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Regiodivergent Addition of Phenols to Allylic Oxides

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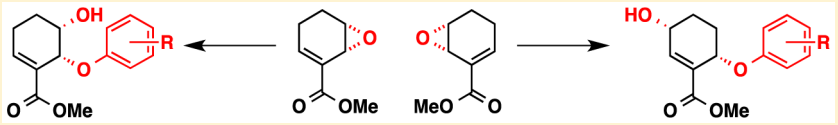
Supporting Information

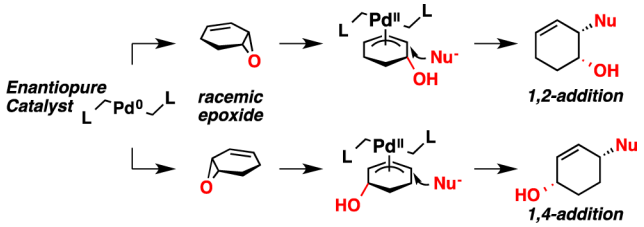


ABSTRACT: The regiodivergent addition of substituted phenols to allylic oxides has been demonstrated using C_2-symmetric palladium complexes. Complex phenol donors tyrosine, estradiol, and griseofulvin follow the predictive model.

INTRODUCTION

The Tsuji–Trost reaction is a powerful method to append both O- and C-donors to η^3-allyl systems.[1] The η^3-allyl progenitor structures include allylic esters, carbonates, halides, and oxides. Internal allylic oxides[2] remain one of the few systems that retain a marker of stereochemical induction with the newly liberated carbinol. The origin of the products can be traced to the diastereomeric η^3-allyl intermediate and stereoisomer of oxide employed. We have recently identified[3] a system capable of the conversion of racemic allylic oxides to distinct enantioenriched regioisomers using achiral phenol donors (Scheme 1). The

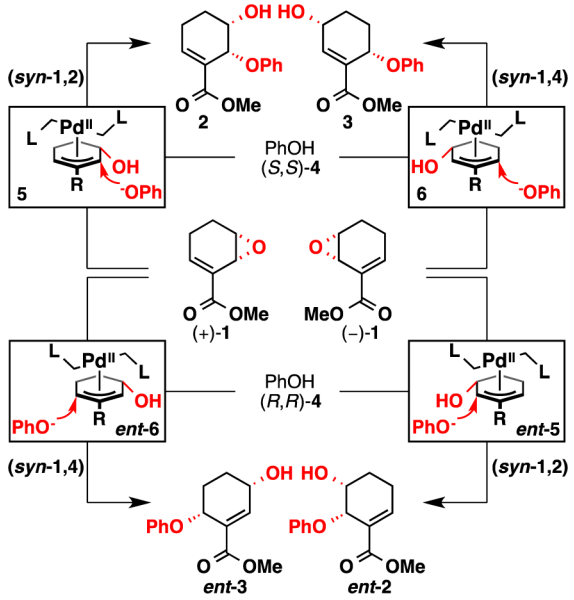
Scheme 1. Allylic Oxide Regio-resolution (AORR)



allylic oxide regio-resolution (AORR) allowed the preparation of enantioenriched carbasugar natural products. We have now expanded this study to include a diverse array of achiral and chiral phenol donors.

The synthesis of aryl ether bonds was chosen for study due to their abundance within natural products, chiral catalyst scaffolds, and availability of phenol precursors. Prior to a full examination of chiral phenol structures with oxide **1**, available in four steps from benzoic acid, a series of achiral phenol donors were studied using the developed predictive model.[3] The absolute stereochemistry of addition was determined using *para*-methoxyphenol under oxidative cleavage conditions.[3,4] The collected data were able to provide a working model for regiodivergence using ligand **4**[5] with the donor phenols. In parallel with Lloyd-Jones[6] and Trost's[1d] studies, a model was generated for oxide **1** that would be necessary for studying the AORR with complex phenol donors. It is predicted the (+)-**1** enantiomer with the (*S*,*S*)-**4** ligand will produce intermediate **5**, and is engaged by phenoxide to produce *syn*-1,2 product **2**. Similarly, the (−)-**1** enantiomer provides intermediate **6** that proceeded to *syn*-1,4 product **3**. The (*R*,*R*)-**4** ligand mirrors the regiodivergence of the (*S*,*S*)-**4** ligand with each enantiomer of oxide producing the alternative *syn*-addition products (Scheme 2).

Scheme 2. Allylic Oxide Regio-resolution Model



RESULTS AND DISCUSSION

The utility of the AORR approach was advanced with numerous phenols. Native phenol provided useful enantioinduction (Table 1, entry 1, 98:2 er for 1,2-addition, 91:9 for 1,4-addition) in a combined yield of 58%. Allylic oxide **1** was not recovered, and the mass balance is suspected to be due to

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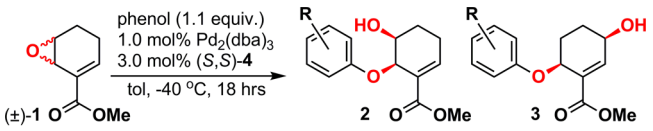
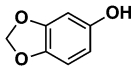
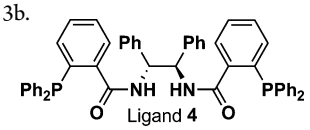
Table 1. Scope of Regiodivergence



entry	phenol	1 er[a]	product	2 er[b]	product	3 er[b]	% yield[c] (1:2:3)
1	R = H	-	2a	98:2	3a	91:9	0:31:27
2[d]	R = 4-Me	57:43	2b	96:4	3b	93:7	2:39:34
3	R = 4-*t*Bu	52:48	2c	96:4	3c	91:9	24:28:34
4[d]	R = 4-OMe	56:44	2d	85:15	3d	95:5	1:48:35
5	R = 4-NHBoc	51:49	2e	90:10	3e	84:16	29:21:23
6	R = 4-NO_2	50:50	2f	97:3	3f	98:2	64:4:4
7	R = 2,4-dimethyl	68:32	2g	94:6	3g	84:16	8:31:34
8	R = 3,5-dimethyl	52:48	2h	90:10	3h	91:9	23:31:34
9	R = 2-nap	-	2i	84:16	3i	84:16	0:33:33
10	R = 1-nap	-	2j	80:20	3j	88:12	0:35:38
11		-	2k	90:10	3k	95:5	0:29:23

[a]Enantiomeric ratio of recovered epoxide was determined by GC analysis. [b]Enantiomeric ratios were determined by LC analysis against prepared racemic standards. [c]Yield refers to isolated yields following silica gel chromatography. [d]Entries 2 and 4 have been previously reported; see ref 3b.

