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Ligand-Controlled Selectivity in the Desymmetrization of *meso* Cyclopenten-1,4-diols via Rhodium(I)-Catalyzed Addition of Arylboronic Acids

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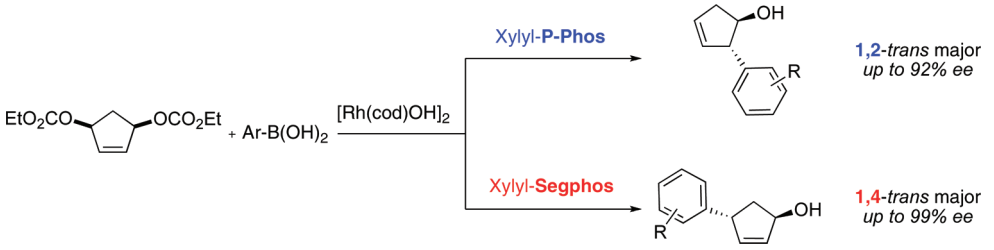

A highly enantioselective desymmetrization of *meso* cyclopent-2-ene-1,4-diethyl dicarbonates has been developed using a Rh-catalyzed asymmetric allylic substitution. Depending on the type of ligand used, each of two regioisomeric products can be obtained in good yield and excellent enantioselectivity. Under rhodium(I) catalysis, bisphosphine P-Phos ligands form *trans*-1,2-arylcyclopentenols as the major product, whereas Segphos ligands lead predominantly to *trans*-1,4-arylcyclopentenols.

Introduction

Enantioselective desymmetrization strategies for the synthesis of small chiral molecules create highly valuable building blocks from simple starting materials.[1] This approach is attractive because it can achieve complete conversion of *meso* substrates into the desired chiral products, whereas traditional kinetic resolution reactions can lead only to a maximum theoretical yield of 50%.[2] Several catalytic protocols have been developed to accomplish such desymmetrizations, many of which make use of enzymatic processes.[1,3] Focusing on the development of new reactions to desymmetrize *meso* substrates, we looked at rhodium(I) complexes to catalyze the enantioselective formation of C−C bonds with activated alkenes.

Transition-metal-catalyzed reactions have allowed us[4] and others[5] to exploit this strategy successfully with symmetrical activated alkenes (Figure 1). Although our work initially looked at highly reactive alkenes **I**,[6] **II**,[7] and **III**,[8] a systematic study led us to explore the generality of the method. More specifically, we sought to extend our methodology to alkenes lacking bicyclic strain, e.g., **IV**, or even to simple linear allylic systems **V**.[9]

The extension to less strained alkenes brought our method conceptually closer to asymmetric allylic substitution (AAS), a field intensively studied with Pd catalysis.[10] The use of this

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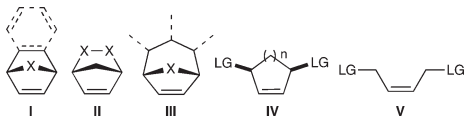
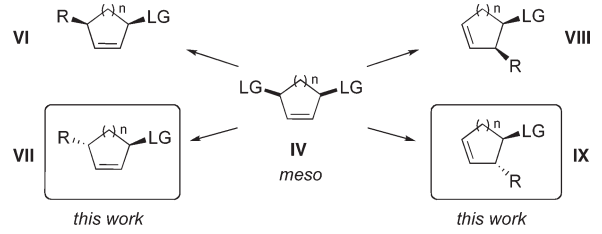


FIGURE 1. Symmetrical substrates bearing decreasingly activated alkenes (X = O, NR; LG = OR, NR_2).

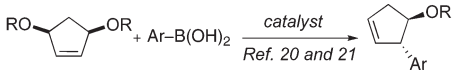
SCHEME 1. Substitution Patterns Accessible via AAS Reactions



transformation has been demonstrated many times in the synthesis of a range of natural products.[11] Metal-catalyzed AAS reactions represent the state of the art in the addition of soft nucleophiles such as enolates and heteroatoms to allylic substrates.[7,12,13] In contrast, the addition of hard nucleophiles has presented significant challenges with respect to both functional group tolerance and selectivity. Recently, efficient solutions were reported with Cu catalysts to effect asymmetric allylic substitution with organomagnesium[14] or organozinc reagents,[15] on both cyclic (**IV**) and acyclic (**V**) substrates. Although these methods allow exceptional levels of selectivity with alkyl nucleophiles, the addition of hard sp^2 nucleophiles such as aryl and vinyl groups still remains a limitation.[16] Our goal was to develop a catalytic system that would use organoboron reagents as hard nucleophiles precursors due to their commercial availability.

