Asymmetric Synthesis of a Series of Chiral AB_2 Monomers for Dendrimer Construction

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Efficient preparation of a series of four chiral, nonracemic AB_2 monomers suitable for the construction of dendrimers is presented. Monomers **1**−**4** possess the common structural features of a diphenolic moiety and a benzylic or aliphatic hydroxyl which render these molecules suitable for convergent dendrimer synthesis. The same basic, high-yielding, five-step sequence is employed for **1**−**4**. Stilbene derivatives **13** and **14** are prepared by a Horner−Wadsworth−Emmons modified Wittig reaction between 3,5- or 3,4-bis(benzyloxy)benzaldehyde (**8** and **10**) and an ester-substituted benzylphosphonate (**11** or **12**). Cinnamate derivatives **21** and **22** are prepared similarly from **8** and **10** and triethyl phosphonoacetate. Chirality is introduced in the form of a 1,2-diol unit by Sharpless asymmetric dihydroxylation (AD) (>97% ee in all cases). Protection of the 1,2-diols as their acetonide derivatives provides dioxolane intermediates **17**, **18**, **25**, and **26**. Reduction of the ester groups followed by hydrogenolysis of the benzyl ethers yields AB_2 monomers **1**−**4** in 57−67% overall yield from **8** and **10**.

Introduction

Dendrimers[1] with chiral terminal groups[2−4] or interiors[5−11] possess the potential for enantioselective clathration of small, chiral molecules, leading to applications in chemical separations, sensor technology, and asymmetric catalysis. The continued successful development of new chiral dendritic structures depends on the efficient preparation of appropriately functionalized (*i.e.*, *n*-connected) monomers.[12−15] Previous syntheses of chiral dendrimers have relied on building blocks from natural sources. The earliest example of a chiral dendrimer was provided by Newkome, who modified an amine-terminated dendrimer with tryptophan residues.[4] Other efforts include the use of nucleic acids,[16] amino acids or derivatives,[2,9,17−19] and tartrates[10,11] as either surface or structural units. The work of Seebach[6−8] uses chirality from synthetic sources—chiral triols are prepared for the central core or linking units throughout the dendrimer—but these building blocks ultimately derive from the natural biopolymer poly[(R)-3-hydroxybutanoate], thus limiting the number of available stereoisomeric triols.[15] In only one instance have chiral dendrimers been prepared from materials outside the chiral pool. Chiral, nonracemic 1,2-diols, introduced by osmium-catalyzed asymmetric dihydroxylation (AD),[20] are used as the branching points to construct polyether dendrimers up to the fourth generation.[5]

We seek to increase the structural diversity of chiral dendrimers by preparing monomers for dendrimer construction through asymmetric synthesis. A greater structural diversity of monomers will facilitate the search for configurationally induced chiral conformations, or macromolecular asymmetry,[21] in dendritic macromolecules. Macromolecular asymmetry in linear macromolecules is crucial for their application to, for example, chiral chromatographic separations,[22,23] preparation of cholesteric liquid crystals,[24] and the development of organic materials for nonlinear optics.[25,26] While much is known of the effect of configuration on the conformation of linear polymers,[27] systematic studies on dendritic

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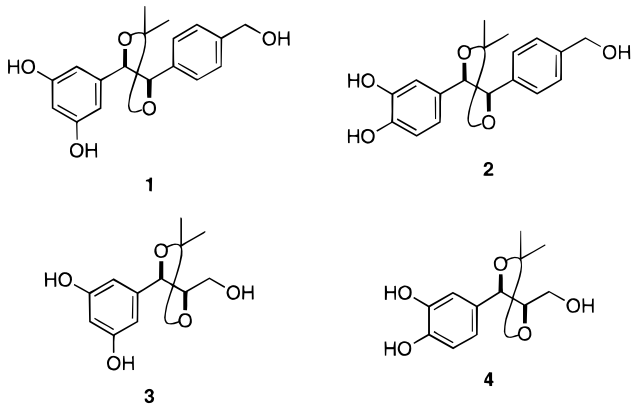
macromolecules are few.[6,7,10,18,28] Although the use of synthetic monomers for chiral dendrimer construction is rare possibly due to the absence of sufficiently functionalized chiral, nonracemic building blocks, synthetic techniques for stereoselectively introducing chirality into prochiral organic substrates are abundant.[29,30]

Our recently initiated program to develop strategies for the incorporation of asymmetric units into dendrimers[31−33] focuses on the development of materials active for the selective clathration of small guest molecules. We anticipate that for selectivity with regards to shape and functionality of the guest, a dendrimer must consist of chiral, nonracemic subunits in the interior for shape selectivity, as well as interior moieties capable of engaging in strong hydrogen bonding with encapsulated guests.[9,17,34] Appropriate functionality at the surface or within the interior of dendrimers also avails the opportunity to anchor well-defined transition metal moieties for catalysis applications.[19,35−39] The monomeric units necessary for preparing dendritic materials must also have the requisite functionality for construction of a highly branched structure; with rare exception,[40,41] dendrimers are constructed by formation of heteroatomic linkages through S_N2 or acyl transfer pathways.[1] In this paper, the preparation and characterization of a series of four new chiral AB_2 monomers are reported. All four monomers contain two phenolic residues and a benzylic or aliphatic hydroxyl group, making them suitable for convergent dendrimer synthesis, and a protected 1,2-diol moiety, which can serve, after deprotection, as a hydrogen bond donor or an anchor point for transition metal moieties in a dendritic structure.

Results and Discussion

Monomer Design. Our primary goal was to prepare AB_2 monomers for chiral dendrimer synthesis in a simple, efficient manner from inexpensive starting materials. In addition, we required the monomers to (a) possess appropriate functionality to allow incorporation into a convergent growth process, (b) be preparable by an asymmetric technique which allows the preparation of both enantiomers, and (c) contain functionality suitable for enthalpic interactions with guest molecules but *not* used to link the monomer units together. Monomers **1**−**4** fulfill these requirements. The common structural features of a diphenolic moiety and a benzylic or aliphatic hydroxyl render these molecules suitable for convergent dendrimer synthesis.[42] The central chiral 1,2-diol unit, masked in **1**−**4** as an acetonide derivative for synthetic



purposes, can be readily introduced by the AD reaction in either enantiomeric sense.[20] Once unmasked in the final dendrimer, the 1,2-diol should be capable of hydrogen bonding interactions with small clathrated guest molecules, especially 1,2-diamines.[43,44] In addition, the ability for 1,2-diols, particularly hydrobenzoins, to act as chiral auxiliaries and ligands for transition metals in catalytic asymmetric synthesis is well precedented. Lewis-acidic metal centers with hydrobenzoin ligands have been used to catalyze the aldol[45] and Diels−Alder reactions.[46] The hydrobenzoin moiety has also been used as a chiral auxiliary for conjugate additions of organolithiums to α,β-unsaturated aldimines[47] and the enantioselective alkylation of prochiral aldehydes by diethylzinc.[48]

