The Application of a Mechanistic Model Leads to the Extension of the Sharpless Asymmetric Dihydroxylation to Allylic 4-Methoxybenzoates and Conformationally Related Amine and Homoallylic Alcohol Derivatives

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Abstract: The scope and utility of the Sharpless asymmetric dihydroxylation has been expanded to include the use of allylic 4-methoxybenzoates as precursors of a wide variety of substituted chiral glycerol derivatives. The allylic 4-methoxybenzoyl group was found to be superior to other allylic alcohol protecting groups with respect to both yield and enantiomeric purity of the product. For example, asymmetric dihydroxylation of allyl 4-methoxybenzoate (**6a**) using the $(DHQD)_2PYDZ{\cdot}OsO_4$ (**1**·OsO_4) catalyst system affords (*S*)-3-(4-methoxybenzoyloxy)-1,2-propanediol (**7a**) in >99% yield and 98% ee. The 4-methoxybenzoates of a variety of other allylic alcohols also serve as excellent substrates, in contrast to the parent alcohols themselves. The efficient asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers (**12a** and **15**), allyl 9-fluorenimine (**18b**), bis(homoallyl) 4-methoxybenzoate (**14**) and other structurally related substrates is also described. This methodology was developed under mechanistic guidance from the transition state model advanced earlier by us for the bis-cinchona alkaloid catalyzed asymmetric dihydroxylation reaction. The 4-methoxybenzoyl group functions not only to selectively protect one of the hydroxy groups of the product triol for subsequent synthetic manipulation but also to provide an extended binding group that participates in hydrophobic and aryl−aryl interactions with the U-shaped binding pocket of the $(DHQD)_2PYDZ{\cdot}OsO_4$ catalyst (**1**·OsO_4), thereby enhancing enantioselectivity.

Introduction

The cinchona alkaloid catalyzed asymmetric dihydroxylation (Sharpless asymmetric dihydroxylation) has emerged as one of the most general methods for the enantioselective functionalization of olefins.[1] Bis-cinchona alkaloids, such as $(DHQD)_2$-PYDZ (**1**), are among the most effective catalysts for the reaction, giving high levels of enantioselectivity for four of the six possible olefin classes with respect to substitution pattern.[1c,3c] Despite the broad scope of the reaction, some limitations still exist with regard to the type of synthetically useful intermediates that can be easily produced. In conjunction with a program directed toward the enantioselective total synthesis of the potent angiogenesis inhibitor (−)-ovalicin (**3**), we developed a method for the asymmetric dihydroxylation of protected allylic alcohols that was guided by the mechanistic model presented earlier.[2] The proposed transition-state assembly for the face-selective dihydroxylation of styrene, for example, in the $(DHQD)_2PYDZ{\cdot}OsO_4$ system is depicted in **2**. The mechanistic pathway has the following characteristics: (1) a preference for the U-shaped conformation as in **2** for the OsO_4 complex, which has the ability to hold olefinic substrates such as styrene in a binding pocket composed of the two parallel methoxyquinoline units, OsO_4 and the pyridazine connector, as shown, (2) staggered geometry about the Os−N bond of the bis-cinchona−OsO_4 complex, (3) the proximity of one axial oxygen (O_a) and one equatorial oxygen (O_e) of the complexed OsO_4 unit to the olefinic carbons of the bound substrate, as shown, and (4) a minimum motion pathway from this arrangement for the [3 + 2] cycloaddition which directly produces the pentacoordinate osmate ester in the energetically most favorable geometry.[3] The rate acceleration for the observed enantioselective pathway relative to other modes is due to the favorable free energy of activation for the reaction from complex **2** in which the reactants are held in a manner which is ideal for the formation of the thermodynamically more stable osmate ester. Dihydroxylation of the opposite olefin face to that shown in **2** is unfavorable due to the fact that there is no three-dimensional arrangement for simultaneous π-facial approach of the olefin to the oxygens labeled as O_a and O_e and favorable interaction with the binding pocket. X-ray crystallographic data suggest that the pyridazine ring at the bottom of the U-shaped cavity tends to be oriented so as to allow conjugation of the ring and the two alkoxy substituents, with the N−N side of the ring participating in binding to the substrate,[3b] though the exact tilt of this ring during reaction probably varies slightly with substrate. This paper reports the successful use of this transition state model to devise structural modifications and derivatives of allylic and homoallylic alcohols

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(1) (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (b) Sharpless, K. B.; Amberg, W.; Beller, M.; Chen H.; Hartung, J.; Kawanami, Y.; Lübben, D.; Manoury, E.; Ogino, Y.; Shibata, T.; Ukita, T. *J. Org. Chem.* **1991**, *56*, 4585. (c) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768. (d) Crispino, G. A.; Jeong, K.-S.; Kolb, H. C.; Wang, Z.-M.; Xu, D.; Sharpless, K. B. *J. Org. Chem.* **1993**, *58*, 3785. (e) Kolb, H. C.; Andersson, P. G.; Bennani, Y. L.; Crispino, G. A.; Jeong, K.-S.; Kwong, H.-L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 12226. (f) Kolb, H. C.; Andersson, P. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1994**, *116*, 1278. (g) Crispino, G. A.; Makita, A.; Wang, Z.-M.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 543. (h) For a review see: Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

(2) Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1994**, *116*, 12109.

(3) (a) Corey, E. J.; Noe, M. C. *J. Am. Chem. Soc.* **1993**, *115*, 12579. (b) Corey, E. J.; Noe, M. C.; Sarshar, S. *Tetrahedron Lett.* **1994**, *35*, 2861. (c) Corey, E. J.; Noe, M. C.; Sarshar, S. *J. Am. Chem. Soc.* **1993**, *115*, 3828. (d) Corey, E. J.; Noe, M. C.; Grogan, M. J. *Tetrahedron Lett.* **1994**, *35*, 6427.

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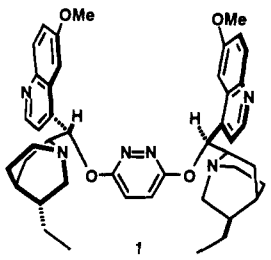
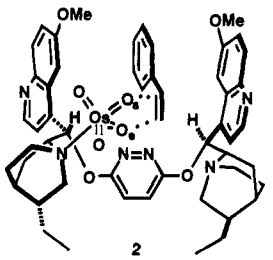
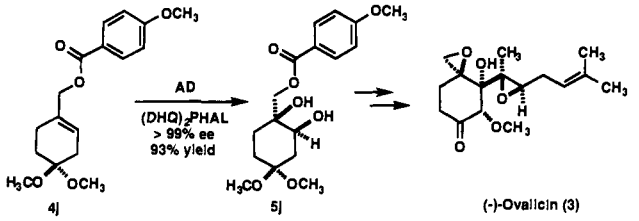




which greatly enhance the enantioselectivity and usefulness of the bis-cinchona alkaloid catalyzed dihydroxylation reaction.

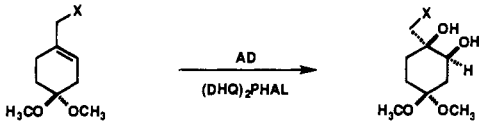
Results

A short asymmetric total synthesis of (−)-ovalicin (**3**) was recently developed on the basis of the enantioselective dihydroxylation of allylic 4-methoxybenzoate **4j** to provide diol **5j** in high enantiomeric purity, in contrast to the results obtained for the corresponding alcohol.[2] The 4-methoxybenzoyl group was initially selected because the mechanistic model suggested that it might direct the dihydroxylation of **4j** due to its ability to interact favorably with the proposed catalytic binding pocket (*vide infra*). In addition, the 4-methoxybenzoyl group can serve to differentiate the original allylic hydroxy group from those introduced in the dihydroxylation step with minimum tendency to undergo oxygen to oxygen acyl rearrangement, as compared, for example, to acetyl or benzoyl groups.



A comprehensive study of the effects of the allylic alcohol protecting group on the enantioselectivity of this step was undertaken for purposes of comparison with this result, as shown in Table 1. For effective dihydroxylation of allylic esters, a modified set of dihydroxylation conditions had to be employed to minimize the extent of acyl migration to the newly introduced hydroxyl groups of the product. Thus, the amount of $K_2OsO_4 \cdot 2H_2O$ was increased to 1 mol % to minimize reaction time, and product isolation was performed immediately upon completion of the reaction as indicated by TLC analysis. Under these conditions, substituted benzoate esters afford the corresponding glycol in high yield and enantiomeric purity. The 4-methoxybenzoate ester offers the specific advantage of suppressing acyl migration of the product glycol under the dihydroxylation conditions and was thus selected for further study. Other derivatives, including the TIPS (**4a**) and benzyl (**4d**) ethers, pivalate ester (**4c**), and the free alcohol[4] (**4b**), afforded the corresponding glycols with poor enantioselectivity.[5] The allylic 4-methoxyphenyl ether **4f** gave the corresponding glycol with intermediate enantioselectivity.[6]

Table 1. Enantioselective Dihydroxylation of 4,4-Dimethoxy-1-cyclohexenyl-1-methanol Derivatives



Entry	Substituent (X- =)	Enantiomeric excess (ee)	Ratio of desired product to acyl migration product[a]
a	TIPSO-	13%[b]	—
b	HO-	18%[c]	—
c	PvO-	35%[b]	12 : 1
d	BnO-	90%[d]	—
e	AcO-	96%[b]	2.5 : 1
f	*p*-MeO-PhO-	96%[d]	—
g	BzO-	>99%[d]	6.5 : 1
h	*p*-NO_2-BzO-	>99%[d]	7 : 1
i	*p*-Br-BzO-	>99%[d]	7 : 1
j	*p*-MeO-BzO-	>99%[d]	32 : 1

[a] Determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Determined by chiral HPLC analysis of the benzoate ester derivative. [c] Determined by ^{1}H NMR analysis of the bis-MTPA ester derivative. [d] Determined by chiral HPLC analysis.

In order to define the scope of the reaction, a series of allylic 4-methoxybenzoates representative of different olefin classes were tested with the results shown in Table 2. Uniformly high enantioselectivities are obtained in the asymmetric dihydroxylation for four of the five olefin classes studied. While the asymmetric dihydroxylation of *trans*-1,2 and trisubstituted olefins, such as **6c**, **6d**, and **6e**, might be expected to proceed with high enantioselectivity based on the uniformly good selectivities observed with these two olefin classes,[1] the extremely selective dihydroxylation of olefins such as the terminal and 1,1-disubstituted allylic 4-methoxybenzoates **6a**, **6b**, and **6g** is truly remarkable and also supportive of the design principles underlying this substrate directed dihydroxylation strategy. Since *cis* olefins generally are observed to react with low enantioselectivities, the selectivity observed for **6f**, although only fair, places it among the best substrates of this olefinic class using the $(DHQD)_2PYDZ \cdot OsO_4$ catalyst system.[1,7] For allylic esters, such as **6a**, **6b**, and **6g**, in which the product can undergo racemization by acyl migration, the 4-methoxybenzoyl group is superior to more nucleophilically reactive acyl groups.[8] The effective dihydroxylation of **6g** is particularly noteworthy due to the synthetic versatility of the protected diol **7g** which possesses a chiral quaternary carbon atom flanked by three differentially protected hydroxymethyl groups.

The 4-methoxybenzoyl group is also useful for influencing the regioselectivity in the asymmetric dihydroxylation of

(4) Although the dihydroxylation of allylic alcohols proceeds with poor enantioselectivity in this case, it has been shown that reaction of tertiary or *cis*-allylic alcohols can proceed with good levels of enantioselectivity: (a) Wang, Z.-M.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 8225. (b) VanNieuwenhze, M. S.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 843. (c) Xu, D.; Park, C. Y.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 2495.

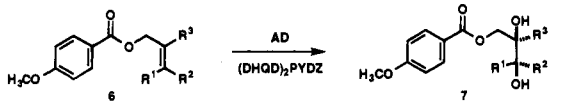
(5) Allyl benzyl ether afforded the corresponding diol in 61% ee and 91% yield, and allyl TIPS ether afforded the corresponding diol in 3% ee and 98% yield in the $(DHQD)_2PYDZ \cdot OsO_4$ catalyzed asymmetric dihydroxylation reaction.

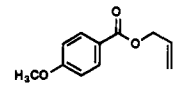
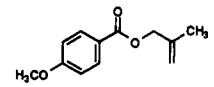
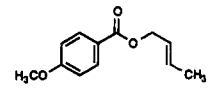
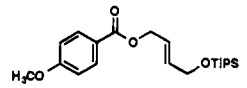
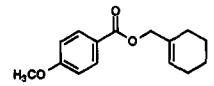
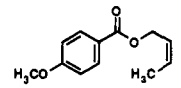
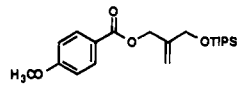
(6) The dihydroxylation of a series of substituted allyl aryl ethers has been reported to give products with ee's averaging 70%. See: (a) Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 2267. On the other hand, allyl *p*-methoxyphenyl ether afforded the corresponding diol of 90−92% ee. See: (b) Vilchèze, C.; Bittman, R. *J. Lipid Res.* **1994**, *35*, 734. (c) Byun, H.-S.; Kumar, E. R.; Bittman, R. *J. Org. Chem.* **1994**, *59*, 2630.

(7) Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568.

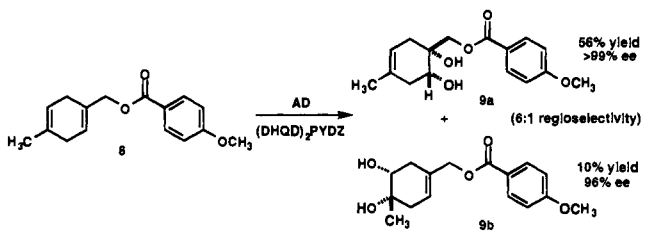
(8) The $(DHQ)_2PHAL$ ligand affords comparably good results in the dihydroxylation of olefins **6a** and **6e** (98% ee and 96% ee, respectively). The parallelism in structure and enantioselectivity of the $(DHQD)_2PYDZ$ and $(DHQD)_2PHAL$ ligands suggests that the latter would perform equally well for all of the dihydroxylation reactions discussed in this paper. For detailed comparisons of these ligands see: (a) Reference 3c. (b) Crispino, G. A.; Makita, A.; Wang, Z.-M.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 543.