Cyclic *meso* allylic diol derivatives **IV** are challenging substrates for the proposed reaction due to the possibility of competing reaction pathways. Indeed, the allylic displacement reaction may take place via an S_N2 or S_N2' type substitution, with overall inversion or retention of stereochemistry in both cases (Scheme 1). The resulting substitution motifs are present in many biologically active compounds and natural products,[17] and excellent asymmetric methods exist for the preparation of substituted products **VI**, **VII** and **IX**.[18] It should be noted that there is currently no enantioselective desymmetrization protocol to obtain products such as **VIII**.[19]

We recently disclosed that a Rh(I)-catalyzed system could achieve the desymmetrization of *meso* allylic diol derivatives **1a** via a formal S_N2' reaction to get **2a** selectively (eq 1).[20] Murakami also reported independently a closely related, elegant approach that used unprotected alcohol **1** directly.[21] Substituted cyclopentenols such as **2** are useful building blocks, particularly because of the alkene, allowing for further transformations.



(1)

Herein, we present a comprehensive study aimed at understanding factors controlling regioselectivity and enantioselectivity in the rhodium(I)-catalyzed desymmetrization of allylic diols with boronic acids. Systematic investigations identified sets of ligands that allow control over the regioselectivity of the products. Moreover, we report conditions leading to improved enantioselectivity compared to our preliminary report.[20]

Results and Discussion

Desymmetrization of *meso* Cyclic Allylic Diols. Initial desymmetrization reactions were attempted on the *meso* diethyl dicarbonate **1a**.[22] The protocol that effected asymmetric ring-opening reactions of oxabicyclic alkenes **II**[23] failed to produce any desired product with substrate **1a**, and only unreacted starting material was observed (Table 1, entry 1). We found that using $[Rh(cod)OH]_2$ in combination with BINAP,[24] the *trans*-1,2-substituted product **2a** was obtained as the major product in a 2:1 ratio over the *trans*-1,4-substituted product **3a** (entry 2).[25] Importantly, none of the diastereomeric *cis* isomers **VI** or **VIII** were observed. Despite low conversion of starting material, the reaction profile was clean: only **2a**, **3a**, and unreacted starting material were present in the mixture. Other metal complexes such as $[Ir(cod)Cl]_2$ or cationic $[Rh(cod)_2]OTf$ gave no reaction or led to deboronation of the boronic acid. Increasing the reaction temperature or using $[Rh(cod)OH]_2$ in the absence of a phosphine ligand led mostly to deboronation.

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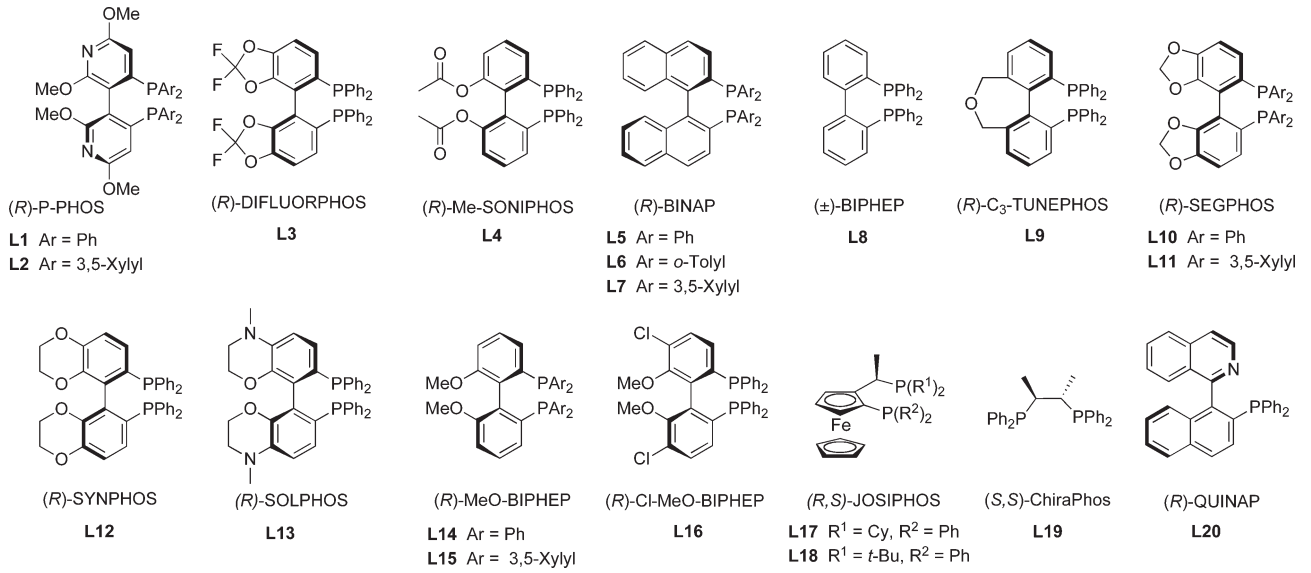
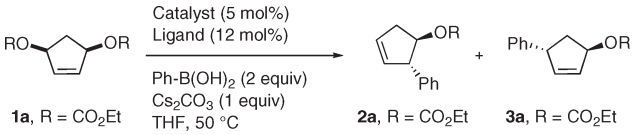


