A Substrate-Based Methodology That Allows the Regioselective Control of the Catalytic Aminohydroxylation Reaction

Hyunsoo Han,* Chang-Woo Cho, and Kim D. Janda*[a]

Abstract: Analogous to the Sharpless osmium-catalyzed asymmetric dihydroxylation (AD) reaction, structure **I** is proposed as the catalytically active species for the asymmetric aminohydroxylation (AA) reaction. Based on this model, the regiochemistry of the reaction can be inferred from the catalyst–substrate complex and is termed either mode **A** or **B** (Figure 1). In an effort to control the regiochemical outcome of the AA reaction, steric, electronic, and substrate–catalyst shape complimentarity were investigated. It was determined that each of these interactions has a modest influence on controlling the regiochemistry of the reaction (Table 1), however, the combination of these factors can greatly control the regioselectivity of the reaction (Tables 2 and 3). Thus, olefin **10** showed greater than a 20:1 preference when both steric and substrate–catalyst shape complimentarity reinforced each other. Furthermore, with α,β-unsaturated carboxylates, the aggregate effect of steric, electronic, and substrate–catalyst shape complimentarity not only increased regioselectivity, but it also *reversed* AA regioselectivity. Considering the natural abundance of vicinal amino alcohols/amino acids and the effectiveness of the Sharpless AA reaction, substrate-based regioselective control should further increase the synthetic utility of this important process.

Keywords: amino alcohols · aminohydroxylations · osmium · oxidations ·

Introduction

Considering the number of vicinal amino alcohols that can be found embedded in natural and manmade compounds,[1] a catalytic regioselective aminohydroxylation reaction of an unsymmetrical olefin could constitute an extremely valuable synthetic transformation. Historically the aminohydroxylation of an olefin dates back to late 1970s.[2] Yet, little attention was paid to this process until Sharpless and co-workers reported an osmium-catalyzed asymmetric aminohydroxylation (AA) reaction using phthalazine (PHAL)-based cinchona alkaloid ligands, chloramine-T as a nitrogen source and oxidant.[3] Subsequently, new nitrogen sources were developed that greatly increased the synthetic utility of this process with respect to both enantioselectivity and substrate specificity.[4] However, little has been done to control the regiochemistry of the catalytic AA reaction, especially with unsymmetrical olefins.[4c, 5] Herein, we report that the regioselectivity of the Sharpless AA reaction of unsymmetrical olefins can be controlled in a highly systematic manner. Our tact in engaging this problem has been to utilize a substrate-based control of the regioselectivity.[6]

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Results and Discussion

Since the Sharpless AA reaction opts to use the same metal/ligands as the asymmetric dihydroxylation (AD) reaction, it would not be unreasonable to assume that the structure of the active complex in both reactions might be very similar. Taking this minimalist approach structure **I** can be proposed for the catalytically active $Ac-N{=}OsO_3-(DHQD)_2PHAL$ complex (Figure 1).[7] In this complex, the $Ac-N{=}OsO_3$ would be coordinated to the *tert*-nitrogen atom of the quinuclidine ring in a distorted trigonal-bipyramid geometry,[8] wherein the two nitrogen ligands occupy axial positions. Based on this model, binding of an olefin would trigger transfer of the axial *N*-acetyl group and one of the equatorial oxygen atoms (O^b in Figure 1) in a [3+2] cycloaddition fashion.[7b, 9] If it is assumed that **I** is a catalytically active species, then the regioselectivity should be programmable as dictated by how an olefin binds to the catalyst. In accordance with this substrate directed AA model two binding modes (**A** and **B**) can be drawn to depict the formation of opposite regioisomers (Figure 1).