Table 2. Enantioselective Dihydroxylation of Representative Allylic 4-Methoxybenzoates



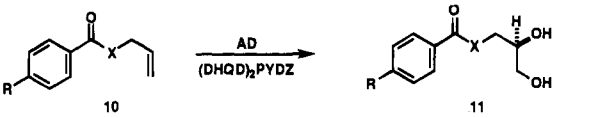
Entry	Substrate	Yield	Enantiomeric excess (ee)	Ratio of desired product to benzoyl migration product (by NMR)
a		>99%	98%	—
b		98%	97%	—
c		96%	>99%	18 : t
d		94%	>99%	>50 : t
e		>99%	98%	>50 : 1 by HPLC
t		99%	49%	25 : t
g		98%	>97%	—

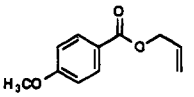
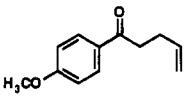
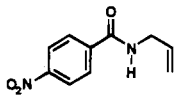
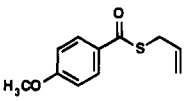
polyolefinic substrates. Thus, while dihydroxylation of **8** with OsO_4 and 4-methylmorpholine *N*-oxide (NMO) in the absence of cinchona alkaloid ligand afforded **9a** and **9b** in a ≤1:10 ratio, asymmetric dihydroxylation under the reported conditions afforded **9a** and **9b** of high enantiomeric purity in a 6:1 ratio.[9]



The scope of this strategy is not limited to allylic esters, but can also be extended to include the structurally related allylic amides, thioesters, and ketones which are shown in Table 3. Products **11** can serve as versatile intermediates for the preparation of a variety of medicinally important compounds, including β-adrenergic blocker drugs.[10] It is noteworthy that the asymmetric dihydroxylation reaction of the allylic amide and thioester analogs **10b** and **10c** proceeded with decidedly lower enantioselectivity than that with the ester **6a** or ketone **10a**. The relative enantioselectivities in Table 3 appear to correlate with the relative stabilities of the corresponding s-*cis*-allylic conformers as assessed through computational molecular modeling studies.[11] Inspection of molecular models indicates that the s-*cis*-allylic conformation offers optimum hydrophobic and π-stacking interactions between the substrate and the catalyst binding pocket (*vide infra*).

Table 3. Enantioselective Dihydroxylation of Hetero Analogs of Allyl 4-Methoxybenzoate **6a**



Entry	Substrate	Yield	Enantiomeric excess (ee)
6a		>99%	98%
10a		96%	>98%
10b		96%	81%
10c		46% (72% based on recovered olefin)	77%

The transition state model[3] which predicted the utility of allylic 4-methoxybenzoates as dihydroxylation substrates also suggested that homoallylic aryl ethers should behave in an analogous way and serve as excellent substrates for enantioselective dihydroxylation. The results of this study are shown in Table 4.[12] Initial studies were performed on derivatives of 3-buten-1-ol as the test system. The specific aryl ether chosen was 4-methoxyphenyl since this aryl group is readily cleaved under mild oxidative conditions to generate the corresponding free alcohol.[13] The catalytic dihydroxylation of 4-methoxyphenyl ether **12a** proceeded with excellent enantioselectivity to afford diol **13a**. Interestingly, the corresponding 4-methoxybenzoate **12b** afforded diol **13b** with only 40% enantiomeric excess. Other derivatives, such as the benzyl (**12c**), TIPS (**12d**), and MEM (**12e**) ethers, gave poor results. The corresponding free alcohols were not tested due to anticipated poor enantioselectivity and problems with extractive isolation of a water-soluble compound.[14]

The asymmetric dihydroxylation of a variety of substituted homoallylic 4-methoxyphenyl ethers proceeded with excellent enantioselectivity as indicated in Table 5. For the homoallylic dienes studied, good regioselectivity is observed, favoring dihydroxylation at the olefin proximal to the 4-methoxyphenyl group. This contrasts with the dihydroxylation of **15d** and **15e** using OsO_4/NMO which reacts preferentially with the olefin distal from the 4-methoxyphenyl group (1.8:1 and 2.4:1, respectively).

(9) For applications of the asymmetric dihydroxylation to the selective oxidation of polyenes, see: (a) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570. (b) Becker, H.; Soler, M.; Sharpless, K. B. *Tetrahedron* **1995**, *51*, 1345.

(10) For studies on the asymmetric dihydroxylations of nitrogen- and sulfur-containing olefins, see: (a) Walsh, P. J.; Bennani, Y. L.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *34*, 5545. (b) Walsh, P. J.; Ho, P. T.; King, S. B.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 5129.

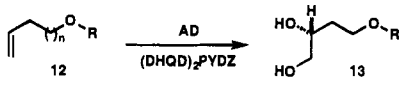
(11) MM2 calculations were performed using Macromodel v 3.5 on a Silicon Graphics Indigo^2 system. A 1000 structure Monte-Carlo conformational search using full matrix Newton Raphson refinement was conducted to locate the global energy minimum.

(12) For a preliminary communication, see: Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *Tetrahedron Lett.* **1995**, *36*, 3481.

(13) For the preparation and cleavage of 4-methoxyphenyl ethers see: Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, *26*, 6291.

(14) Methyl 3-butenoate afforded 3-hydroxybutyrolactone in 45% ee and 41% yield (due to high water solubility of the product) when dihydroxylated using the $(DHQD)_2PYDZ{\cdot}OsO_4$ system.

Table 4. Enantioselective Dihydroxylation of 3-Buten-1-ol Derivatives



12 13

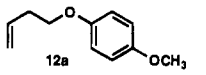
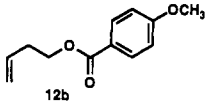
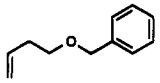
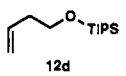
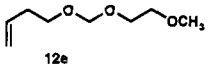
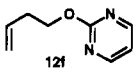
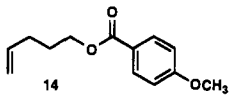
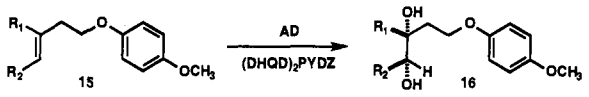
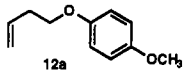
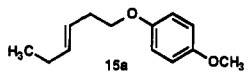
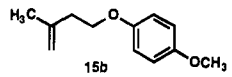
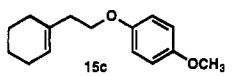
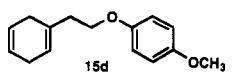
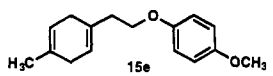
Substrate	Yield	Enantiomeric excess (ee)
 12a	96%	91%
 12b	>99%	40%
 12c	97%	52%
 12d	97%	16%
 12e	99%	38%
 12f	91%	50%
 14	99%	82%

Table 5. Enantioselective Dihydroxylation of Representative Homoallylic 4-Methoxyphenyl Ethers

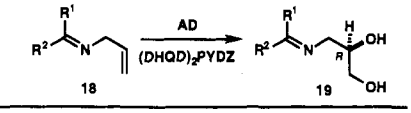


15 16

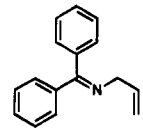
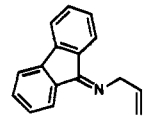
Substrate	Yield	Enantiomeric excess (ee)
 12a	96%	91%
 15a	>99%	>98%
 15b	99%	96%
 15c	99%	95%
 15d	74% of major product (≥30 : 1 regioselectivity)	95%
 15e	62% of major product (16e) 8% of minor product (17) (7 : 1 regioselectivity)	95% (major, 16e) 99% (minor, 17)

While the degree of asymmetric induction in the dihydroxylation of *N*-allyl-4-nitrobenzamide is acceptable, a more complete investigation of mechanistically guided choices of protecting groups was carried out in an attempt to improve the enantioselectivity to the levels observed for allylic alcohol derivatives. Allylic imines were chosen on the basis of their rigid conformation and ease of preparation and protecting group removal. The results are shown in Table 6. Several imines were tested, and only the benzophenone and 9-fluorenone imines were stable to the reaction conditions. *N*-Allyl-9-fluorenimine (**18b**) affords the corresponding glycol (**19b**) in high enantiomeric purity, whereas the corresponding benzophenone imine (**18a**) gives poor results, presumably due to the non-coplanarity of its two phenyl groups.[15]

Table 6. Enantioselective Dihydroxylation of Allyl Imines

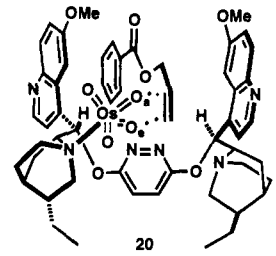


18 19

Substrate	Yield	Enantiomeric excess (ee)
 18a	53%	58%
 18b	90%	90%

Mechanistic Discussion

The successful dihydroxylation of allylic 4-methoxybenzoates and related compounds validates the principles used in the design of this substrate-directed dihydroxylation technique. The proposed transition state for enantioselective dihydroxylation of allyl 4-methoxybenzoate (**6a**) is shown in **20** (the methoxy group of the substrate was omitted for clarity) and Figure 1.



20

Examination of the above complex reveals several interesting structural features. As denoted in earlier crystallographic studies,[3b] dimeric ligands such as **1** possess a U-shaped binding pocket approximately 7.7 Å (internuclear distance) wide. When positioned within the cavity as shown in Figure 1, allyl 4-methoxybenzoate is oriented such that the aryl ring of the substrate is centered within the binding pocket and parallel to the methoxyquinoline rings of the catalyst with approximately 3.9 Å internuclear separation between them. In this orientation, the carbonyl group of the substrate lies directly above the N−N bond of the pyridazine linker group. This places the *cis*-vinylic proton and the *cis*-ortho aromatic proton of the substrate approximately 2.2 Å from the pyridazine nitrogens. The proximity of one axial and one equatorial oxygen atom of the catalyst bound OsO_4 to the olefinic carbons of the bound substrate (approximately 2.7 Å internuclear distance) allows for a minimum motion pathway for production of the thermodynamically more stable osmate ester through a [3 + 2] cycloaddition reaction across the *si* face of the olefin. This transition

(15) The asymmetric dihydroxylation of **18b** with the $(DHQ)_2PHAL$ ligand afforded the (*S*)-enantiomer of **19b** in 80% ee and 91% yield.

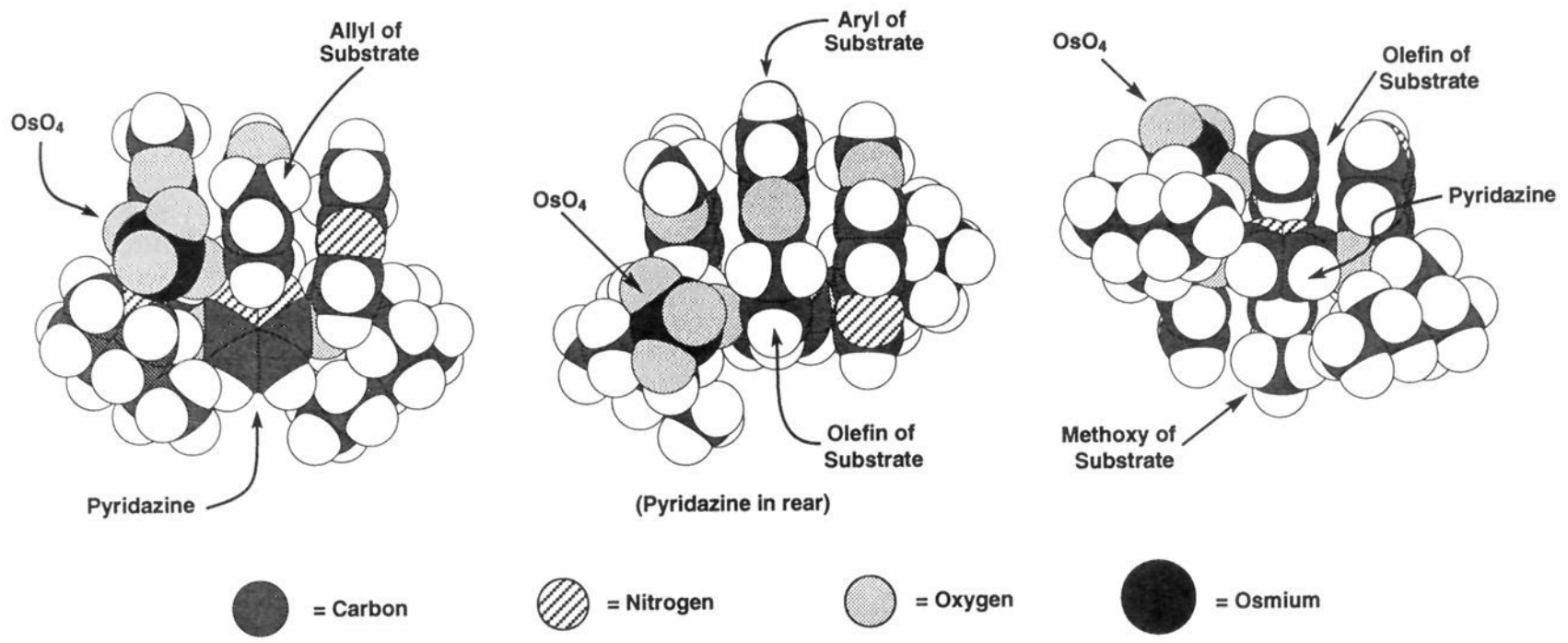


Figure 1. Three views of the proposed geometry for the complex between the allyl s-*cis*-form of allyl 4-methoxybenzoate (**6a**), OsO_4, and ligand **1**. The catalyst geometry was based on the X-ray crystal structure of **1**·CH_3I[3b] with the following modifications: (a) the methyl group of the methiodide salt was replaced by OsO_4 with the staggered arrangement about the N−Os bond and the bond distances demonstrated from X-ray studies,[3c] and (b) the H(8)−C(8)−C(9)−H(9) dihedral angle was adjusted to *ca.* 90°.[3b]

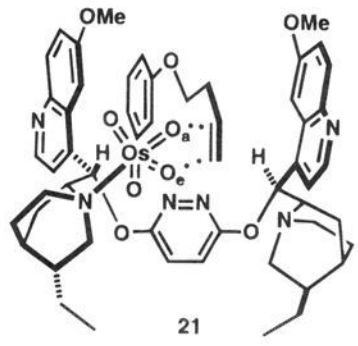
state model correctly predicts the direction and levels of enantioselectivity for each of the substrates presented above.