FIGURE 2. Ligand examined in the asymmetric allylic substitution reaction.

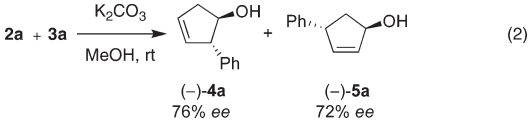
TABLE 1. Finding a Suitable Rhodium Precatalyst



entry	catalyst	ligand[a]	yield (%)[b,c]	ratio **2a**:**3a**
1	$[Rh(cod)OH]_2$	(*R,S*)-**L18**	0[c]	
2	$[Rh(cod)OH]_2$	(*S*)-**L5**	45	2:1
3	$[Rh(cod)Cl]_2$	(*S*)-**L5**	0[c]	
4	$[Rh(cod)OH]_2$	None	10[d]	20:1

[a]See Figure 2 for ligand structures. [b]Determined by ^{1}H NMR analysis of crude mixture. [c]Yield balance was recovered starting material. [d]Deboronation observed.

Carbonate products **2a** and **3a** could not be separated at this stage, but they were readily converted to the corresponding alcohols **4a** and **5a**[26] by simple hydrolysis (eq 2). The resulting alcohols were easily separable by chromatography, and their enantiomeric enrichment was determined by chiral HPLC.[27,28] The reaction was next investigated thoroughly to identify key factors controlling selectivity.



(2)

Synthesis of Chiral *trans*-1,2-Arylcyclopentenols. The initial goal was to find reaction conditions to increase conversion and regioselectivity of 1,2-arylcyclopentenol derivatives **2a**, while at least maintaining the enantioselectivity.

A study of the impact of solvent showed that aprotic, weakly coordinating solvents worked best, with THF being the solvent of choice in terms of yield (Table 2, entries 1−6). Regioisomeric ratios were not affected by the solvent. It is noteworthy that, whereas enantioselectivity was constant for **2a**, the solvent strongly influenced the ee of 1,4-product **3a** (entries 1−3). The nature of the base had a marked effect on yield, product distribution, and on the enantioselectivity of **2a** (entries 1, and 7−11). The absence of base showed a best local maximum in terms of regioselectivity, but the yield was unsatisfactory (entry 8). Since the primary goal was to improve conversion, Cs_2CO_3 was used for further studies.

Substrates carrying different leaving groups were investigated in the asymmetric allylic substitution reaction, but ethyl carbonate appeared to be the best leaving group for the desired reaction.[29] The hexafluoroisopropyl carbonate leaving group (HFIP), which had proved successful for the rhodium allylic substitution reported by Evans, gave only trace conversion under our conditions.[30] The impact of ligands was then examined in hope to modulate the intrinsic reactivity of the rhodium catalyst.

Biaryl bisphosphane ligands are the only class of ligands that showed any appreciable activity (Figure 2).[31] Two ligand families proved to be unique in giving *trans*-2-phenylcyclopentenyl carbonate (**2a**) with good regioselectivity: Chan's P-PHOS ligands[32] and Genêt's DiFluorPhos[33] (entries 1−3, Table 3).[34]

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(28) The stereochemistry of (1*R*,2*S*)-**4a** shown in eq 2 arose from (*S*)-biaryl bisphospine ligands; that of (1*R*,4*R*)-**5a** was assigned by correlation.