Based on these binding modes we set out to examine substrate–catalyst specificity. Table 1 shows the regioselec-

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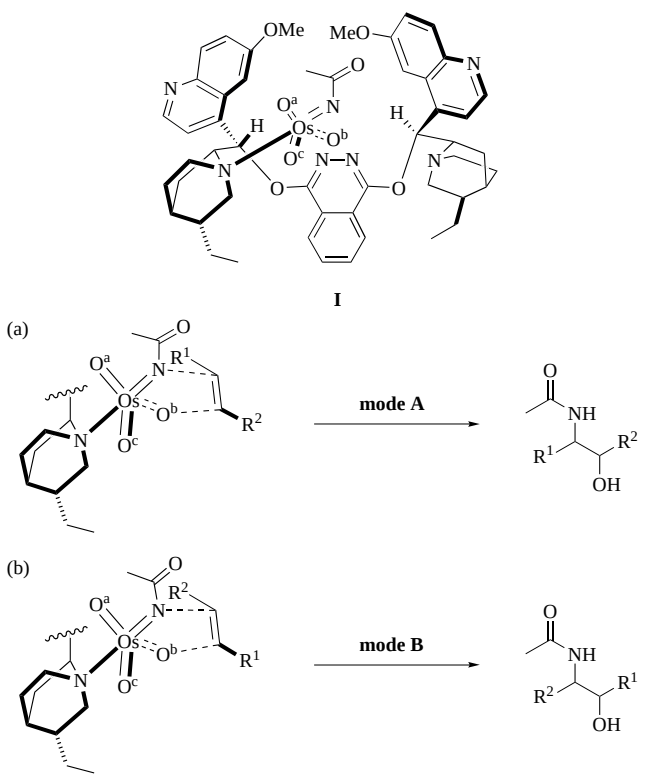
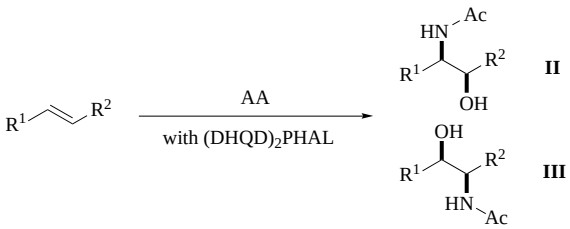
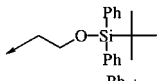
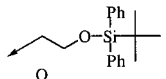
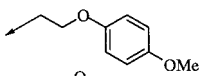
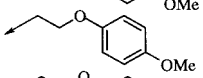
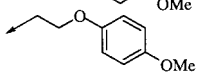


Figure 1. Proposed structure of the Ac–N=OsO_3–$(DHQD)_2PHAL$ catalyst.

Table 1. AA Reaction with selected olefins.[a]



	Olefins	Regioselectivity (**II**:**III**)[b]
1	R^1 = H, R^2 = 	> 20.0:1
2	R^1 = Et, R^2 = 	2.0:1
3	R^1 = H, R^2 = 	15.2:1
4	R^1 = Me, R^2 = 	1.4:1
5	R^1 = H, R^2 = 	1.2:1
6	R^1 = Me, R^2 = 	1:3.2
7	R^1 = Et, R^2 = 	1:3.5

[a] Os = 4 mol %, ligand = 5 mol %, *t*BuOH:H_2O = 2:3, $LiOH \cdot H_2O$ = 1.1 equiv, olefin = 1 mmol, and *N*-bromoacetamide = 1.0 equiv. [b] Regioselectivity was determined by measuring relative peak heights of the corresponding ^1H NMR spectra for the two regioisomers.

tivity obtained with some representative olefins. Each alkene was carefully chosen so as to examine steric, electronic, and/or substrate–catalyst shape complimentarity for the regioselectivity of the reactions. For compounds **1** and **2**, a sterically demanding *tert*-butyldiphenylsilyl group was appended to the olefin. In accordance with the model this moiety would not be expected to fit into the relatively narrow U-shape binding pocket of the catalyst, and thus would tend to point into solvent (mode **A**). Therefore, the difference in regioselectivity as seen for olefins **1** and **2** could be rationalized in terms of the relative size of R^1. Olefins **3** and **4** collectively showed an electronic influence on the regiochemistry. In both cases the more nucleophilic nitrogen ligand of the osmium complex prefers to add to the more electrophilic β-carbon atom of the α,β-unsaturated ester, and the oxygen atom to the α-carbon atom. It should also be noted that hydrophobicity might also play some role in orienting the substrate molecule to mode **A** as the polar ester group seeks a more hydrophilic environment away from the binding cleft. Olefins **5**, **6**, and **7** demonstrate a more subtle interplay between substrate–catalyst binding. Considering just simple steric considerations it could be argued that the *p*-methoxyphenoxy moiety would prefer mode **A**. The *p*-methoxyphenoxy functionality is much larger than any of the R^1 moieties found in **5**–**7**, yet, regioselectivities observed were opposite to what might be predicted based on simple steric considerations. These apparently contradicting results could be rationalized if aryl–aryl interactions between the substrate and the cleft of the catalyst prevail, thus mode **B** would be favored over mode **A**.[7b, 10] From Table 1, it is clear that steric, electronic, and shape complimentarity all have some influence on the regioselectivity of the Sharpless AA reaction. Furthermore, it suggests that a proper combination of these interactions could be utilized to greatly increase regioselectivity of the AA reaction.

