidazole (236.0 mg, 3.77 mmol), DMAP (15.0 mg, 0.126 mmol), and TBDPSCl (0.40 ml, 1.51 mmol) in DCM, following the general procedure, (*E*)-**SI-**

1c was obtained. Chromatographic purification (hexanes/EtOAc 100:1 to 70:1) provided (*E*)-**SI-1c** (458.7 mg, 90.8%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.71 (m, 4H), 7.31-7.41 (m, 6H), 6.76 (s, 1H), 6.60 (s, 2H), 6.25 (dd, *J* = 15.6, 1.6 Hz, 1H), 6.02 (dq, *J* = 15.6, 6.4 Hz, 1H), 3.57 (s, 3H), 1.82 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.10 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 150.3, 144.1, 135.3, 133.6, 131.6, 130.7, 129.6, 127.5, 123.5, 120.1, 118.5, 109.6, 55.4, 26.9, 20.0, 18.6; IR (Film) 2931, 1577, 1509, 1427, 1278, 1112, 1037 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M + H]$^+$ Calcd for $C_{26}H_{31}O_2Si$ 403.2093; Found 403.2087.

*(E)-Ethyl 3-(4-((tert-Butyldiphenylsilyl)oxy)-3-methoxyphenyl)acrylate [(E)-**SI-1d**].* From ethyl 4-hydroxy-3-methoxycinnamate (267.0 mg, 1.20 mmol), imidazole (245.1 mg, 3.60 mmol), DMAP (14.7 mg, 0.12 mmol), and TBDPSCl (0.37 ml, 1.44 mmol) in DCM, following the general procedure, (*E*)-**SI-1d** was obtained. Chromatographic purification (hexanes/EtOAc 20:1) provided (*E*)-**SI-1d** (553.4 mg, 100%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.70 (m, 4H), 7.54 (d, *J* = 16.0 Hz ,1H), 7.32-7.43 (m, 6H), 6.93 (d, *J* = 1.6 Hz, 1H), 6.84 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.59 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.12 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.1, 150.7, 147.3, 144.6, 135.3, 133.1, 129.7, 128.1, 127.6, 122.0, 120.3, 115.9, 111.0, 60.5, 55.5, 26.8, 20.1, 14.6; IR (Film) 2931, 1705, 1595, 1509, 1428, 1262, 1155, 1035 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M + H]$^+$ Calcd for $C_{28}H_{33}O_4Si$ 461.2148; Found 461.2152.

General Procedure for the Synthesis of Aryl-Substituted 1,2-*syn*-Diols

To a stirred solution of (*E*)-styrene or (*E*)-ethyl cinnamate (1.0 equiv.) in acetone/H_2O (2:1, v/v, 10.0 mL) at room temperature was added 4-methylmorpholine *N*-oxide (1.2 equiv.) and OsO_4 (0.02 M in H_2O, 0.025 equiv.). The reaction mixture was stirred at room temperature for 12 hours under N_2 atmosphere, then quenched by the addition of saturated $Na_2S_2O_3$ solution

(10 mL) and diluted with EtOAc (10 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 30 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using the appropriate mixture of eluents, provided the corresponding 1,2-diols.

*(±)-(2S,3R)-Ethyl 3-(3,4-Dimethoxyphenyl)-2,3-dihydroxypropanoate [syn-(±)-**7b**].* From (*E*)-Ethyl 3-(3,4-Dimethoxyphenyl)acrylate[24] (316.0 mg, 1.338 mmol), OsO_4 (0.02 M, 1.67 mL, 0.033 mmol), 4-methylmorpholine *N*-oxide (203.7 mg, 1.739 mmol) in acetone/H_2O, following the general procedure, *syn*-(±)-**7b** was obtained. Chromatographic purification (hexanes/EtOAc 1:1 to 1:2) provided *syn*-(±)-**7b** (317.0 mg, 1.173 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (d, *J* = 2.0 Hz, 1H), 6.94 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 4.94 (d, *J* = 2.8 Hz, 1H), 4.33 (d, *J* = 2.8 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.14 (brs, 1H), 2.74 (brs, 1H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.3, 148.4, 148.2, 132.3, 118.4, 110.5, 109.4, 75.1, 74.3, 61.6, 55.7, 55.6, 13.9; IR (Film) 3472, 2938, 1732, 1594, 1515, 1464, 1258, 1139, 1023 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{13}H_{18}O_6$ 270.1103; Found 270.1106.

*(±)-(1R,2R)-1-(4-((tert-Butyldiphenylsilyl)oxy)-3-methoxyphenyl)propane-1,2-diol [syn-(±)-**7c**].* From (*E*)-**SI-1c** (243.0 mg, 0.604 mmol), OsO_4 (0.02 M, 0.75mL, 0.015 mmol), 4-methylmorpholine *N*-oxide (91.9 mg, 0.785 mmol) in acetone/H_2O, following the general procedure, *syn*-(±)-**7c** was obtained. Chromatographic purification (hexanes/EtOAc 4:1 to 2:1) provided *syn*-(±)-**7c** (263.5 mg, 0.604 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.69 (m, 4H), 7.29-7.40 (m, 6H), 6.73 (d, *J* = 2.4 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.58 (dd, *J* = 8.0, 2.4 Hz, 1H), 4.20 (d, *J* = 7.2 Hz, 1H), 3.75 (dq, *J* = 7.2, 6.4 Hz, 1H), 3.55 (s, 3H),

2.55 (brs, 1H), 2.47 (brs, 1H), 1.11 (s, 9H), 0.97 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.6, 144.9, 135.4, 134.2, 133.4, 129.6, 127.5, 120.1, 119.1, 110.6, 80.0, 72.4, 55.5, 26.9, 20.0, 18.9; IR (Film) 3378, 2931, 1589, 1513, 1428, 1266, 1139, 1113 (cm^{-1}); HRMS (FAB-magnetic sector) m/z: $[M]^+$ Calcd for $C_{26}H_{32}O_4Si$ 436.2070; Found 436.2067.

*(±)-(2S,3R)-Ethyl 3-(4-((tert-butyldiphenylsilyl)oxy)-3-methoxyphenyl)-2,3-dihydroxypropanoate [syn-(±)-**7d**].* From (*E*)-**SI-1d** (724.0 mg, 1.572 mmol), OsO_4 (0.02 M, 1.96 mL, 0.040 mmol), 4-methylmorpholine *N*-oxide (239.4 mg, 2.043 mmol) in acetone/H_2O, following the general procedure, *syn*-(±)-**7d** was obtained. Chromatographic purification (hexanes/EtOAc 1:1 to 1:2) provided *syn*-(±)-**7d** (476.2 mg, 0.963 mmol) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.70 (m, 4H), 7.31-7.41 (m, 6H), 6.85 (s, 1H), 6.63-6.67 (m, 2H), 4.83 (dd, J = 6.0, 3.2 Hz, 1H), 4.27 (dd, J = 5.6, 3.6 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.58 (s, 3H), 3.02 (d, J = 6.0 Hz, 1H), 2.61 (d, J = 6.8 Hz, 1H), 1.23 (t, J = 7.2 Hz, 3H), 1.10 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.6, 150.3, 144.7, 135.2, 133.4, 133.0, 129.5, 127.5, 119.7, 118.5, 110.6, 75.0, 74.6, 62.1, 55.5, 26.8, 20.0, 14.3; IR (Film) 3456, 2932, 1732, 1589, 1514, 1428, 1265, 1155, 1106 (cm^{-1}); HRMS (FAB-magnetic sector) m/z: $[M]^+$ Calcd for $C_{28}H_{34}O_6Si$ 494.2125; Found 494.2128.