The following substrate features have emerged as crucial for high enantioselectivity in the reactions presented above: (1) the presence of a suitable binding group on the substrate that allows extensive π-contact and other favorable binding interactions with the U-shaped binding pocket of the catalyst, (2) accessibility of the s-*cis*-allylic conformation of the substrate that places this binding group in the correct spatial orientation for interaction with the catalyst, and (3) stability of the protecting group with regard to potential acyl migration reactions of the product that can lead to racemization and reduced yield.

Unlike conjugated aromatic olefins such as styrene, the allylic 4-methoxybenzoates, which bind to the catalyst via the 4-methoxyphenyl ring, possess a binding group remotely located from the olefinic carbon atoms. In the transition state model depicted in Figure 1, this group participates in extensive aryl π-stacking and hydrophobic interactions with each of the methoxyquinoline rings of the catalyst. In this complex, the aromatic ring of the substrate participates in offset parallel π-stacking interactions with the rearward methoxyquinoline ring of the catalyst and hydrophobic interactions with the methoxy group and upper portion of the forward methoxyquinoline group. Additional favorable van der Waals contacts occur between the allylic methylene and carboxyl group of the ester and the pyridazine linker group of the catalyst. The "thickness" of the 4-methoxybenzoate group of the substrate is optimum for achieving maximum van der Waals contacts with the interior of the catalyst binding pocket without imposing unfavorable steric interactions upon binding. The poor enantioselectivities observed in the case of allylic TIPS ether (**4a**), allylic pivalate (**4c**), and allylic benzyl ether (**4d**) can be understood based on unfavorable steric interactions between the bulky protecting group and the binding pocket.[16] Free allylic alcohols such as **4b** cannot participate in favorable hydrophobic interactions with the catalyst pocket and prefer to be solvated, resulting in low enantioselectivities.

Binding to the catalyst is facilitated by the s-*cis*-allylic geometry of the substrate that allows the 4-methoxybenzoate group to penetrate deep within the catalyst binding pocket and participate in extensive π-facial interaction with both methoxyquinoline units of the catalyst. The enantioselectivities in the dihydroxylation of allyl 4-methoxybenzoate **6a** and the structurally related ketone **10a**, amide **10b**, and thioester **10c** correlate with the relative stabilities of their s-*cis*-allylic conformational isomers. From the above transition state model, the importance of an energetically accessible s-*cis*-allylic conformation to binding of the substrate and enantioselective dihydroxylation is readily apparent. Steric factors may contribute to the weaker binding of **10b** and **10c** to the catalyst. Positioning amide **10b** inside the catalyst binding pocket according to the geometry depicted for **6a** in Figure 1 places the amide N−H group in close proximity to the pyridazine nitrogen atoms of the catalyst, resulting in mildly unfavorable steric repulsion. Similar analysis of thioester **10c** indicates that the bulky sulfur atom and the reduced C−S−C bond angle contribute to less favorable binding interactions between the substrate and the catalyst. Examination of the X-ray crystal structure of diol **11c** indicates that the C−S−C bond angle is approximately 100° which is considerably more acute than the expected 115° C−O−C bond angle of **6a**. The angle change for the thioester **10c** causes a displacement of the methoxyphenyl binding group further out of the top of the catalyst U-shaped binding pocket, resulting in reduced hydrophobic binding interactions relative to **6a**. Thus, enantioselectivity in this reaction is quite sensitive to the geometric parameters of the substrate that determine the effectiveness of the binding interactions between the olefin and the catalyst.

A similar analysis of the critical features governing enantioselective dihydroxylation of allylic 4-methoxybenzoates can be applied to the corresponding reaction of homoallylic ethers and esters. The proposed transition state model for dihydroxylation of homoallyl 4-methoxyphenyl ether is depicted in **21** (the methoxy group of the substrate is omitted for clarity) and Figure 2.



(16) Unfavorable steric interactions in the case of benzyl ethers result from a substrate conformational preference that places the phenyl group perpendicular to the plane of the olefin, according to MM2 calculations.

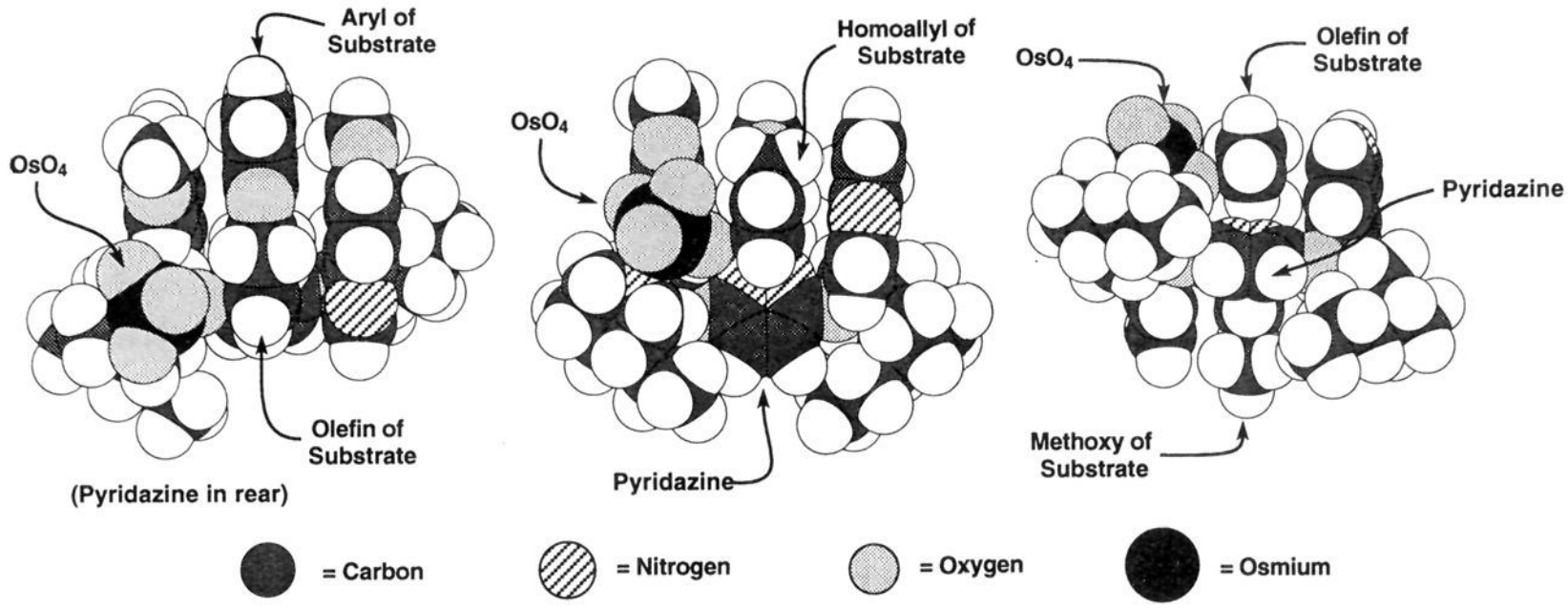


Figure 2. Three views of the proposed geometry for the complex between the allyl s-*cis* form of homoallyl 4-methoxyphenyl ether (**12a**), OsO_4, and ligand **1**. The catalyst geometry is identical to that in Figure 1.

Examination of the above complex reveals critical binding features similar to those found for allyl 4-methoxybenzoate. In this case, an additional rotational degree of freedom exists for **12a** compared to **6a** resulting from the replacement of a rigid ester carbonyl functionality by a more flexible ether methylene group. However, MM2 calculations indicate that the conformation of the substrate shown in **21** is energetically accessible.[11] This conformation of the substrate is topologically related to the s-*cis*-allylic geometry of allyl 4-methoxybenzoate and can participate in similar π-facial and hydrophobic interactions with the catalyst binding pocket. The lower enantioselectivities observed for homoallyl benzyl ether **12c**, TIPS ether **12d**, and MEM ether **12e** parallel those observed with the corresponding allylic compounds, and can be understood in terms of unfavorable steric interactions and poorer hydrophobic interactions with the catalyst. The asymmetric dihydroxylation of homoallyl 4-methoxybenzoate **12b** represents a special case in that lower enantioselectivity is observed for this substrate compared to the corresponding allylic (**6a**) and bishomoallylic (**14**) 4-methoxybenzoates. This observation can be understood by examination of the topology of each of these substrates and their interactions with the catalyst binding pocket. In the planar s-*cis* orientation, the ester carbonyl group of the homoallylic substrate is directed into close proximity with the pyridazine nitrogen atoms of the catalyst, creating unfavorable electrostatic interactions, whereas the corresponding conformation of the allylic or bishomoallylic 4-methoxybenzoates directs the ester carbonyl out of the top of the binding cavity toward solvent and orients the 4-methoxyphenyl group into the lower rear region of the pocket. These unfavorable electrostatic interactions are also absent in homoallyl 4-methoxyphenyl ether (**12a**). Homoallyl 2-pyrimidyl ether (**12f**) was subjected to the asymmetric dihydroxylation for purposes of testing this hypothesis. As indicated by MM2 calculations, the planar s-*cis* conformation of this substrate is accessible.[11] In this orientation, one of the electronegative pyrimidine nitrogen atoms is proximal to the pyridazine nitrogen atoms of the catalyst, resulting in similar electrostatic destabilization of the transition state as with the corresponding 4-methoxybenzoate ester (**12b**). As shown in Figure 3, RHF/3-21G*//RHF/3-21G* calculations[17] indicate substantial negative

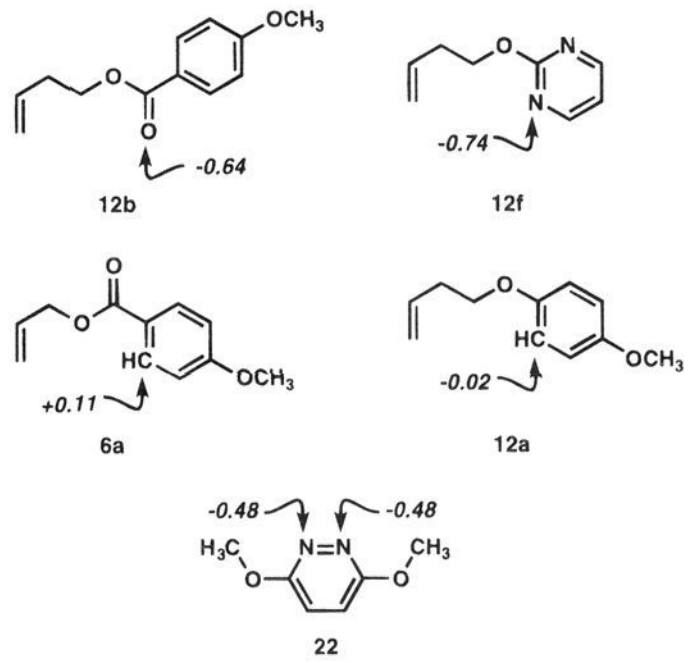


Figure 3. RHF/3-21G*//RHF/3-21G* calculated charge distributions on selected atoms of various allylic and homoallylic alcohol derivatives (H-atom charges summed into heavy atoms).

partial charge on the carbonyl group of homoallyl 4-methoxybenzoate (**12b**) (−0.64), the pyrimidine nitrogen atoms of allyl 2-pyrimidyl ether (**12f**) (−0.74), and the two nitrogen atoms of 3,6-dimethoxypyridazine (**22**) (−0.48), as a model for the $(DHQD)_2PYDZ$ catalyst linker group. The corresponding carbon atoms of homoallyl 4-methoxyphenyl ether (**12a**) and the allyl 4-methoxybenzoate ester (**6a**) exhibited much lower charges (−0.02 and +0.11 respectively).

Each of the doubly unsaturated substrates **8**, **15d**, and **15e** is more rapidly dihydroxylated at the site proximal to the aromatic binding group, although the more remote double bound is preferentially oxidized by OsO_4/NMO. Regioselectivity in the case of these substrates is expected based on the effective binding of the aryl protecting group as compared with hydrogen or methyl groups. It is noteworthy that, in the case of **8** and **15e**, high enantioselectivity is observed for minor regioisomers **9b** and **17**, respectively, as compared with the 51% ee that is obtained for the dihydroxylation of 1-methylcyclohexene using $(DHQD)_2PHAL$ ligand.[1h] It is possible that kinetic resolution of the less abundant regioisomer leads to enhanced enantiomeric excess in the case of these compounds.