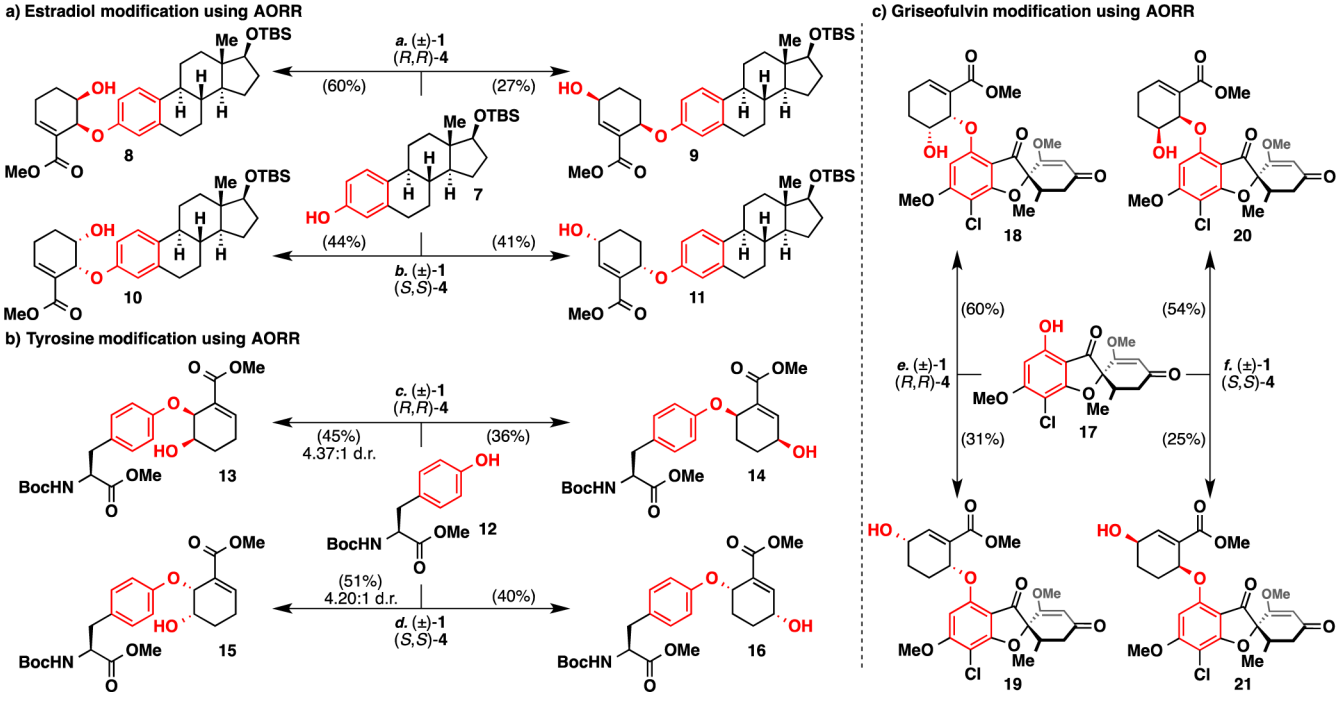


competitive β-hydride elimination. Alkyl substitution (entries 2,[7] 3) proved similar in stereoinduction, and the recovered allylic oxide was weakly enantiomerically enriched. One possible explanation for the lack of resolution of recovered oxide **1** is each oxide enantiomer is forming the palladium-allyl at an identical rate. The newly formed allyl complexes are then steered toward each phenol addition product with high fidelity. Other phenol donors such as electron releasing substituents were similarly well tolerated (entries 4[7] and 5) with the Boc-protected aniline providing lower conversion. 4-Nitrophenol provided the highest enantioinduction (97:3 and 98:2 for 1,2- and 1,4-addition respectively, entry 6) albeit with low yield and degradation upon standing. Sterically larger arenes, including *ortho*- and *meta*-substitution (entry 7 and 8 respectively) behaved similarly, and both 1- and 2-naphthol offered less selectivity overall (entries 9 and 10). Interestingly, sesamol provided high enantioinduction for both addition modes (entry 11). In all cases, the absence of palladium did not result in any conversion.

With these data in hand, the application of the AORR method upon chiral phenolic scaffolds was examined. The substrates were chosen for their biological activity and for the emergence of diastereomers by competitive 1,2- or 1,4-addition to the palladium-allyl. Estradiol, tyrosine, and griseofulvin were selected and regiodiverged into four distinct diastereomers under catalyst control.

Silyl protected estradiol[8] was first examined to gauge the suitability of larger phenol substrates with remote stereochemical elements for the regiodivergence (Scheme 3a). Interestingly, the regiodivergence provided high stereoselectivity for the 1,2- and 1,4-addition products with no detectable diastereomers. Using (*R*,*R*)-**4**, the 1,2-adduct was obtained in

Scheme 3. Applying the AORR Method with Estradiol, Tyrosine, and Griseofulvin[a]



[a]Reagents and conditions: (a) 5.0 mol % $Pd_2(dba)_3$, 15.0 mol % (*R*,*R*)-**4**, toluene, **1** (1.4 equiv), −40 °C, 96 h; (b) 5.0 mol % $Pd_2(dba)_3$, 15.0 mol % (*S*,*S*)-**4**, **1** (1.4 equiv), toluene, −40 °C, 96 h; (c) 1.0 mol % $Pd_2(dba)_3$, 3.0 mol % (*R*,*R*)-**4**, **1** (1.0 equiv), toluene, −40 °C, 72 h; (d) 1.0 mol % $Pd_2(dba)_3$, 3.0 mol % (*S*,*S*)-**4**, **1** (1.1 equiv), toluene, −40 °C, 72 h; (e) 5.0 mol % $Pd_2(dba)_3$, 15.0 mol % (*R*,*R*)-**5**, toluene, **1** (1.8 equiv), −40 °C, 18 h; (f) 5.0 mol % $Pd_2(dba)_3$, 15.0 mol % (*S*,*S*)-**4**, toluene, **1** (1.8 equiv), −40 °C, 18 h.

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60% yield and the 1,4-adduct in 27% yield. The enhanced yield of the 1,2-product was surprising considering the achiral phenols were roughly equal in reactivity to produce 1,2- and 1,4-products. Switching to the (*S*,*S*)-**4** ligand, the 1,2-adduct was obtained in 44% yield with an increase to 41% for the 1,4-addition product as compared to the (*R*,*R*)-**4** ligand.

A more challenging regiodivergence was examined using tyrosine (Scheme 3b). The protected amino acid, as compared to estradiol, was predicted to be prone to mixtures of diastereomers from carbamate chelation to palladium[9] and/or populations of rotamers. Applying the AORR conditions resulted in the isolation of the 1,2- and 1,4-addition products in similar yield for each enantiomer of applied ligand. The additional constraints of the tyrosine moiety were reflected in the appearance of diastereomers for the 1,2-addition products: 4.37:1 for **13** and 4.20:1 for **15** in 45% and 51% yield, respectively. The 1,4-adducts were isolated as single diastereomers in 40% yield for **14** and 36% yield for **16**. The similarity in structure required the isolation of the 1,2- and 1,4-adducts as a comixture with ^{1}H NMR integration to determine the yield of each isomer. The estradiol and tyrosine phenol substrates provided high regiodivergence to the desired stereoisomers. Moving forward, the application of this method toward a multiply substituted hindered chiral phenol would demonstrate the robustness of the method with diverse phenolic substrates.

Polyketides continue to provide diverse functionality including spirocoumaranones such as griseofulvin,[10] geodin,[11] and Sch202596.[12] The interesting biological properties of these phenolic spirocycles make them ideal substrates for analog generation using AORR.

The native structure of griseofulvin has recently been advanced as a cancer treatment[13] and is readily available in large quantities. Cleavage of the C-4 methyl[14] provided a chiral phenol donor that was then studied for the AORR (Scheme 3c).

In parallel with the estradiol and tyrosine studies, applying the (*R*,*R*)-**4** ligand resulted in two products. The 1,2-adduct **18** (60%) was dominant as compared to the 1,4-adduct **19** (31%) with the remaining mass balance attributed to recovered griseofulvin (**17**). Similar to the tyrosine studies, the complexity of the 1,2- and 1,4-adducts required isolation as a comixture and determination of yield by ^{1}H NMR integration. Crude reaction mixture analysis showed no starting material remained, with griseofulvin being regenerated from degradation of the 1,2- and 1,4-adducts during isolation.[15] The (*S*,*S*)-**4** ligand proved similar in reactivity to provide 1,2-adduct **20** (54%) and 1,4-adduct **21** (25%) and recovered griseofulvin. The 1,2-addition products for both reactions was approximately double in yield as compared to the 1,4-products, a result we had observed previously with estradiol (Scheme 2a, **8**, (*R*,*R*)-**4** ligand), which appears to substrate dependent. The presence of diastereomers associated with off-catalyst addition modes was less than 2% when examining the ^{1}H NMR of the product mixture for both ligands.

In conclusion, an asymmetric addition to an allylic oxide has been applied to a series of achiral phenol donors resulting in an asymmetric regiodivergent reaction. The extension of the allylic oxide regioresolution was then tested upon three complex natural products using the predicted model and efficiently generated the desired targets.

EXPERIMENTAL SECTION

Preparation and characterization of oxide **1**, as well as compounds **2b**, **3b**, **2d**, and **3d**, have been reported previously.[3]

General Procedure A. Racemic epoxide **1** (43.0 mg, 0.279 mmol, 1.0 equiv) was dissolved in 2.0 mL of toluene in a flame-dried vial outfitted with a septum followed by the addition of phenol (15.8 mg, 0.149 mmol, 0.6 equiv). The resulting solution was degassed with argon and cooled to −40 °C. In a separate vial, $Pd_2(dba)_3$ (2.4 mg, 1.0 mol %) and (*S*,*S*)-**4**[5] (6.6 mg, 3.0 mol %) were dissolved in 1.0 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. The reaction was allowed to stir for 6 h before additional phenol (16.4 mg (0.174 mmol, 0.6 equiv) was added, and the solution was purged with argon. The reaction was stirred for an additional 12 h at −40 °C before the reaction was quenched with an aqueous NH_4Cl solution, extracted with ether (2 × 1.5 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The crude oil was purified by column chromatography (9:1 hexanes/EtOAc v/v) to give 1,2-product **2a** (21.5 mg, 31% yield, 98:2 e.r.) and 1,4-product **3a** (18.7 mg, 27% yield, 91:9 e.r.) as white solids.