Procedure for the Synthesis of Cyclic Boronic Ester

*(±)-(4R,5R)-4-(3,4-Dimethoxyphenyl)-5-methyl-2-((E)-styryl)-1,3,2-dioxaborolane [trans-(±)-**9a**].* To a stirred solution of *syn*-(±)-**7a**[15] (713.0 mg, 3.359 mmol) in anhydrous DCM (22.4 mL) at room temperature was added *trans*-2-phenylvinylboronic acid **8a** (994.2 mg, 6.719 mmol). The reaction mixture was stirred for 1 hour under N_2 atmosphere and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using (hexanes/EtOAc 2:1 to 1:1) as elutant, provided *trans*-(±)-**9a** (1.089 g, 3.359 mmol) as a

colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.53 (m, 3H), 7.29-7.38 (m, 3H), 6.85-6.91 (m, 3H), 6.26 (d, *J* = 18.0 Hz, 1H), 4.87 (d, *J* = 7.6 Hz, 1H), 4.37 (dq, *J* = 7.6, 6.4 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 1.47 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.1, 149.0, 148.8, 137.0, 132.5, 128.8, 128.4, 126.9, 118.2, 115.2, 110.9, 108.5, 85.6, 80.9, 55.8, 20.8; IR (Film) 2930, 1623, 1577, 1516, 1450, 1348, 1233, 1139 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{19}H_{21}BO_4$ 324.1533; Found 324.1535.

General Procedure for the Synthesis of *syn*-Alcohol (±)-10 from Aryl-Substituted *syn*-1,2-Diol (±)-7 with Aryl-, Heteroaryl, Polyaryl Boronic Acids Promoted by a Lewis acid (One-Pot Protocol).

To a stirred solution of *syn*-(±)-1,2-diol (1.0 equiv.) in anhydrous DCM (1.0 mL/mmol) at room temperature was added the corresponding boronic acid (1.5 equiv.). The reaction mixture was stirred for 1 hour under N_2 atmosphere, and the appropriate Lewis acid (2.0 equiv.) was added to the resulting mixture at 0 °C. The reaction mixture was stirred at room temperature for 1.5 hours under N_2 atmosphere, then quenched by the addition of saturated $NaHCO_3$ solution (1.0 mL/mmol) and diluted with DCM (1.0 mL/mmol) and the layers were separated. The aqueous layer was extracted with DCM (2 × 10 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using the appropriate mixture of eluents, provided the corresponding *syn*-alcohol.

*(±)-(2R,3R,E)-3-(3,4-Dimethoxyphenyl)-5-phenylpent-4-en-2-ol [syn-(±)-**10a**].* From *syn*-(±)-**7a**[15] (68.5 mg, 0.323 mmol, (*E*)-styrylboronic acid **8a** (71.6 mg, 0.484 mmol) and $In(OTf)_3$ (362.8 mg, 0.646 mmol) in DCM, following the general procedure, *syn*-(±)-**10a** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 2:1) provided *syn*-(±)-**10a**

(84.7 mg, 0.316 mmol, dr = 95:5) as a colorless oil. From *anti*-(±)-**7a**[15] (93.6 mg, 0.441 mmol), (*E*)-styrylboronic acid **8a** (97.9 mg, 0.661 mmol) and $In(OTf)_3$ (495.3 mg, 0.882 mmol) in DCM, following the general procedure, *syn*-(±)-**10a** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 2:1) provided *syn*-(±)-**10a** (111.8 mg, 0.375 mmol, dr = 95:5) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.38 (m, 2H), 7.28-7.32 (m, 2H), 7.22-7.24 (m, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.81 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 6.55 (d, *J* = 15.6 Hz, 1H), 6.46 (dd, *J* = 15.6, 8.4 Hz, 1H), 4.01-4.08 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.29 (dd, *J* = 8.4, 7.2 Hz, 1H), 1.86 (d, *J* = 2.8 Hz, 1H), 1.14 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.9, 147.6, 136.8, 134.2, 132.6, 129.7, 128.4, 127.3, 126.2, 119.8, 111.4, 111.3, 70.8, 57.6, 56.0, 55.9, 21.0; IR (Film) 3440, 2931, 1709, 1590, 1513, 1449, 1259, 1141, 1025 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{19}H_{22}O_3$ 298.1569; Found 298.1570.

(±)-(2S,3R,E)-Ethyl 3-(3,4-Dimethoxyphenyl)-2-hydroxy-5-phenylpent-4-enoate [syn-(±)-10b]. From a solution of *syn*-(±)-**7b**[18] (78.0 mg, 0.289 mmol) in DCM, (*E*)-styrylboronic acid **8a** (64.0 mg, 0.433 mmol) and $In(OTf)_3$ (324.4 mg, 0.577 mmol), following the general procedure, benzylic substituted alcohol *syn*-(±)-**10b** was obtained. Chromatographic purification (hexanes/EtOAc 6:1 to 3:1) provided *syn*-(±)-**10b** (68.4 mg, 0.192 mmol, dr = 95:5) as a colorless oil.^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.36 (m, 2H), 7.20-7.31 (m, 3H), 6.93-6.96 (m, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.52 (dd, *J* = 16.0, 7.2 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.53 (dd, *J* = 5.6, 3.2 Hz, 1H), 4.16-4.30 (m, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.87-3.89 (m, 1H), 2.94 (d, *J* = 5.6 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.4, 148.8, 148.0, 136.9, 133.0, 132.9, 128.5, 127.5, 126.8, 126.4, 120.3, 111.2, 111.1, 74.6, 62.1, 56.1, 52.4, 14.6; IR (Film) 3479, 2936, 1727, 1590, 1513, 1464, 1261, 1142 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{21}H_{24}O_5$ 356.1624; Found 356.1624.

*(±)-(2R,3R,E)-3-(4-((tert-Butyldiphenylsilyl)oxy)-3-methoxyphenyl)-5-phenylpent-4-en-2-ol [syn-(±)-**10c**].* From a solution of *syn*-(±)-**7c** (132.0 mg, 0.302 mmol) in DCM, (*E*)-styrylboronic acid **8a** (67.1 mg, 0.454 mmol) and $In(OTf)_3$ (339.8 mg, 0.605 mmol), following the general procedure, *syn*-(±)-**10c** was obtained. Chromatographic purification (hexanes/EtOAc 15:1 to 6:1) provided *syn*-(±)-**10c** (103.4 mg, 0.198 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.70 (m, 4H), 7.19-7.40 (m, 11H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 2.0 Hz, 1H), 6.48-6.54 (m, 2H), 6.40 (dd, *J* = 15.6, 8.8 Hz, 1H), 3.91-3.95 (m, 1H), 3.56 (s, 3H), 3.18 (dd, *J* = 8.8, 7.6 Hz, 1H), 1.82 (d, *J* = 2.8 Hz, 1H), 1.11 (s, 9H), 1.05 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.7, 144.0, 137.1, 135.6, 135.0, 133.7, 132.9, 130.0, 129.8, 128.7, 127.69, 127.65, 126.5, 120.5, 120.0, 112.4, 71.1, 58.1, 55.8, 27.1, 21.1, 20.2; IR (Film) 3439, 2936, 1588, 1512, 1463, 1266, 1113 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{34}H_{38}O_3Si$ 522.2590; Found 522.2598.