The successful dihydroxylation of allyl 9-fluorenimine (**18b**) can be understood in terms of a transition state model analogous to that discussed above for allylic 4-methoxybenzoates. Molecular mechanics studies indicate that the s-*cis*-allylic conformation for **18b** is energetically accessible.[11] This conformation

(17) The calculations were performed using Gaussian 92 on a Silicon Graphics Indigo^2 workstation. *Gaussian 92*, Revision A, Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, J.; Baker, J.; Stewart, J. J. P.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1992.

of fluorenimine **18b** is topologically related to the s-*cis*-allylic conformation of allyl 4-methoxybenzoate (**6a**) and homoallyl 4-methoxyphenyl ether (**12a**), and similar interactions between the aryl groups of these substrates and the interior of the catalyst U-shaped binding pocket are observed upon docking of the olefins onto the catalyst. Each of these factors contribute to the high enantioselectivities obtained in the corresponding dihydroxylation reactions.

Conclusions

The scope and utility of the cinchona alkaloid catalyzed asymmetric dihydroxylation has been expanded to include the production of a variety of substituted chiral glycerol derivatives through the use of allylic 4-methoxybenzoates as substrates. The 4-methoxybenzoyl group serves to (1) differentiate between enantiotopic hydroxy groups in some derivatives, (2) to selectively protect one hydroxy group of the product triol for subsequent synthetic manipulation, and (3) to provide an effective binding group for the enantioselective dihydroxylation of these substrates, and in this sense, acts as an achiral controller group. This strategy has been extended both to the asymmetric dihydroxylation of homoallylic and bishomoallylic alcohol derivatives and to the dihydroxylation of allylic amine and thiol derivatives. The rational extension of the scope of the asymmetric dihydroxylation provides additional support to the previously proposed transition state model for the reaction that was the basis for each of these improvements. Our results on the successful asymmetric dihydroxylation of allylic 4-methoxybenzoates and related compounds conflict with the mechanistic model for dihydroxylation recently advanced by Sharpless *et al.*, which offers no basis for understanding the high enantioselectivities associated with the dihydroxylation of substrates, such as **6a**, that possess distal binding groups.[18]

Experimental Section

General Methods. All moisture and air sensitive reactions were performed in oven or flame dried glassware equipped with rubber septa under a positive pressure of nitrogen or argon. When necessary, solvents and reagents were distilled prior to use and were transferred using a syringe or cannula. Reaction mixtures were magnetically stirred. Thin layer chromatography was performed on Merck precoated silica gel F-254 plates (0.25 mm). Concentration *in vacuo* was generally performed using a Büchi rotary evaporator. Kugelrohr distillation temperatures are reported as oven temperatures. Flash column chromatography was performed on Baker 230−400 mesh silica gel. Melting points were determined using a Fisher-Johns hot stage apparatus and are reported uncorrected for all crystalline products. Optical rotations were determined using a Perkin-Elmer 241 polarimeter. Infrared spectra were recorded on a Nicolet 5ZDX FT-IR. Nuclear magnetic resonance spectra were recorded on Bruker AM500, AM400, AM300, and AM250 instruments. Proton NMR spectra were recorded in ppm using the residual solvent signal as an internal standard: $CDCl_3$ (7.26 ppm), C_6D_6 (7.15 ppm), or $(CD_3)_2CO$ (2.05 ppm). Carbon NMR were recorded in ppm relative to solvent signal: $CDCl_3$ (77.07 ppm), C_6D_6 (128.0 ppm), or $(CD_3)_2CO$ (29.8 ppm). Mass spectra and high resolution mass spectra (HRMS) were recorded on JEOL Model AX-505 or SX-102 spectrometers and are reported in units of mass to charge (*m/e*). Chiralcel and Chiralpak HPLC columns were obtained from Daicel Chemical Industries, Ltd.

(18) The Sharpless model invokes stabilizing interactions between the substrate and a catalyst L-shaped binding pocket in the transition state for a [2 + 2] cycloaddition reaction to form a postulated metallaoxetane intermediate which ultimately produces the product diol. See: (a) Göbel, T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329, (b) Becker, H.; Ho, P. T.; Kolb, H. C.; Loren, S.; Norrby, P.-O.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 7315, (c) Norrby, P.-O.; Kolb, H. C.; Sharpless, K. B. *J. Am. Chem. Soc.* **1994**, *116*, 8470. (d) Reference 1f.

General Procedure for the Preparation of Allylic 4-Methoxybenzoates. A solution of the corresponding alcohol in methylene chloride (0.3 M) at 23 °C was treated with triethylamine (1.5 equiv), followed by 4-methoxybenzoyl chloride (1.0 equiv). The resulting homogenous solution was treated with 4-(dimethylamino)pyridine (DMAP) (0.05 equiv) and stirred for 3 h. The resulting heterogeneous mixture was poured into water and extracted with ether. The organic extract was washed with HCl (1 M aqueous), brine, $NaHCO_3$ (saturated aqueous solution), and brine, dried with $MgSO_4$ (anhydrous), and concentrated *in vacuo*. The residue was purified by either Kugelrohr distillation or flash chromatography to afford the indicated yield of product.

1-(((4-Methoxybenzoyl)oxy)methyl)-4,4-dimethoxy-1-cyclohexene (4j). Following the general procedure for the preparation of allylic 4-methoxybenzoates, alcohol **4b**[2] (0.353 g, 2.05 mmol) afforded, after flash chromatography (hexane−EtOAc 70:30), 0.616 g (98% yield) of desired product **4j** as an oil: $R_f = 0.29$ (hexane−EtOAc 70:30); FTIR (film) 2941, 1714, 1607, 1511, 1461, 1316, 1272, 1257, 1168, 1115, 1103, 1054, 1029, 851 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, $J = 6.9$, 2.0 Hz, 2H), 6.91 (dd, $J = 6.9$, 2.0 Hz, 2H), 5.67 (br s, 1H), 4.71 (s, 2H), 3.85 (s, 3H), 3.24 (s, 6H), 2.33 (br s, 2H), 2.16 (m, 2H), 1.89 (t, $J = 6.5$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.3, 133.0, 131.6, 122.7, 121.8, 113.6, 99.3, 67.7, 55.4, 47.8, 34.0, 28.3, 24.3; EIMS 306 $[M]^+$, 154, 135 [4-methoxybenzoyl (An)]$^+$; HRMS calcd for $[C_{17}H_{22}O_5]^+$ 306.1468, found 306.1483.

Allyl 4-Methoxybenzoate (6a). Following the general procedure for the preparation of allylic 4-methoxybenzoates, allyl alcohol (0.408 mL, 6.00 mmol) afforded, after Kugelrohr distillation (150 °C (1.5 mmHg)), 1.013 g (88% yield) of the desired product **6a** as an oil: $R_f = 0.45$ (hexane−EtOAc 80:20); FTIR (film) 1716, 1607, 1511, 1460, 1361, 1317, 1257, 1169, 1102, 1030, 848 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (m, 2H), 6.90 (m, 2H), 6.02 (ddt, $J = 17.2$, 10.5, 5.6 Hz, 1H), 5.38 (dd, $J = 17.2$, 1.5 Hz, 1H), 5.26 (dd, $J = 10.5$, 1.2 Hz, 1H), 4.79 (dt, $J = 5.6$, 1.3 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 163.4, 132.6, 131.6, 122.7, 117.8, 113.6, 65.2, 55.3; EIMS 192 $[M]^+$, 135 $[An]^+$; HRMS calcd for $[C_{11}H_{12}O_3]^+$ 192.0787, found 192.0785.

Methallyl 4-Methoxybenzoate (6b). Following the general procedure for the preparation of allylic 4-methoxybenzoates, methallyl alcohol (1.035 mL, 12.3 mmol) afforded, after Kugelrohr distillation (160 °C (0.6 mmHg)), 2.301 g (91% yield) of the desired product **6b** as an oil: $R_f = 0.44$ (hexane−EtOAc 80:20); FTIR (film) 1715, 1607, 1511, 1458, 1317, 1257, 1168, 1103, 1031, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, $J = 6.9$, 2.1 Hz, 2H), 6.90 (dd, $J = 6.9$, 2.1 Hz, 2H), 5.05 (m, 1H), 4.95 (m, 1H), 4.70 (s, 2H), 3.82 (s, 3H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 163.4, 140.2, 131.6, 122.6, 113.6, 112.6, 67.7, 55.3, 19.5; EIMS 206 $[M]^+$, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{14}O_3]^+$ 206.0943, found 206.0953.

***trans*-Crotyl 4-Methoxybenzoate (6c).** Following the general procedure for the preparation of allylic 4-methoxybenzoates, *trans*-crotyl alcohol (1.280 mL, 15.0 mmol) afforded, after Kugelrohr distillation (150−160 °C (0.5 mmHg)), 2.874 g (93% yield) of the desired product **6c** as an oil: $R_f = 0.49$ (hexane−EtOAc 80:20); FTIR (film) 2941, 1713, 1607, 1582, 1511, 1459, 1446, 1421, 1376, 1316, 1257, 1168, 1102, 1031, 967, 848, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (m, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 5.83 (m, 1H), 5.68 (m, 1H), 4.70 (dd, $J = 6.4$, 0.7 Hz, 2H), 3.81 (s, 3H), 1.72 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.3, 131.5, 130.9, 125.4, 122.8, 113.5, 65.2, 55.3, 17.7; EIMS 206 $[M]^+$, 152, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{14}O_3]^+$ 206.0943, found 206.0932.

***trans*-1-((4-Methoxybenzoyl)oxy)-4-((triisopropylsilyl)oxy)-2-butene (6d).** (*E*)-2-Butene-1,4-diol was mono-acylated with 4-methoxybenzoyl chloride according to the general procedure. The mono- and bis-acylated materials were separated by flash chromatography, and the former was subsequently silylated with triisopropylsilyl trifluoromethanesulfonate and 2,6-lutidine in methylene chloride at 0 °C to afford **6d** as a colorless oil: $R_f = 0.53$ (hexane−EtOAc 80:20); FTIR (film) 2943, 2893, 2866, 1716, 1607, 1511, 1463, 1257, 1168, 1104, 1032, 883, 771, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 2H), 6.90 (m, 2H), 5.94 (m, 2H), 4.80 (m, 2H), 4.29 (d, $J = 2.6$ Hz, 2H), 3.83 (s, 3H), 1.16−1.02 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 163.4, 134.0, 131.6, 123.6, 122.8, 113.6, 64.6, 63.1,

55.4, 18.0, 12.1; CIMS 396 $[M + NH_4]^+$, 205 $[M - TIPSO]^+$; HRMS calcd for $[C_{21}H_{34}O_4Si + NH_4]^+$ 396.2570, found 396.2558.

1-Cyclohexenylmethyl 4-Methoxybenzoate (6e). Following the general procedure for the preparation of allylic 4-methoxybenzoates, 1-cyclohexenylmethanol (0.240 g, 2.14 mmol) afforded, after flash chromatography (hexane−EtOAc 90:10), 0.499 g (95% yield) of the desired product **6e** as an oil: $R_f = 0.47$ (hexane−EtOAc 80:20); FTIR (film) 2931, 2837, 1711, 1606, 1510, 1254, 1166, 1100, 1029, 847 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, $J = 8.8$ Hz, 2H), 6.91 (d, $J = 8.8$ Hz, 2H), 5.81 (s, 1H), 4.66 (s, 2H), 3.86 (s, 3H), 2.05 (m, 4H), 1.67 (m, 2H), 1.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.4, 133.2, 131.6, 125.8, 123.0, 113.6, 69.0, 55.4, 26.0, 25.0, 22.5, 22.2; EIMS 246 $[M]^+$, 153, 135 $[An]^+$; HRMS calcd for $[C_{15}H_{18}O_3]^+$ 246.1256, found 246.1252.

***cis*-Crotyl 4-Methoxybenzoate (6f).** Following the general procedure for the preparation of allylic 4-methoxybenzoates, *cis*-crotyl alcohol (1.18 mL, 14.23 mmol) afforded, after Kugelrohr distillation (160−170 °C (1.0 mmHg)), 2.829 g (96% yield) of the desired product **6f** as an oil: $R_f = 0.45$ (hexane−EtOAc 80:20); FTIR (film) 1713, 1607, 1511, 1461, 1349, 1316, 1256, 1168, 1101, 1030, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (m, 2H), 6.87 (m, 2H), 5.75−5.62 (m, 2H), 4.83 (d, $J = 6.8$ Hz, 2H), 3.79 (s, 3H), 1.73 (dd, $J = 6.6$, 1.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 163.3, 131.5, 129.3, 124.6, 122.8, 113.5, 60.2, 55.2, 13.0; EIMS 206 $[M]^+$, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{14}O_3]^+$ 206.0943, found 206.0943.

1-((4-Methoxybenzoyl)oxy)-2-methylene-3-((triisopropylsilyl)oxy)propane (6g). Methallyl alcohol was protected as its triisopropylsilyl ether using triisopropylsilyl trifluoromethanesulfonate and 2,6-lutidine in methylene chloride and was subsequently epoxidized using *m*-chloroperoxybenzoic acid in methylene chloride. The resulting epoxide was rearranged using lithium diisopropylamide in THF at reflux temperature, followed by acylation of the resulting alcohol with 4-methoxybenzoyl chloride as indicated in the general procedure to afford **6g** as a colorless oil: $R_f = 0.51$ (hexane−EtOAc 80:20); FTIR (film) 2943, 2866, 1719, 1607, 1511, 1463, 1257, 1168, 1100, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (m, 2H), 6.89 (m, 2H), 5.33 (d, $J = 1.4$ Hz, 1H), 5.22 (d, $J = 1.4$ Hz, 1H), 4.81 (s, 2H), 4.33 (s, 2H), 3.82 (s, 3H), 1.16−1.02 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 163.4, 143.5, 131.6, 122.6, 113.6, 112.4, 64.8, 64.1, 55.3, 17.9, 12.0; CIMS 396 $[M + NH_4]^+$, 379 $[M + H]^+$; HRMS calcd for $[C_{21}H_{34}O_4Si + NH_4]^+$ 396.2570, found 396.2569.