Analytical standards used for the characterization of **2a** and **3a** were prepared from a separate trial giving enantiomeric ratios of 97:3 and 95:5 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(phenoxy)-cyclohex-1-enecarboxylate (2a). $[\alpha]_D^{20.0}$ −127.7 (*c* 1.00, $CHCl_3$); Mp 63−66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.25 (m, 2H), 7.20−7.15 (m, 2H), 7.15−7.12 (m, 1H), 7.02−6.91 (m, 1H), 5.28 (d, *J* = 3.7 Hz, 1H), 3.92 (dt, *J* = 11.5, 3.8 Hz, 1H), 3.61 (s, 3H), 2.54 (m, 1H), 2.39−2.26 (m, 1H), 2.10−1.93 (m, 1H), 1.93−1.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 159.7, 144.1, 129.6, 122.0, 117.4, 115.9, 73.2, 69.6, 51.9, 25.4, 25.3; IR (film, cm^{-1}) 3435, 2950, 2360, 1710, 1595, 1490, 1250, 1227, 750; TLC R_f = 0.37 (7:3 hexanes/EtOAc v/v); HPLC 97:3 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/methanol. Retention times: R_T = 8.0 min, 10.7 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1047.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(phenoxy)-cyclohex-1-enecarboxylate (3a). $[\alpha]_D^{20.0}$ −20.8 (*c* 0.50, $CHCl_3$); Mp 36−39 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.25 (m, 2H), 7.12 (t, *J* = 1.8 Hz, 1H), 7.04−6.95 (m, 3H), 5.14 (br s, 1H), 4.34 (d, *J* = 8.5 Hz, 1H), 3.75 (s, 3H), 2.24−2.14 (m, 1H), 2.05−1.96 (m, 1H), 1.91−1.77 (m, 1H), 1.61 (tt, *J* = 14.2, 3.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 158.0, 145.8, 130.6, 129.7, 121.7, 117.0, 68.2, 67.9, 52.2, 26.5, 25.4; IR (film, cm^{-1}) 3403, 2950, 2358, 1718, 1490, 1250, 1226, 751; TLC R_f = 0.25 (7:3 hexanes/EtOAc v/v); HPLC 95:5 e.r., Chiral HPLC eluting at 1.0 mL/min with 90% hexanes/isopropanol. Retention times: R_T = 5.9 min, 6.6 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1055.

1,2-Product **2c** (21.9 mg, 28%, 96:4 e.r.) and 1,4-product **3c** (26.9 mg, 34%, 91:9 e.r.). Recovered epoxide **1** (9.5 mg, 24%, 52:48 e.r.).

Analytical standards used for the characterization of **2c** and **3c** were prepared from a separate trial giving enantiomeric ratios of 96:4 and 91:9 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(4-*tert*-butylphenoxy)-cyclohex-1-enecarboxylate (2c). $[\alpha]_D^{20.0}$ −92.4 (*c* 1.00, $CHCl_3$); Mp 53−56 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.24 (m, 2H), 7.15 (dd, *J* = 4.7, 3.0 Hz, 1H), 7.11−7.03 (m, 2H), 5.26 (d, *J* = 3.8 Hz, 1H), 3.90 (dt, *J* = 11.2, 3.7 Hz, 1H), 3.61 (s, 3H), 2.61−2.46 (m, 1H), 2.39−2.23 (m, 1H), 2.15−1.90 (m, 1H), 1.91−1.79 (m, 1H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 157.3, 144.7, 144.0, 129.4, 126.4, 116.7, 73.1, 69.5, 51.9, 34.3, 31.6, 25.4, 25.3; IR (film, cm^{-1}) 3435, 2953, 2358, 1716, 1509, 1220, 1043; TLC R_f = 0.42 (7:3 hexanes/EtOAc v/v); HPLC 96:4 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/isopropanol. Retention times: R_T = 6.7 min, 7.2 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{18}H_{24}O_4$ 304.1675, found 304.1661.

Methyl (3*R*,6*S*)-3-Hydroxy-6-O-(4-*tert*-butylphenoxy)-cyclohex-1-enecarboxylate (3c). $[\alpha]_D^{20.0}$ −10.1 (*c* 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.27 (m, 2H), 7.11 (br s, 1H), 6.96−6.91 (m, 2H), 5.11 (br s, 1H), 4.37−4.28 (m, 1H), 3.75 (s, 3H),

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2.24−2.15 (m, 1H), 2.03−1.95 (m, 1H), 1.88−1.77 (m, 1H), 1.58 (tt, J = 14.2, 3.4 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 155.7, 145.8, 144.3, 130.7, 126.4, 116.3, 68.0, 67.9, 52.2*, 52.2*, 34.3, 31.7, 26.5, 25.3; IR (film, cm^{-1}) 3399, 2952, 2867, 2359, 1718, 1508, 1250, 1225, 1030, 757; TLC R_f = 0.29 (7:3 hexanes/EtOAc v/v); HPLC 91:9 e.r., Chiral HPLC eluting at 1.0 mL/min with 90% hexanes/isopropanol. Retention times: R_T = 4.6 min, 6.0 min; HRMS (EI$^+$) m/z calcd for $C_{18}H_{24}O_4$ 304.1675, found 304.1673. * denotes presumed rotamers in a 1:1 ratio.

1,2-Product **2e** (20.7 mg, 21%, 90:10 e.r.) and 1,4-product **3e** (22.3 mg, 23%, 84:16 e.r.). Recovered epoxide **1** (12.1 mg, 29%, 51:49 e.r.).

Analytical standards used for the characterization of **2e** and **3e** were prepared from a separate trial giving enantiomeric ratios of 94:6 and 89:11 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(4-*N*-Bocphenoxy)-cyclohex-1-enecarboxylate (2e). $[\alpha]_D^{20.0}$ −92.4 (c 0.50, $CHCl_3$); Mp 134−136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27−7.23 (m, 2H), 7.15 (dd, J = 4.7, 3.0 Hz, 1H), 7.10−7.04 (m, 2H), 6.35 (s, 1H), 5.15 (d, J = 3.6 Hz, 1H), 3.88 (ddt, J = 12.2, 8.5, 3.8 Hz, 1H), 3.61 (s, 3H), 2.58−2.47 (m, 1H), 2.37−2.24 (m, 1H), 2.03−1.91 (m, 1H), 1.90−1.81 (m, 1H), 1.50 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.6, 155.6, 153.2, 144.1, 132.7, 129.3, 120.2, 118.1, 80.5, 73.9, 69.5, 51.9, 28.5, 25.4, 25.3; IR (film, cm^{-1}) 3481, 3358, 2974, 2921, 1720, 1695, 1511, 1210, 1150; TLC R_f = 0.13 (7:3 hexanes/EtOAc v/v); HPLC 94:6 e.r., Chiral HPLC eluting at 1.00 mL/min with 95% hexanes/isopropanol for 20.00 min and then a gradient from 5% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 33.1 min, 35.5 min; HRMS (EI$^+$) m/z calcd for $C_{19}H_{25}O_6N$ 363.1682, found 363.1686.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(4-*N*-Bocphenoxy)-cyclohex-1-enecarboxylate (3e). $[\alpha]_D^{20.0}$ −19.8 (c 0.50, $CHCl_3$); Mp 61−65 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28−7.23 (m, 2H), 7.10 (dd, J = 1.9, 1.6 Hz, 1H), 6.97−6.92 (m, 2H), 6.37 (s, 1H), 5.01 (t, J = 3.0 Hz, 1H), 4.36−4.29 (m, 1H), 3.74 (s, 3H), 2.18−2.09 (m, 1H), 2.02−1.94 (m, 1H), 1.81 (tdd, J = 13.0, 10.4, 2.9 Hz, 1H), 1.58 (tt, J = 14.5, 3.0 Hz, 1H), 1.49 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 154.1, 153.2, 145.8, 132.5, 130.6, 120.7, 118.0, 80.5, 69.2*, 69.2*, 67.9, 52.2*, 52.2*, 28.5, 26.5, 25.3; IR (film, cm^{-1}) 3342, 2950, 1702, 1509, 1254, 1220, 1160; TLC R_f = 0.12 (7:3 hexanes/EtOAc v/v); HPLC 89:11 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/isopropanol for 20.00 min and then a gradient from 5% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 31.9 min, 34.0 min; HRMS (EI$^+$) m/z calcd for $C_{19}H_{25}O_6N$ 363.1682, found 363.1688. * denotes presumed rotamers in a 1:1 ratio.