Table 2 presents data, wherein the olefin was designed so as to contain both steric and substrate–catalyst shape complimentarity which would reinforce each other. Thus **8** and **9** display the *p*-methoxyaryl group for binding and a sterically demanding moiety enforcing steric constraints. Mode **B** type binding is expected and this prediction was borne out with these olefins, showing very good regioselectivity. To further extend this 'additive' effect compound **10** was synthesized and examined. Here regioselectivity was further increased by added aryl–aryl interactions. Interestingly, when the carbonyl group of **10** is replaced by a simple methylene unit, **11**, the regioselectivity drops considerably. We believe this result is due to increased freedom of rotation and a potential loss of aryl–aryl interactions.[9a] Based on these results other additive combinations of steric, electronic, and shape complimentarity were retooled into new substrates (Table 3). With olefins **12**–**15**, shape complimentarity and electronic interaction were used to direct the regioselectivity of the reaction. Based on these factors mode **A** binding is expected and **12** and **13** showed excellent regioselectivity. A comparison between olefins **3**, **4** (Table 1), **12**, **13** (Table 3) clearly demonstrates not only the importance of binding, but also the cooperative influence between binding and electronic effects on the regiochemistry. As seen with **11**, alkenes **14** and **15** displayed lower regioselectivity due to increased mobility.

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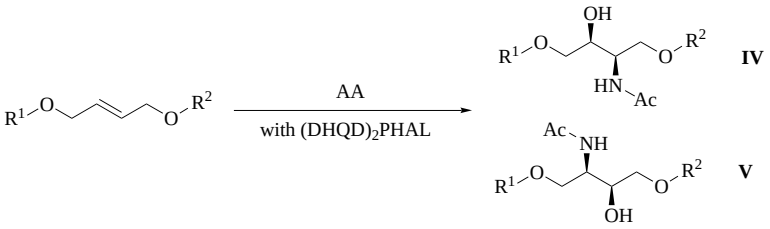
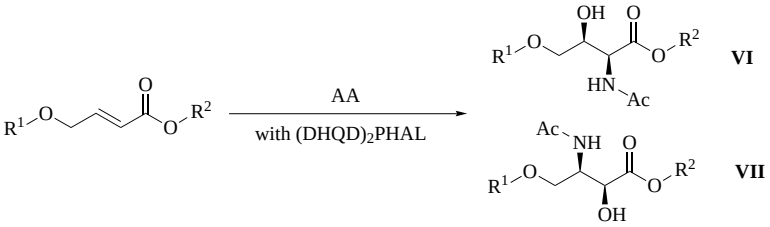
Table 2. AA reaction with *trans*-disubstituted olefins.[a]



	Olefins	Regioselectivity (**IV:V**)[b]	*ee* [%][c]	Yield [%][d]
8	R^1 = TBDPS			
	R^2 = *p*-methoxybenzoyl	11.9:1	> 95	59[e]
9	R^1 = *tert*-butyl			
	R^2 = *p*-methoxybenzoyl	14.2:1[f]	> 95	67
10	R^1 = TBDPS			
	R^2 = 2-naphthoyl	> 20.0:1	> 95	83
11	R^1 = TBDPS			
	R^2 = (2-naphthyl)methyl	3.0:1	ND	23[e]

[a] Os = 5 mol %, ligand = 6 mol %, *t*BuOH:H_2O = 2:1, LiOH · H_2O = 1.1 equiv, olefin = 0.5 mmol, and *N*-bromoacetamide = 1.0 equiv. [b] Regioselectivity was determined by measuring the relative peak heights of the corresponding ^{1}H NMR spectra for the two regioisomers. [c] Enantioselectivity was determined by ^{1}H NMR analysis of the Mosher ester derivative. [d] Combined yield of two regioisomers. [e] The reaction did not go to completion even after 48 h. [f] *t*BuOH:H_2O = 2:3 solvent.