*(±)-(2S,3R,E)-Ethyl 3-(4-((tert-Butyldiphenylsilyl)oxy)-3-methoxyphenyl)-2-hydroxy-5-phenylpent-4-enoate [syn-(±)-**10d**].* From a solution of *syn*-(±)-**7d** (159.0 mg, 0.321 mmol) in DCM, (*E*)-styrylboronic acid **8a** (71.3 mg, 0.482 mmol) and $In(OTf)_3$ (227.9 mg, 0.643 mmol), following the general procedure, *syn*-(±)-**10d** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 5:1) provided *syn*-(±)- **10d** (145.6 mg, 0.251 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.71 (m, 4H), 7.18-7.40 (m, 11H), 6.80 (s, 1H), 6.64-6.65 (m, 2H), 6.45 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 4.45 (dd, *J* =6.0, 4.0 Hz, 1H), 4.13-4.21 (m, 2H), 3.79 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.58 (s, 3H), 2.83 (d, *J* = 6.0 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.10 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.4, 150.3, 144.1, 137.0, 135.3, 133.62, 133.60, 133.3, 132.8, 129.6, 128.5, 127.5, 127.1, 126.4, 120.3, 120.0, 112.7, 74.6, 61.9, 55.7, 52.5, 26.9, 20.0, 14.6; IR (Film) 3478, 2931, 1730,

1587, 1513, 1464, 1278, 1251 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M + H]^+$ Calcd for $C_{36}H_{41}O_5Si$ 581.2723; Found 581.2721.

*(±)-(2R,3R,E)-3-(4-Methoxyphenyl)-5-phenylpent-4-en-2-ol [syn-(±)-**10e**].* From a solution of *syn*-(±)-**7e**[25] (41.0 mg, 0.225 mmol) in DCM, (*E*)-styrylboronic acid **8a** (49.9 mg, 0.338 mmol) and $InBr_3$ (159.5 mg, 0.450 mmol), following the general procedure, *syn*-(±)-**10e** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 8:1) provided *syn*-(±)-**10e** (40.0 mg, 0.149 mmol, dr = 95:5) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.39 (m, 2H), 7.27-7.31 (m, 2H), 7.19-7.23 (m, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.46 (dd, *J* = 16.0, 8.4 Hz, 1H), 3.99-4.07 (m, 1H), 3.80 (s, 3H), 3.30 (dd, *J* = 8.4, 7.6 Hz, 1H), 1.87 (d, *J* = 2.8 Hz, 1H), 1.12 (d, *J* = 6.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.3, 136.9, 133.7, 132.8, 129.9, 128.9, 128.5, 127.5, 126.3, 114.2, 70.9, 57.4, 55.4, 21.0; IR (Film) 3440, 2929, 1609, 1582, 1509, 1449, 1244, 1177 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{18}H_{20}O_2$ 268.1463; Found 268.1461.

*(±)-(2S,3R,E)-Ethyl 2-Hydroxy-3-(4-methoxyphenyl)-5-phenylpent-4-enoate [syn-(±)-**10f**].* From a solution of *syn*-(±)-**7f**[26] (82.0 mg, 0.341 mmol) in DCM, (*E*)-styrylboronic acid **8a** (75.7 mg, 0.512 mmol) and $InBr_3$ (242.0 mg, 0.683 mmol), following the general procedure, *syn*-(±)-**10f** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 8:1) provided *syn*-(±)-**10f** (66.5 mg, 0.204 mmol, dr = 95:5) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.35 (m, 6H), 7.19-7.23 (m, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.52 (dd, *J* = 15.6, 8.0 Hz, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 4.51 (dd, *J* = 5.6, 3.6 Hz, 1H), 4.15-4.29 (m, 2H), 3.90 (dd, *J* = 8.0, 4.0 Hz, 1H), 3.80 (s, 3H), 2.93 (d, *J* = 5.6 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 158.5, 136.9, 132.9, 132.4, 129.3, 128.5, 127.5, 127.0, 126.4, 114.0, 74.6, 62.0, 55.4, 52.1, 14.6; IR (Film) 3478, 2982, 1726, 1610, 1583, 1511, 1447, 1245, 1177

(cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{20}H_{22}O_4$ 326.1518; Found 326.1521.

*(±)-(2R,3R,E)-5-Phenyl-3-(2,4,5-trimethoxyphenyl)pent-4-en-2-ol [syn-(±)-**10g**].* From a solution of *syn*-(±)-**7g**[27] (70.4 mg, 0.291 mmol) in DCM, (*E*)-styrylboronic acid **8a** (64.5 mg, 0.436 mmol) and In(OTf)$_3$ (326.6 mg, 0.581 mmol), following the general procedure, *syn*-(±)-**10g** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 1:1) provided *syn*-(±)-**10g** (84.1 mg, 0.256 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.39 (m, 2H), 7.27-7.31 (m, 2H), 7.19-7.22 (m, 1H), 6.76 (s, 1H), 6.54-6.56 (m, 3H), 4.12 (m, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.72 (m, 1H), 2.05 (d, *J* = 3.2 Hz, 1H), 1.13 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.0, 148.1, 143.0, 137.1, 132.7, 129.3, 128.4, 127.3, 126.2, 121.6, 113.1, 98.1, 70.0, 56.9, 56.7, 56.2, 51.5, 20.9; IR (Film) 3439, 2931, 1598, 1507, 1451, 1201, 1177 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{20}H_{24}O_4$ 328.1675; Found 328.1674.

*(±)-(2R,3R,E)-3-(3,4-Dimethoxyphenyl)-5-(4-(trifluoromethyl)phenyl)pent-4-en-2-ol [syn-(±)-**10h**].* From a solution of *syn*-(±)-**7a**[15] (65.1 mg, 0.307 mmol) in DCM, *trans*-2-[4-(trifluoromethyl)phenyl]vinylboronic acid **8b** (104.6 mg, 0.460 mmol) and $InBr_3$ (217.5 mg, 0.613 mmol), following the general procedure, *syn*-(±)-**10h** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 5:1) provided *syn*-(±)- **10h** (97.0 mg, 0.265 mmol, dr = 95:5) as a white soild. mp 111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.81 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.62 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 4.04-4.12 (m, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.33 (dd, *J* = 8.0, 7.2 Hz, 1H), 1.76 (d, *J* = 4.0 Hz, 1H), 1.16 (d, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.1, 147.9, 140.4 (d, $J_{C\text{-}F}$ = 1.5 Hz), 133.8, 132.6, 131.4, 129.2 (q, $J_{C\text{-}F}$ = 31.9 Hz) 126.4, 125.5 (q, $J_{C\text{-}F}$ = 3.8 Hz), 119.9, 111.4, 111.2, 70.9, 57.6,

56.1, 56.0, 21.3; IR (Film) 3477, 2963, 1614, 1591, 1514, 1464, 1321, 1259 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{20}H_{21}F_3O_3$ 366.1443; Found 366.1443.

*(±)-(2R,3R,E)-3-(3,4-Dimethoxyphenyl)-5-(4-fluorophenyl)pent-4-en-2-ol [syn-(±)-**10i**].* From a solution of *syn*-(±)-**7a**[15] (66.4 mg, 0.313 mmol) in DCM, *trans*-2-[4-fluorophenyl]vinylboronic acid **8c** (82.0 mg, 0.469 mmol) and $InBr_3$ (221.8 mg, 0.626 mmol), following the general procedure, *syn*-(±)-**10i** was obtained. Chromatographic purification (hexanes/EtOAc 8:1 to 4:1) provided *syn*-(±)-**10i** (77.8 mg, 0.246 mmol, dr = 95:5) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.8, 5.6 Hz, 2H), 6.99 (t, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.50 (d, *J* = 16.4 Hz, 1H), 6.38 (dd, *J* = 16.4, 8.8 Hz, 1H), 4.02-4.06 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.27 (dd, *J* = 8.8, 7.6 Hz, 1H), 1.82 (d, *J* = 3.2 Hz, 1H), 1.14 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.1 (d, $J_{C\text{-}F}$ = 244.3 Hz), 149.0, 147.8, 134.2, 133.1 (d, $J_{C\text{-}F}$ = 3.8 Hz), 131.6, 129.4 (d, $J_{C\text{-}F}$ = 2.3 Hz), 127.8 (d, $J_{C\text{-}F}$ = 7.6 Hz), 119.8, 115.4 (d, $J_{C\text{-}F}$ = 21.2 Hz), 111.4, 111.2, 70.9, 57.7, 56.1, 56.0, 21.1; IR (Film) 3446, 2965, 1601, 1507, 1464, 1263, 1224 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{19}H_{21}FO_3$ 316.1475; Found 316.1475.