Synthesis of AB_2 Monomers. A logical pathway to monomers **1**−**4** proceeds through a Wittig preparation of the appropriately substituted olefin AD substrates. This Wittig strategy requires bis(benzyloxy)benzaldehydes **8** and **10**. While commercially available, both are prohibitively expensive. Fortunately, efficient routes to **8** from α-resorcylic acid esters have been reported.[49−51] We have made modifications to these routes to avoid the use of benzyl bromide and 18-crown-6 as well as chromatography (Scheme 1). Thus, benzylation of methyl 3,5-dihydroxybenzoate (**5**) with benzyl chloride proceeded smoothly in K_2CO_3/DMF to provide **6** in yields consistently exceeding 90% after recrystallization. Reduction to benzyl alcohol **7**, followed by oxidation (PCC/CH_2Cl_2), provided **8** in 77% overall yield from **5**. Benzylation of

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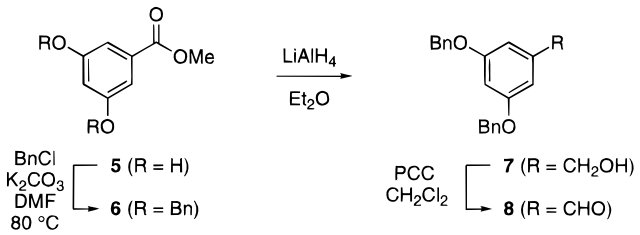
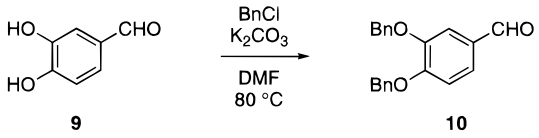
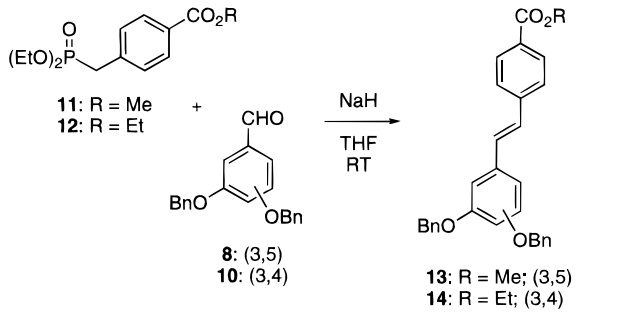
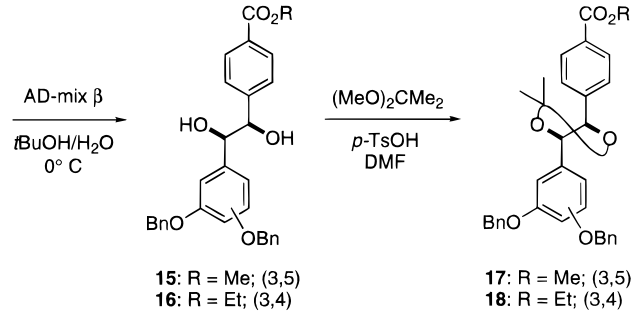
Scheme 1

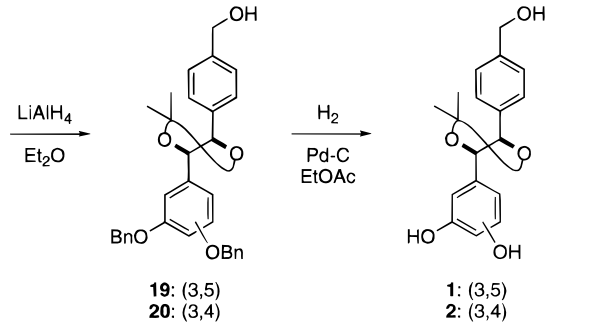




Scheme 2



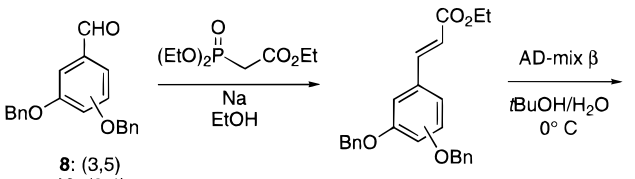


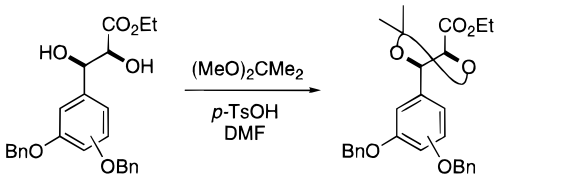


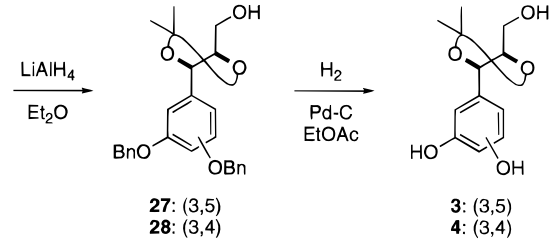
commercially available protocatechualdehyde (**9**) under identical conditions provided crystalline **10** in 95% yield after a single recrystallization.

The phosphonate-stabilized Wittig coupling of aldehydes **8** and **10** to an ester-substituted benzyl phosphonate (**11** or **12**)[52] provided stilbenes **13** and **14** in 95 and 80% yields, respectively (Scheme 2). Asymmetric dihydroxylation of stilbenes **13** and **14** yielded (*R*,*R*)-hydrobenzoins **15** and **16** in 74 and 90% yields, respectively, both in >97% ee. No attempt was made to increase the optical purity of **15** or **16** through physical manipulation. We found that the AD reactions were best performed in a 3:3:5 toluene/*tert*-butanol/water mixture to dissolve the substrate. Acetonide protection of the 1,2-diol moiety, reduction of the ester group, and hydrogenolysis of the benzyl ether protecting groups of both **15** and **16** were all carried out under standard conditions to provide target monomers **1** and **2** in 62 and 57% overall yields from **8** and **10**, respectively (five steps).[53] **1** and **2** were crystalline solids readily soluble in acetone, ether, and ethyl acetate. Although we anticipated catechol **2** be susceptible to oxidation to the orthoquinone, multigram samples of **2** have been stored over a period of months on the benchtop with no decomposition as confirmed by ^{1}H NMR.

Scheme 3







Preparation of **3** and **4** from cinnamate precursors follows a pathway analogous to that presented above (Scheme 3). Accordingly, bis(benzyloxy)cinnamate esters **21** and **22** were prepared by a phosphonate-stabilized Wittig coupling of aldehydes **8** and **10** to commercially available triethyl phosphonoacetate in 84 and 76% yields, respectively, under milder conditions than those used in the preparation of **13** and **14**. Asymmetric dihydroxylation of cinnamates **21** and **22** yielded (*R*,*R*)-diols **23** and **24** in 83 and 91% yields, respectively. The same solvent system as above was employed (3:3:5 toluene/*tert*-butanol/water), although the electronic nature of the cinnamate substrates necessitated a higher reaction temperature (20 °C rather than 0 °C)[54] for a reasonable reaction rate. The

(52) Transesterification between the phosphonate ester and the substrate was observed to occur during this reaction resulting in a small amount of **13** existing as the ethyl, rather than methyl, ester (see Experimental Section). This was avoided in the preparation of **14** by employing ethyl ester **12**, rather than methyl ester **11**.

(53) The optical purity of **1** was essentially the same as that of diol **15** (>97% ee by chiral HPLC). We were not able to ascertain the optical purity of **2** but believe it to be similarly high since no diastereomeric products were observed in the ^{1}H or ^{13}C NMR of crude **18**.