1,2-Product **2f** (3.2 mg, 4%, 97:3 e.r.) and 1,4-product **3f** (2.9 mg, 4%, 98:2 e.r.). Recovered epoxide **1** (27.6 mg, 64%, 50:50 e.r.).

Analytical standards used for the characterization of **2f** and **3f** were prepared from a separate trial giving enantiomeric ratios of 98:2 and 98:2 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-O-(4-nitrophenoxy)-cyclohex-1-enecarboxylate (2f). $[\alpha]_D^{20.0}$ −108.2 (c 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) 8.22−8.17 (m, 2H), 7.26−7.21 (m, 3H), 5.44 (d, J = 3.7 Hz, 1H), 3.96 (ddt, J = 12.0, 8.0, 3.8 Hz, 1H), 3.66 (s, 3H), 2.58 (dtd, J = 20.3, 5.4, 2.3 Hz, 1H), 2.45−2.32 (m, 1H), 2.05−1.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.1, 165.0, 145.1, 141.9, 128.2, 125.9, 116.7, 73.1, 69.8, 52.1*, 52.1*, 25.7, 25.2; IR (film, cm^{-1}) 3458, 2952, 1710, 1590, 1509, 1493, 1330, 1250; TLC R_f = 0.12 (7:3 hexanes/EtOAc v/v); HPLC 98:2 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/isopropanol for 20.00 min and then a gradient from 5% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 35.9 min, 38.4 min; HRMS (EI$^+$) m/z calcd for $C_{14}H_{15}NO_6$ 239.0899, found 239.0898. * denotes presumed rotamers in a 1:1 ratio

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(4-nitrophenoxy)-cyclohex-1-enecarboxylate (3f). $[\alpha]_D^{20.0}$ +37.5 (c 0.50, $CHCl_3$) (analytical standard was obtained as the enantiomer of **3f** from the (*R*,*R*)-**4**); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24−8.17 (m, 2H), 7.18 (dd, J = 2.2, 1.4 Hz, 1H), 7.06−7.00 (m, 2H), 5.28 (s, 1H), 4.38 (s, 1H), 3.74 (s, 3H), 2.21−2.13 (m, 1H), 2.10−2.02 (m, 1H), 1.88−1.69 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.9, 163.2, 146.7, 141.8, 129.4, 126.2, 115.9, 68.5, 67.6, 52.3, 26.4, 25.6; IR (film, cm^{-1}) 3391, 2950, 1708, 1438, 1255, 1041, 756; TLC R_f = 0.09 (7:3 hexanes/EtOAc v/v); HPLC 98:2 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/isopropanol for 20.00 min then a gradient from 5% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 31.9 min, 34.0 min; HRMS (EI$^+$) m/z calcd for $C_{14}H_{15}NO_6$ 239.0899, found 239.0895.

1,2-Product **2g** (23.4 mg, 31%, 96:4 e.r.) and 1,4-product **3g** (25.8 mg, 34%, 84:16 e.r.). Recovered epoxide **1** (0.4 mg, 1%, 68:32 e.r.).

Analytical standards used for the characterization of **2g** and **3g** were prepared from a separate trial giving enantiomeric ratios of 85:15 and 90:10 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(2,4-dimethylphenoxy)-cyclohex-1-enecarboxylate (2g). $[\alpha]_D^{20.0}$ −106.6 (c 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.19−7.11 (m, 2H), 7.00−6.89 (m, 2H), 5.20 (d, J = 3.7 Hz, 1H), 3.89 (ddt, J = 12.0, 8.0, 3.7 Hz, 1H), 3.57 (s, 3H), 2.62−2.47 (m, 1H), 2.41−2.31 (m, 1H), 2.25 (s, 3H), 2.14 (s, 3H), 2.07−1.96 (m, 1H), 1.93−1.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7, 155.6, 143.8, 131.5, 131.0, 129.8, 127.7, 127.3, 115.7, 73.6, 69.6, 51.8, 25.4, 25.4, 20.7, 16.6; IR (film, cm^{-1}) 3434, 2949, 1716, 1489, 1250, 1217, 1042; TLC R_f = 0.50 (7:3 hexanes/EtOAc v/v); HPLC 85:15 e.r., Chiral HPLC eluting at 1.0 mL/min with 90% hexanes/isopropanol. Retention times: R_T = 3.7 min, 4.2 min; HRMS (EI$^+$) m/z calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1357.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(2,4-dimethylphenoxy)-cyclohex-1-enecarboxylate (3g). $[\alpha]_D^{20.0}$ −19.4 (c 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.10 (dd, J = 2.2, 1.3 Hz, 1H), 7.03−6.92 (m, 3H), 5.09 (br s, 1H), 4.39−4.27 (m, 1H), 3.74 (s, 3H), 2.26 (s, 3H), 2.15 (s, 3H), 2.13−2.06 (m, 1H), 2.05−1.96 (m, 1H), 1.93−1.78 (m, 1H), 1.65−1.58 (dt, J = 13.9, 3.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 154.1, 145.3, 131.5, 130.8, 130.4, 128.0, 127.1, 114.3, 68.7, 67.8, 52.0, 26.6, 25.6, 20.5, 16.5; IR (film, cm^{-1}) 3415, 2949, 1719, 1499, 1250, 1219, 1032; TLC R_f = 0.40 (7:3 hexanes/EtOAc v/v); HPLC 90:10 e.r., Chiral HPLC eluting at 1.0 mL/min with 90% hexanes/methanol. Retention times: R_T = 4.2 min, 5.0 min; HRMS (EI$^+$) m/z calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1367.

1,2-Product **2h** (21.5 mg, 31%, 90:10 e.r.) and 1,4-product **3h** (24.5 mg, 34%, 91:9 e.r.). Recovered epoxide **1** (9.2 mg, 23%, 52:48 e.r.).

Analytical standards used for the characterization of **2h** and **3h** were prepared from a separate trial giving enantiomeric ratios of 90:10 and 92:8 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(3,5-dimethylphenoxy)-cyclohex-1-enecarboxylate (2h). $[\alpha]_D^{20.0}$ −93.3 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.15 (dd, J = 4.7, 3.0 Hz, 1H), 6.77 (s, 2H), 6.63 (s, 1H), 5.26 (d, J = 3.7 Hz, 1H), 3.90 (ddt, J = 12.3, 8.2, 3.7 Hz, 1H), 3.64 (s, 3H), 2.53 (dtd, J = 20.0, 5.2, 3.0 Hz, 1H), 2.33 (dddd, J = 9.7, 6.4, 3.1, 1.1 Hz, 1H), 2.28 (s, 6H), 2.02−1.92 (m, 1H), 1.90−1.82 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.6, 159.6, 143.9, 139.3, 129.4, 123.8, 114.9, 72.8, 69.5, 51.9*, 51.9*, 25.4, 25.2, 21.6; IR (film, cm^{-1}) 3434, 2949, 1714, 1590, 1293, 1246, 1150, 1039, 755; TLC R_f = 0.53 (7:3 hexanes/EtOAc v/v); HPLC 90:10 e.r., Chiral HPLC eluting at 1.25 mL/min with 97% hexanes/methanol. Retention times: R_T = 6.0 min, 6.4 min; HRMS (EI$^+$) m/z calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1352. * denotes presumed rotamers in a 1:1 ratio.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(3,5-dimethylphenoxy)-cyclohex-1-enecarboxylate (3h). $[\alpha]_D^{20.0}$ −14.0 (c 0.75, $CHCl_3$); Mp 93−95 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.10 (dd, J = 2.2, 1.4 Hz, 1H), 6.63 (s, 3H), 5.11 (br s, 1H), 4.37−4.28 (m, 1H), 3.76 (s, 3H), 2.28 (s, 6H), 2.18 (ddt, J = 14.5, 4.0, 2.6 Hz, 1H), 2.04−1.95 (m, 1H), 1.86−1.78 (m, 1H), 1.58 (dt, J = 14.0, 3.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.4, 158.0, 145.7, 139.4, 130.7, 123.4, 114.6, 67.9, 67.8, 52.2, 26.6, 25.3, 21.6; IR (film, cm^{-1}) 3408, 2949, 1717, 1590, 1292, 1252, 1150, 1031; TLC R_f = 0.29 (7:3 hexanes/EtOAc v/v); HPLC 92:8 e.r., Chiral HPLC eluting at 1.25 mL/min with 90% hexanes/isopropanol. Retention times: R_T = 3.6 min, 4.2 min; HRMS (EI$^+$) m/z calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1370.