Table 3. AA reactions with α,β-unsaturated carboxylic acid esters.[a]



	Entry	Regioselectivity (**VI:VII**)[b]	*ee* [%][c]	Yield [%][d]
12	R^1 = *p*-methoxybenzoyl			
	R^2 = ethyl	1: > 20.0	> 95	79
13	ethyl *trans*-cinnamate	1: > 20.0	> 95	65
14	R^1 = benzyl			
	R^2 = ethyl	1:2.4	ND	51
15	R^1 = (2-naphthyl)methyl			
	R^2 = ethyl	1:4.3	ND	53
16	R^1 = *tert*-butyl			
	R^2 = *p*-methoxybenzyl	1.5:1	ND	60
17	R^1 = TBDPS			
	R^2 = *p*-methoxybenzyl	6.0:1	83 (> 95)	36[e]
18	R^1 = TBDPS			
	R^1 = (2-naphthyl)methyl	17.0:1	92 (> 95)	63

[a, b, c, d, and e] See footnotes a, b, c, d, and e, respectively, in Table 2. In note c, numbers in parentheses are *ee* values after one recrystallization from ethyl acetate/hexane.

In contrast to the previous examples presented olefins **16**, **17**, and **18** (Table 3) provide test cases where both steric and shape complimentarity combine in a positive manner and electronic effects detract from the system. With this type of 'push–pull' system **16** display a slight reversal in regioselectivity compared with **12**–**15**. Encouraged by this finding we replaced the *tert*-butyl group in **16** by the bulkier *tert*-butyldiphenylsilyl (TBDPS) functionality to give **17**, which now shows enhanced regioselectivity for the formation of **VI** as was evidenced by 6.0:1 ratio. If now shape complimentarity between substrate and catalyst are further enhanced as is the case with **18**, then regioselectivity can be further skewed towards amino alcohol **VI** versus **VII**. Consequently, we see that a judicious choice of functionalities appended to the olefin can strongly impact the orientation of substrate binding to the catalyst and thus the regioselectivity of the AA reaction. Finally, since these R groups are in essence typical protecting groups their manipulation to more recognizable biologically and/or chemically relevant materials or their precursors is eminently evident.

In summary, a proposed working model for the active catalyst conformation in the Sharpless AA reaction was put forth. Based on this model, it has been shown for the first time that regiochemistry of the Sharpless AA reaction can be controlled by a combination of steric, electronic, and/or shape complimentarity of suitable protecting groups. This work highlights the ability to control the regioselectivity of the AA reaction not by an extensive catalyst redesign but rather by simple substrate alterations.

Experimental Section

NMR spectra were recorded in $CDCl_3$ at 250, 400, or 600 MHz. Flash chromatography was carried out with Mallinckrodt silica gel 60 (230-400 mesh). Analytical TLC was performed on Merck glass plates coated with 0.25 mm silica. Chloroform and dichloromethane were distilled from calcium hydride, and THF was distilled from sodium metal. *Trans*-4-(*tert*-butyldiphenylsiloxy)but-2-en-1-ol,[11] *trans*-4-(*tert*-butyldiphenylsiloxy)but-2-enoic acid,[11, 12] 3-(4-methoxyphenoxy)-1-butene (**5**),[10a] and *trans*-5-(4-methoxyphenoxy)-3-hexene (**7**)[10a] were prepared according to literature procedures. Synthetic procedures for all other olefins used in this study are detailed below.