(29) Among other leaving groups tested, most did not give any desired product (carbonates: Me, Ph; acetate; benzoate; 4-nitrobenzoate; ethyl phosphonate). In the case of HFIP carbonate, only trace of product was observed.

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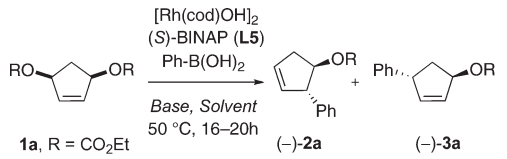
(34) Despite the promising ee obtained with Difluorphos (**L3**), we pursued our studies with a ligand having comparable behaviour, namely, P-PHOS (**L1**). The main reason was the prohibitive price of research quantities of Difluorphos from its manufacturer.

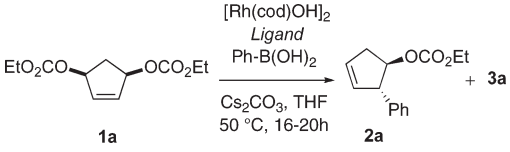
TABLE 2. Variation of Solvent and Base with BINAP and Phenylboronic Acid[a]



					ee (%)[d]	
entry	solvent	base	yield (%)[b]	ratio **2**:**3**[c]	**2**	**3**
1	THF	Cs_2CO_3	45	2:1	76	72
2[e]	dioxane	Cs_2CO_3	21	2:1	74	57
3[e]	toluene	Cs_2CO_3	19	2:1	76	36
4[e]	DMF	Cs_2CO_3	9	2:1	nd	nd
5[f]	MeCN	Cs_2CO_3	0			
6	*i*-PrOH	Cs_2CO_3	0			
7	THF	Na_2CO_3	15	3:1	74	36
8	THF		26	5:1	84	56
9	THF	KOH	29	3:1	82	46
10	THF	KF	16	2.5:1	66	38
11	THF	DIPEA	12	1:1	72	71

[a]Reactions performed using biscarbonate **1a** (0.164 mmol), Rh catalyst (5 mol % dimer), ligand (10 mol %), base (1.0 equiv), and $PhB(OH)_2$ (2.0 equiv) in THF (0.20 M) under Ar atmosphere. [b]Isolated yield. [c]Determined by ^1H NMR analysis of crude mixture. [d]Determined by chiral HPLC analysis on deprotected alcohols. [e]Reaction conducted at 90 °C. [f]Reaction conducted at 80 °C.

TABLE 3. Effect of Ligands on Regioselectivity of the Rh(I)-Catalyzed AAS[a]



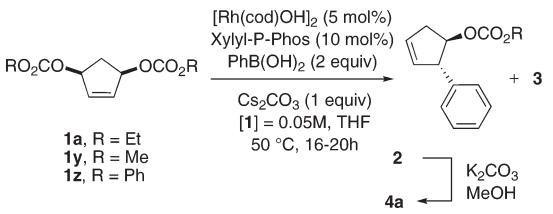
					ee (%)[d]	
entry	ligand	yield (%)[b]	ratio[c] **2**:**3**	**2**	**3**
1	**L1**, P-Phos	**74**	**> 20:1**	82	
2	**L2**, Xyl-P-Phos	**65**	**13:1**	**88**	98
3	**L3**, DiFluorPhos	58	17:1	92	
4	**L4**, Me-SoniPhos	16	**10:1**	nd	
5	**L5**, BINAP	45[c]	2:1	76	72
6	**L6**, Tol-BINAP	32	1:1	95	32
7	**L7**, Xyl-BINAP	**59**	2:1	82	60
8	**L9**, C_3-TunePhos	30	1.5:1	42	80
9	**L10**, SegPhos	**60**	2.3:1	92	> 98
10	**L11**, Xyl-SegPhos	**76**	1:1	96	> 98
11	**L16**, Cl-MeO-BIPHEP	**60**	1:1	90	98
12	**L13**, SolPhos	11	nd		
13	**L20**, QUINAP	3	nd		
14	**L19**, ChiraPhos	2	nd		
15	**L18**, *t*-Bu-JosiPhos	0			

[a]Reactions performed using biscarbonate **1a** (0.164 mmol), 5 mol % $[Rh(cod)OH]_2$, ligand (10 mol %), Cs_2CO_3 (1.0 equiv), and $ArB(OH)_2$ (2.0 equiv) in solvent (0.20 M) under Ar atmosphere. [b]Isolated yield. [c]Determined by ^1H NMR analysis of crude mixture. [d]Determined by chiral HPLC analysis on deprotected alcohols.