*(±)-(2R,3R,E)-5-(4-Chlorophenyl)-3-(3,4-dimethoxyphenyl)pent-4-en-2-ol [syn-(±)-**10j**].* From a solution of *syn*-(±)-**7a**[15] (63.0 mg, 0.297 mmol) in DCM, *trans*-2-[4-chlorophenyl]vinylboronic acid **8d** (81.2 mg, 0.445 mmol) and $InBr_3$ (210.5 mg, 0.594 mmol), following the general procedure, *syn*-(±)-**10j** was obtained. Chromatographic purification (hexanes/EtOAc 3:1) provided *syn*-(±)-**10j** (80.7 mg, 0.242 mmol, dr = 95:5) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.79 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.46-6.47 (m, 2H), 4.01-4.09 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.26-3.30 (m, 1H), 1.77 (d, *J* = 3.6 Hz, 1H), 1.14 (d, *J*

= 6.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 149.1, 147.9, 135.5, 134.1, 133.0, 131.5, 130.5, 128.6, 127.5, 119.9, 111.5, 111.4, 70.9, 57.6, 56.09, 56.05, 21.2; IR (Film) 3469, 2964, 1590, 1513, 1489, 1463, 1258 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{19}H_{21}ClO_3$ 332.1179; Found 332.1172.

(±)-(2R,3R,E)-5-([1,1'-Biphenyl]-4-yl)-3-(3,4-dimethoxyphenyl)pent-4-en-2-ol [syn-(±)-10k]. From a solution of *syn*-(±)-**7a**[15] (15.2 mg, 0.0716 mmol) in DCM, *trans*-2-[4-biphenyl]vinylboronic acid **8e** (24.1 mg, 0.107 mmol) and $InBr_3$ (50.8 mg, 0.143 mmol), following the general procedure, *syn*-(±)-**10k** was obtained. Chromatographic purification (hexanes/Et_2O 4: 1 to 2:1) provided *syn*-(±)-**10k** (18.4 mg, 0.0491 mmol, dr = 95:5) as a white solid. mp 95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.59 (m, 4H), 7.40-7.47 (m, 4H), 7.31-7.34 (m, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.82 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.78 (d, *J* = 1.6 Hz, 1H), 6.58 (d, *J* = 15.6 Hz, 1H), 6.51 (dd, *J* = 15.6, 8.0 Hz, 1H), 4.03-4.09 (m, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.31 (dd, *J* = 8.0, 7.6 Hz, 1H), 1.87 (brs, 1H), 1.15 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 149.0, 147.8, 140.6, 140.2, 135.9, 134.2, 132.4, 129.8, 128.8, 127.3, 127.2, 126.9, 126.7, 119.9, 111.4, 111.3, 70.9, 57.8, 56.10, 56.06, 21.1; IR (Film) 3440, 2964, 1591, 1513, 1486, 1463, 1260 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{25}H_{26}O_3$ 374.1882; Found 374.1883.

(±)-(2R,3R,E)-3-(3,4-Dimethoxyphenyl)-5-(p-tolyl)pent-4-en-2-ol [syn-(±)-10l]. From a solution of *syn*-(±)-**7a**[15] (18.4 mg, 0.0867 mmol) in DCM, *trans*-2-[4-methylphenyl]vinylboronic acid **8f** (21.1 mg, 0.130 mmol) and $InBr_3$ (61.5 mg, 0.173 mmol), following the general procedure, *syn*-(±)-**10l** was obtained. Chromatographic purification (hexanes/EtOAc 2:1 to 1:1) provided *syn*-(±)-**10l** (13.5 mg, 0.0432 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H),

6.84 (d, *J* = 8.0 Hz, 1H), 6.80 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.52 (d, *J* = 15.6 Hz, 1H), 6.40 (dd, *J* = 15.6, 8.4 Hz, 1H), 3.99-4.05 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.26 (dd, *J* = 8.4, 7.6 Hz, 1H), 2.32 (s, 3H), 1.92 (brs, 1H), 1.13 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 149.0, 147.7, 137.3, 134.3, 134.1, 132.8, 129.2, 128.6, 126.2, 119.9, 111.4, 111.2, 70.9, 57.9, 56.08, 56.06, 21.4, 21.0; IR (Film) 3437, 2927, 1590, 1512, 1463, 1418, 1261 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{20}H_{24}O_3$ 312.1725; Found 312.1726.

(±)-(2R,3R,E)-3-(3,4-Dimethoxyphenyl)-5-(4-methoxyphenyl)pent-4-en-2-ol [syn-(±)-10m]. From a solution of *syn*-(±)-**7a**[15] (18.0 mg, 0.0848 mmol) in DCM, *trans*-2-[4-methoxyphenyl]vinylboronic acid **8g** (22.6 mg, 0.127 mmol) and $BF_3{\cdot}OEt_2$ (0.013 mL, 0.103 mmol), following the general procedure, *syn*-(±)-**10m** was obtained. Chromatographic purification (hexanes/EtOAc 3:1) provided *syn*-(±)- **10m** (11.0 mg, 0.0335 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.80 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.49 (d, *J* = 15.6 Hz, 1H), 6.30 (dd, *J* = 15.6, 8.8 Hz, 1H), 3.98-4.07 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.80 (s, 3H), 3.25 (dd, *J* = 8.8, 8.0 Hz, 1H), 1.92 (brs, 1H), 1.13 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.1, 149.0, 147.7, 134.5, 132.4, 129.7, 127.5, 127.4, 119.9, 114.0, 111.5, 111.3, 70.9, 58.0, 56.11, 56.10, 55.5, 21.0; IR (Film) 3437, 2927, 1590, 1512, 1463, 1418, 1261 (cm^{-1}); HRMS (EI-magnetic sector) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}O_4$ 328.1675; Found 328.1672.

(±)-(1R,2R)-1-(3,4-Dimethoxyphenyl)-1-(4-methoxyphenyl)propan-2-ol [syn-(±)-10n]. From a solution of *syn*-(±)-**7a**[15] (66.4 mg, 0.313 mmol) in DCM, 4-methoxyphenylboronic acid **8h** (71.3 mg, 0.469 mmol) and $BF_3{\cdot}OEt_2$ (0.077 ml, 0.626 mmol), following the general

procedure, *syn*-(±)-**10n** was obtained. Chromatographic purification (hexanes/EtOAc 6:1 to 3:1) provided *syn*-(±)-**10n** (69.0 mg, 0.228 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.82 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 4.41-4.49 (m, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.78 (s, 3H), 3.70 (d, *J* = 8.4 Hz, 1H), 1.62 (d, *J* = 3.2 Hz, 1H), 1.20 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.3, 148.7, 147.4, 135.4, 133.5, 129.5, 119.8, 114.2, 111.5, 111.2, 70.3, 59.2, 55.97, 55.95, 55.4, 21.6; IR (Film) 3517, 2930, 1607, 1509, 1463, 1244, 1142 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd $C_{18}H_{22}O_4$ 302.1518; Found 302.1519.