1,2-Product **2i** (25.8, 33%, 84:16 e.r.) and 1,4-product **3i** (25.7 mg, 33%, 84:16 e.r.). No recovered epoxide **1**.

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Analytical standards used for the characterization of **2i** and **3i** were prepared from a separate trial giving enantiomeric ratios of 89:11 and 97:3 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(2-naphthoxy)-cyclohex-1-enecarboxylate (2i). $[\alpha]_D^{20.0}$ −124.3 (*c* 2.00, $CHCl_3$); Mp 82−86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78−7.74 (m, 3H), 7.57 (d, *J* = 2.5 Hz, 1H), 7.43 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.34 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.30 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.19 (dd, *J* = 4.8, 3.0 Hz, 1H), 5.44 (d, *J* = 3.6 Hz, 1H), 4.02−3.92 (m, 1H), 3.58 (s, 3H), 2.62−2.50 (m, 1H), 2.40−2.27 (m, 1H), 2.07−1.97 (m, 1H), 1.94−1.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.5, 157.5, 144.2, 134.6, 129.6, 129.5, 129.2, 127.7, 127.2, 126.4, 124.1, 119.7, 111.4, 73.2, 69.6, 51.9, 25.4, 25.4; IR (film, cm^{-1}) 3431, 3055, 2949, 1709, 1250, 1212, 1041, 747; TLC R_f = 0.29 (7:3 hexanes/EtOAc v/v); HPLC 89:11 e.r., Chiral HPLC eluting at 1.25 mL/min with 99% hexanes/isopropanol then a gradient of 1% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 26.2 min, 29.9 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1215.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(2-naphthoxy)-cyclohex-1-enecarboxylate (3i). $[\alpha]_D^{20.0}$ −5.7 (*c* 0.50, $CHCl_3$); Mp 63−66 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79−7.71 (m, 3H), 7.44 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.34 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.20 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.16 (dd, *J* = 2.2, 1.4 Hz, 1H), 5.30 (t, *J* = 2.9 Hz, 1H), 4.36 (dddd, *J* = 10.5, 6.1, 2.2, 1.1 Hz, 1H), 3.75 (s, 3H), 2.32−2.25 (m, 1H), 2.07−1.98 (m, 1H), 1.94−1.81 (m, 1H), 1.67 (tt, *J* = 14.2, 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 155.8, 146.0, 134.6, 130.5, 129.7, 129.5, 127.8, 127.0, 126.4, 124.0, 120.0, 109.9, 68.1*, 68.1*, 67.9, 52.2*, 52.2*, 26.6, 25.2; IR (film, cm^{-1}) 3420, 2949, 2359, 1717, 1250, 1214, 1031, 748; TLC R_f = 0.18 (7:3 hexanes/EtOAc v/v); HPLC 97:3 e.r., Chiral HPLC eluting at 1.25 mL/min with 99% hexanes/isopropanol and then a gradient from 1% to 30% isopropanol in hexanes from 20.01 to 40.00 min. Retention times: R_T = 31.0 min, 31.5 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1194. * denotes presumed rotamers in a 1:1 ratio.

1,2-Product **2j** (27.3 mg, 35%, 80:20 e.r.) and 1,4-product **3j** (29.8 mg, 38%, 88:12 e.r.). No recovered epoxide **1**.

Analytical standards used for the characterization of **2j** and **3j** were prepared from a separate trial giving enantiomeric ratios of 80:20 and 90:10 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(1-naphthoxy)-cyclohex-1-enecarboxylate (2j). $[\alpha]_D^{20.0}$ −123.2 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.19−8.13 (m, 1H), 7.83−7.77 (m, 1H), 7.49−7.39 (m, 5H), 7.24 (dd, *J* = 4.9, 2.9 Hz, 1H), 5.52 (d, *J* = 3.7 Hz, 1H), 3.99 (ddt, *J* = 11.7, 9.8, 3.7 Hz, 1H), 3.44 (s, 3H), 2.69−2.58 (m, 1H), 2.47−2.33 (m, 1H), 2.21−2.09 (m, 1H), 2.01−1.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 155.3, 144.1*, 144.0*, 134.6, 129.3, 127.6*, 127.6*, 126.5, 126.2*, 126.1*, [126.0, 126.0, 126.0, 125.9] − single carbon signal, 125.3*, 125.3*, 121.8*, 121.8*, 121.4*, 121.3*, 109.3, 73.8*, 73.7*, 69.6, 51.7*, 51.6*, 25.5, 25.4; IR (film, cm^{-1}) 3390, 2951, 1709, 1395, 1246, 1235, 1091, 1042, 770; TLC R_f = 0.28 (7:3 hexanes/EtOAc v/v); HPLC 80:20 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/methanol. Retention times: R_T = 10.7 min, 15.4 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1201. * denotes presumed rotamers in a 1:1 ratio.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(1-naphthoxy)-cyclohex-1-enecarboxylate (3j). $[\alpha]_D^{20.0}$ +67.0 (*c* 1.00, $CHCl_3$); Mp 132−135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.25−8.18 (m, 1H), 7.82−7.77 (m, 1H), 7.50−7.35 (m, 4H), 7.20 (dd, *J* = 2.2, 1.3 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 5.41 (t, *J* = 3.0 Hz, 1H), 4.42−4.35 (m, 1H), 3.70 (s, 3H), 2.30−2.22 (m, 1H), 2.07−1.87 (m, 2H), 1.68 (dt, *J* = 14.0, 3.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.5, 153.9, 146.0, 134.8, 130.6, 127.6, 126.8, 126.4, 126.0, 125.3, 122.4, 120.9, 107.3, 68.2, 67.9, 52.2*, 52.2*, 26.9, 25.5; IR (film, cm^{-1}) 3244, 3052, 2950, 2359, 1717, 1256, 1234, 771; TLC R_f = 0.19 (7:3 hexanes/EtOAc v/v); HPLC 90:10 e.r., Chiral HPLC eluting at 1.0 mL/min with 98% hexanes/methanol. Retention times: R_T = 7.9 min, 11.6 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1207. * denotes presumed rotamers in a 1:1 ratio.

1,2-Product **2k** (23.1 mg, 29%, 90:10 e.r.) and 1,4-product **3k** (18.5 mg, 23%, 95:5 e.r.). No recovered epoxide **1**.

Analytical standards used for the characterization of **2k** and **3k** were prepared from a separate trial giving enantiomeric ratios of 92:8 and 95:5 respectively.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(1,3-benzodioxol-5-yl)-cyclohex-1-enecarboxylate (2k). $[\alpha]_D^{20.0}$ +104.4 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.14 (dd, *J* = 4.7, 3.0 Hz, 1H), 6.74 (d, *J* = 2.5 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.60 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.91 (s, 2H), 5.08 (d, *J* = 3.7 Hz, 1H), 3.87 (ddt, *J* = 11.5, 9.2, 3.8 Hz, 1H), 3.65 (s, 3H), 2.52 (dtd, *J* = 20.1, 5.3, 2.8 Hz, 1H), 2.37−2.25 (m, 1H), 2.02−1.91 (m, 1H), 1.90−1.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.5, 155.0, 148.2, 144.0, 142.6, 129.3, 109.9, 108.0, 101.4, 100.8, 74.8, 69.6, 51.9*, 51.9*, 25.4, 25.3; IR (film, cm^{-1}) 3446, 2950, 2360, 1710, 1480, 1242, 1175, 1035, 746; TLC R_f = 0.20 (7:3 hexanes/EtOAc v/v); HPLC 92:8 e.r., Chiral HPLC eluting at 1.0 mL/min with 95% hexanes/isopropanol. Retention times: R_T = 20.4 min, 23.4 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{15}H_{16}O_6$ 292.0947, found 292.0952.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(1,3-benzodioxol-5-yl)-cyclohex-1-enecarboxylate (3k). $[\alpha]_D^{20.0}$ −16.7 (*c* 0.75, $CHCl_3$); Mp 70−73 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.09 (s, 1H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 6.48 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.92 (dd, *J* = 1.43, 1.41 Hz, 2H), 4.93 (t, *J* = 2.8 Hz, 1H), 4.35−4.29 (m, 1H), 3.78 (s, 3H), 2.21−2.10 (m, 1H), 2.04−1.97 (m, 1H), 1.91−1.76 (m, 1H), 1.54 (tt, *J* = 14.4, 3.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 153.4, 148.3, 145.8, 142.6, 130.6, 109.8, 108.2, 101.3, 101.0, 70.2, 67.9, 52.2*, 52.2*, 26.5, 25.2; IR (film, cm^{-1}) 3408, 2950, 1715, 1482, 1254, 1177, 1033; TLC R_f = 0.14 (7:3 hexanes/EtOAc v/v); HPLC 95:5 e.r., Chiral HPLC eluting at 1.0 mL/min with 90% hexanes/isopropanol. Retention times: R_T = 8.9 min, 12.4 min; HRMS (EI$^+$) *m*/*z* calcd for $C_{15}H_{16}O_6$ 292.0947, found 292.0935. * denotes presumed rotamers in a 1:1 ratio.