4-(*tert*-Butyldiphenylsiloxy)-1-butene (1):[13] 60 % Sodium hydride (0.180 g, 4.50 mmol) was suspended in THF, and to the mixture was added 3-buten-1-ol (0.324 g, 4.49 mmol). The resulting mixture was stirred for 30 min at room temperature. Then, *tert*-butyldiphenyl silyl chloride (1.24 g, 4.51 mmol) was added, and vigorous stiring was continued until 3-buten-1-ol disappeared as judged by TLC. The mixture was partitioned between

diethyl ether and 10% aqueous K_2CO_3. The ether layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The resulting oil was purified by column chromatography (hexane:ethyl acetate = 70:30) (1.22 g, 3.93 mmol, 87.5%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9H), 2.33 (q, $J = 6.7$ Hz, 2H), 3.72 (t, $J = 6.7$ Hz, 2H), 5.03 (m, 2H), 5.83 (m, 1H), 7.41 (m, 6H), 7.67-7.79 (m, 4H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{20}H_{26}OSiNa$ 333.1651, found 333.1658.

***trans*-6-(Butyldiphenylsiloxy)-3-hexene (2)**: This compound was prepared according to the procedure described for **1** (1.31 g, 3.87 mmol, 86.2%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.5$ Hz, 3H), 1.05 (s, 9H), 1.99 (q, $J = 7.4$ Hz, 2H), 2.26 (q, $J = 6.8$ Hz, 2H), 3.67 (t, $J = 6.8$ Hz, 2H), 5.45 (m, 2H), 7.30-7.54 (m, 6H), 7.66-7.70 (m, 4H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{22}H_{30}OSiNa$ 361.1964, found 361.1674.

***trans*-5-(4-Methoxyphenoxy)-2-pentene (6)**:[10a] Diethyl azodicarboxylate (2.20 g, 12.6 mmol) was slowly added to a mixture of 3-buten-1-ol (0.838 g, 9.73 mmol), 4-methoxyphenol (3.62 g, 29.2 mmol), and triphenylphosphane (3.30 g, 12.6 mmol) in THF at room temperature. The resulting mixture was refluxed for 3 h, and cooled to room temperature. After all volatiles were removed, the residue was purified by column chromatography (hexane:ethyl acetate = 90:10) (1.59 g, 8.28 mmol, 85.1%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.76$ (d, $J = 6.1$ Hz, 3H), 3.82 (s, 3H), 4.69 (d, $J = 6.2$ Hz, 2H), 5.61–5.91 (m, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 7.98 (d, $J = 8.8$ Hz, 2H); HR-MS: FAB $[M + H^+]$: calcd for $C_{12}H_{17}O_2$ 193.1229, found 192.1239.

***trans*-4-(*tert*-Butyldiphenylsiloxy)-2-buten-1-yl 4-methoxybenzoate (8)**:[10b] A mixture of *trans*-4-(*tert*-butyldiphenylsiloxy)but-2-en-1-ol (1.27 g, 3.89 mmol) and triethylamine (0.433 g, 4.28 mmol) in dichloromethane was added to 4-methoxybenzoyl chloride (0.730 g, 4.28 mmol) in dichloromethane at 4 °C. After stirring overnight at room temperature, the reaction mixture was diluted with dichloromethane, washed with 1N HCl and saturated sodium bicarbonate solutions. The organic layer was dried over magnesium sulfate. Removal of the solvent and purification of the residue by column chromatography (hexane:ethyl acetate = 70:30) gave the desired product (1.52 g, 3.30 mmol, 84.8%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9H), 3.86 (s, 3H), 4.24 (s, 2H), 4.79 (d, $J = 4.9$ Hz, 2H), 5.86-6.05 (m, 2H), 6.92 (d, $J = 8.8$ Hz, 2H), 7.33–7.45 (m, 6H), 7.66–7.73 (m, 4H), 8.02 (d, $J = 8.9$ Hz, 2H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{28}H_{32}O_4SiNa$ 483.1968, found 483.1984.

***trans*-4-(*tert*-Butyldiphenylsiloxy)-2-buten-1-yl 2-naphthoate (10)**: This compound was prepared according to the procedure described for **8** (0.820 g, 1.71 mmol, 88.1%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.08$ (s, 9H), 4.27 (m, 2H), 4.89 (m, 2H), 5.94-6.10 (m, 2H), 7.37-8.08 (m, 16H), 8.64 (s, 1H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{31}H_{32}O_3SiNa$ 503.2018, found 503.2008.