*(±)-(R)-1,1-Bis(3,4-dimethoxyphenyl)propan-2-ol [(±)-**10o**].* From a solution of *syn*-(±)-**7a**[15] (63.4 mg, 0.298 mmol) in DCM, 3,4-dimethoxyphenylboronic acid **8i** (81.4 mg, 0.447 mmol) and $BF_3{\cdot}OEt_2$ (0.074 ml, 0.596 mmol), following the general procedure, (±)-**10o** was obtained. Chromatographic purification (hexanes/EtOAc 3:1 to 3:2) provided (±)-**10o** (70.6 mg, 0.212 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.84 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 4.40-4.47 (m, 1H), 3.86 (s, 3H), 3.854 (s, 3H), 3.850 (s, 3H), 3.84 (s, 3H), 3.68 (d, *J* = 8.4 Hz, 1H), 1.72 (brs, 1H), 1.20 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.0, 148.7, 147.8, 147.5, 135.2, 134.0, 120.1, 119.8, 112.1, 111.5, 111.4, 111.2, 70.3, 59.7, 55.98, 55.97, 21.5; IR (Film) 3516, 2931, 1589, 1509, 1463, 1415, 1240 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd $C_{19}H_{24}O_5$ 332.1624; Found 332.1629.

*(±)-(1S,2R)-1-(2,4-Dimethoxyphenyl)-1-(3,4-dimethoxyphenyl)propan-2-ol [syn-(±)-**10p**].* From a solution of 1,2-diol *syn*-(±)-**7a**[15] (63.0 mg, 0.297 mmol) in DCM, 2,4-dimethoxyphenylboronic acid **8j** (81.0 mg, 0.445 mmol) and $BF_3{\cdot}OEt_2$ (0.073 ml, 0.594 mmol),

following the general procedure, *syn*-(±)-**10p** was obtained. Chromatographic purification (hexanes/EtOAc 4:1 to 2:1) provided *syn*-(±)-**10p** (65.3 mg, 0.196 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.0 Hz, 1H), 6.81-6.83 (m, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.50 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.45 (d, *J* = 2.0 Hz, 1H), 4.48-4.51 (m, 1H), 4.20 (d, *J* = 8.8 Hz, 1H,) 3.84 (s, 3H), 3.82 (s, 3H), 3.783 (s, 3H), 3.776 (s, 3H), 1.90 (brs, 1H), 1.18 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4, 158.5, 148.5, 147.2, 135.4, 128.4, 122.3, 120.2, 111.8, 110.9, 104.5, 99.2, 70.0, 56.0, 55.9, 55.7, 55.5, 51.6, 21.8; IR (Film) 3516, 2935, 1585, 1504, 1463, 1416, 1258 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{19}H_{24}O_5$ 332.1624; Found 332.1627.

(±)-4-((1R,2R)-1-(3,4-Dimethoxyphenyl)-2-hydroxypropyl)phenol [syn-(±)-10q]. From a solution of *syn*-(±)-**7a**[15] (64.5 mg, 0.304 mmol) in DCM, 4-hydroxyphenylboronic acid **8k** (62.9 mg, 0.456 mmol) and $BF_3{\cdot}OEt_2$ (0.075 ml, 0.608 mmol), following the general procedure, *syn*-(±)-**10q** was obtained. Chromatographic purification (hexanes/EtOAc 2:1 to 1:1) provided *syn*-(±)-**10q** (61.0 mg, 0.212 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.8 Hz, 2H), 6.81 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.74-6.79 (m, 4H), 5.57 (s, 1H), 4.41-4.48 (m, 1H), 3.833 (s, 3H), 3.825 (s, 3H), 3.68 (d, *J* = 8.8 Hz, 1H), 1.80 (brs, 1H), 1.20 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.8, 148.7, 147.5, 135.3, 133.2, 129.6, 119.9, 115.8, 111.5, 111.2, 70.6, 59.2, 56.03, 55.99, 21.6; IR (Film) 3478, 3266, 2949, 1594, 1511, 1456, 1416, 1227 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{17}H_{20}O_4$ 288.1362; Found 288.1362.

(±)-(2S,3R)-Ethyl 2-Hydroxy-3-(4-hydroxyphenyl)-3-(4-methoxyphenyl)propanoate [syn-(±)-10r]. From a solution of *syn*-(±)-**7f**[25] (81.0 mg, 0.337 mmol) in DCM, 4-hydroxyphenylboronic acid **8k** (69.8 mg, 0.506 mmol) and $BF_3{\cdot}OEt_2$ (0.083 ml, 0.674 mmol),

following the general procedure, *syn*-(±)-**10r** was obtained. Chromatographic purification (hexanes/EtOAc 8:1 to 4:1) provided *syn*-(±)-**10r** (76.5 mg, 0.242 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 4.96 (s, 1H), 4.84 (dd, *J* = 6.8, 4.0 Hz, 1H), 4.37 (d, *J* = 4.0 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 2.81 (d, *J* = 6.8 Hz, 1H), 1.19 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.8, 158.1, 154.5, 133.7, 131.5, 130.5, 129.5, 115.3, 113.8, 73.8, 62.0, 55.4, 52.8, 14.4; IR (Film) 3487, 2983, 1723, 1610, 1509, 1463, 1442, 1243 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M + H]$^+$ Calcd for $C_{18}H_{21}O_5$ 317.1389; Found 317.1382.

*(±)-(2S,3R)-Ethyl 3-(3,4-Dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)-propanoate [syn-(±)-**10s**].* From a solution of *syn*-(±)-**7b**[18] (84.8 mg, 0.314 mmol) in DCM, 4-methoxyphenyl boronic acid **8h** (71.6 mg, 0.471 mmol) and $BF_3{\cdot}OEt_2$ (0.08 mL, 0.628 mmol), following the general procedure, *syn*-(±)-**10s** was obtained. Chromatographic purification (hexanes/EtOAc 4:1 to 1:3) provided *syn*-(±)- **10s** (85.7 mg, 0.238 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H), 6.97 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.91 (d, *J* = 2.4 Hz, 1H), 6.80-6.83 (m, 3H), 4.85 (dd, *J* = 6.4, 4.0 Hz, 1H), 4.39 (d, *J* = 4.0 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.83 (s, 3H), 3.77 (s, 3H), 2.78 (d, *J* = 6.4 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.6, 158.4, 148.6, 147.6, 134.2, 131.2, 130.2, 120.5, 113.7, 111.9, 110.9, 73.8, 61.9, 56.0, 55.9, 55.3, 53.1, 14.4; IR (Film) 3495, 2936, 1730, 1608, 1508, 1463, 1416, 1243 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M]$^+$ Calcd for $C_{20}H_{24}O_6$ 360.1573; Found 360.1556.

*(±)-(1R,2R)-1-(Benzofuran-2-yl)-1-(3,4-dimethoxyphenyl)propan-2-ol [syn-(±)-**10t**].* From a solution of *syn*-(±)-**7a**[15] (64.5 mg, 0.304 mmol) in DCM, benzofuran-2-boronic acid **8l**

(73.9 mg, 0.456 mmol) and $InBr_3$ (215.5 mg, 0.608 mmol), following the general procedure, *syn*-(±)-**10t** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 4:1) provided *syn*-(±)-**10t** (80.2 mg, 0.257 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.52 (m, 1H), 7.43-7.45 (m, 1H), 7.22 (td, *J* = 7.6, 1.2 Hz, 1H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 6.90 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 6.82 (d, *J* =8.0 Hz, 1H), 6.62 (s, 1H), 4.46 (dqd, *J* = 8.0, 6.0, 4.0 Hz, 1H) , 3.98 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 2.09 (d, *J* = 4.0 Hz, 1H), 1.20 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.2, 154.6, 148.8, 148.0, 131.7, 128.3, 123.6, 122.7, 120.61, 120.58, 111.6, 111.2, 111.0, 104.1, 70.2, 56.0, 55.9, 54.1, 21.4; IR (Film) 3440, 2931, 1591, 1513, 1454, 1253, 1140 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{19}H_{20}O_4$ 312.1362; Found 312.1368.