Fortunately, they also showed reasonable enantioselectivity, which could be improved upon further optimization.

Sterically, xylyl-substituted bisphosphanes gave enantiomeric excesses 4−6% higher than those of their phenyl-substituted analogues but did not increase regioselectivity for **2a** (entries 1 and 2; 5 and 7; 9 and 10). The SegPhos family gave good conversion and exceptional ee for both products **2** and **3**, but in an almost equimolar mixture (entries 9 and 10). Intriguingly, a dramatic difference in regioselectivity was observed by replacing two hydrogens of **L10** by two fluorine atoms on the catecholic methylene of **L3**, a site remote from the reacting groups (17:1 vs almost 1:1). Among several other chiral ligands that were screened but are not shown, some returned only traces of products (e.g., Monophos, C2-Ferriphos, KenPhos) or did not react at all (*i*-Pr-PHOX, Me-DuPhos).

TABLE 4. Optimization of Experimental Parameters with Xylyl-P-PHOS



entry	variation from standard conditions	yield (%)[a]	ratio **2**:**3**[b]	ee **4** (%)[c]
1	*standard*	70	> 15:1	90
2	substrate: **1y**	74	> 15:1	90
3	substrate: **1z**	41	1.2:1	82
4	0.5 equiv Cs_2CO_3	0		
5	2.0 equiv Cs_2CO_3	73	7:1	84
6	5.0 equiv $PhB(OH)_2$	79	3.5:1	90
7	L:Rh = 2.0:1	79	> 20:1	90
8	L:Rh = 1.2:1	70	> 20:1	90
9	L:Rh = 1.2:1; 7.5 mol % $[Rh]_2$	87	20:1	88
10	P-PHOS, instead of Xyl-P-PHOS, L:Rh = 1.2:1	74	> 20:1	82

[a]Isolated yield. [b]Determined by ^1H NMR analysis of crude mixture. [c]Determined by chiral HPLC analysis on deprotected alcohols.

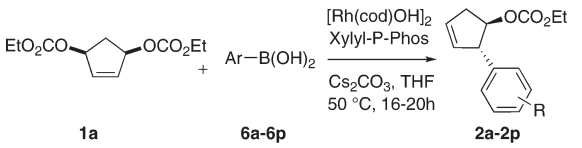
Xylyl-SegPhos attracted our attention because it gave exceptional ee for *both* products and gave good conversion (**L11**, entry 10). As will be discussed below, this result was later exploited in reactions aimed at synthesizing the complementary 1,4-product **3**.

Optimization of Reaction Conditions. An optimization study was undertaken to increase the yield and enantioselectivity of the 1,2-product **2a** with Xyl-P-Phos as ligand. A summary of the most significant results is shown in Table 4. A second look at the nature of the leaving group revealed that small alkyl carbonates worked equally well, whereas aryl carbonates led to a complete loss of regioselectivity (entries 1−3). The amount of Cs_2CO_3 was found to significantly impact the reaction, and the initial 1.0 equiv was best (entries 4 and 5). Increasing the equivalents of phenylboronic acid gave higher conversion, but at the expense of regioselectivity (entry 6). Increasing the ratio of ligand to catalyst resulted in higher conversion and increased selectivity (entries 7 and 8). This positive effect is presumed to arise from a higher concentration of the chiral active complex, otherwise lower than expected due to ready oxidation of ligand **L2**.[35]

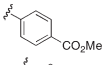
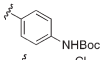
The lower ratio of 1.2:1 was preferred for cost economy. Increasing the amount of rhodium dimer led to significantly

(35) ^{31}P NMR analyses revealed that Xyl-P-PHOS is highly sensitive to oxidation in solution. Phosphine oxides of Xyl-P-PHOS: ^{31}P NMR (THF-d_8) = 27.1 ppm for dioxide; 25.3 and −14.2 for monoxide; −12.5 ppm for the free diphosphine.