(4-Methylcyclohexa-1,4-dienyl)methyl 4-Methoxybenzoate (8). Following the general procedure for the preparation of allylic 4-methoxybenzoates, (4-methylcyclohexa-1,4-dienyl)methanol[19] (0.518 g, 4.2 mmol) afforded, after flash chromatography (hexane−EtOAc 85:15), 0.976 g (91% yield) of desired product **8** as a white solid: mp 57−59 °C; $R_f = 0.31$ (hexane−EtOAc 90:10); FTIR (film) 2670, 2934, 2864, 1708, 1608, 1509, 1449, 1367, 1313, 1281, 1255, 1168, 959, 842 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (m, 2H), 6.91 (m, 2H), 5.83 (m, 1H), 5.45 (m, 1H), 4.71 (s, 2H), 3.85 (s, 3H), 2.73 (m, 2H), 2.65 (m, 2H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 163.4, 131.7, 130.9, 130.5, 123.3, 122.8, 118.1, 113.6, 68.4, 55.4, 31.3, 27.8, 23.0; EIMS 258 $[M]^+$, 256 $[M - H_2]^+$, 153 $[AnOH_2]^+$, 135 $[An]^+$, 106 $[M - AnOH]^+$; HRMS calcd for $[C_{16}H_{18}O_3]^+$ 258.1256, found 258.1231.

***N*-(2-Propen-1-yl)-4-nitrobenzamide (10b).** To a suspension of 4-nitrobenzoic acid (9.0 g, 0.06 mol) in 500 mL of CH_2Cl_2 was added oxalyl chloride (5.7 mL, 8.3 g, 0.065 mol) and 1 mL of DMF. The resulting suspension was stirred for 2 h at 23 °C, during which time vigorous gas evolution occurred. The mixture was concentrated, and the residual solid was dissolved in 500 mL of CH_2Cl_2 and treated with allylamine (4.5 mL, 3.4 g, 0.06 mol) and triethylamine (9.8 mL, 7.1 g, 0.07 mol). After being stirred for 1 h at 23 °C, the solution was washed twice with 1 M HCl, once with $NaHCO_3$ (saturated aqueous), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was crystallized from cold methanol, giving 10.5 g (85%) of **10b** as a colorless solid: mp 116−117 °C; $R_f = 0.70$ (2:1 EtOAc−hexane); FTIR (KBr Pellet) 3321, 2950, 1654, 1640, 1600, 1548, 1518, 1490, 1424, 1411, 1361, 1345, 1327, 1303, 1258, 1107, 932 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, $J = 8.6$ Hz, 2H), 7.94 (d, $J = 8.6$ Hz, 2H), 6.48 (br s, 1H), 5.91 (ddd, $J = 5.8$, 10.5, 16.2 Hz, 1H), 5.26 (dd, $J = 1.3$, 17.2 Hz, 1H), 5.20 (d, $J = 10.2$ Hz, 1H), 4.09 (t, $J = 5.8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 149.6, 140.0, 133.4, 128.1, 123.8, 117.3, 42.7; EIMS 206 $[M]^+$, 191, 150, 135 $[An]^+$, 104; HRMS calcd for $[C_{10}H_{10}N_2O_3]^+$ 206.0691, found 206.0694.

2-Propen-1-yl 4-Methoxythiobenzoate (10c). To a solution of allylmercaptan (0.9 g, 12 mmol) in 60 mL of CH_2Cl_2 was added triethylamine (2.0 mL, 1.5 g, 14 mmol), DMAP (10 mg), and 4-methoxybenzoyl chloride (2.0 g, 12 mmol). The mixture was stirred for 1 h at 23 °C and was then diluted with 50 mL of CH_2Cl_2 and washed with 50 mL of 1 M HCl and 50 mL of $NaHCO_3$ (saturated aqueous). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by Kugelrohr distillation (200 °C (0.3 mmHg)), giving 2.3 g (94%) of **10c** as a colorless liquid: $R_f = 0.65$ (4:1 hexane−EtOAc); FTIR (film) 3009, 2967, 2934, 2839, 1658, 1603, 1578, 1509, 1462, 1419, 1310, 1260, 1215, 1169, 1030, 913, 838 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.97 (dt, $J = 2.8$, 9.7 Hz, 2H), 6.90 (dt, $J = 2.8$, 9.7 Hz, 2H), 5.88 (m, 1H), 5.30 (dt, $J = 1.4$, 15.8 Hz, 1H), 5.13 (dd, $J = 1.0$, 10.2 Hz, 1H), 3.86 (s, 3H), 3.70 (dd, $J = 1.0$, 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 163.8, 133.3, 129.8, 129.4, 117.8, 113.7, 55.5, 31.7; EIMS 208 $[M]^+$, 135 $[An]^+$; HRMS calcd for $[C_{11}H_{12}SO_2]^+$ 208.0558, found 208.0563.

4-Penten-1-yl 4-Methoxybenzoate (14). Following the general procedure for the preparation of allylic 4-methoxybenzoates, 4-penten-1-ol (1.30 mL, 12.6 mmol) afforded, after Kugelrohr distillation (160−170 °C (0.3 mmHg)), 2.61 g (94% yield) of the desired product **14** as an oil: $R_f = 0.42$ (hexane−EtOAc 80:20); FTIR (film) 2958, 1713, 1607, 1512, 1463, 1318, 1278, 1256, 1169, 1105, 1032, 915, 849 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (m, 2H), 6.91 (m, 2H), 5.84 (m, 1H), 5.06 (m, 1H), 4.99 (m, 1H), 4.30 (t, $J = 6.6$ Hz, 2H), 3.84 (s, 3H), 2.20 (m, 2H), 1.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 163.3, 137.6, 131.5, 122.9, 115.3, 113.6, 64.0, 55.4, 30.2, 28.0; EIMS 220 $[M]^+$, 152, 135 $[An]^+$; HRMS calcd for $[C_{13}H_{16}O_3]^+$ 220.1100, found 220.1104.

(1*S*,2*S*)-1-(((4-Methoxybenzoyl)oxy)methyl)-4,4-dimethoxy-1,2-cyclohexanediol (5j). A mixture of K_2CO_3 (0.112 g, 0.813 mmol), $K_3Fe(CN)_6$ (0.268 g, 0.813 mmol), $K_2OsO_4 \cdot 2H_2O$ (0.0010 g, 0.0027 mmol), $(DHQ)_2PHAL$ (0.0021 g, 0.0027 mmol), and $CH_3SO_2NH_2$ (0.026 g, 0.271 mmol) in *tert*-butyl alcohol (1.7 mL) and water (1.7 mL) was cooled to 0 °C. The resulting suspension was treated with olefin **4j** (0.083 g, 0.271 mmol), then stirred for 4 h, and then quenched by addition of Na_2SO_3 (0.50 g, 4.0 mmol). The mixture was stirred for 5 min, warmed to 23 °C over 5 min, and partitioned between EtOAc and minimal water. The organic extract was washed with KOH (1 M in water) and brine (2×), dried with Na_2SO_4 (anhydrous), and concentrated *in vacuo*. The residue was filtered through a silica gel plug eluting with EtOAc and was concentrated *in vacuo* to afford 0.086 g (93% yield) of desired compound **5j** as an oil of >99% ee (determined by HPLC) and 32:1 ratio of **5j** to products of acyl migration (determined by HPLC): $R_f = 0.34$ (hexane−EtOAc 20:80); $[\alpha]^{20}_D$ +1.61° (*c* 3.73, $CHCl_3$); FTIR (film) 3459, 2956, 1714, 1607, 1512, 1359, 1318, 1278, 1259, 1170, 1103, 1053, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, $J = 8.8$ Hz, 2H), 6.79 (d, $J = 8.8$ Hz, 2H), 4.32 (d, $J = 11.2$ Hz, 1H), 4.12 (d, $J = 11.2$ Hz, 1H), 3.73 (s, 3H), 3.64 (m, 1H), 3.58 (br s, 1H), 3.21 (br s, 1H), 3.10 (s, 3H), 3.04 (s, 3H), 2.04 (m, 1H), 1.74−1.64 (m, 4H), 1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.4, 131.6, 121.9, 113.5, 100.3, 71.8, 68.3, 68.2, 55.2, 47.5, 47.4, 35.5, 28.3, 26.4; FABMS 363 $[M + Na]^+$, 291 $[M - H_2O - OCH_3]^+$; HRMS calcd for $[C_{17}H_{24}O_7 + Na]^+$ 363.1420, found 363.1431; HPLC (chiral) Chiralcel OD at 23 °C, $\lambda = 254$ nm, hexane−2-propanol 85:15, retention times 21.9 (1*S*,2*S*), 26.3 min (1*R*,2*R*) at 1 mL/min flow rate. The absolute stereochemistry was established by transformation of **5j** to (−)-ovalicin ($[\alpha]^{27}_D$ −114° (*c* 0.20, $CHCl_3$), lit. $[\alpha]^{20}_D$ −117° (*c* 0.4, $CHCl_3$)).[2,20]

General Procedure for the Asymmetric Dihydroxylations of Allylic 4-Methoxybenzoates. A mixture of K_2CO_3 (3.00 equiv), $K_3Fe(CN)_6$ (3.00 equiv), $K_2OsO_4 \cdot 2H_2O$ (0.01 equiv), $(DHQD)_2PYDZ$ (0.01 equiv), and $CH_3SO_2NH_2$ (only for 1,2-disubstituted and trisubstituted olefins, 1.00 equiv) in *tert*-butyl alcohol−water 1:1 was cooled

(19) Prepared according to: (a) Bailey, W. J.; Baylouny, R. A. *J. Org. Chem.* **1962**, *27*, 3476. (b) Sugawara, F.; Sugiyama, T.; Kobayashi, A.; Yamashita, K. *Agric. Biol. Chem.* **1978**, *42*, 847.

(20) Bollinger, P.; Sigg, H. P.; Weber, H. P. *Helv. Chim. Acta* **1973**, *56*, 819.

to 0 °C. The resulting suspension was treated with the corresponding olefin (0.1 M with respect to total reaction volume). The mixture was stirred until all of the starting material disappeared by TLC (1.5−3.5 h) and quenched by addition of Na_2SO_3 (12 equiv). The mixture was stirred for 5 min, warmed to 23 °C over 5 min, and partitioned between EtOAc and minimal water. The organic extract was washed twice with brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was filtered through a silica gel plug, eluting with EtOAc. The filtrate was concentrated *in vacuo* to afford the indicated yield of product.

(*S*)-3-((4-Methoxybenzoyl)oxy)-1,2-propanediol (7a). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, allyl 4-methoxybenzoate (**6a**) (0.057 g, 0.297 mmol) afforded 0.067 g (>99% yield) of the desired product **7a** as a white solid of 98% ee (determined by HPLC): mp 75−77 °C; R_f = 0.34 (EtOAc); $[\alpha]^{25}_D$ +5.2° (*c* 1.61, EtOAc), $[\alpha]^{25}_D$ +13.4° (*c* 1.32, pyridine), lit. for (*R*)-enantiomer: $[\alpha]_D$ −13.8° (*c* 1.36, pyridine);[21] FTIR (film) 3407, 1710, 1606, 1512, 1319, 1277, 1258, 1170, 1104, 1028, 848 cm^{-1}; ^{1}H NMR (400 MHz, d_6-acetone) δ 8.00 (m, 2H), 7.01 (m, 2H), 4.37 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.28 (dd, *J* = 11.2, 6.2 Hz, 1H), 4.22 (d, *J* = 5.3 Hz, 1H), 3.98 (m, 1H), 3.87 (s, 3H), 3.85 (m, 1H), 3.66 (m, 2H); ^{13}C NMR (100 MHz, d_6-acetone) δ 166.6, 164.5, 132.3, 123.7, 114.6, 71.1, 66.8, 64.2, 55.9; EIMS 226 $[M]^+$, 195 $[M - OCH_3]^+$, 152, 135 $[An]^+$; HRMS calcd for $[C_{11}H_{14}O_5]^+$ 226.0841, found 226.0847; HPLC (chiral) Chiralpak AS at 23 °C, λ = 254 nm, hexane−2-propanol 75:25, retention times 17.06 (*S*), 23.91 min (*R*) at 1 mL/min flow rate.