Allylic Oxide Regio-resolution of Estradiol. 17-*O*-*tert*-Butyldimethylsilylestradiol (**7**) was prepared according to literature procedures using a bis-TBS protection followed by selective removal of the phenolic silane.[8] In addition to the discussed use of the (*S*,*S*)-**4**, (*R*,*R*)-**4** was also used and the results are included below. Products are a single diastereomer unless otherwise noted.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (68.0 mg, 0.44 mmol, 1.4 equiv) was dissolved in 6.5 mL of toluene followed by 17-O-*tert*-butyldimethylsilylestradiol **7** (120.0 mg, 0.31 mmol, 1.0 equiv). The resulting solution was degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (14.7 mg, 5.0 mol %) and (*R*,*R*)-**4** (36.7 mg, 15.0 mol %) were dissolved in 4.0 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. After 96 h at −40 °C, the reaction was concentrated to a volume of 2.0 mL and then purified by flash chromatography (9:1, hexanes/EtOAc v/v) to yield **8** (101.5 mg, 60%) and **9** (46.9 mg, 27%), both as white solids and single diastereomers. The epoxide (**1**, 22%) was recovered in 93:7 enantiomeric ratio.

Methyl (5*R*,6*S*)-5-Hydroxy-6-*O*-(17-*O*-*tert*-butyldimethylsilyl-estradiol)-cyclohex-1-enecarboxylate (8). $[\alpha]_D^{20.0}$ −97.3 (*c* 1.00, $CHCl_3$); Mp 38−42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 4.6, 3.1 Hz, 1H), 6.92 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.87 (d, *J* = 2.8 Hz, 1H), 5.25 (d, *J* = 3.7 Hz, 1H), 3.91 (dt, *J* = 11.3, 3.7 Hz, 1H), 3.66 (s, 3H), 3.64 (t, *J* = 7.7 Hz, 1H), 2.88−2.77 (m, 1H), 2.57−2.48 (m, 1H), 2.37−2.22 (m, 2H), 2.21−2.11 (m, 1H), 2.11−1.79 (m, 6H), 1.66−1.63 (m, 1H), 1.55−1.03 (m, 7H), 0.89 (s, 9H), 0.73 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 157.3, 143.8, 138.1, 134.1, 129.4, 126.4, 117.2, 114.2, 81.9, 72.7, 69.4, 51.9, 49.8, 44.3, 43.7, 38.9, 37.3, 31.1, 29.9, 27.4, 26.5, 26.0, 25.4, 25.2, 23.4, 18.2, 11.5, −4.3, −4.6; IR (film, cm^{-1}) 3433, 2926, 2854, 1717, 1495, 1246, 1094, 834, 773; TLC R_f = 0.57 (7:3 hexanes/EtOAc v/v). HRMS (EI$^+$) *m*/*z* calcd for $C_{32}H_{48}SiO_5$ 540.3271, found 540.3263.

Methyl (3*S*,6*R*)-3-Hydroxy-6-*O*-(17-*O*-*tert*-butyldimethylsilyl-estradiol)-cyclohex-1-enecarboxylate (9). $[\alpha]_D^{20.0}$ −25.6 (*c* 1.00, $CHCl_3$); Mp 43−47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* =

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8.1 Hz, 1H), 7.10 (dd, J = 2.2, 1.3 Hz, 1H), 6.79 (dd, J = 8.6, 2.8 Hz, 1H), 6.73 (d, J = 2.7 Hz, 1H), 5.09 (br s, 1H), 4.32 (dddd, J = 10.6, 6.1, 2.1, 1.0 Hz, 1H), 3.76 (s, 3H), 3.64 (t, J = 7.9 Hz, 1H), 2.89−2.78 (m, 1H), 2.34−2.10 (m, 3H), 2.04−1.76 (m, 5H), 1.71−1.03 (m, 10H), 0.89 (s, 9H), 0.74 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 155.7, 145.9, 138.3, 133.9, 130.6, 126.5, 117.1, 114.1, 81.9, 68.0*, 68.0*, 67.8, 52.2*, 52.2*, 49.8, 44.3, 43.7, 39.0, 37.3, 31.1, 20.0, 27.4, 26.5, 26.5, 26.0, 25.3, 23.4, 18.3, 11.5, −4.3, −4.7; IR (film, cm^{-1}) 3389, 2926, 2853, 1719, 1496, 1247, 1094, 834, 773; TLC R_f = 0.43 (7:3 hexanes/EtOAc v/v). HRMS (EI$^+$) m/z calcd for $C_{32}H_{48}SiO_5$ 540.3271, found 540.3263. * denotes presumed rotamers in a 1:1 ratio.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (121.6 mg, 0.788 mmol, 1.4 equiv) was dissolved in 7.0 mL of toluene followed by 17-O-*tert*-butyldimethylsilylestradiol **7** (208.1 mg, 0.539 mmol, 1.0 equiv). The resulting solution was degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (26.2 mg, 5.0 mol %) and (*S*,*S*)-**4** (67.0 mg, 15.0 mol %) were dissolved in 4.0 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. After 96 h at −40 °C, the reaction was concentrated to a volume of 2.0 mL and then purified by flash chromatography (9:1, hexanes/EtOAc v/v) to yield **10** (127.9 mg, 44%) and **11** (119.2 mg, 41%) both as white solids and single diastereomers. The epoxide (**1**, 18%) was recovered in 66:34 enantiomeric ratio.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(17-*O*-*tert*-butyldimethylsilyl-estradiol)-cyclohex-1-enecarboxylate (10). $[\alpha]_D^{20.0}$ −28.0 (*c* 1.00, $CHCl_3$); Mp 56−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, J = 8.7 Hz, 1H), 7.14 (dd, J = 4.6, 3.1 Hz, 1H), 6.94 (dd, J = 8.6, 2.8 Hz, 1H), 6.85 (d, J = 2.6 Hz, 1H), 5.25 (d, J = 3.7 Hz, 1H), 3.91 (ddt, J = 11.3, 9.1, 3.7 Hz, 1H), 3.65 (s, 3H), 3.64 (t, J = 8.5 Hz, 1H), 2.86−2.79 (m, 1H), 2.58−2.47 (m, 1H), 2.37−2.23 (m, 2H), 2.20−2.11 (m, 1H), 2.06−1.80 (m, 6H), 1.71−1.59 (m, 1H), 1.54−1.07 (m, 7H), 0.89 (s, 9H), 0.74 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 157.3, 143.8, 138.0, 134.0, 129.4, 126.3, 117.0, 114.3, 81.8, 72.7, 69.4, 51.8*, 51.8*, 49.7, 44.2, 43.6, 38.9, 37.2, 31.0, 29.9, 27.4, 26.4, 25.9, 25.2, 25.1, 23.3, 18.2, 11.4, −4.4, −4.7; IR (film, cm^{-1}) 3435, 2928, 2855, 1719, 1496, 1246, 1095, 834, 774; TLC R_f = 0.57 (7:3 hexanes/EtOAc v/v). HRMS (EI$^+$) m/z calcd for $C_{32}H_{48}SiO_5$ 540.3271, found 540.3264. * denotes presumed rotamers in a 1:1 ratio.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(17-*O*-*tert*-butyldimethylsilyl-estradiol)-cyclohex-1-enecarboxylate (11). $[\alpha]_D^{20.0}$ +27.5 (*c* 0.50, $CHCl_3$); Mp 64−69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 8.6 Hz, 1H), 7.10 (dd, J = 2.4, 1.3 Hz, 1H), 6.80 (dd, J = 8.3, 2.5 Hz, 1H), 6.71 (d, J = 2.6 Hz, 1H), 5.09 (br s, 1H), 4.34−4.30 (m, 1H), 3.75 (s, 3H), 3.64 (t, J = 8.0 Hz, 1H), 2.88−2.77 (m, 1 H), 2.32−2.11 (m, 3H), 2.04−1.76 (m, 5H), 1.74−1.03 (m, 10H), 0.89 (s, 9H), 0.74 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 155.6, 146.1, 138.2, 133.8, 130.5, 126.5, 116.9, 114.3, 81.9, 68.0, 67.7, 52.2, 49.8, 44.3, 43.7, 39.0, 37.3, 31.1, 30.0, 27.4, 26.5, 26.3, 26.0, 25.3, 23.4, 18.2, 11.5, −4.3, −4.7; IR (film, cm^{-1}) 3410, 2928, 2855, 1720, 1496, 1247, 1095, 834, 773; TLC R_f = 0.43 (7:3 hexanes/EtOAc v/v). HRMS (EI$^+$) m/z calcd for $C_{32}H_{48}SiO_5$ 540.3271, found 540.3268.