(±)-(1R,2R)-1-(3,4-Dimethoxyphenyl)-1-(thiophen-2-yl)propan-2-ol [syn-(±)-10u]. From a solution of *syn*-(±)-**7a**[15] (65.0 mg, 0.306 mmol) in DCM, 2-thiopheneboronic acid **8m** (58.8 mg, 0.459 mmol) and $InBr_3$ (217.2 mg, 0.613 mmol), following the general procedure, *syn*-(±)-**10u** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 4:1) provided *syn*-(±)-**10u** (53.3 mg, 0.191 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.00-7.01 (m, 1H), 6.97 (dd, *J* = 5.2, 3.2 Hz, 1H), 6.87 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.83 (d, *J* = 2.0 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.32 (dqd, *J* = 8.0, 6.0, 3.2 Hz, 1H), 4.03 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 1.90 (d, *J* = 3.2 Hz, 1H), 1.17 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.8, 147.8, 144.7, 134.4, 126.8, 125.6, 124.6, 120.0, 111.24, 111.16, 71.5, 55.99, 55.98, 55.5, 21.4; IR (Film) 3516, 2936, 1591, 1514, 1464, 1262, 1141 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{15}H_{18}O_3S$ 278.0977; Found 278.0976.

(±)-tert-Butyl 2-((1S,2R)-1-(3,4-Dimethoxyphenyl)-2-hydroxypropyl)-1H-pyrrole-1-

*carboxylate [syn-(±)-**10v**].* From a solution of *syn*-(±)-**7a**[15] (62.0 mg, 0.292 mmol) in DCM, *N*-Boc-2-pyrroleboronic acid **8n** (92.5 mg, 0.438 mmol) and $BF_3 \cdot OEt_2$ (0.072 ml, 0.584 mmol), following the general procedure, *syn*-(±)-**10v** was obtained. Chromatographic purification (hexanes/EtOAc 8:1 to 4:1) provided *syn*-(±)- **10v** (63.0 mg, 0.174 mmol, dr = 92:8) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.78 (s, 1H), 6.75 (s, 2H), 6.40 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.17 (dd, *J* = 3.6, 3.2 Hz, 1H), 4.76 (d, *J* = 8.8 Hz, 1H), 4.25 (dqd, *J* = 8.8, 6.0, 2.8 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.25 (d, *J* = 2.8 Hz, 1H), 1.52 (s, 9H), 1.13 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.1, 148.4, 147.5, 136.1, 133.6, 122.0, 120.6, 112.3, 110.9, 110.6, 110.0, 83.7, 71.2, 56.01, 55.98, 51.8, 28.2, 21.2; IR (Film) 3533, 2977, 1740, 1591, 1513, 1464, 1314, 1123 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{20}H_{27}NO_5$ 361.1889; Found 361.1891.

*(±)-(1S,2R)-1-(3,4-Dimethoxyphenyl)-1-(naphthalen-1-yl)propan-2-ol [syn-(±)-**10w**].* From a solution of *syn*-(±)-**7a**[15] (65.5 mg, 0.309 mmol) in DCM, 1-naphthaleneboronic acid **8o** (79.6 mg, 0.463 mmol) and $BF_3 \cdot OEt_2$ (0.076 ml, 0.617 mmol), following the general procedure, *syn*-(±)-**10w** was obtained. Chromatographic purification (hexanes/EtOAc 10:1 to 3:1) provided *syn*-(±)- **10w** (89.5 mg, 0.278 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 1H), 7.83 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.79 (d, *J* = 6.8 Hz, 1H), 7.78 (d, *J* = 6.8 Hz, 1H), 7.54 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.46 (td, *J* = 6.8, 1.6 Hz, 2H), 6.88 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.81 (d, *J* = 2.0 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 4.62-4.67 (m, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 1.90 (brs, 1H), 1.29 (d, *J* = 5.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.7, 147.5, 137.2, 134.4, 134.3, 132.6, 128.8, 127.5, 126.1, 125.6, 125.3, 123.63, 123.57, 120.6, 111.6, 111.1, 70.3, 56.0, 55.9, 54.4, 21.6; IR (Film) 3516, 2936, 1591, 1511, 1464, 1262, 1121 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{21}H_{22}O_3$ 322.1569; Found 322.1566.

*(±)-(1S,2R)-1-(3,4-Dimethoxyphenyl)-1-(phenanthren-9-yl)propan-2-ol [syn-(±)-**10x**].* From a solution of *syn*-(±)-**7a**[15] (65.3 mg, 0.307 mmol) in DCM, 9-phenanthreneboronic acid **8p** (102.5 mg, 0.462 mmol) and $BF_3{\cdot}OEt_2$ (0.076 ml, 0.615 mmol), following the general procedure, *syn*-(±)-**10x** was obtained. Chromatographic purification (hexanes/Et_2O 4:1 to 2:1) provided *syn*-(±)-**10x** (87.6 mg, 0.235 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.4 Hz, 1H), 8.66 (d, *J* = 7.6 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.96 (d, *J* = 7.2 Hz, 1H), 7.54-7.68 (m, 4H), 6.92 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.72-4.78 (m, 1H), 4.62 (d, *J* = 8.8 Hz, 1H), 3.803 (s, 3H), 3.795 (s, 3H), 2.13 (brs, 1H), 1.33 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.9, 147.8, 135.3, 134.0, 131.6, 131.4, 131.2, 129.9, 128.7, 126.84, 126.76, 126.72, 126.4, 124.5, 123.2, 122.5, 120.8, 111.9, 111.2, 70.3, 56.1, 56.0, 54.9, 21.6; IR (Film) 3447, 2930, 1590, 1512, 1450, 1262, 1140 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{25}H_{24}O_3$ 372.1725; Found 372.1726.

*(±)-(1S,2R)-1-(3,4-Dimethoxyphenyl)-1-(pyren-1-yl)propan-2-ol [syn-(±)-**10y**].* From a solution of *syn*-(±)-**7a**[15] (62.5 mg, 0.295 mmol) in DCM, 1-pyreneboronic acid **8q** (108.7 mg, 0.442 mmol) and $BF_3{\cdot}OEt_2$ (0.073 ml, 0.589 mmol), following the general procedure, *syn*-(±)-**10y** was obtained. Chromatographic purification (hexanes/EtOAc 1:1 to 1:3) provided *syn*-(±)-**10y** (67.9 mg, 0.200 mmol, dr = 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 9.2 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 7.6 Hz, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 8.04 (s, 2H), 7.98 (t, *J* = 7.6 Hz, 1H), 6.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.88 (d, *J* = 2.0 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 4.97 (d, *J* = 8.4 Hz, 1H), 4.83-4.87 (m, 1H), 3.797 (s, 3H), 3.795 (s, 3H), 1.82 (d, *J* = 2.8 Hz, 1H), 1.39 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.8, 147.5, 135.2, 135.0, 131.3, 130.6,

130.1, 129.9, 127.8, 127.3, 127.2, 126.0, 125.4, 125.2, 125.0, 124.9, 124.8, 124.4, 123.0, 120.6, 111.8, 111.2, 70.6, 56.0, 55.9, 54.5, 21.9; IR (Film) 3439, 2964, 1589, 1515, 1463, 1242, 1141 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{27}H_{24}O_3$ 396.1725; Found 396.1726.