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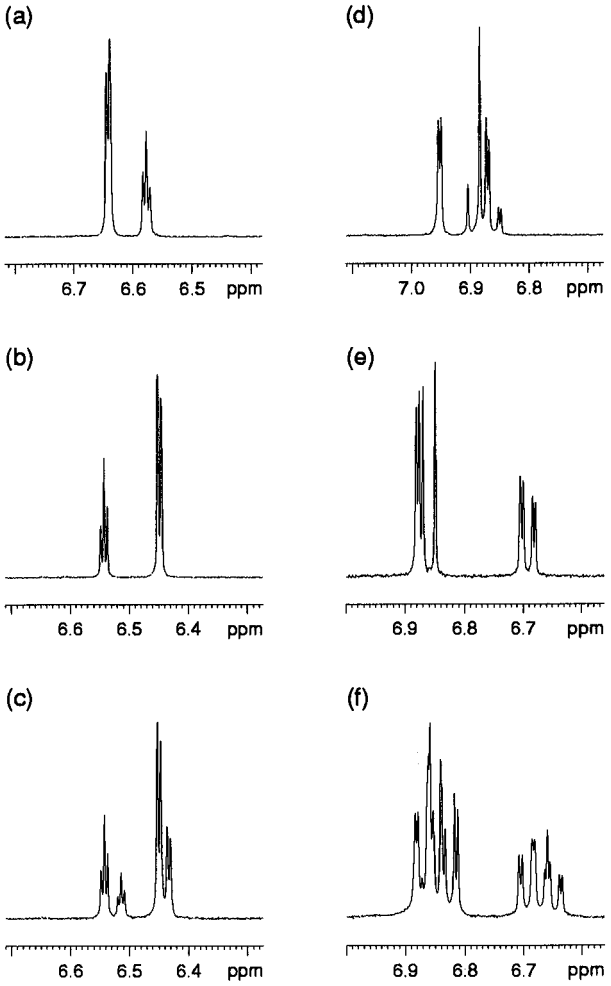

Figure 1. Selected regions of the ^{1}H NMR spectra of (a) **19**, (b) **27**, (c) **29**, (d) **20**, (e) **28**, and (f) **30** exhibiting the resonances for the oxygen-substituted aryl rings.

enantiomeric excesses of **23** and **24**, both >99%, did not suffer as a result. Acetonide protection of the 1,2-diol moiety, reduction of the ester group, and hydrogenolysis of the benzyl ether protecting groups of both **23** and **24** were again carried out under standard conditions to provide target monomers **3** and **4** in 64 and 67% overall yields from **8** and **10**, respectively (five steps).[55] **3** and **4** were both crystalline solids which were readily soluble in acetone, ether, and ethyl acetate.

Characterization. All compounds have been thoroughly characterized by ^{1}H and ^{13}C NMR and, with the exception of compounds **13** and **15**, which were obtained as mixtures of methyl and ethyl esters, give satisfactory combustion analyses. While constructing dendrimers from monomers **1**−**4**, we find the characteristic resonances appearing in the 6.6−7.0 ppm region for the three protons on the diphenolic aryl rings useful in identifying new structures. For example, consider dendrons built from monomers **1**−**4**. In the **1**- and **3**-based zeroth-generation dendrons **19** and **27** the three protons on the symmetrical 1,3,5-substituted aromatic ring appear as a doublet and a triplet in a 2:1 ratio by integration (Figure 1, parts a and b). The corresponding **1**-based first-generation dendron **29**[31] (Chart 1) gives rise to two *sets* of doublet/triplet patterns in a 1:2 ratio, indicative of the one A and two equivalent B rings (Figure 1c). Similarly, **2**- and **4**-based zeroth-generation dendrons **20** and **28**, with nonsymmetrical 1,3,4-substituted aromatic rings, both exhibit three resonances—two doublets and a doublet of doublets—in a 1:1:1 ratio (Figure 1, parts d and e). The corresponding **2**-based first-generation dendron **30**[31] (Chart 1) exhibits a more complicated pattern in this region which is nevertheless indicative of overlapping resonances for the three inequivalent C, D, and E rings in a 1:1:1 ratio (Figure 1f).

(55) The optical purities of both **3** and **4** were essentially the same as that of diols **21** and **22** (>99% ee by chiral HPLC).

Summary

We have prepared a series of four chiral, nonracemic AB_2 monomers for dendrimer synthesis. These monomers are suitable for convergent dendrimer synthesis since each possesses two phenolic residues and a benzylic or aliphatic hydroxyl group.[42] The monomers were prepared in five-step sequences with the chirality in the form of a 1,2-diol unit introduced in excellent %ee by the Sharpless AD reaction. The 1,2-diol was protected as an acetonide derivative which will be removed after the final dendrimers are prepared. These interior functional groups are intended to provide strong enthalpic contributions to guest binding. The protons on the trisubstituted aromatic rings of the monomer units provide useful ^{1}H NMR spectroscopic handles for structure identification during preparation of higher generation materials. The details of dendrimer construction using these monomers will be presented in due course.

Experimental Section

Materials and Methods. Elemental analyses were performed by Supersun Technology of Stony Brook, NY. Optical rotations and high performance liquid chromatography (HPLC) were performed on commercially available instrumentation. Melting points were measured on a Thomas-Hoover capillary melting point apparatus which was calibrated with commercial standards. Anhydrous ether was purchased from J. T. Baker and used as received. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen (N_2). Toluene and methylene chloride (CH_2Cl_2) were distilled from sodium and calcium hydride, respectively, under N_2. Dimethyl formamide (DMF) was distilled at reduced pressure under N_2 and stored in the dark. Potassium carbonate (granular) was dried at 150 °C at reduced pressure for at least 12 h and stored in a desiccator. Methyl 3,5-dihydroxybenzoate (**5**), 3,4-dihydroxybenzaldehyde (**9**), $(DHQD)_2PHAL$ (dihydroquinidine 1,4-phthalazinediyl diether), and methyl 4-(bromomethyl)benzoate (**11**) were purchased from Aldrich or Acros and used as received. Ethyl 4-(bromomethyl)benzoate (**12**) was prepared from *p*-toluic acid (Aldrich) by published procedures.[56] Triethyl phosphonoacetate was prepared from ethyl bromoacetate and triethyl phosphite. Pyridinium chlorochromate (PCC) was prepared according to the literature.[57] Flash chromatography was performed by the method of Still et al.[58] using silica gel (32−63 μm, Scientific Adsorbants, Inc.). Thin-layer chromatography (TLC) was performed on precoated TLC plates (Silica Gel HLO, F-254, Scientific Adsorbants, Inc.).

Methyl 3,5-Bis(benzyloxy)benzoate (6). A slurry of methyl 3,5-dihydroxybenzoate (**5**) (50.0 g, 0.30 mol), anhydrous potassium carbonate (164.5 g, 1.19 mol), benzyl chloride (69 mL, 0.60 mol), and DMF (400 mL) was stirred at 80 °C for 24 h under N_2. The reaction mixture was allowed to cool to ambient temperature, and the DMF was removed in vacuo.