Allylic Oxide Regio-resolution of Tyrosine. In addition to the discussed use of (*S*,*S*)-**4**, (*R*,*R*)-**4** was also tested and the results are shown below. Products are shown to be a single diastereomer unless otherwise noted.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (264.7 mg, 1.71 mmol, 1.05 equiv) was dissolved in 12.0 mL of toluene followed by the addition of Boc-L-Tyr-OMe **12** (482.5 mg, 1.63 mmol, 1.0 equiv). The resulting solution was degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (12.4 mg, 1.0 mol %) and (*R*,*R*)-**4** (34.2 mg, 3.0 mol %) were dissolved in 1.0 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. The reaction was allowed to stir for 72 h before being worked up as in general procedure A. The reaction was purified by flash chromatography (7:3 hexanes/EtOAc v/v) to yield 664.3 mg of an inseparable mixture of **13** and **14** and 0.8 mg of recovered oxide (59:41 e.r.). Analytical standards of **13** and **14** were purified by preparatory HPLC (90:10 to 1:99 water/acetonitrile v/v) and yields **13** (45% yield, 4.37 d.r. as determined by ^{1}H NMR) and **14** (36% yield as a single diastereomer) as determined by ^{1}H NMR analysis of the homogeneous mixture.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(Boc-L-Tyr-OMe)-cyclohex-1-enecarboxylate (13). Note: The following data are for the major diastereomer isolated (4.37:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 4.7, 3.0 Hz, 1H), 7.08−7.00 (m, 4H), 5.23 (d, J = 3.7 Hz, 1H), 4.95 (br d, J = 8.1 Hz, 1H), 4.56−4.50 (m, 1H), 3.90 (dt, J = 11.2, 3.8 Hz, 1H), 3.71 (s, 3H), 3.61 (s, 3H), 3.07−2.95 (m, 2H), 2.58−2.48 (m, 1H), 2.38−2.25 (m, 1H), 2.04−1.84 (m, 2H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 166.5, 158.8, 155.2, 144.1, 130.6, 130.4 129.3, 117.5, 80.1, 73.3, 69.5, 54.6, 52.3, 51.8, 37.6, 28.4, 25.4, 23.5. Optical rotation, IR, and HRMS were not obtained due to the mixture of diastereomers.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(Boc-L-Tyr-OMe)-cyclohex-1-enecarboxylate (14). $[\alpha]_D^{20.0}$ +36.4 (*c* 1.00, $CHCl_3$); Mp 38−42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, J = 1.6 Hz, 1H), 7.01 (d, J = 8.1 Hz, 2H), 6.94−6.88 (m, 2H), 5.07 (t, J = 2.8 Hz, 1H), 5.01 (d, J = 8.3 Hz, 1H), 4.53 (dt, J = 8.7, 6.0 Hz, 1H), 4.36−4.26 (m, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 3.01 (tt, J = 14.1, 6.8 Hz, 2H), 2.17−2.09 (m, 1H), 2.00−1.92 (m, 1H), 1.80 (tdd, J = 12.9, 10.3, 2.7 Hz, 1H), 1.57 (tt, J = 14.3, 3.2 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 166.4, 157.1, 155.3, 145.8, 130.5, 128.9, 128.6, 117.1, 80.1, 68.3, 67.9, 54.6, 52.4*, 52.4*, 52.2*, 52.2*, 37.6, 28.5, 26.5, 25.3; IR (film, cm^{-1}) 3370, 2951, 1718, 1508, 1255, 1167, 1031; TLC R_f = 0.17 (7:3 hexanes/EtOAc v/v). HRMS (EI$^+$) m/z calcd for $C_{23}H_{31}O_8N$ 449.2049, found 449.2056. * denotes presumed rotamers in a 1:1 ratio.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (301.0 mg, 1.02 mmol, 1.0 equiv) was dissolved in 12.0 mL of toluene followed by the addition of Boc-L-Tyr-OMe **12** (562.1 mg, 1.0 mmol, 0.98 equiv). The resulting solution was degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (14.5 mg, 1.0 mol %) and (*S*,*S*)-**4** (39.3 mg, 3.0 mol %) were dissolved in 6.0 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. The reaction was allowed to stir for 72 h before being worked up as in general procedure A. The reaction was purified by flash chromatography (7:3 hexanes/EtOAc v/v) to yield 712.0 mg of an inseparable mixture of **15** and **16** and 43.4 mg of recovered oxide (53:47 e.r.). Analytical standards of **15** and **16** were purified by preparatory HPLC (90:10 to 1:99 water/acetonitrile v/v) and yields **15** (51% yield, 4.20 d.r. as determined by ^{1}H NMR) and **16** (40% yield as a single diastereomer) as determined by ^{1}H NMR analysis of the homogeneous mixture.

Methyl (5*R*,6*S*)-5-Hydroxy-6-*O*-(Boc-L-Tyr-OMe)-cyclohex-1-enecarboxylate (15). Note: The following data are for the major diastereomer isolated (4.20:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (dd, J = 4.7, 3.0 Hz, 1H), 7.08−6.99 (m, 4H), 5.22 (d, J = 3.6 Hz, 1H), 5.00−4.96 (m, 1H), 4.55−4.50 (m, 1H), 3.89 (dt, J = 11.4, 3.7 Hz, 1H), 3.70 (s, 3H), 3.60 (s, 3H), 3.06−2.96 (m, 2H), 2.57−2.48 (m, 1H), 2.36−2.27 (m, 1H), 2.02−1.93 (m, 1H), 1.89−1.80 (m, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 166.5, 158.8, 155.2, 144.1, 130.7, 130.4, 129.3, 117.5, 80.1, 73.3, 69.5, 54.6, 52.4, 51.9, 37.6, 28.4, 25.4, 25.3. Optical rotation, IR, and HRMS were not obtained due to the mixture of diastereomers.

Methyl (3*S*,6*R*)-3-Hydroxy-6-*O*-(Boc-L-Tyr-OMe)-cyclohex-1-enecarboxylate (16). $[\alpha]_D^{20.0}$ +10.2 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, J = 1.7 Hz, 1H), 7.03−6.99 (m, 2H), 6.95−6.90 (m, 2H), 5.10 (t, J = 2.9 Hz, 1H), 4.96 (d, J = 8.3 Hz, 1H), 4.54 (q, J = 6.7 Hz, 1H), 4.40−4.27 (m, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.02 (qd, J = 14.0, 5.9 Hz, 2H), 2.19−2.13 (m, 1H), 2.04−1.96 (m, 1H), 1.87−1.73 (m, 1H), 1.59 (tt, J = 14.2, 3.2 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 166.4, 157.1, 155.3, 146.2,

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130.5, 130.2, 129.0, 117.0, 80.1, 68.3, 67.7, 54.6, 52.3*, 52.3*, 52.2*, 52.1*, 37.5, 28.4, 26.3, 25.3; IR (film, cm^{-1}) 3369, 2951, 1718, 1508, 1256, 1167, 1031; TLC R_f = 0.17 (7:3 hexanes/EtOAc v/v). HRMS (EI^+) m/z calcd for $C_{23}H_{31}O_8N$ 449.2049, found 449.2042. * denotes presumed rotamers in a 1:1 ratio.

Allylic Oxide Regio-resolution of Griseofulvin. 4-Des-methyl-griseofulvin **17** was prepared by the demethylation of griseofulvin following a literature procedure.[14] In addition to the discussed use of (*S*,*S*)-**4**, (*R*,*R*)-**4** was also tested and the results are shown below. Products are shown to be a single diastereomer unless otherwise noted.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (81.2 mg, 0.527 mmol, 1.8 equiv) was dissolved in 1.3 mL of toluene followed by the addition of 4-des-methyl-griseofulvin **17** (99.5 mg, 0.294 mmol, 1.0 equiv). The resulting solution was thoroughly degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (17.1 mg, 5.0 mol %) and (*R*,*R*)-**4** (39.9 mg, 15.0 mol %) were dissolved in 0.6 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. The reaction was continued at −40 °C and monitored by ^{1}H NMR until total consumption of the starting phenol was observed (approximately 18 h). The reaction was then concentrated to dryness and was purified by flash chromatography (100% DCM, then 95:5 DCM/MeOH v/v) using Florisil as the stationary phase to yield 132.4 mg of a mixture containing **18** (60% yield), **19** (31% yield), and 9.0 mg of recovered phenol **17** (9%). Degradation of the products on Florisil is suspected to regenerate griseofulvin **17**. Similar degradation, but to a much greater extent, was observed when using silica as the stationary phase. Analytical standards of **18** and **19** could be separated from one another and purified by a silica column (5:1 toluene/acetone v/v) and then by preparatory HPLC (80:20 to 35:65 water/acetonitrile v/v over 35 min) to remove **17**. Both products were isolated as white solids.