Confirmation of the Relative Configuration of Major and Minor Diastereomers

(±)-4-((3R,4R,E)-4-(Allyloxy)-1-phenylpent-1-en-3-yl)-1,2-dimethoxybenzene [syn-(±)-11]. To a cooled (0 °C) stirred solution of *syn*-(±)-**10a** (105.3 mg, 0.353 mmol) in THF/DMF (3.40 mL, 1:1 v/v) was added 95% NaH (89.2 mg, 3.530 mmol) under argon atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, allyl bromide (0.15 mL, 1.77 mmol) was added. The reaction mixture was stirred at 0°C for 30 minutes under argon atmosphere, then quenched with saturated aqueous NH_4Cl solution (3 mL) and diluted with Et_2O (10 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL), and the combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/Et_2O (5:1 to 1:1) as elutant, provided *syn*-(±)-**11** (69.6 mg, 0.206 mmol, 58.3% isolated yield, 86.5% **B**ased **O**n **R**ecovered **S**tarting **M**aterial) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.36 (m, 2H), 7.25-7.29 (m, 2H), 7.16-7.19 (m, 1H), 6.83 (s, 1H), 6.81 (s, 2H), 6.58 (dd, *J* = 15.6, 8.0 Hz, 1H), 6.38 (d, *J* = 15.6 Hz, 1H), 5.89 (ddt, *J* = 17.2, 10.4, 5.2 Hz, 1H), 5.27 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.13 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.09 (dd, *J* = 12.8, 5.2 Hz, 1H), 3.91 (dd, *J* = 12.8, 5.2 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.69-3.77 (m, 1H), 3.40 (dd, *J* = 7.6, 6.4 Hz, 1H), 1.11 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.7, 147.5, 137.6, 135.3, 135.0, 131.4, 130.7, 128.4, 127.0, 126.2, 120.4, 116.4, 111.6, 111.1, 78.6, 70.4, 56.01, 55.99, 55.4, 18.5; IR (Film) 2930, 1590, 1514, 1463, 1260, 1140, 1027 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{22}H_{26}O_3$ 338.1882; Found 338.1884.

*(±)-(2R,3R)-3-(3,4-Dimethoxyphenyl)-2-methyl-3,6-dihydro-2H-pyran [trans-(±)-**12**].* To a stirred solution of *syn*-(±)-**11** (52.2 mg, 0.154 mmol) in DCM (3.10 mL) was added Grubbs second-generation catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh, Grubbs II] (26.2 mg, 0.031 mmol) under N_2 atmosphere at room temperature. The reaction mixture was stirred for 3 hours under N_2 atmosphere and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/Et_2O (4:1) as elutant, provided *trans*-(±)-**12** (33.3 mg, 0.142 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 8.0 Hz, 1H), 6.73 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.67 (d, *J* = 2.0 Hz, 1H), 5.87-5.91 (m, 1H), 5.75 (dd, *J* = 10.4, 2.4 Hz, 1H), 4.23-4.36 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.50 (dq, *J* = 8.8, 6.0 Hz, 1H), 3.14-3.18 (m, 1H), 1.14 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.6, 147.6, 134.4, 128.8, 125.9, 120.4, 111.2, 110.9, 76.3, 65.6, 55.9, 48.6, 19.5; IR (Film) 2930, 1590, 1514, 1463, 1260, 1134, 1026 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{18}O_3$ 234.1256; Found 234.1254.

*(±)-(2R,3R)-3-(3,4-Dimethoxyphenyl)-2-methyltetrahydro-2H-pyran [trans-(±)-**13**].* To a solution of *trans*-(±)-**12** (31.7 mg, 0.135 mmol) in MeOH (1.35 mL) were added 10% Pd/C (6.3 mg) at room temperature. The reaction mixture was stirred under H_2 atmosphere for 3 h, then filtered through a pad of Celite 545 and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/EtOAc (5:1) as elutant, provided *trans*-(±)-**13** (31.2 mg, 0.126 mmol) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 8.0 Hz, 1H), 6.71 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.66 (d, *J* = 2.0 Hz, 1H), 4.03-4.06 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.56 (td, *J* = 11.2, 2.4 Hz, 1H), 3.48 (dq, *J* = 10.0, 6.0 Hz, 1H), 2.33 (td, *J* = 11.2, 3.6 Hz, 1H), 1.93-1.97 (m, 1H), 1.65-1.80 (m, 3H), 0.98 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.7, 147.5, 136.4, 119.5, 111.2, 110.9, 78.6, 68.6, 56.05, 56.03, 50.3,

32.6, 26.8, 20.4; IR (Film) 2930, 1588, 1511, 1463, 1259, 1134, 1025 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{20}O_3$ 236.1412; Found 236.1412.

(±)-4-((3S,4R,E)-4-(Allyloxy)-1-phenylpent-1-en-3-yl)-1,2-dimethoxybenzene [anti-(±)-11]. To a cooled (0 °C) stirred solution of *anti*-(±)-**10a** (100.1 mg, 0.335 mmol) in THF/DMF (3.20 mL, 1:1 v/v) was added 95% NaH (84.6 mg, 3.350 mmol) under argon atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, allyl bromide (0.14 mL, 1.68 mmol) was added. The reaction mixture was stirred at 0 °C for 30 minutes under argon atmosphere, then quenched with saturated aqueous NH_4Cl solution (3 mL) and diluted with Et_2O (10 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL), and the combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/Et_2O (5:1 to 1:1) as elutant, provided *anti*-(±)-**11** (69.7 mg, 0.206 mmol, 61.4% isolated yield, 92.3% **B**ased **O**n **R**ecovered **S**tarting **M**aterial) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.36 (m, 2H), 7.26-7.30 (m, 2H), 7.17-7.21 (m, 1H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.85 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.43-6.44 (m, 2H), 5.78 (dddd, *J* = 17.2, 10.4, 5.2, 5.2 Hz, 1H), 5.17 (dddd, *J* = 17.2, 1.6, 1.6, 1.6 Hz, 1H), 5.08 (dddd, *J* = 10.4, 1.6, 1.6, 1.6 Hz, 1H), 4.00 (dddd, *J* = 12.8, 5.6, 1.2, 1.2 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.83 (dddd, *J* = 12.8, 5.6, 1.2, 1.2 Hz, 1H), 3.77 (dq, *J* = 6.8, 6.4 Hz, 1H), 3.46 (ddd, *J* = 6.8, 5.2, 2.4 Hz, 1H), 1.19 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.6, 147.5, 137.5, 135.3, 134.5, 131.1, 130.8, 128.5, 127.2, 126.2, 120.6, 116.3, 112.2, 111.1, 78.3, 70.3, 56.0, 55.5, 18.4; IR (Film) 2929, 1590, 1513, 1463, 1260, 1140, 1027 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{22}H_{26}O_3$; Found 338.1884.

(±)-(2R,3S)-3-(3,4-Dimethoxyphenyl)-2-methyl-3,6-dihydro-2H-pyran [cis-(±)-12]. To a

stirred solution of *anti*-(±)-**11** (51.8 mg, 0.153 mmol) in DCM (3.10 mL) was added Grubbs second-generation catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh, Grubbs II] (26.0 mg, 0.031 mmol) under N_2 atmosphere at room temperature. The reaction mixture was stirred for 3 hours under N_2 atmosphere and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/Et_2O (4:1) as elutant, provided *cis*-(±)-**12** (35.0 mg, 0.149 mmol) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 1.6 Hz, 1H), 6.76 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.91-5.92 (m, 2H), 4.27-4.36 (m, 2H), 3.92 (qd, *J* = 6.0, 3.2 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.07-3.08 (m, 1H), 0.90 (d, *J* = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.4, 147.7, 132.4, 128.4, 125.9, 121.8, 112.9, 110.6, 72.8, 66.4, 56.02, 55.96, 45.8, 19.3; IR (Film) 2930, 1588, 1510, 1463, 1250, 1143, 1027 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{18}O_3$ 234.1256; Found 234.1258.

*(±)-(2R,3S)-3-(3,4-Dimethoxyphenyl)-2-methyltetrahydro-2H-pyran [cis-(±)-**13**].* To a solution of *cis*-(±)-**12** (29.8 mg, 0.140 mmol) in MeOH (1.27 mL) were added 10% Pd/C (6.0 mg) at room temperature. The reaction mixture was stirred under H_2 atmosphere for 3 h, then filtered through a pad of Celite 545 and concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel, using hexanes/EtOAc (5:1) as elutant, provided *cis*-(±)-**13** (26.9 mg, 89.5%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, *J* = 2.0 Hz, 1H), 6.93 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.01-4.06 (m, 1H), 3.89-3.93 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.58-3.64 (m, 1H), 2.78 (q, *J* = 4.0 Hz, 1H), 1.82-1.99 (m, 3H), 1.41-1.46 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 148.3, 147.2, 135.3, 121.3, 112.8, 110.8, 75.8, 66.8, 56.1, 56.0, 44.5, 29.5, 22.5, 18.1; IR (Film) 2930, 1590, 1514, 1463, 1260, 1099, 1027 (cm^{-1}); HRMS (EI-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{20}O_3$ 236.1412; Found 236.1411.