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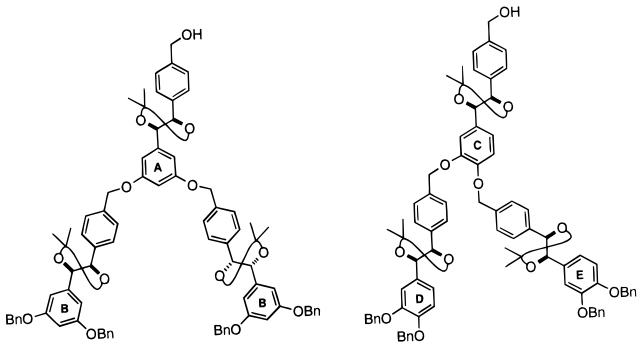
Chart 1



29 **30**

The residue was extracted with ethyl acetate and filtered through Celite. Concentration of the resulting solution gave crude product as a yellow solid. Recrystallization from methanol/water yielded pure **6** as colorless crystals (97.4 g, 94%): mp 69−71 °C (lit.[50] 68−70 °C); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.24−7.41 (m, 10 H), 6.79 (s, 3H), 5.05 (s, 4H), 3.90 (s, 3H).

3,5-Bis(benzyloxy)benzyl alcohol (7). A literature procedure[59] was used with modification as follows. To a cold (0 °C) suspension of $LiAlH_4$ (3.04 g, 80 mmol) in anhydrous ether (300 mL) was added with stirring **6** (15.0 g, 43 mmol). The reaction was allowed to warm to rt under N_2 while stirring (1 h) and then quenched by slow addition of water (150 mL) followed by 5% H_2SO_4 (150 mL). After the mixture was allowed to stir at ambient temperature (1 h), the organic layer was separated, the aqueous phase was further extracted with ether (3 × 100 mL), and the combined organic phase was dried over Na_2SO_4. Concentration in vacuo yielded **7** as a colorless solid (12.0 g, 87%) which was used without further purification: mp 78−80 °C (lit.[50] 79−81 °C); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.33−7.42 (m, 10 H), 6.60 (d, J = 2.2 Hz, 2H), 6.54 (t, J = 2.2 Hz, 1H) , 5.02 (s, 4H), 4.61 (d, J = 8.8 Hz, 2H), 1.64 (t, J = 8.8 Hz, 1H).

3,5-Bis(benzyloxy)benzaldehyde (8). A solution of **7** (15.2 g, 47.6 mmol) in dry CH_2Cl_2 was added to a slurry of PCC (15.5 g, 71.4 mmol), Celite (15.0 g), and 3 Å molecular sieves (10 g) in dry CH_2Cl_2 (125 mL) . The reaction was left to stir at rt until complete by TLC (SiO_2, 3:1 petroleum ether−ethyl acetate) at which time the solvent was removed in vacuo. The remaining dark brown solids were then extracted with ether which was filtered through florisil. Concentration of the pale yellow filtrate resulted in the precipitation of **8** (14.3 g, 94%) as colorless crystals: mp 80.5−81 °C (lit.[50] 79−81); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.33−7.43 (m, 10 H), 7.10 (d, J = 2.2 Hz, 2H), 6.86 (t, J = 2.2 Hz, 1H), 5.08 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5, 160.3, 138.4, 136.2, 128.6, 128.2, 127.5, 108.6, 108.3, 70.3.

3,4-Bis(benzyloxy)benzaldehyde (10). A literature procedure[60] was used with modification as follows: A mixture of **9** (32.7 g, 236 mmol), dry K_2CO_3 (163 g, 1.18 mol), and dry DMF (ca. 150 mL) was stirred at room temperature for 1 h under N_2. Benzyl chloride (54.4 mL, 473 mmol) was then added, and the mixture was refluxed for 24 h. The dark brown slurry was allowed to cool to ambient temperature and was then filtered through Celite. The filtrate was concentrated to a brown solid. Recrystallization from ethanol yielded tan crystals (71.6 g, 95%): mp 90−91 °C (lit.[60] 90−92 °C); ^{1}H NMR (270 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.30−7.47 (m, 12H), 7.00 (d, J = 8.2 Hz, 1H), 5.24 (s, 2H), 5.20 (s, 2H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 191.0, 154.4, 149.4, 136.7, 136.4, 130.5, 128.7, 128.6, 128.2, 128.1, 127.5, 127.2, 126.7, 113.4, 112.7, 71.1, 71.0. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.23; H, 5.70. Found: C, 79.05; H, 5.73.

4-Carbomethoxy-3′,5′-Bis(benzyloxy)-*trans*-stilbene (13). Methyl 4-(bromomethyl)benzoate (5.04 g, 22 mmol) was dissolved in triethyl phosphite (5.2 mL, 30 mmol), and the solution was heated to 120 °C under a reflux condenser. After 24 h, at which time the reaction was complete by TLC (SiO_2, 4:1 petroleum ether−ethyl acetate), the reaction was cooled to room temperature, and excess triethyl phosphite was removed in vacuo. A slurry of the resulting phosphonate ester, **8** (6.85 g, 21.5 mmol), and sodium hydride (1.26 g, 50% dispersion in mineral oil, 26.3 mmol) in dry THF (250 mL) was stirred at rt until analysis by TLC (SiO_2, 3:1 petroleum ether−ethyl acetate) indicated consumption of starting materials (approximately 36 h). The reaction was quenched with H_2O (40 mL) and acidified with 1 N HCl (60 mL). The organic layer was separated, and the aqueous layer was further extracted with ether (3 × 50 mL). The combined organic fractions were washed with saturated $NaHCO_3$ (50 mL), dried ($MgSO_4$), and concentrated to yield crude **13** (9.21 g, 95%) as a pale tan solid which was used without further purification. Spectroscopic characterization indicated that a 4:1 mixture of methyl and ethyl ester was present: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 7.45−7.32 (m, 10H), 7.13 and 7.04 (AB pattern, J = 15.8 Hz, 2H), 6.77 (d, J = 2.2 Hz, 2H), 6.57 (t, J = 2.2 Hz, 1H), 5.06 (s, 4H), 4.37 (q, J = 7.1 Hz, 0.4H), 3.91 (s, 2.4H), 1.39 (t, J = 7.1 Hz, 0.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 160.2, 141.6, 138.8, 136.8, 131.1, 130.0, 129.0, 128.6, 128.2, 128.0, 127.5, 126.4, 106.1, 102.2, 70.2, 60.9 (Et), 52.1 (Me), 14.3 (Et).