Methyl (5*R*,6*S*)-5-Hydroxy-6-*O*-(4-des-methyl-griseofulvin)-cyclohex-1-enecarboxylate (18). $[\alpha]_D^{20.0}$ +366.6 (*c* 1.00, $CHCl_3$); Mp 90−92 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 (dd, *J* = 4.9, 2.7 Hz, 1H), 7.18 (s, 1H), 5.55 (s, 1H), 5.24 (d, *J* = 3.4 Hz, 1H), 4.05 (s, 3H), 3.79 (dt, *J* = 12.0, 3.8 Hz, 1H), 3.75 (s, 3H), 3.63 (s, 3H), 2.93 (dd, *J* = 16.2, 13.3 Hz, 1H), 2.82 (ddd, *J* = 13.4, 6.7, 4.3 Hz, 1H), 2.59 (dt, *J* = 20.4, 5.3 Hz, 1H), 2.48−2.30 (m, 2H), 2.24−2.09 (m, 1H), 2.00−1.89 (m, 1H), 0.95 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 196.9, 194.2, 170.8, 169.0, 166.7, 165.2, 158.6, 146.8, 127.9, 106.9, 105.2, 98.5, 97.2, 91.1, 77.3, 69.3, 57.4, 56.9, 52.2, 40.2, 36.6, 25.8, 24.6, 14.5; IR (film, cm^{-1}) 3457, 2949, 1709, 1611, 1584, 1224, 1210, 753; TLC R_f = 0.28 (1:4 acetone/toluene v/v); HRMS (DART) m/z calcd for $C_{24}H_{26}ClO_9$ $(M + H)^+$: 493.1260, found 493.1269.

Methyl (3*S*,6*R*)-3-Hydroxy-6-*O*-(4-des-methyl-griseofulvin)-cyclohex-1-enecarboxylate (19). $[\alpha]_D^{20.0}$ +298.9 (*c* 1.00, $CHCl_3$); Mp 126−128 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18 (d, *J* = 1.3 Hz, 1H), 6.55 (s, 1H), 5.52 (s, 1H), 5.35 (br s, 1H), 4.33 (ddd, *J* = 9.2, 6.2, 2.0 Hz, 1H), 4.02 (s, 3H), 3.71 (s, 3H), 3.63 (s, 3H), 2.95 (dd, *J* = 16.5, 13.4 Hz, 1H), 2.88−2.73 (m, 1H), 2.60 (br s, 1H), 2.39 (dd, *J* = 16.6, 4.6 Hz, 1H), 2.18−1.92 (m, 3H), 1.71 (tt, *J* = 13.7, 3.5 Hz, 1H), 0.91 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.1, 192.3, 171.1, 169.3, 166.2, 164.6, 156.7, 147.7, 129.0, 106.6, 105.0, 97.8, 93.9, 90.7, 70.9, 67.5, 57.2, 56.8, 52.2, 40.1, 36.7, 27.0, 26.5, 14.3; IR (film, cm^{-1}) 3399, 2950, 1711, 1611, 1585, 1357, 1224, 751; TLC R_f = 0.17 (1:4 acetone/toluene v/v); HRMS (DART) m/z calcd for $C_{24}H_{26}ClO_9$ $(M + H)^+$: 493.1260, found 493.1268.

In a flame-dried flask outfitted with a septum, racemic epoxide **1** (81.2 mg, 0.527 mmol, 1.8 equiv) was dissolved in 1.3 mL of toluene followed by the addition of 4-des-methyl-griseofulvin **17** (99.5 mg, 0.294 mmol, 1.0 equiv). The resulting solution was thoroughly degassed with argon and cooled to −40 °C. In a separate flask, $Pd_2(dba)_3$ (16.7 mg, 5.0 mol %) and (*S*,*S*)-**4** (38.9 mg, 15.0 mol %) were dissolved in 0.6 mL of toluene. The resulting purple solution was degassed and stirred at room temperature until it became yellow (approximately 10 min). The solution was then cooled to −40 °C and added to the epoxide solution via syringe. The reaction was continued at −40 °C and monitored by ^{1}H NMR until total consumption of the starting phenol was observed (approximately 18 h). The reaction was then concentrated to dryness and purified by flash chromatography (100% DCM, then 95:5 DCM/MeOH v/v) using Florisil as the stationary phase to yield 132.4 mg of a mixture containing **20** (54% yield), **21** (25% yield), and 6.2 mg of recovered phenol **17** (6%). Degradation of the products on Florisil is suspected to regenerate griseofulvin **17**. Similar degradation, but to a much greater extent, was observed when using silica as the stationary phase. Analytical standards of **20** and **21** could be separated from one another and purified by a silica column (5:1 toluene/acetone v/v) and then by preparatory HPLC (80:20 to 35:65 water/acetonitrile v/v over 35 min) to remove **17**. Both products were isolated as white solids.

Methyl (5*S*,6*R*)-5-Hydroxy-6-*O*-(4-des-methyl-griseofulvin)-cyclohex-1-enecarboxylate (20). $[\alpha]_D^{20.0}$ +61.0 (*c* 1.00, $CHCl_3$); Mp 196−198 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32−7.27 (m, 1H), 7.20 (s, 1H), 5.53 (s, 1H), 5.23 (d, *J* = 3.8 Hz, 1H), 4.05 (s, 3H), 3.81 (dt, *J* = 11.7, 3.9 Hz, 1H), 3.74 (s, 3H), 3.60 (s, 3H), 3.05 (dd, *J* = 16.5, 13.5 Hz, 1H), 2.91−2.81 (m, 1H), 2.64−2.52 (m, 1H), 2.50−2.28 (m, 2H), 2.23−2.09 (m, 1H), 2.04−1.91 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 196.9, 194.7, 170.7, 169.1, 166.7, 165.3, 158.8, 146.8, 128.0, 107.2, 104.9, 98.6, 97.8, 90.9, 77.7, 69.3, 57.5, 56.8, 52.2, 40.2, 36.6, 25.8, 24.7, 14.4; IR (film, cm^{-1}) 3468, 2949, 1709, 1611, 1224, 1046, 753; TLC R_f = 0.26 (1:4 acetone/toluene v/v); HRMS (DART) m/z calcd for $C_{24}H_{26}ClO_9$ $(M + H)^+$: 493.1260, found 493.1268.

Methyl (3*R*,6*S*)-3-Hydroxy-6-*O*-(4-des-methyl-griseofulvin)-cyclohex-1-enecarboxylate (21). $[\alpha]_D^{20.0}$ +96.9 (*c* 1.00, $CHCl_3$); Mp 102−104 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.15 (dd, *J* = 2.4, 1.2 Hz, 1H), 6.53 (s, 1H), 5.51 (s, 1H), 5.34 (d, *J* = 3.2 Hz, 1H), 4.33 (ddd, *J* = 10.3, 6.2, 2.6 Hz, 1H), 4.01 (s, 3H), 3.70 (s, 3H), 3.60 (s, 3H), 3.04−2.93 (m, 1H), 2.87−2.78 (m, 1H), 2.47−2.35 (m, 2H), 2.20−1.94 (m, 2H), 1.73 (tt, *J* = 13.9, 3.6 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.0, 192.3, 171.1, 169.4, 166.2, 164.6, 156.6, 147.5, 129.1, 106.7, 104.8, 97.9, 94.2, 90.7, 71.0, 67.5, 57.2, 56.8, 52.2, 40.1, 36.6, 27.1, 26.5, 14.4; IR (film, cm^{-1}) 3400, 2940, 1712, 1612, 1357, 1177, 750; TLC R_f = 0.17 (1:4 acetone/toluene v/v); HRMS (DART) m/z calcd for $C_{24}H_{26}ClO_9$ $(M + H)^+$: 493.1260, found 493.1272.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds is provided. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00671.

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Notes

The authors declare no competing financial interest.

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