A Short and Efficient Enantioselective Total Synthesis of Cherylline Dimethyl Ether (–)-16.

*(2R,3S)-Ethyl 3-(3,4-Dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate [syn-(+)-**10s**].* To a stirred solution of *syn*-(+)-**7b**[18] (84.8 mg, 0.314 mmol) in DCM (3.10 mL) at room temperature was added 4-methoxyphenylboronic acid **8h** (71.6 mg, 0.471 mmol). The reaction mixture was stirred at room temperature for 1 hour under N_2 atmosphere, and $BF_3{\cdot}OEt_2$ (0.08 mL, 0.628 mmol) was added dropwise *via* syringe to the resulting mixture at 0 °C. The reaction mixture was stirred at room temperature for 1.5 hours under N_2 atmosphere, then quenched by the addition of saturated $NaHCO_3$ solution (3 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using hexanes/EtOAc (4:1 to 1:3) as elutant, provided *syn*-(+)-**10s** (85.7 mg, 0.238 mmol, dr = 92:8) as a colorless oil. $[\alpha]^{25}_D$ +41.7 (*c* 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H), 6.97 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.91 (d, *J* = 2.4 Hz, 1H), 6.80-6.83 (m, 3H), 4.85 (dd, *J* = 6.4, 4.0 Hz, 1H), 4.39 (d, *J* = 4.0 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.83 (s, 3H), 3.77 (s, 3H), 2.78 (d, *J* = 6.4 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.6, 158.4, 148.6, 147.6, 134.2, 131.2, 130.2, 120.5, 113.7, 111.9, 110.9, 73.8, 61.9, 56.0, 55.9, 55.3, 53.1, 14.4; IR (Film) 3495, 2936, 1730, 1608, 1508, 1463, 1416, 1243 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: [M]+ Calcd for $C_{20}H_{24}O_6$ 360.1573; Found 360.1556.

*(2R,3S)-3-(3,4-Dimethoxyphenyl)-3-(4-methoxyphenyl)propane-1,2-diol [(–)-**14**].* To a stirred solution of *syn*-(+)-**10s** (161.4 mg, 0.448 mmol) in MeOH (4.50 mL) at room temperature was added $NaBH_4$[19] (254.2 mg, 6.72 mmol). The reaction mixture was stirred at

room temperature for 3.5 hours under N_2 atmosphere, then quenched by the addition of H_2O (10 mL). The aqueous layer was extracted with EtOAc (2 × 30 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using hexanes/acetone (2:1 to 1:2) as elutant, provided (−)-**14** (142.6 mg, 0.448 mmol, 100% yield) as a colorless oil. $[\alpha]^{25}_D$ -23.7 (*c* 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.82 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.76-6.78 (m, 2H), 4.35 (ddd, *J* = 9.2, 6.4, 2.8, 1H), 3.92 (d, *J* = 9.2 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 3.64 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.46 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.16 (brs, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.5, 149.0, 147.8, 134.4, 133.1, 129.5, 112.0, 114.4, 111.6, 111.5, 74.3, 65.0, 56.1, 56.1, 55.5, 53.7; IR (Film) 3402, 2936, 1609, 1508, 1442, 1245, 1141, 1025 (cm^{-1}); HRMS (FAB-magnetic sector) *m*/*z*: $[M]^+$ Calcd for $C_{18}H_{22}O_5$ 318.1467; Found 318.1464.

*(S)-2-(3,4-Dimethoxyphenyl)-2-(4-methoxyphenyl)-N-methylethanamine [(−)-**15**].* To a stirred solution of (−)-**14** (87.6 mg, 0.275 mmol) in acetone/H_2O (2:1 (v/v), 2.70 mL) at room temperature was added $NaIO_4$ (117.7 mg, 0.550 mmol). The reaction mixture was stirred at room temperature for 1 hour under N_2 atmosphere. The aqueous layer was extracted with DCM (2 × 20 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was used for the next step without further purification. To a stirred solution of aldehyde prepared above (78.8 mg, 0.275 mmol) in MeOH (11.0 mL) at room temperature was added methylamine hydrochloride (185.8 mg, 2.752 mmol, 10 eq), sodium cyanoborohydride[20] (69.2 mg, 1.101 mmol), 4Å molecular sieves (200 times). The reaction mixture was stirred at room temperature for 60 hours under N_2

atmosphere. The aqueous layer was extracted with DCM (2 × 20 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using hexanes/EtOAc/acetone/Et_3N (1%) (1:1:1 to 1:3:3) as elutant, provided (-)-**15** (46.2 mg, 0.153 mmol) as a colorless oil. $[\alpha]^{25}_D$ -1.17 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.74-6.80 (m, 3H), 4.09 (t, *J* = 7.6 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.13 (d, *J* = 7.6 Hz, 2H), 2.45 (s, 3H), 1.44 (brs, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 158.1, 148.9, 147.5, 135.8, 135.2, 128.8, 119.6, 114.0, 111.5, 111.3, 57.2, 56.0, 56.0, 55.4, 49.9, 36.6; IR (Film) 3337, 2931, 1607, 1509, 1463, 1246, 1142, 1028 (cm^{-1}); HRMS (FAB-magnetic sector) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_3$ 302.1756; Found 302.1752.

*(S)-6,7-Dimethoxy-4-(4-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline [Cherylline Dimethyl Ether (-)-**16**].* To a stirred solution of (-)-**15** (17.0 mg, 0.056 mmol) in CH_3CO_2H (0.56 mL) at room temperature was added formaldehyde[21] (2.2 mg, 0.073 mmol). The reaction mixture was stirred at 95 °C for 4 hours under N_2 atmosphere, then cooled to room temperature and basified by the addition of 50% NaOH solution (0.50 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL), and the combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification of the crude residue by flash chromatography on silica gel, using hexanes/EtOAc/acetone (1:5:0.25) as elutant, provided cherylline dimethyl ether (–)-**16** (16.6 mg, 0.053 mmol, 93.9 % yield) as a white solid. $[\alpha]^{25}_D$ -12.44 (*c* 0.5, MeOH); mp 90-92 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.55 (s, 1H), 6.34 (s, 1H), 4.15 (dd, *J* = 8.8, 5.6 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.65 (s, 3H), 3.52-3.67 (m, 2H), 2.97 (dd, *J* = 11.6, 5.6 Hz,

1H), 2.48 (dd, J = 11.6, 8.8 Hz, 1H), 2.41 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.1, 147.5, 147.4, 136.9, 129.9, 129.2, 127.3, 113.7, 111.9, 108.8, 62.3, 58.3, 56.0, 56.0, 55.4, 46.1, 44.9; IR (Film) 2935, 1608, 1508, 1461, 1244, 1138, 1032 (cm^{-1}); HRMS (FAB-magnetic sector) m/z: $[M + H]^+$ Calcd for $C_{19}H_{24}NO_3$ 314.1756; Found 314.1752.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website at DOI:

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AUTHOR INFORMATION

Corresponding Authors

*E-mail: dongjoo@ajou.ac.kr

Tel.: +82-31-219-3455; fax: +82-31-219-3435.

ORCID

Dongjoo Lee: 0000-0002-6337-2229

Hyoungsu Kim: 0000-0002-2774-8727

Notes

The authors declare no competing financial interest.

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