4-Carbethoxy-3′,4′-bis(benzyloxy)-*trans*-stilbene (14). Ethyl 4-(bromomethyl)benzoate (15.6 g, 68.1 mmol) was dissolved in triethyl phosphite (11.7 mL, 68.1 mmol), and the solution was heated to 120 °C under a reflux condenser. After 72 h, at which time the reaction was complete by TLC (SiO_2, 4:1 petroleum ether−ethyl acetate), the reaction was cooled to room temperature, and excess triethyl phosphite was removed in vacuo to give diethyl (4-carbethoxybenzyl)phosphonate as a clear liquid which was used without further purification: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.96 (d, J = 8.1 Hz, 2H), 7.35 (dd, J = 2.3, 8.1 Hz, 2H), 3.94−4.13 (m, 6H), 3.88 (s, 3H), 3.18 (d, J = 22.1 Hz, 2H), 1.07−1.37 (m, 9H). The phosphonate ester (22.8 g, 75.9 mmol) was dissolved in dry THF (500 mL) over 3 Å molecular sieves stirred at room temperature. After 20 min, NaH (7.28 g, 50% dispersion in mineral oil, 152 mmol) was added and stirring was continued for another 30 min. Aldehyde **10** (24.2 g, 76.0 mmol) was added, and the reaction was monitored by TLC (SiO_2, 7:3 petroleum ether−ethyl acetate) until completion (approximately 48 h). The reaction was quenched with H_2O (150 mL) and 1 N HCl (150 mL), the organic layer was separated, and the aqueous layer was extracted with ether (2 × 200 mL). The combined organic layers were washed with concentrated $NaHCO_3$ (200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated. Recrystallization from hot ethanol gave pale yellow crystals (27.4 g, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.25−7.51 (m, 12H), 7.14 (d, J = 2.0 Hz, 1H), 7.08 (d, J = 15.8 Hz, 1H), 7.04 (dd, J = 2.0, 8.4 Hz, 1H), 6.91 (d, J = 8.5 Hz, 1H), 6.90 (d, J = 15.8 Hz, 1H), 5.20 (s, 2H), 5.17 (s, 2H), 4.36 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 150.0, 142.8, 138.0, 131.6, 131.5, 130.8, 129.8, 129.40, 129.38, 128.76, 128.73, 128.2, 128.1, 126.9, 121.8, 115.8, 114.0, 72.4, 72.1, 61.7, 15.2. A sample for combustion analysis was prepared by recrystallization from Et_2O (colorless needles). Anal. Calcd for $C_{31}H_{28}O_4$: C, 80.15; H, 6.08. Found: C, 79.87; H, 6.34.

(*R*,*R*)-1-(4′-Carbomethoxyphenyl)-2-[3′,5′-bis(benzyloxy)phenyl]-1,2-ethanediol (15). To a cold (0 °C) slurry of $K_3Fe(CN)_6$ (39.5 g, 0.12 mol), K_2CO_3 (16.6 g, 0.12 mol), potassium osmate(VI) dihydrate ($K_2[OsO_2(OH)_4]$) (148 mg, 0.40 mmol, 1.0 mol %), $(DHQD)_2PHAL$ (312 mg, 0.40 mmol, 1.0 mol %), and methanesulfonamide (3.80 g, 40.0 mmol) in *tert*-butyl alcohol (120 mL), water (200 mL), and toluene (120 mL) was added **13** (18.0 g, 40.0 mmol). Stirring was continued at 0 °C until TLC (SiO_2, 1:1 petroleum ether−ethyl acetate) indicated consumption of starting material (48 h). Na_2SO_3 (60 g, 0.48 mol) was added, and the reaction mixture was allowed to warm to rt over the course of 5 h. The resulting green emulsion was extracted with ethyl acetate (4 × 50 mL). The combined organic layers were washed with 5% NaOH, dried ($MgSO_4$),

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(60) Ramage, R.; Griffiths, G. J.; Shutt, F. E.; Sweeney, J. N. A. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1539.

and concentrated to yield crude diol. Purification by flash chromatography (SiO_2 1:1 ethyl acetate−hexane) afforded diol **15** (14.3 g, 74%, >97% ee) as a pale yellow solid. The enantiomeric excess was determined by HPLC analysis of the diol on a Chiralcel OD column. Spectroscopic characterization indicated a 15:1 mixture of methyl and ethyl ester was present: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.25−7.40 (m, 10H), 7.14 (d, J = 8.3 Hz, 2H), 6.47 (t, J = 2.2 Hz, 1H), 6.33 (d, J = 2.2 Hz, 2H), 4.91 and 4.87 (AB pattern, J = 11.7 Hz, 4H), 4.68 (dd, J = 2.5, 7.0 Hz, 1H), 4.52 (dd, J = 3.0, 7.0 Hz, 1H), 4.35 (q, J = 7.1 Hz, 0.13H), 3.86 (s, 2.8H), 2.99 (d, J = 2.5 Hz, 1H), 2.80 (d, J = 3.0 Hz, 1H), 1.35 (t, J = 7.1 Hz, 0.19H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.9, 159.7, 145.0, 141.9, 136.7, 129.5, 129.3, 128.5, 128.0, 127.4, 126.9, 106.1, 102.0, 79.0, 78.5, 70.0, 52.0; $[\alpha]_D$ = +120.8 (c = 1.00, CH_2Cl_2).

(*R*,*R*)-1-(4′-Carbethoxyphenyl)-2-[3′,4′-bis(benzyloxy)-phenyl]-1,2-ethanediol (16). Following the procedure for **15**, $K_3Fe(CN)_6$ (52.6 g, 160 mmol), K_2CO_3 (22.0 g, 160 mmol), $K_2[OsO_2(OH)_4]$ (196 mg, 0.53 mmol, 1 mol %), $(DHQD)_2$-PHAL (414 mg, 0.53 mmol, 1.0 mol %), methanesulfonamide (5.06 g, 53.2mmol), *tert*-butyl alcohol (160 mL), water (266 mL), toluene (160 mL), and **14** (24.0 g, 53.2 mmol) yielded **16** as a pale tan oil (23.3 g, 90%, >97% ee) which was used without further purification. The enantiomeric excess was determined by HPLC analysis of the diol on a Chiralcel OD column. A small quantity of crude product was purified by flash chromatography to give the diol as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.27−7.40 (m, 10H), 7.01 (d, J = 8.2 Hz, 2H), 6.72 (d, J = 8.2 Hz, 1H), 6.71 (d, J = 2.0 Hz, 1H), 6.50 (dd, J = 2.0, 8.2 Hz, 1H), 5.09 (s, 2H), 5.03 and 5.01 (AB pattern, J = 12.2 Hz, 2H), 4.61 (d, J = 7.7 Hz, 1H), 4.51 (d, J = 7.7 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.90 (br s, 1H), 2.65 (br s, 1H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 164.6, 146.5, 146.4, 143.4, 135.12, 135.10, 131.0, 127.6, 127.1, 126.5, 125.9, 125.4, 125.1, 118.4, 112.5, 112.0, 76.8, 69.18, 69.15, 59.1, 12.3; $[\alpha]_D$ = +144.0 (c = 2.63, CH_2Cl_2). Anal. Calcd for $C_{31}H_{30}O_6$: C, 74.68; H, 6.06. Found: C, 74.84; H, 6.42.

(*R*,*R*)-4-(4′-Carbomethoxyphenyl)-5-[3′,5′-bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (17). A solution of **15** (22.7 g, 47 mmol), 2,2-dimethoxypropane (280 mL), *p*-toluenesulfonic acid monohydrate (372 mg, 2.0 mmol), and DMF (95 mL) was heated at reflux (100 °C bath) for 2 h. The reaction mixture was cooled to rt, poured into 0.5% $NaHCO_3$ (150 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Recrystallization from hot hexane yielded acetal **17** (22.3 g, 91%) as colorless needles in two crops: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 1.7, 6.6 Hz, 2H), 7.25−7.34 (m, 12H), 6.56 (t, J = 2.2 Hz, 1H), 6.43 (d, J = 2.2 Hz, 2H), 4.96 (s, 4H), 4.73 (d, J = 8.4 Hz, 1H), 4.59 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H), 1.64 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 166.8, 160.0, 142.1, 138.9, 136.7, 130.1, 129.7, 128.6, 128.0, 127.5, 126.6, 109.8, 105.9, 102.1, 85.3, 84.7, 70.1, 52.1, 27.12, 27.07; $[\alpha]_D$ = +113.0 (c = 2.05, CH_2Cl_2). Anal. Calcd for $C_{33}H_{32}O_6$: C, 75.55; H, 6.15. Found: C, 75.65; H, 6.27.