TABLE 5. Scope of Arylboronic Acids in the Rh(I)-Catalyzed Enantioselective Desymmetrization with Xylyl-P-PHOS[a]



1a **6a-6p** **2a-2p**

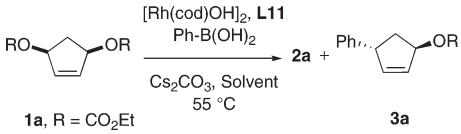
entry	2	Ar	Hammet σ cst	yield (%)[b]	2:3[c]	% ee (2)[d]
1	**2b**		0.54	86	13:1	88
2	**2c**		0.50	94	>20:1	88
3	**2d**		0.39	95	>20:1	90
4	**2e**		0.23	53	13:1	90
5	**2f**		0.23	35	10:1	86
6	**2g**		0.06	46	7:1	86
7	**2h**		-0.17	70	20:1	84
8	**2a**		0.00	87	18:1	92
9	**2i**		-0.27	49	>20:1	89
10	**2j**		-	32	>20:1	84
11	**2k**		0.37	87	10:1	90
12	**2l**		0.12	63	>20:1	92
13	**2m**		-0.07	78	20:1	92
14	**2n**		-	78	>20:1	90
15	**2o**		-	50	1:1	70
16	**2p**		-	25	6:1	92

[a]Protocol A: reactions were performed using biscarbonate **1a** (0.164 mmol), Rh catalyst (5 mol % dimer), (*S*)-**L2** (12 mol %), Cs_2CO_3 (1.0 equiv), and $ArB(OH)_2$ (2.0 equiv) in THF (0.20 M) under Ar atmosphere. [b]Isolated yields of carbonates, average of at least two runs. [c]Determined by ^1H NMR analysis of crude mixture. [d]Determined by chiral HPLC analysis on deprotected alcohol (**4**).

higher conversion (entries 7 and 8), but it was considered that a loading above the already high 5 mol % of dimer (10 mol % rhodium) was undesirable, so the catalyst loading was maintained at 5 mol % of dimer for further experiments. Finally, reexamining P-Phos at a 1.2:1 Rh:L ratio showed better selectivity, but the ee remained lower than with Xyl-P-Phos (entry 10).

Scope and Limitations of Arylboronic Acids. The enantioselective desymmetrization of dicarbonate **1a** proved to be efficient with a wide range of arylboronic acids (Table 5). Some trends were observed when comparing sterics and electronic effects. First, *meta*-substituted arylboronic acids gave the best results in terms of both yield and ee (entries 11−14). Then, within the *para*-substituted series, yields seem to correlate with electron density of the substituents as indicated by Hammett sigma constants, whereas ee was not significantly affected (entries 2−9). In general, lower conversion with electron-rich arylboronic acids was associated by an increased amount of homocoupling products, which

TABLE 6. Influence of Leaving Group, Solvent, and Concentration using Xyl-SEGPHOS as Chiral Ligand[a]



1a, R = CO_2Et **3a**

entry	1	solvent (conc, M)	yield (%)[b]	ratio[c] 3:2	ee (%)[d] 3 (2)
1	**1a**	THF (0.12)	26	1:1.2	99 (84)
2	**1a**	THF (0.31)	56	1.5:1	99 (93)
3	**1a**	dioxane (0.31)	63	1.3:1	99 (92)
4	**1a**	benzene (0.31)	60	1.7:1	99 (93)
5	**1a**	benzene (0.47)	**80**	**2.0:1**	**99 (97)**
6	**1a**	benzene (0.69)	70	1.8:1	99 (96)
7	**1a**	toluene (0.31)	70	1.5:1	99 (88)

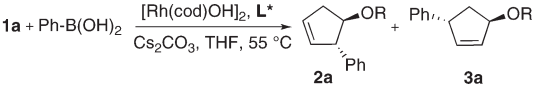
[a]All reactions were performed using **1** (0.135 mmol), catalyst (4 mol %), Xyl-SegPhos (**L11**, 12 mol %), base (1 equiv), and solvent at the indicated concentration of **1**. [b]Isolated yield. [c]Determined by ^1H NMR of purified mixture. [d]Determined by chiral HPLC analysis of deprotected alcohol.

seemed detrimental to catalytic activity (e.g., *N*-Boc-4-aminophenylboronic acid, entry 10).[36]

The reaction showed a limitation with arylboronic acids bearing *ortho* substituents as a marked decrease in both conversion and selectivity was observed (entries 15 and 16). Other cases where no conversion occurred included heterocyclic boronic acids such as 4-pyridineboronic acid, 3-furanboronic acid, 3-thiopheneboronic acid, and 2-furanboronic acid. Electron-deficient 3-nitrophenylboronic acid gave only very low conversion (less than 10%). Also, sp^3 nucleophiles such as methylboronic acid gave no reaction.