(*S*)-3-((4-Methoxybenzoyl)oxy)-2-methyl-1,2-propanediol (7b). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, methallyl 4-methoxybenzoate (**6b**) (0.079 g, 0.383 mmol) afforded 0.090 g (98% yield) of the desired product **7b** as an oil of 97% ee (determined by HPLC): R_f = 0.31 (hexane−EtOAc 20:80); $[\alpha]^{22}_D$ −1.7° (*c* 4.12, EtOAc); FTIR (film) 3420, 1710, 1607, 1512, 1319, 1259, 1170, 1106, 1055, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (m, 2H), 6.87 (m, 2H), 4.30 (d, *J* = 11.2 Hz, 1H), 4.17 (d, *J* = 11.2 Hz, 1H), 3.81 (s, 3H), 3.56 (d, *J* = 11.6 Hz, 1H), 3.46 (d, *J* = 11.6 Hz, 1H), 3.36 (br s, 2H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.6, 131.8, 121.9, 113.7, 72.2, 68.0, 66.9, 55.4, 21.3; EIMS 240 $[M]^+$, 209 $[M - OCH_3]^+$, 166, 152, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{16}O_5]^+$ 240.0998, found 240.1008; HPLC (chiral) Chiralpak AS at 23 °C, λ = 254 nm, hexane−2-propanol 75:25, retention times 8.03 (*S*), 11.88 min (*R*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) acetonide formation with 2-methoxypropene and catalytic $POCl_3$ in CH_2Cl_2, followed by (2) treatment with K_2CO_3 in CH_3OH to afford (*R*)-2,2,4-trimethyl-1,3-dioxolane-4-methanol: $[\alpha]^{24}_D$ +6.8° (*c* 1.17, CH_2Cl_2), lit. $[\alpha]^{20}_D$ +5.35° (*c* 0.28, CH_2Cl_2).[22]

(2*R*,3*R*)-1-((4-Methoxybenzoyl)oxy)-2,3-butanediol (7c). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, *trans*-crotyl 4-methoxybenzoate (**6c**) (0.066 g, 0.320 mmol) afforded 0.074 g (96% yield) of the desired product **7c** as a white solid of >99% ee (determined by HPLC) and 18:1 ratio of **7c** to products of acyl migration (determined by ^{1}H NMR): mp 66−67 °C; R_f = 0.20 (ether); $[\alpha]^{23}_D$ +3.3° (*c* 2.15, $CHCl_3$); FTIR (film) 3428, 1711, 1607, 1512, 1319, 1278, 1259, 1170, 1105, 1076, 1029, 848, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 2H), 6.87 (m, 2H), 4.40 (dd, *J* = 11.7, 4.3 Hz, 1H), 4.30 (dd, *J* = 11.7, 6.4 Hz, 1H), 3.82 (s, 3H), 3.84−3.81 (m, 1H), 3.71 (m, 1H), 3.46 (d, *J* = 4.7 Hz, 1H), 3.13 (br s, 1H), 1.25 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 163.6, 131.8, 122.0, 113.7, 73.9, 67.7, 66.0, 55.4, 19.2; EIMS 240 $[M]^+$, 195 $[M - CH_3CHOH]^+$, 152, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{16}O_5]^+$ 240.0998, found 240.0996; HPLC (chiral) Chiralpak AS at 23 °C, λ = 254 nm, hexane−2-propanol 60:40, retention times 9.57 (2*R*,3*R*), 24.65 min (2*S*,3*S*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) treatment with K_2CO_3 in CH_3OH followed by (2) peracylation with 4-nitrobenzoyl chloride, triethylamine, and DMAP in CH_2Cl_2 to afford (2*R*,3*R*)-1,2,3-tris((4-nitrobenzoyl)oxy)butane: $[\alpha]^{25}_D$ −5.8° (*c* 2.30, $CHCl_3$), lit. $[\alpha]^{23}_D$ −9.05° (*c* 2.19, $CHCl_3$).[23]

(2*R*,3*R*)-1-((4-Methoxybenzoyl)oxy)-4-((triisopropylsilyl)oxy)-2,3-butanediol (7d). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, *trans*-1-((4-methoxybenzoyl)oxy)-4-((triisopropylsilyl)oxy)-2-butene (**6d**) (0.103 g, 0.272 mmol) afforded 0.106 g (94% yield) of the desired product **7d** as an oil of >99% ee (determined by HPLC) and >50:1 ratio of **7d** to products of acyl migration (determined by ^{1}H NMR): R_f = 0.46 (hexane−EtOAc 50:50); $[\alpha]^{22}_D$ −2.0° (*c* 4.29, EtOAc); FTIR (film) 3469, 2944, 2894, 2867, 1716, 1607, 1512, 1463, 1317, 1258, 1170, 1117, 1066, 1032, 883 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (m, 2H), 6.87 (m, 2H), 4.41 (m, 2H), 4.05 (m, 1H), 3.85 (m, 2H), 3.82 (s, 3H), 3.76 (m, 1H), 3.22 (d, *J* = 4.8 Hz, 1H), 2.94 (d, *J* = 5.8 Hz, 1H), 1.15−1.00 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 163.6, 131.8, 122.3, 113.6, 71.0, 70.3, 65.7, 65.4, 55.4, 17.9, 11.8; FABMS 435 $[M + Na]^+$, 413 $[M + H]^+$, 395 $[M - OH]^+$, 239 $[M - TIPSO]^+$; HRMS calcd for $[C_{21}H_{36}O_6Si + Na]^+$ 435.2179, found 435.2171; HPLC (chiral) Chiralcel OD at 23 °C, λ = 254 nm, hexane−2-propanol 90:10, retention times 10.81 (2*R*,3*R*), 15.83 min (2*S*,3*S*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) acetonide formation with 2-methoxypropene and catalytic $POCl_3$ in CH_2Cl_2, (2) treatment with tetrabutylammonium fluoride in THF, followed by (3) treatment with K_2CO_3 in CH_3OH to afford (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol: $[\alpha]^{23}_D$ −3.52° (*c* 0.51, EtOH), lit. $[\alpha]^{20}_D$ −3° (*c* 5, EtOH).[24]

(1*R*,2*R*)-1-(((4-Methoxybenzoyl)oxy)methyl)-1,2-cyclohexanediol (7e). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, 1-cyclohexenylmethyl 4-methoxybenzoate (**6e**) (0.082 g, 0.333 mmol) afforded 0.093 g (>99% yield) of the desired product **7e** as a white solid of 98% ee (determined by HPLC) and >50:1 ratio of **7e** to products of acyl migration (determined by HPLC): mp 72−73 °C; R_f = 0.35 (hexane−EtOAc 40:60); $[\alpha]^{24}_D$ +4.04° (*c* 2.60, $CHCl_3$); FTIR (film) 3374, 3318, 2938, 1713, 1606, 1511, 1316, 1280, 1253, 1169, 1106, 1032 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (m, 2H), 6.90 (m, 2H), 4.50 (d, *J* = 11.3 Hz, 1H), 4.03 (d, *J* = 11.3 Hz, 1H), 3.84 (s, 3H), 3.49 (m, 1H), 3.13 (d, *J* = 5.2 Hz, 1H), 2.78 (s, 1H), 1.82 (m, 1H), 1.73−1.56 (m, 4H), 1.46 (m, 2H), 1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.8, 131.9, 122.1, 113.8, 72.7, 70.6, 68.8, 55.5, 32.6, 29.3, 23.8, 20.4; EIMS 280 $[M]^+$, 210, 166, 152, 135 $[An]^+$; HRMS calcd for $[C_{15}H_{20}O_5]^+$ 280.1311, found 280.1312; HPLC (chiral) Chiralcel OD at 23 °C, λ = 254 nm, hexane−2-propanol 85:15, retention times 15.30 (1*S*,2*S*), 21.04 min (1*R*,2*R*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) Swern oxidation followed by (2) treatment with K_2CO_3 in CH_3OH to afford (*R*)-2-hydroxycyclohexanone-2-methanol: $[\alpha]^{23}_D$ −76.4° (*c* 0.77, $CHCl_3$), lit. for (*S*)-enantiomer $[\alpha]^{20}_D$ +42.5° (*c* 1.0, $CHCl_3$, 92% ee).[25]

(2*R*,3*S*)-1-((4-Methoxybenzoyl)oxy)-2,3-butanediol (7f). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, *cis*-crotyl 4-methoxybenzoate (**6f**) (0.060 g, 0.291 mmol) afforded 0.069 g (99% yield) of the desired product **7f** as a white solid of 49% ee (determined by HPLC) and 25:1 ratio of **7f** to products of acyl migration: mp 56−59 °C; R_f = 0.36 (hexane−EtOAc 10:90); $[\alpha]^{24}_D$ +4.74° (*c* 3.02, $CHCl_3$); FTIR (film) 3442, 2973, 1710, 1607, 1512, 1459, 1421, 1378, 1320, 1279, 1259, 1172, 1108, 1074, 1029, 849 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (m, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.36 (d, *J* = 5.0 Hz, 2H), 3.87 (m, 2H), 3.79 (s, 3H), 3.58 (d, *J* = 4.5 Hz, 1H), 3.29 (d, *J* = 4.3 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.6, 131.8, 122.0, 113.7, 73.7, 68.4, 65.7, 55.4, 18.0; EIMS 240 $[M]^+$, 195 $[M - CH_3CHOH]^+$, 152, 135 $[An]^+$; HRMS calcd for $[C_{12}H_{16}O_5]^+$ 240.0998, found 240.0986; HPLC (chiral) Chiralpak AS at 23 °C, λ = 254 nm, hexane−2-propanol 60:40, retention times 12.79 (2*S*,3*R*), 19.76 min (2*R*,3*S*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) acetonide formation with 2-methoxypropene and catalytic $POCl_3$ in CH_2Cl_2 and (2) treatment with K_2CO_3 in CH_3OH to

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afford (4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolane-4-methanol: $[\alpha]^{24}_D$ +25.5° (*c* 0.42, $CHCl_3$, 49% ee), lit. $[\alpha]^{20}_D$ +52° (*c* 1, $CHCl_3$).[26]

(*S*)-2-(((Triisopropylsilyl)oxy)methyl)-3-((4-methoxybenzoyl)oxy)-1,2-propanediol (7g). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, 1-((4-methoxybenzoyl)oxy)-2-methylene-3-((triisopropylsilyl)oxy)propane (**6g**) (0.108 g, 0.285 mmol) afforded 0.115 g (98% yield) of the desired product **7g** as an oil of >97% ee (determined by HPLC): R_f = 0.43 (hexane−EtOAc 50:50); $[\alpha]^{25}_D$ −1.3° (*c* 5.19, $CHCl_3$); FTIR (film) 3472, 2944, 2892, 2867, 1717, 1607, 1512, 1463, 1317, 1257, 1170, 1101, 1064, 1033, 883 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (m, 2H), 6.88 (m, 2H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.34 (d, *J* = 11.5 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 2H), 3.65 (s, 2H), 3.24 (s, 1H), 2.85 (br s, 1H), 1.13−1.00 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.6, 131.7, 122.0, 113.7, 74.1, 65.1, 64.6, 64.1, 55.4, 17.9, 11.8; FABMS 435 $[M + Na]^+$, 413 $[M + H]^+$, 395 $[M - OH]^+$, 369; HRMS calcd for $[C_{21}H_{36}O_6Si + Na]^+$ 435.2179, found 435.2183; HPLC (chiral) Chiralcel OD at 23 °C, λ = 254 nm, hexane−2-propanol 90:10, retention times 10.81 (*S*), 15.83 min (*R*) at 1 mL/min flow rate. The absolute stereochemistry was established by converting this material to (*R*)-**7b** by (1) treatment with iodine, triphenylphosphine, and imidazole in toluene, (2) reduction with tributyltin hydride and AIBN in toluene, followed by (3) desilylation with HF in acetonitrile and comparison of the chiral HPLC retention time with that of (*S*)-**7b**.

(1*R*,2*R*)-1-(((4-Methoxybenzoyl)oxy)methyl)-4-methyl-4-cyclohexene-1,2-diol (9a). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, (4-methylcyclohexa-1,4-dienyl)methyl 4-methoxybenzoate (**8**) (0.126 g, 0.488 mmol) afforded a 6:1 mixture of regioisomers **9a** and **9b** (determined by ^1H NMR analysis of the crude product), which was purified by flash chromatography (hexane−EtOAc 30:70−0:100) to provide 0.080 g (56% yield) of desired product **9a** as an oil of >99% ee (determined by HPLC) and 0.014 g (10% yield) of regioisomer **9b** of 96% ee (determined by ^1H NMR analysis in $CDCl_3$ of the MTPA ester). Data for **9a**: R_f = 0.37 (hexane−EtOAc 30:70); $[\alpha]^{18}_D$ −43.6° (*c* 3.7, $CHCl_3$); FTIR (film) 3442, 2911, 1711, 1607, 1512, 1458, 1422, 1370, 1318, 1278, 1258, 1169, 1105, 1064, 1029, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 2H), 6.89 (m, 2H), 5.24 (m, 1H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.10 (d, *J* = 11.4 Hz, 1H), 3.83 (s, 3H), 3.81 (m, 1H), 3.25 (br s, 1H), 2.97 (br s, 1H), 2.36−2.20 (m, 4H), 1.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 163.7, 131.8, 131.3, 121.8, 117.4, 113.7, 72.0, 68.4, 67.6, 55.4, 35.0, 33.3, 22.9; CIMS 310 $[M + NH_4]^+$, 293 $[M + H]^+$, 135 $[An]^+$; HRMS calcd for $[C_{16}H_{20}O_5 + H]^+$ 293.1389, found 293.1382; HPLC (chiral) Chiralpak AD at 23 °C, λ = 254 nm, hexane−2-propanol 80:20, retention times 24.2 (1*R*,2*R*), 18.6 min (1*S*,2*S*) at 1 mL/min flow rate. Data for **9b**: R_f = 0.16 (hexane−EtOAc 30:70); ^1H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.67 (m, 1H), 4.67 (s, 2H), 3.83 (s, 3H), 3.69 (dd, *J* = 9.9, 4.9 Hz, 1H), 2.71 (d, *J* = 5.1 Hz, 1H), 2.56 (s, 1H), 2.43−2.12 (m, 4H), 1.22 (s, 3H).