(*R*,*R*)-4-(4′-Carbethoxyphenyl)-5-[3′,4′-bis(benzyloxy)-phenyl]-2,2-dimethyl-1,3-dioxolane (18). Following the procedure for **17**, diol **16** (22.5 g, 46.0 mmol), 2,2-dimethoxypropane (340 mL), *p*-toluenesulfonic acid monohydrate (880 mg, 4.6 mmol), and anhydrous DMF (135 mL) yielded acetal **18** as a brown oil (2.24 g, 89%) which was carried directly to the next step. A small quantity of crude product was purified by flash chromatography to give the acetal as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.43−7.24 (m, 10H), 7.17 (d, J = 8.3 Hz, 2H), 6.84 (d, J = 8.3 Hz, 1H), 6.82 (d, J = 2.0 Hz, 1H), 6.67 (dd, J = 2.0, 8.3 Hz, 1H), 5.14 (s, 2H), 5.12 and 5.09 (AB pattern, J = 12.3 Hz, 2H), 4.65 (d, J = 8.5 Hz, 1H), 4.53 (d, J = 8.5 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.62 (s, 3H), 1.61 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 166.3, 149.2, 148.9, 142.0, 137.1, 130.3, 129.6, 129.3, 128.4, 127.8, 127.3, 126.2, 120.3, 114.9, 113.9, 109.5, 85.1, 84.7, 71.4, 71.3, 60.9, 27.2, 27.0, 14.3; $[\alpha]_D$ = +103.6 (c = 4.22, CH_2Cl_2). Anal. Calcd for $C_{34}H_{34}O_6$: C, 75.82; H, 6.36. Found: C, 75.82; H, 5.96.

(*R*,*R*)-4-[4′-(Hydroxymethyl)phenyl]-5-[3′,5′-bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (19). To a cold (0 °C) solution of $LiAlH_4$ (2.46 g, 65 mmol) and anhydrous ether (300 mL) was added a solution of **17** (19.4 g, 37 mmol) and anhydrous ether (300 mL) dropwise over 30 min. Stirring was continued for 1 h at 0 °C, after which time the reaction was allowed to warm to ambient temperature. The reaction was quenched with H_2O (2 mL), 15% NaOH (2 mL), and H_2O (6 mL), stirred at rt for 2 h, filtered through a pad of Celite, and concentrated to yield **19** (17.9 g, 97%) as a colorless oil which solidified on standing: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.2−7.4 (m, 14H), 6.54 (t, J = 2.3 Hz, 1H), 6.45 (d, J = 2.3 Hz, 2H), 4.96 (s, 4H), 4.69 (d, J = 8.5 Hz, 1H), 4.67 (d, J = 5.3 Hz, 1H), 4.63 (d, J = 8.5 Hz, 1H), 1.66 (br t, J = 5.3 Hz, 1H), 1.64 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 140.9, 139.3, 136.7, 136.3, 128.5, 128.0, 127.5, 126.97, 126.95, 109.4, 105.9, 101.8, 85.2, 84.9, 70.08, 65.0, 27.16, 27.10; $[\alpha]_D$ = +94.2 (c = 2.05, CH_2Cl_2). Anal. Calcd for $C_{32}H_{32}O_5$: C, 77.40; H, 6.49. Found: C, 77.67; H, 6.62.

(*R*,*R*)-4-[4′-(Hydroxymethyl)phenyl]-5-[3′,4′-bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (20). Ester **18** (21.8 g, 40.5 mmol) was dissolved in diethyl ether (20 mL) and cooled to 0 °C, and solid $LiAlH_4$ (1.69 g, 44.6 mmol) was added portionwise. After 20 min, the reaction mixture was allowed to warm to room temperature and stirred for 24 h. The reaction was quenched with H_2O (1.5 mL), 15% NaOH (1.5 mL), and H_2O (4.5 mL), stirred at rt for 2 h, filtered through a pad of Celite, and concentrated to yield benzyl alcohol **20** (20.1 g, 100%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (m, 14H), 7.13 (d, J = 8.1 Hz, 2H), 6.88 (d, J = 2.0 Hz, 1H), 6.86 (d, J = 8.3 Hz, 1H), 6.69 (dd, J = 2.0, 8.3 Hz, 1H), 5.15 (s, 2H), 5.14 and 5.09 (AB pattern, J = 12.1 Hz, 2H), 4.69 (s, 2H), 4.64 (d, J = 8.5 Hz, 1H), 4.59 (d, J = 8.5 Hz, 1H), 1.64 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 148.6, 140.8, 137.0, 136.9, 135.8, 129.5, 128.3, 127.6, 127.19, 127.15, 126.7, 126.5, 120.1, 114.5, 113.5, 109.0, 84.9, 84.8, 71.2, 71.0, 64.4, 27.03, 26.98; $[\alpha]_D$ = +118.6° (c = 2.05, CH_2Cl_2). Anal. Calcd for $C_{32}H_{32}O_5$: C, 77.40; H, 6.49. Found: C, 77.32; H, 6.58.

(*R*,*R*)-4-[4′-(Hydroxymethyl)phenyl]-5-(3′,5′-dihydroxyphenyl)-2,2-dimethyl-1,3-dioxolane (1). A solution of benzyl alcohol **19** (7.09 g, 14.3 mmol) in ethyl acetate (150 mL) was charged with 10% Pd/C (280 mg) and stirred under 1 atm H_2 at rt. After completion by TLC (SiO_2, 1:1 petroleum ether−ethyl acetate), the reaction mixture was filtered through a Celite column and concentrated to yield **1** (4.52 g, 100%, >97% ee) as a colorless solid which may be recrystallized from petroleum ether/ethyl acetate. The enantiomeric excess was determined by HPLC analysis on a Chiralcel OD column. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.18 (s, 2H), 7.32 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 6.28 (t, J = 2.2 Hz, 1H), 6.23 (d, J = 2.2 Hz, 2H), 4.68 (d, J = 8.5 Hz, 1H), 4.63 (d, J = 5.8 Hz, 2H), 4.59 (d, J = 8.5 Hz, 2H), 4.23 (t, J = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 159.3, 143.3, 140.7, 136.8, 127.8, 127.3, 109.6, 106.0, 103.1, 86.1, 86.0, 64.4, 27.5, 27.4; $[\alpha]_D$ = +112.2 (c = 1.58, EtOH); Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37; Found: C, 68.63; H, 6.61.