***trans*-4-Hydroxy-2-buten-1-yl 4-methoxybenzoate (19)**:[11] nBu$_4$NF (2.60 mL of 1M solution in THF) was added to a solution of **8** (1.00 g, 2.08 mmol) in THF. The reaction mixture was stirred until **8** had disappeared as judged by TLC at room temperature. The mixture was then diluted with ethyl acetate, and washed with a saturated ammonium chloride solution. Drying over magnesium sulfate, followed by removal of the solvent, and purification of the residue by column chromatography (hexane:ethyl acetate = 80:20) gave the desired product (0.383 g, 1.73 mmol, 83.2%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.43$ (s, 1H), 3.80 (s, 3H), 4.15 (d, $J = 4.1$ Hz, 2H), 4.75 (d, $J = 4.7$ Hz, 2H), 5.82–6.01 (m, 2H), 6.87 (d, $J = 8.9$ Hz, 2H), 7.95 (d, $J = 8.8$ Hz, 2H); HR-MS: FAB $[M + H^+]$: calcd for $C_{12}H_{15}O_4$ 223.0971, found 223.0980.

***trans*-4-*tert*-Butoxy-2-buten-1-yl 4-methoxybenzoate (9)**:[14] Compound **19** (0.340 g, 1.53 mmol) and *tert*-butyl trichloroacetimidate (0.463 g, 1.68 mmol) were dissolved in a dichloromethane/cyclohexane co-solvent, and then a catalytic amount of boron trifluoride etherate (40 µL, 0.326 mmol) was added. After the mixture had been stirred for 24 h at room tempertaure, solid sodium bicarbonate was added, and the precipitate formed was removed by filtration. The filtrate was purified by column chromatography (hexane:ethyl acetate = 80:20) (0.276 g, 0.993 mmol, 64.9%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.19$ (s, 9H), 3.82 (s, 3H), 3.92 (s, 2H), 4.76 (d, $J = 2.0$ Hz, 2H), 5.91 (m, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 7.98 (d, $J = 8.8$ Hz, 2H); HR-MS: FAB $[M + H^+]$: calcd for $C_{16}H_{23}O_4$ 279.1596, found 279.1600.

4-Methoxybenzyl *trans*-4-(*tert*-butyldiphenylsiloxy)-2-butenoate (17):[15] *trans*-4-(*tert*-Butyldiphenylsiloxy)-2-butenoic acid (1.50 g, 4.41 mmol) was added to a suspension of cesium carbonate (1.44 g, 4.42 mmol) in DMF, and stirred for 10 min at room temperature. 4-Methoxybenzyl chloride (0.668 g, 4.27 mmol) was then added, and the resulting mixture was stirred overnight at room temperature. The reaction mixture was partitioned between water and ethyl acetate. The organic layer was washed with brine, and dried over magnesium sulfate. The solvent was removed, and the remaining residue was purified by column chromatography (hexane:ethyl acetate = 70:30) (1.79 g, 3.89 mmol, 88.2%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9H), 3.81 (s, 3H), 4.33 (m, 2H), 5.14 (s, 2H), 6.32 (dt, $J = 15.6$ and 2.4 Hz, 1H), 6.90 (d, $J = 6.9$ Hz, 2H), 7.00 (dt, $J = 15.5$ and 3.3 Hz, 1H), 7.32–7.46 (m, 8H), 7.62–7.66 (m, 4H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{28}H_{32}O_4SiNa$ 483.1968, found 483.1984.

(2-Naphthyl)methyl *trans*-4-(*tert*-butyldiphenylsiloxy)-2-butenoate (18): This compound was prepared according to the procedure described for **17** (1.24 g, 2.58 mmol, 87.8%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.09$ (s, 9H), 4.37 (m, 2H), 5.39 (s, 2H), 6.38 (dt, $J = 15.5$ and 2.3 Hz, 1H), 7.08 (dt, $J = 15.4$ & 3.2 Hz, 1H), 7.37–7.87 (m, 17H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{31}H_{32}O_3SiNa$ 503.2018, found 503.2006.