Synthesis of Chiral *trans*-1,4-Arylcyclopentenols. The successful enantioselective synthesis of 1,4-substituted cyclopentenols was very recently reported by the group of Alexakis using Cu catalysis with a new family of chiral phosphine ligands, SimplePhos.[37] The reaction was described with alkyl Grignard reagents.

During the above studies, the fact that both regioisomers **2** and **3** were formed hinted at the possibility of developing a complementary protocol to obtain **3** selectively. Ligand studies identified bisphosphine ligand Xyl-SegPhos[38] as the least selective for the 1,2-product **2a** and hence the most promising for **3a** (eq 3). More importantly, Xyl-SegPhos showed exceptional enantioselectivity for the 1,4-product **3a** (98% ee), as well as improved ee for **2a** (96% ee). Encouraged by these observations, the reaction was reinvestigated with the specific goal of finding conditions that would allow selective preparation of *trans*-1,4-arylcyclopentenols as useful chiral building blocks.

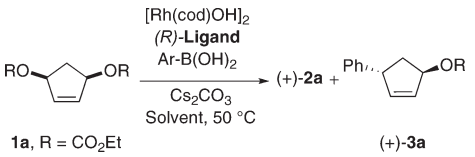


(3)

The effect of solvent was examined using Xyl-SegPhos (**L11**). Dioxane and benzene gave similar results for the reaction, with benzene favoring slightly the desired regioisomer **3** (Table 6). Non-coordinating solvents like benzene and toluene provided the highest yield and ratio of desired

(36) Control experiments showed that homocoupling of the boronic acid occurs as a background reaction under the reaction conditions.
(37) Millet, R.; Alexakis, A. *Synlett* **2008**, 1797.
(38) Shimizu, H.; Nagasaki, I.; Matsumura, K.; Sayo, N.; Saito, T. *Acc. Chem. Res.* **2007**, *40*, 1385.

TABLE 7. Effect of Bisphosphane Ligands on Regioselectivity[a]



entry	L	ligand	yield (%)[b]	ratio[c] 2a:3a	ee (%)[d] 3a (2a)
1		none	10	20:1	
2	L1	P-Phos	74	20:1	98 (82)
3	L2	Xyl-P-Phos	87	18:1	nd (92)
4	L3	DiFluorphos	58	17:1	nd (92)
5[e]	L7	Xyl-BINAP	43	12:1	nd (12)
6[e]	L5	BINAP	42	2.5:1	95 (87)
7	L10	SegPhos	60	2.3:1	98 (92)
8	L11	Xyl-Segphos	26	1.2:1	99 (84)
9[e]	L11	Xyl-Segphos	56	1:1.4	99 (93)
10[f]	L11	Xyl-Segphos	80	1:2.0	99 (97)
11[e]	L12	SynPhos	76	1:1.7	99 (93)
12[g]	L16	Cl-MeO-BIPHEP	60	1:2.0	>99 (93)
13[e]	L16	Cl-MeO-BIPHEP	73	1:2.5	99 (94)
14[f]	L16	Cl-MeO-BIPHEP	82	1:2.8	99 (95)

[a]All reactions were performed using **1a** (0.135 mmol) with the listed catalyst (8 mol % in Rh), ligand (12 mol %), and THF (0.12 M). [b]Isolated yield. [c]Determined by ^{1}H NMR of purified mixture. [d]Determined by chiral HPLC analysis of deprotected alcohols. [e]In PhH (0.31 M). [f]In PhH (0.47 M). [g]In dioxane (0.47 M).

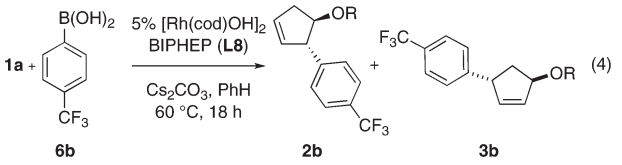
1,4-products as well as the highest ee for both regioisomers. Toluene gave a yield similar to that of benzene, but the latter was still preferred for its superior solubilizing ability.