(*R*,*R*)-4-[4′-(Hydroxymethyl)phenyl]-5-(3′,4′-dihydroxyphenyl)-2,2-dimethyl-1,3-dioxolane (2). Following the procedure for **1**, benzyl alcohol **20** (5.00 g, 10.1 mmol), ethyl acetate (100 mL), and 10% Pd/C (645 mg) stirred under 1 atm H_2 at room temperature yielded **2** (2.83 g, 89%) as a colorless solid after purification by flash chromatography (SiO_2, 1:1 petroleum ether−ethyl acetate): ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.23 (d, J = 8.1 Hz, 4H), 7.13 (d, J = 8.1 Hz, 4H), 6.51−6.68 (m, 3H), 6.07 (s, 2H), 4.65 (d, J = 8.5 Hz, 1H), 4.58 (s, 2H), 4.51 (d, J = 8.6 Hz, 1H), 1.62 (s, 6H); ^{13}C NMR (67.5 MHz, acetone-d_6) δ 145.2, 145.0, 142.2, 136.2, 128.8, 126.8, 126.6, 118.9, 115.1, 114.1, 108.6, 85.4, 85.2, 63.7, 26.84, 26.78; $[\alpha]_D$ = +124.0 (c = 2.30, CH_3CN). Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.10; H, 6.52.

Ethyl 3,5-Bis(benzyloxy)cinnamate (21). Sodium metal (0.11 g, 4.7 mmol) was dissolved in anhydrous EtOH (50 mL). Triethyl phosphonoacetate (0.70 g, 3.1 mmol) was added at once followed by **8** (1.0 g, 3.1 mmol) after 20 min. The reaction was stirred at rt under N_2 and monitored by TLC (SiO_2, 4:1 petroleum ether−ethyl acetate). The reaction was quenched

with water (100 mL) and extracted with ether (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to yield crude product. Recrystallization from hexane yielded **21** as a pale yellow solid (1.03 g, 84%): ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.57 (d, J = 15.9 Hz, 1H), 7.34−7.42 (m, 10H), 6.74 (d, J = 2.2 Hz, 2H), 6.63 (t, J = 2.2 Hz, 1H), 6.36 (d, J = 15.9 Hz, 1H), 4.24 (q, J = 7.3 Hz, 2H), 1.32 (t, J = 7.3 Hz, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 167.0, 160.2, 144.4, 136.6, 136.4, 128.6, 128.1, 127.5, 118.9, 107.2, 104.2, 70.2, 60.5, 14.3. Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23; Found: C, 77.22; H, 6.23.

Ethyl 3,4-Bis(benzyloxy)cinnamate (22). Following the procedure for **21**, sodium metal (3.13 g, 0.136 mmol), EtOH (750 mL), triethyl phosphonacetate (15.0 g, 66.7 mmol), and **10** (17.4 g, 54.5 mmol) yielded **22** as a pale yellow solid from hexane (16.0 g, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 15.9 Hz, 1H), 7.27−7.45 (m, 10H), 7.10 (d, J = 2.0 Hz, 1H), 7.04 (dd, J = 2.0, 8.3 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 6.22 (d, J = 15.9 Hz, 1H), 5.24 (s, 2H), 5.23 (s, 2H), 4.22 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 149.0, 144.3, 136.9, 136.8, 128.7, 128.6, 127.97, 127.95, 127.3, 127.2, 122.8, 116.2, 114.3, 113.8, 71.4, 71.0. 60.4, 14.3. Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23; Found: C, 77.30; H, 6.42.

***(R,R)*-1-[3′,5′-Bis(benzyloxy)phenyl]-2-(carbethoxy)-1,2-ethanediol (23)**. To a slurry of $K_3Fe(CN)_6$ (988 mg, 3.0 mmol), K_2CO_3 (415 mg, 3.0 mmol), $K_2[OsO_2(OH)_4]$ (3.7 mg, 0.01 mmol, 1 mol %), $(DHQD)_2PHAL$ (7.8 mg, 0.01 mmol, 1.0 mol %), and methanesulfonamide (95 mg, 1.0 mmol) in *tert*-butyl alcohol (3 mL), water (5 mL), and toluene (3 mL) was added **21** (388 mg, 1.0 mmol). Stirring was continued at room temperature until TLC (SiO_2, 7:3 petroleum ether−ethyl acetate) indicated comsumption of starting material (72 h). Na_2SO_3 (1.5 g, 12 mmol) was added, and the reaction mixture was allowed to stir for an additional 2.5 h. The resulting green emulsion was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with 5% NaOH, dried ($MgSO_4$), and concentrated to yield crude diol. Purification by flash chromatography (SiO_2, 3:2 petroleum ether−ethyl acetate) yielded **23** as a colorless solid (350 mg, 83%, >99% ee). The enantiomeric excess was determined by HPLC analysis of the diol on a Chiralcel OD column. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.30−7.42 (m, 10H), 6.65 (d, J = 2.2 Hz, 2H), 6.55 (t, J = 2.2 Hz, 1H), 5.02 (s, 4H), 4.93 (dd, J = 2.8, 5.7 Hz, 1H), 4.32 (dd, J = 2.8, 7.4 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 3.03 (d, J = 5.7 Hz, 1H), 2.65 (d, J = 7.4 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 172.6, 160.1, 142.5, 136.8, 128.6, 128.0, 127.6, 105.5, 101.6,74.5, 74.3, 70.2, 62.2, 14.1; H, 6.48; $[\alpha]_D$ = −6.64 (c = 1.96, CH_2Cl_2). Anal. Calcd for $C_{25}H_{26}O_6$: C, 71.07; H, 6.20. Found: C, 70.99; H, 6.48.

***(R,R)*-1-[3′,4′-Bis(benzyloxy)phenyl]-2-Carbethoxy-1,2-ethanediol (24)**. Following the procedure for **23**, $K_3Fe(CN)_6$ (43.0 g, 0.13 mol), K_2CO_3 (18.1 g, 0.13 mol), $K_2[OsO_2(OH)_4]$ (0.16 g, 0.44 mmol, 1 mol %), $(DHQD)_2PHAL$ (343 mg, 0.44 mmol, 1 mol %), methanesulfonamide (4.1 g, 43 mmol), *tert*-butyl alcohol (130 mL), water (220 mL), toluene (130 mL), and **22** (16.9 g, 43.4 mmol) yielded **24** (16.7 g, 91%, >99% ee) as a colorless solid after flash chromatography (SiO_2, 3:2 petroleum ether−ethyl acetate). The enantiomeric excess was determined by HPLC analysis of the diol on a Chiralcel OD column. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.44 (m, 10H), 7.04 (s, 1H), 6.91 and 6.89 (AB pattern, J = 8.2 Hz, 2H), 5.15 (s, 2H), 5.14 (s, 2H), 4.86 (dd, J = 3.2, 6.7 Hz, 1H), 4.26 (dd, J = 3.2, 5.9 Hz, 1H), 4.21 (q, J = 7.1 Hz, 1H), 4.19 (q, J = 7.1 Hz, 1H), 3.02 (d, J = 5.9 Hz, 1H), 2.59 (d, J = 6.7 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 149.0, 148.8, 137.22, 137.16, 133.3, 128.4, 127.80, 127.76, 127.4, 127.2, 119.5, 114.9, 113.5, 74.6, 74.2, 71.4, 71.3, 62.1, 14.5; $[\alpha]_D$ = −2.70 (c = 2.33, CH_2Cl_2). A small amount was recrystallized from ethyl acetate−petroleum ether for analysis. Anal. Calcd for $C_{25}H_{26}O_6$: C, 71.07; H, 6.20. Found: C, 71.14; H, 6.24.