(*R*)-5-(4-Methoxyphenyl)-1,2-dihydroxy-5-pentanone (11a). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, 1-(4-methoxyphenyl)-4-penten-1-one (**10a**)[27] (0.400 g, 2.11 mmol) afforded 0.452 g (96%) of **11a** as a colorless solid of >98% enantiomeric excess (determined by ^1H NMR integration of the corresponding bis-MPTA esters): mp 39−40 °C; R_f = 0.2 (2:1 EtOAc−hexane); $[\alpha]^{23}_D$ +16.3° (*c* 0.46, EtOH); IR (film) 3600−3400, 2935, 1673, 1601, 1576, 1512, 1461, 1419, 1365, 1313, 1260, 1212, 1174, 1100, 1028, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (dt, *J* = 2.8, 9.8 Hz, 2H), 6.92 (dt, *J* = 2.8, 9.8 Hz, 2H), 3.87 (s, 3H), 3.77 (m, 1H), 3.69 (dd, *J* = 3.4, 11.1 Hz, 1H), 3.50 (dd, *J* = 6.9, 11.1 Hz, 1H), 3.15 (t, *J* = 6.7 Hz, 2H), 1.93 (m, 2H), 1.64 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 163.7, 130.4, 129.7, 113.8, 71.7, 66.7, 55.5, 34.4, 27.2; CIMS (NH_3) 242 $[M + NH_4]^+$, 225 $[M + H]^+$, 207; HRMS calcd for $[C_{12}H_{16}O_4 + H]^+$ 225.1127, found 225.1118. The absolute stereochemistry was established by (1) enol ether formation and protection of the alcohols with *tert*-butyldimethylsilyl trifluoromethanesulfonate and diisopropylethylamine in methylene chloride, (2) ozonolysis in 2:1 CH_2Cl_2−methanol, (3) reduction with sodium borohydride in THF−EtOH, followed by (4) deprotection with tetrabutylammonium fluoride in THF to afford (*R*)-1,2,4-butanetriol: $[\alpha]^{23}_D$ +24° (*c* 0.57, MeOH), lit. for (*S*)-enantiomer $[\alpha]_D$ −28° (*c* 1.07, MeOH).[28]

(*R*)-2,3-Dihydroxy-1-propyl 4-Nitrobenzamide (11b). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, *N*-(2-propen-1-yl)-4-nitrobenzamide (**10b**) (0.198 g, 0.96 mmol) afforded 0.220 g (96%) of diol **11b** of 81% ee (determined by ^1H NMR integration of the corresponding bis-MPTA esters): mp 99−105 °C; R_f = 0.52 (20:80:2 MeOH−$CHCl_3$−NH_4OH); $[\alpha]^{23}_D$ + 13.0° (*c* 0.27, EtOH); IR (KBr Pellet) 3600−3200, 2900, 1648, 1601, 1562, 1524, 1489, 1434, 1349, 1329, 1302, 1110, 1086, 1064, 860 cm^{-1}; ^1H NMR (500 MHz, d_6-acetone) δ 8.32 (dt, *J* = 2.3, 9.2 Hz, 2H), 8.15 (dt, *J* = 2.3, 9.2 Hz, 2H), 8.15 (br s, 1H), 4.12 (d, *J* = 5.1 Hz, 1H), 3.85 (br m, 2H), 3.59 (m, 1H), 3.50 (m, 4H); ^{13}C NMR (d_6-acetone, 100 MHz) δ 166.6, 150.4, 141.2, 129.4, 124.2, 71.8, 64.8, 44.1; FABMS 241 $[M + H]^+$, 225; HRMS calcd for $[C_{10}H_{12}N_2O_5 + H]^+$ 241.0824, found 241.0831. The absolute stereochemistry was established by synthesis of an authentic sample of (*S*)-**11b** from (*S*)-2,2-dimethyl-1,3-dioxolane-4-methylamine[29] by (1) acylation with 4-nitrobenzoyl chloride, triethylamine, and DMAP in CH_2Cl_2 followed by (2) treatment with HCl in methanol: $[\alpha]^{23}_D$ −17.9° (*c* 0.75, EtOH).

(*S*)-2,3-Dihydroxy-1-propyl 4-Methoxythiobenzoate (11c). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, 2-propen-1-yl 4-methoxythiobenzoate (**10c**) (0.200 g, 0.96 mmol) afforded a 0.107 g (46%) yield of diol **11c** of 77% ee (determined by ^1H NMR integration of the corresponding bis-MPTA esters) plus 0.072 g (36%) of recovered **10c**. Data for **11c**: mp 57−60 °C; R_f = 0.30 (2:1 EtOAc−hexane); $[\alpha]^{23}_D$ +15.7° (*c* 0.46, C_6H_6); IR (KBr Pellet) 3700−3100, 2933, 1654, 1603, 1577, 1509, 1458, 1311, 1263, 1217, 1170, 1115, 1028, 916, 837 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.95 (dt, *J* = 2.9, 9.8 Hz, 2H), 6.90 (dt, *J* = 2.9, 9.8 Hz, 2H), 3.93 (m, 1H), 3.86 (s, 3H), 3.69 (dd, *J* = 3.8, 11.6 Hz, 1H), 3.60 (dd, *J* = 5.3, 11.6 Hz, 1H), 3.28 (dd, *J* = 5.8, 14.2 Hz, 1H), 3.20 (dd, *J* = 6.4, 14.2 Hz, 1H), 2.80 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.6, 164.1, 129.7, 129.3, 113.9, 71.4, 64.6, 55.5, 31.5; CIMS (NH_3) 243 $[M + H]^+$; HRMS calcd for $[C_{11}H_{14}SO_4]^+$ 242.0613, found 242.0613. The absolute stereochemistry was established by X-ray crystallographic analysis of **11c**. See the supporting information for details.

(*R*)-4,5-Dihydroxypent-1-yl 4-Methoxybenzoate. Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, 4-penten-1-yl 4-methoxybenzoate (**14**) (0.078 g, 0.354 mmol) afforded 0.089 g (99% yield) of the desired product as a white solid of 82% ee (determined by ^1H NMR analysis in $CDCl_3$ of the bis-MTPA ester): mp 39−40 °C; R_f = 0.28 (EtOAc); $[\alpha]^{20}_D$ +2.6° (*c* 2.74, $CHCl_3$); FTIR (film) 3396, 2939, 1709, 1607, 1512, 1319, 1281, 1259, 1170, 1106, 1072, 1029, 849 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 4.29 (t, *J* = 6.6 Hz, 2H), 3.82 (s, 3H), 3.75 (br s, 1H), 3.63 (m, 1H), 3.42 (m, 2H), 3.27 (br s, 1H), 1.93−1.78 (m, 2H), 1.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.4, 131.6, 122.6, 113.6, 71.8, 66.7, 64.6, 55.4, 29.5, 25.1; CIMS 272 $[M + NH_4]^+$, 255 $[M + H]^+$; HRMS calcd for $[C_{13}H_{18}O_5 + H]^+$ 255.1232, found 255.1238.

General Procedure for the Preparation of Homoallylic 4-Methoxyphenyl Ethers.[13] A solution of the corresponding homoallylic alcohol, 4-methoxyphenol (3.0 equiv) and triphenylphosphine (1.3 equiv), in THF (0.3 M), at 23 °C, was treated with diethyl azodicarboxylate (1.3 equiv). The resulting homogenous solution was heated at reflux for 1−3 h, cooled to room temperature, and concentrated *in vacuo*. The residue was subjected to flash chromatography (hexane−CH_2Cl_2 90:10−50:50) to afford the indicated yield of product.

1-(4-Methoxyphenoxy)-3-butene (12a). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, 3-buten-1-ol (1.02 mL, 11.9 mmol) afforded 1.84 g (87% yield) of desired product **12a** as an oil: R_f = 0.42 (hexane−EtOAc 90:10); FTIR (film) 2948, 1509, 1470, 1442, 1233, 1181, 1042, 991, 918, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.84 (m, 4H), 5.91 (m, 1H), 5.17 (m,

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1H), 5.10 (m, 1H), 3.97 (t, J = 6.7 Hz, 2H), 3.77 (s, 3H), 2.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.0, 134.6, 116.8, 115.5, 114.5, 67.8, 55.6, 33.7; EIMS 178 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{11}H_{14}O_2]^+$ 178.0994, found 178.0999.

(*E*)-1-(4-Methoxyphenoxy)-3-hexene (15a). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, (*E*)-3-hexen-1-ol (1.23 mL, 10.0 mmol) afforded 1.93 g (94% yield) of desired product **15a** as an oil: R_f = 0.46 (hexane−EtOAc 90:10); FTIR (film) 2961, 2933, 1509, 1468, 1232, 1042, 969, 825 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (m, 4H), 5.64 (dt, J = 15.3, 6.2 Hz, 1H), 5.51 (dt, J = 15.3, 6.7 Hz, 1H), 3.94 (t, J = 6.9 Hz, 2H), 3.78 (s, 3H), 2.48 (q, J = 6.8 Hz, 2H), 2.07 (quintet, J = 7.1 Hz, 2H), 1.03 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.2, 134.7, 124.6, 115.5, 114.6, 68.5, 55.6, 32.6, 25.7, 13.7; EIMS 206 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{13}H_{18}O_2]^+$ 206.1307, found 206.1305.

1-(4-Methoxyphenoxy)-3-methyl-3-butene (15b). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, 3-methyl-3-buten-1-ol (1.01 mL, 10.0 mmol) afforded 1.79 g (93% yield) of desired product **15b** as an oil: R_f = 0.39 (hexane−EtOAc 90:10); FTIR (film) 2939, 1509, 1470, 1444, 1231, 1043, 891, 826 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (m, 4H), 4.87 (s, 1H), 4.83 (s, 1H), 4.05 (t, J = 6.8 Hz, 2H), 3.78 (s, 3H), 2.51 (t, J = 6.8 Hz, 2H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.1, 142.3, 115.6, 114.6, 111.9, 67.1, 55.6, 37.3, 22.8; EIMS 192 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{12}H_{16}O_2]^+$ 192.1151, found 192.1142.

1-(2-(4-Methoxyphenoxy)ethyl)-1-cyclohexene (15c). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, 2-(1-cyclohexenyl) ethanol[30] (1.212 g, 9.60 mmol) afforded 2.055 g (92% yield) of desired product **15c** as an oil: R_f = 0.48 (hexane−EtOAc 90:10); FTIR (film) 2929, 2860, 2834, 1508, 1469, 1442, 1232, 1042, 825 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (m, 4H), 5.54 (s, 1H), 4.00 (t, J = 7.1 Hz, 2H), 3.78 (s, 3H), 2.42 (t, J = 7.0 Hz, 2H), 2.02 (m, 4H), 1.62 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 153.2, 134.3, 123.1, 115.6, 114.6, 67.6, 55.7, 37.7, 28.7, 25.3, 22.9, 22.3; EIMS 232 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{15}H_{20}O_2]^+$ 232.1464, found 232.1466.

1-(2-(4-Methoxyphenoxy)ethyl)-1,4-cyclohexadiene (15d). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, 2-(1,4-cyclohexadienyl)ethanol[31] (1.24 g, 10.0 mmol) afforded 1.153 g (50% yield) of desired product **15d** as an oil: R_f = 0.44 (hexane−EtOAc 90:10); FTIR (film) 3027, 2944, 2906, 2878, 2823, 1507, 1469, 1440, 1289, 1231, 1180, 1107, 1040, 958, 825 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (m ,4H), 5.76 (d, J = 11.5 Hz, 1H), 5.73 (d, J = 11.5 Hz, 1H), 5.58 (s, 1H), 4.03 (t, J = 6.9 Hz, 2H), 3.78 (s, 3H), 2.72 (m, 4H), 2.46 (t, J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 153.0, 131.6, 124.1 (2C), 120.4, 115.4, 114.5, 67.1, 55.6, 37.0, 29.3, 26.7; EIMS 230 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{15}H_{18}O_2]^+$ 230.1307, found 230.1314.

1-(2-(4-Methoxyphenoxy)ethyl)-4-methyl-1,4-cyclohexadiene (15e). Following the general procedure for the preparation of homoallylic 4-methoxyphenyl ethers, 2-(4-methyl-1,4-cyclohexadienyl)ethanol[31] (0.799 g, 5.78 mmol) afforded 1.311 g (93% yield) of desired product **15e** as a white solid: mp 38−39 °C; R_f = 0.48 (hexane−EtOAc 90:10); FTIR (film) 2956, 2928, 2909, 2874, 2833, 2818, 1508, 1470, 1444, 1232, 1179, 1043, 952, 825 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (m, 4H), 5.55 (m, 1H), 5.42 (m, 1H), 4.01 (t, J = 6.9 Hz, 2H), 3.77 (s, 3H), 2.65 (m, 4H), 2.44 (t, J = 6.9 Hz, 2H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.1, 131.6, 131.2, 120.5, 118.5, 115.5, 114.6, 67.3, 55.7, 36.7, 31.7, 30.4, 23.0; EIMS 244 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{16}H_{20}O_2]^+$ 244.1464, found 244.1469.

General Procedure for the Asymmetric Dihydroxylations of 4-Methoxyphenyl Ethers. A mixture of K_2CO_3 (3.00 equiv), $K_3Fe(CN)_6$ (3.00 equiv), $K_2OsO_4{\cdot}2H_2O$ (0.002 equiv), $(DHQD)_2PYDZ$ (0.01 equiv), and $CH_3SO_2NH_2$ (only for 1,2-disubstituted and trisubstituted olefins, 1.00 equiv) in *tert*-butyl alcohol−water 1:1 was cooled to 0 °C. The resulting suspension was treated with the corresponding olefin (0.09−0.10 M with respect to total reaction volume). The mixture was stirred for 4−22 h and was quenched by addition of Na_2SO_3 (12 equiv). The resulting mixture was stirred for 5 min, warmed to 23 °C over 5 min, and partitioned between EtOAc and minimal water. The organic extract was washed twice with brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was filtered through a silica gel plug eluting with EtOAc. The filtrate was concentrated *in vacuo* and, if necessary, purified by flash chromatography to afford the indicated yield of product.