4-Methoxybenzyl *trans*-4-*tert*-butoxy-2-butenoate (16): This compound was prepared from **17** according to the procedure described for **9** (0.265 g, 0.953 mmol, 43.9% from **17**): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.56$ (s, 9H), 4.16 (s, 3H), 4.42 (m, 2H), 5.47 (s, 2H), 6.49 (dt, $J = 15.4$ & 2.0 Hz, 1H), 7.24 (d, $J = 8.4$ Hz, 2H), 7.37 (dt, $J = 15.4$ & 4.0 Hz, 1H), 7.67 (d, $J = 8.5$ Hz, 2H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{16}H_{22}O_4Na$ 301.1416, found 301.1426.

Ethyl *trans*-4-(4-methoxybenzoyloxy)-2-butenoate (12):[15] This compound was prepared from *p*-anisic acid (1.00 g, 6.57 mmol) and 75% ethyl 4-bromocrotonate (1.64 g, 6.37 mmol) according to the procedure described for **17** (1.45 g, 5.49 mmol, 86.2%): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.27$ (t, $J = 7.1$ Hz, 3H), 3.82 (s, 3H), 4.17 (q, $J = 7.1$ Hz, 2H), 4.92 (dd, $J = 4.4$ & 2.0 Hz, 2H), 6.07 (dt, $J = 15.8$ and 2.0 Hz, 1H), 6.90 (d, $J = 6.8$ Hz, 2H), 7.01 (dt, $J = 15.8$ and 4.4 Hz, 1H), 7.98 (d, $J = 6.8$ Hz, 2H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{14}H_{17}O_5$ 265.1076, found 265.1081.

Ethyl *trans*-4-benzyloxy-2-butenoate (14):[16] Benzyl alcohol (0.964 g, 8.91 mmol), ethyl 2-butynoate (1.00 g, 8.92 mmol), triphenylphosphane (0.117 g, 0.446 mmol), and acetic acid (0.107 g, 1.78 mmol) were dissolved in toluene. The resulting mixture was heated at 80 °C overnight. All volatiles were removed, and the residue was purified by column chromatography (hexane:ethyl acetate = 70:30) (1.67 g, 7.59 mmol, 85.2%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.28$ (t, $J = 7.3$ Hz, 3H), 4.10–4.26 (m, 4H), 4.55 (s, 2H), 6.13 (dt, $J = 15.7$ & 2.1 Hz, 1H), 6.96 (dt, $J = 15.7$ & 4.4 Hz, 1H), 7.32 (m, 5H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{13}H_{17}O_3$ 221.1178, found 221.1184.

Ethyl *trans*-4-(2-naphthyl)methyl-2-butenoate (15): This compound was prepared according to the procedure described for **14** (2.00 g, 7.41 mmol, 83.2%): ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.30$ (t, $J = 7.1$ Hz, 3H), 4.17 (m, 2H), 4.23 (q, $J = 7.1$ Hz, 2H), 4.68 (s, 2H), 6.20 (dt, $J = 15.7$ and 2.0 Hz, 1H), 7.03 (dt, $J = 15.7$ & 4.3 Hz, 1H), 7.44–7.52 (m, 3H), 7.77-7.85 (m, 4H); HR-MS: FAB $[M + Na^+]$: calcd for $C_{17}H_{19}O_3$ 271.1334, found 271.1342.

General procedure for the Sharpless catalytic asymmetric aminohydroxylation (AA) reaction:[4c] Basically the methodology of Sharpless was followed with the following modifications: i) for Table 1, $K_2OsO_2(OH)_4$ (4 mol%), $(DHQD)_2PHAL$ (5 mol%), *tert*-BuOH:H_2O = 6 mL:9 mL, and 1.0 mmol olefin and ii) for Tables 2 and 3, $K_2OsO_2(OH)_4$ (5 mol%), $(DHQD)_2PHAL$ (6 mol%), *tert*-BuOH:H_2O = 12 mL:6 mL, and 0.5 mmol olefin. The regioselectivity of the Sharpless AA reaction was determined by measuring relative peak heights of corresponding ^{1}H NMR spectra for the two regioisomers. The optical purity (*ee*) of the major regioisomers was determined from the ^{1}H NMR spectrum of their Mosher ester derivatives.

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