***(R,R)*-4-(Carbethoxy)-5-[3′,5′-Bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (25).** Following the procedure for **17**, diol **23** (296 mg, 0.70 mmol), 2,2-dimethoxypropane (10.5 mL), *p*-toluenesulfonic acid monohydrate (14 mg, 0.074 mmol), and anhydrous DMF (3.5 mL) yielded **25** (310.5 mg, 96%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.42 (m, 10H), 6.67 (d, J = 2.2 Hz, 2H), 6.56 (t, J = 2.2 Hz, 1H), 5.09 (d, J = 7.4 Hz, 1H), 5.02 (s, 4H), 4.30 (d, J = 7.4 Hz, 1H), 4.23 (q, J = 7.1 Hz, 2H), 1.56 (s, 3H), 1.52 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 160.2, 140.6, 136.9, 128.7, 128.1, 127.6, 111.8, 105.7, 102.0, 81.3, 80.6, 70.3, 61.6, 27.0, 25.9, 14.3; $[\alpha]_D$ = +28.7 (c = 3.41, CH_2Cl_2). Anal. Calcd for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.82; H, 6.69.

***(R,R)*-4-(Carbethoxy)-5-[3′,4′-Bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (26).** Following the procedure for **17**, diol **24** (15.6 g, 36.9 mmol), 2,2-dimethoxypropane (550 mL), *p*-toluenesulfonic acid monohydrate (740 mg, 3.9 mmol), and anhydrous DMF (185 mL) yielded **26** (17.0 g, 100%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.44 (m, 10H), 7.01 (s, 1H), 6.89 and 6.92 (AB pattern, J = 8.2 Hz, 2H), 5.17 and 5.12 (AB pattern, J = 11.4 Hz, 2H), 5.03 (d, J = 7.6 Hz, 1H), 4.22 (d, J = 7.6 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.54 (s, 3H), 1.51 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 149.2, 149.1, 137.2, 130.9, 128.5, 127.83, 127.80, 127.4, 127.3, 119.9, 114.9, 113.4, 111.4, 81.2, 80.5, 71.4, 71.3, 61.4, 26.9, 25.8, 14.2; $[\alpha]_D$ = +34.67 (c = 2.32, CH_2Cl_2). A small amount was purified by flash chromatography (SiO_2, 4:1 petroleum ether−ethyl acetate) for analysis. Anal. Calcd for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.54; H, 6.65.

***(R,R)*-4-(Hydroxymethyl)-5-[3′,5′-bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (27).** To a cold (0 °C) solution of $LiAlH_4$ (1.10 g, 28.9 mmol) and anhydrous ether (200 mL) was added a solution of **25** (7.20 g, 15.6 mmol) and anhydrous ether (200 mL) dropwise over 30 min. The reaction was then allowed to warm to rt under N_2 and left to stir until TLC (SiO_2 7:3 petroleum ether−ethyl acetate) indicated consumption of starting material (45 min). The reaction was quenched with water (80 mL), acidified with 5% H_2SO_4 (80 mL), and allowed to stir at rt (1 h). The mixture was then extracted with ether (3 × 100 mL), dried (Na_2SO_4), and concentrated to yield **27** as a colorless solid (6.29 g, 96%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.41 (m, 10H), 6.62 (d, J = 2.1 Hz, 2H), 6.55 (t, J = 2.1 Hz), 5.02 (s, 4H), 4.82 (d, J = 8.5 Hz, 1H), 3.77−3.84 (m, 2H), 3.59 (m, 1H), 1.87 (m, 1H), 1.52 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 160.2, 140.4, 136.7, 128.6, 128.0, 127.5, 109.3, 105.5, 101.8, 83.3, 78.4, 70.2, 60.4, 27.1; $[\alpha]_D$ = −4.05 (c = 2.05, CH_2Cl_2). Anal. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71. Found: C, 74.41; H, 6.90.

***(R,R)*-4-(Hydroxymethyl)-5-[3′,4′-bis(benzyloxy)phenyl]-2,2-dimethyl-1,3-dioxolane (28).** Following the procedure for **27**, $LiAlH_4$ (2.45 g, 63.9 mmol), anhydrous ether (400 mL), and **26** (16.4 g, 35.5 mmol) yielded **28** as a white solid (14.5 g, 97%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.28 (m, 10H), 6.95 (d, J = 1.8 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.86 (dd, J = 1.8, 8.2 Hz, 1H), 5.17 and 5.14 (AB pattern, J = 12.4 Hz, 2H), 5.14 (s, 2H), 4.77 (d, J = 8.5 Hz, 1H), 3.74 (m, 2H), 3.52 (m, 1H), 1.85 (dd, J = 4.0, 8.4 Hz, 1H), 1.50 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 137.2, 130.8, 128.5, 127.82, 127.79, 127.4, 127.3, 119.8, 115.0, 113.8, 109.1, 83.3, 78.3, 71.4, 71.3, 60.3, 27.1, 27.0; $[\alpha]_D$ = −8.31 (c = 3.02, CH_2Cl_2). Anal. Calcd for $C_{26}H_{28}O_5$: C, 74.26; H, 6.71. Found: C, 74.16; H, 6.71.

***(R,R)*-4-(Hydroxymethyl)-5-[3′,5′-dihydroxyphenyl]-2,2-dimethyl-1,3-dioxolane (3).** Following the procedure for **1**, benzyl alcohol **27** (2.90 g, 6.90 mmol), ethyl acetate (50 mL), and 10% Pd/C (250 mg) stirred under 1 atm H_2 at room temperature yielded **8** (1.67 g, 100%, >99% ee) as a colorless solid (mp 147−148 °C). The enantiomeric excess was determined by HPLC analysis on a Chiralcel OD column. ^{1}H NMR (400 MHz, acetone-d_6) δ 8.21 (s, 2H), 6.41 (d, J = 2.2 Hz, 2H), 6.27 (t, J = 2.2 Hz, 1H), 4.70 (d, J = 8.1 Hz, 1H), 3.57−3.83 (m, 4H), 1.44 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (67.5 MHz, acetone-d_6) δ 159.4, 142.5, 109.4, 105.6, 102.9, 85.2, 79.6, 61.6, 27.4, 27.3; $[\alpha]_D$ = −7.08 (c = 1.56, EtOH). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.36; H, 7.04.

***(R,R)*-4-(Hydroxymethyl)-5-[3′,4′-dihydroxyphenyl]-2,2-dimethyl-1,3-dioxolane (4).** Following the procedure for **1**, **28** (4.15 g, 9.87 mmol), ethyl acetate (150 mL), and 10% Pd/C (370 mg) yielded **4** (1.67 g, 100%) as a colorless, sticky solid. Evaporation of a CH_2Cl_2 solution yielded a colorless

powder (mp 112−113 °C). The enantiomeric excess was determined by HPLC analysis on a Chiralcel OD column. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.89 (s, 1H), 7.88 (s, 1H), 6.92 (d, J = 1.9 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.74 (dd, J = 2.0, 8.1 Hz, 1H), 4.71 (d, J = 8.5 Hz, 1H), 3.8 (m, 1H), 3.7 (m, 1H), 3.55 (m, 1H), 1.46 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) d 145.9, 145.7, 131.4, 119.2, 115.9, 114.5, 109.1, 85.3, 79.8, 61.5, 27.47, 27.43; $[\alpha]_D$ = +18.0 (c = 1.91, EtOH). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.85; H, 6.95.

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