(*R*)-4-(4-Methoxyphenoxy)butane-1,2-diol (13a). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, 1-(4-methoxyphenoxy)but-3-ene (**12a**) (0.070 g, 0.393 mmol) afforded 0.080 g (96% yield) of desired product **13a** as a white solid of 91% ee (determined by ^{1}H NMR analysis in $CDCl_3$ of the bis-MTPA ester): mp 64−65 °C; R_f = 0.32 (EtOAc); $[\alpha]^{18}_D$ +5.4° (*c* 1.9, $CHCl_3$); FTIR (film) 3289, 3258, 2945, 2880, 1513, 1292, 1242, 1116, 1069, 1049, 1034, 826 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (m, 4H), 4.03 (m, 2H), 3.95 (m, 1H), 3.74 (s, 3H), 3.73 (m, 1H), 3.64 (m, 1H), 3.49 (m, 2H), 1.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 152.7, 115.5, 114.7, 70.0, 66.7, 65.7, 55.7, 32.6; EIMS 212 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{11}H_{16}O_4]^+$ 212.1049, found 212.1046. The absolute stereochemistry was established by (1) acetonide formation with 2-methoxypropene and catalytic $POCl_3$ in CH_2Cl_2 and (2) treatment with ceric ammonium nitrate in CH_3CN-H_2O to afford (*R*)-2,2-dimethyl-1,3-dioxolane-4-ethanol: $[\alpha]^{20}_D$ +2.3° (*c* 1.12, MeOH), lit. $[\alpha]^{25}_D$ +2.3° (*c* 3.125, MeOH).[32]

(3*R*,4*R*)-1-(4-Methoxyphenoxy)hexane-3,4-diol (16a). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, (*E*)-1-(4-methoxyphenoxy)-3-hexene (**15a**) (0.082 g, 0.398 mmol) afforded 0.096 g (>99% yield) of desired product **16a** as a white solid of >98% ee (determined by ^{1}H NMR analysis in $CDCl_3$ of the bis-MTPA ester): mp 74−75 °C; R_f = 0.23 (hexane−EtOAc 50:50); $[\alpha]^{18}_D$ +11.5° (*c* 3.0, $CHCl_3$); FTIR (film) 3396, 2961, 2934, 1509, 1467, 1232, 1041, 826 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (m, 4H), 4.06 (m, 2H), 3.74 (s, 3H), 3.71 (m, 1H), 3.37 (m, 1H), 3.25 (br s, 1H), 2.96 (br s, 1H), 1.90 (m, 2H), 1.57 (m, 1H), 1.48 (m, 1H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.7, 115.4, 114.6, 75.8, 71.7, 65.9, 55.7, 33.1, 26.3, 10.0; EIMS 240 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{13}H_{20}O_4]^+$ 240.1362, found 240.1373. The absolute stereochemistry was established by (1) methylation with sodium hydride and methyl iodide in THF followed by (2) treatment with ceric ammonium nitrate in CH_3CN-H_2O to afford (3*R*,4*R*)-3,4-dimethoxy-1-hexanol: $[\alpha]^{22}_D$ +46.1° (*c* 2.13, EtOH), lit. $[\alpha]^{23.5}_D$ +48.5° (*c* 4.14, EtOH).[33]

(*R*)-4-(4-Methoxyphenoxy)-2-methylbutane-1,2-diol (16b). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, 1-(4-methoxyphenoxy)-3-methyl-3-butene (**15b**) (0.083 g, 0.432 mmol) afforded 0.097 g (99% yield) of desired product **16b** as a white solid of 96% ee (determined by HPLC): mp 57−58 °C; R_f = 0.26 (hexane−EtOAc 30:70); $[\alpha]^{18}_D$ −7.7° (*c* 2.8, $CHCl_3$); FTIR (film) 3264, 2946, 2919, 2872, 1511, 1468, 1289, 1241, 1168, 1114, 1058, 1034, 829 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (m, 4H), 4.13 (ddd, J = 9.7, 7.5, 4.9 Hz, 1H), 4.06 (ddd, J = 9.6, 6.4, 5.3 Hz, 1H), 3.74 (s, 3H), 3.51 (dd, J = 11.1, 4.9 Hz, 1H), 3.45 (dd, J = 11.1, 5.3 Hz, 1H), 3.19 (br s, 1H), 3.05 (m, 1H), 2.06 (ddd, J = 14.7, 7.5, 5.2 Hz, 1H), 1.89 (ddd, J = 14.7, 6.4, 5.1 Hz, 1H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 152.4, 115.5, 114.6, 72.4, 69.9, 65.2, 55.6, 37.4, 23.9; EIMS 226 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{12}H_{18}O_4]^+$ 226.1205, found 226.1205; HPLC (chiral) Chiralpak AS at 23 °C, λ = 254 nm, hexane−2-propanol 60:40, retention times 13.5 (*R*), 27.3 min (*S*) at 1 mL/min flow rate. The absolute stereochemistry was established by (1) acetonide formation with 2-methoxypropene and catalytic $POCl_3$ in CH_2Cl_2 and (2) treatment with ceric ammonium nitrate in CH_3CN-H_2O to afford (*R*)-2,2,4-trimethyl-1,3-dioxolane-4-ethanol: $[\alpha]^{21}_D$ +8.02° (*c* 1.97, $CHCl_3$), lit. $[\alpha]^{22}_D$ +8.07° (*c* 1.66, $CHCl_3$).[34]

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(1*R*,2*R*)-1-(2-(4-Methoxyphenoxy)ethyl)cyclohexane-1,2-diol (16c). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, 1-(2-(4-methoxyphenoxy)-ethyl)-1-cyclohexene (**15c**) (0.080 g, 0.344 mmol) afforded 0.091 g (99% yield) of desired product **16c** as a white solid of 95% ee (determined by ^{1}H NMR analysis in $CDCl_3$ of the MTPA ester): mp 55−57 °C; R_f = 0.42 (hexane−EtOAc 30:70); $[\alpha]^{18}_D$ −9.6° (*c* 3.8, $CHCl_3$); FTIR (film) 3438, 2936, 2862, 1509, 1468, 1446, 1289, 1231, 1182, 1109, 1066, 1039, 970, 826 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (m, 4H), 4.14 (ddd, J = 9.6, 8.0, 4.6 Hz, 1H), 4.05 (ddd, J = 9.7, 6.0, 5.2 Hz, 1H), 3.74 (s, 3H), 3.45 (m, 1H), 3.00 (d, J = 5.7 Hz, 1H), 2.89 (s, 1H), 2.17 (ddd, J = 14.9, 8.0, 5.1 Hz, 1H), 1.87 (ddd, J = 14.9, 6.2, 4.8 Hz, 1H), 1.81 (m, 1H), 1.71−1.53 (m, 4H), 1.42−1.19 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 152.3, 115.5, 114.7, 73.8, 72.8, 65.0, 55.6, 38.4, 34.8, 29.9, 23.3, 21.0; EIMS 266 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{15}H_{22}O_4]^+$ 266.1519, found 266.1526.

(1*R*,2*R*)-1-(2-(4-Methoxyphenoxy)ethyl)-4-cyclohexene-1,2-diol (16d). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, 1-(2-(4-methoxyphenoxy)ethyl)-1,4-cyclohexadiene (**15d**) (0.092 g, 0.399 mmol) afforded a mixture with a ≥30:1 ratio of regioisomers (determined by ^{1}H NMR analysis of the crude product), which was purified by flash chromatography (hexane−EtOAc 30:70), to provide 0.078 g (74% yield) of desired product **16d** as a white solid of 95% ee (determined by ^{1}H NMR analysis in C_6D_6 of the MTPA ester): mp 61−62 °C; R_f = 0.33 (hexane−EtOAc 30:70); $[\alpha]^{18}_D$ −18.8° (*c* 1.7, $CHCl_3$); FTIR (film) 3367, 2911, 1509, 1479, 1288, 1234, 1109, 1042, 884, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (m, 4H), 5.58 (m, 2H), 4.15 (ddd, J = 9.6, 7.1, 4.7 Hz, 1H), 4.08 (ddd, J = 9.6, 7.0, 4.7 Hz, 1H), 3.77 (m, 1H), 3.75 (s, 3H), 3.02 (s, 1H), 2.84 (d, J = 5.1 Hz, 1H), 2.41−2.20 (m, 4H), 2.10 (ddd, J = 14.9, 7.1, 4.7 Hz, 1H), 1.97 (ddd, J = 14.9, 7.0, 4.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.3, 124.2, 123.7, 115.5, 114.7, 72.5, 71.1, 65.1, 55.7, 36.6, 35.4, 31.1; EIMS 264 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{15}H_{20}O_4]^+$ 264.1362, found 264.1364.

(1*R*,2*R*)-1-(2-(4-Methoxyphenoxy)ethyl)-4-methyl-4-cyclohexene-1,2-diol (16e). Following the general procedure for the asymmetric dihydroxylation of homoallylic 4-methoxyphenyl ethers, 1-(2-(4-methoxyphenoxy)ethyl)-4-methyl-1,4-cyclohexadiene (**15e**) (0.095 g, 0.389 mmol) afforded a mixture with a 7:1 ratio of regioisomers **16e** and **17** (determined by ^{1}H NMR analysis of the crude product), which was purified by flash chromatography (hexane−EtOAc 40:60−30:70) to provide 0.067 g (62% yield) of the desired product **16e** as a white solid of 95% ee (determined by ^{1}H NMR analysis in $CDCl_3$ of the MTPA ester) and 0.009 g (8% yield) of regioisomer **17** of 99% ee (determined by HPLC). Data for **16e**: mp 69−70 °C; R_f = 0.38 (hexane−EtOAc 30:70); $[\alpha]^{18}_D$ −16.9° (*c* 5.6, $CHCl_3$); FTIR (film) 3434, 2910, 1509, 1470, 1442, 1231, 1108, 1062, 1040, 826 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (m, 4H), 5.26 (m, 1H), 4.15 (ddd, J = 9.6, 7.2, 4.7 Hz, 1H), 4.08 (ddd, J = 9.6, 6.9, 4.7 Hz, 1H), 3.77 (m, 1H), 3.75 (s, 3H), 2.83 (br s, 2H), 2.30−2.16 (m, 4H), 2.12 (ddd, J = 14.9, 7.2, 4.7 Hz, 1H), 1.95 (ddd, J = 14.9, 6.9, 4.7 Hz, 1H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 152.4, 131.1, 118.1, 115.5, 114.7, 72.3, 71.5, 65.2, 55.7, 36.6, 35.9, 35.4, 22.9; EIMS 278 $[M]^+$, 124 $[CH_3OC_6H_4OH]^+$; HRMS calcd for $[C_{16}H_{22}O_4]^+$ 278.1519, found 278.1510. Data for **17**: R_f = 0.18 (hexane−EtOAc 30:70); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 4H), 5.40 (m, 1H), 3.98 (t, J = 6.7 Hz, 2H), 3.75 (s, 3H), 3.63 (t, J = 5.1 Hz, 1H), 2.47−2.14 (m, 8H), 1.21 (s, 3H); HPLC (chiral) Chiralcel OD at 23 °C, λ = 230 nm, hexane−2-propanol 85:15, retention times 28.3 (major), 18.8 min (minor) at 1 mL/min flow rate.

***N*-Allyl-9-fluorenimine (18b).**[35] A vigorously stirred solution of 9-fluorenone (2.70 g, 15.0 mmol) and allylamine (6.75 mL, 90.0 mmol) in toluene (40 mL) at 0 °C was treated dropwise with titanium tetrachloride (1.64 mL, 15.0 mmol). The mixture was stirred for 10 min, warmed to 23 °C, and stirred for 2 h. The resulting mixture was poured into water and extracted with EtOAc. The organic extract was washed with pH = 7 buffer solution and brine, dried with Na_2SO_4, and concentrated *in vacuo* to afford 3.17 g (96% yield) of desired product **18b** as a yellow solid: mp 70−72 °C; R_f = 0.42 (hexane−EtOAc 80:20); FTIR (film) 3059, 1644, 1602, 1448, 1412, 1326, 1302, 993, 918 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.66 (d, J = 7.5 Hz, 1H), 7.57 (d, J = 7.4 Hz, 1H), 7.42 (m, 2H), 7.29 (m, 2H), 6.30 (m, 1H), 5.44 (dd, J = 17.2, 1.7 Hz, 1H), 5.28 (dd, J = 10.3, 1.6 Hz, 1H), 4.83 (d, J = 5.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 143.7, 141.0, 138.4, 136.0, 131.8, 131.3, 130.9, 128.4, 128.0, 127.7, 122.6, 120.4, 119.3, 116.0, 55.6; EIMS 219 $[M]^+$, 191, 164 [fluorenylidine]$^+$; HRMS calcd for $[C_{16}H_{13}N]^+$ 219.1049, found 219.1049.

(*R*)-*N*-(2,3-Dihydroxyprop-1-yl)-9-fluorenimine (19b). Following the general procedure for the asymmetric dihydroxylation of allylic 4-methoxybenzoates, *N*-allyl-9-fluorenimine (**18b**) (0.073 g, 0.333 mmol) afforded, after flash chromatography (CH_2Cl_2−acetone−triethylamine 60:40:1), 0.076 g (90% yield) of desired product **19b** as a yellow solid of 90% ee (determined by HPLC): mp 124−126 °C; R_f = 0.24 (EtOAc); $[\alpha]^{20}_D$ +22.0° (*c* 0.71, $CHCl_3$); FTIR (film) 3299, 2921, 1648, 1602, 1450, 1307, 1087, 1045 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 7.7 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.30 (m, 2H), 4.31 (dd, J = 15.8, 4.0 Hz, 1H), 4.21 (dd, J = 15.8, 6.0 Hz, 1H), 4.17 (m, 1H), 3.95 (dd, J = 11.3, 3.9 Hz, 1H), 3.88 (dd, J = 11.4, 4.3 Hz, 1H), 3.44 (br s, 1H), 2.96 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 143.7, 141.2, 137.8, 132.0, 131.8, 131.3, 128.5, 128.1, 127.7, 122.4, 120.5, 119.6, 70.8, 65.4, 56.2; EIMS 253 $[M]^+$, 222 $[M - CH_2OH]^+$, 192 $[M - CH(OH)CH_2OH]^+$; HRMS calcd for $[C_{16}H_{15}O_2N]^+$ 253.1104, found 253.1109; HPLC (chiral) Chiralcel OD at 23 °C, λ = 254 nm, hexane−2-propanol 65:35, retention times 23.4 (*R*), 16.7 min (*S*) at 1 mL/min flow rate.

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Supporting Information Available: Text and tables giving full details of the X-ray crystallographic analysis of **11c** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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