The concentration of substrate was found to have a significant effect on the regioselectivity with Xyl-SegPhos ligand (**L11**). Increasing the concentration from 0.12 M to ~0.5 M favored the desired 1,4-product **3** (entries 4−6). Intriguingly, we also observed that the ee of the 1,2-product is affected by the concentration. A local maximum of concentration was observed at 0.47 M and was selected as optimal concentration.

A second look was taken at ligands in solvents such as benzene, dioxane, and THF. Again, only bidentate bisphophanes were successful at giving the desymmetrized products **2** and **3**. The most significant results of the ligand study are summarized in Table 7. An interesting general trend is observed as regioselectivity seems to correlate with the electronic density of the phosphorus atoms. From the pyridine-based P-PHOS family, which was shown to be selective for **2**, an incremental ratio drift can be seen toward the desired 1,4-substituted cyclopentene **3** (entries 2−12). The ligand Cl-MeO-BIPHEP[39] gave the highest **3**:**2** ratio. The noted dependence on concentration observed with Xyl-SEGPHOS was also confirmed with Cl-MeO-BIPHEP (entries 8−10 and 12−14, respectively).

Importantly, the electron-rich biphenyl-based ligands **L10**, **L11**, **L12**, and **L16** consistently gave outstanding ee values for **3a** (entries 7−14). It should also be noted that the ee of 1,2-substituted products **2** are notably higher with **L10**−**L16** than those we found previously with Xyl-P-PHOS (**L2**). Despite our best efforts, the highest regioselectivity for **3** that could be achieved was close to 3:1 (entry 14). However, the method is still synthetically useful since once the carbonate is cleaved, the parent alcohols **4** and **5** are easily separated by chromatography. Furthermore, results from Table 7 indicate that *both* cyclopentenols **4** and **5** can be prepared with unprecedented enantioselectivity in a *single operation* from readily available starting materials (i.e., entry 10).

Cl-MeO-BIPHEP was selected as optimal ligand to study the influence of the boronic acid on the regioselectivity of the reaction. While benzene is the solvent of choice to favor formation of **3a**, solubility issues arose when boronic acids other than $PhB(OH)_2$ were used. As we surveyed more arylboronic acids, it became apparent that yields were generally low. Experimentally, the optimized reaction protocol of Table 5 required canulating simultaneously **1a** and the boronic acid as a stock solution. Polar boronic acids would often not fully solubilize in benzene and could not be added this way. A solution to this issue was found by changing the addition technique of reagents. Instead of adding the substrate and boronic acid as a solution, dicarbonate **1a** was added while the premixed complex solution was still at 60 °C, and the remaining solids were added by opening of the reaction vessel. For instance, *p*-trifluoromethylphenylboronic acid (**6b**) is insoluble in benzene, but the modified procedure (protocol B) gave the arylcyclopentenes **2b** and **3b** in 87% yield as opposed to 18% when added at rt. (eq 4).



Scope of the Reaction with Cl-MeO-BIPHEP. The Rh-catalyzed enantioselective desymmetrization was shown to tolerate a wide range arylboronic acids and gave both regioisomeric arylcyclopentenols cleanly. The results with Cl-MeO-BIPHEP are summarized in Table 8. Importantly, the 1,4-substituted products **3** were obtained with outstandingly robust enantioselectivity. The regioisomeric ratio was fairly constant at about 2:1, favoring the products **3**. A limitation was observed with *ortho*-substituted arylboronic acids. In these cases, the reactivity is likely hampered by steric factors, otherwise the regioselectivity and enantioselectivity is similar to that of the other examples.

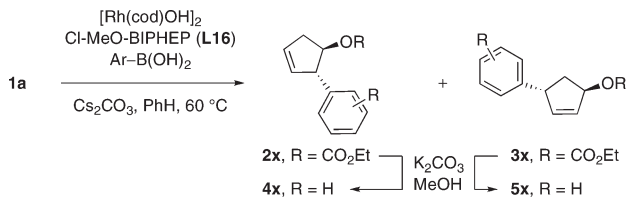
Mechanistic Considerations. Our working hypothesis for the mechanism of the reaction is depicted in Scheme 2. At least two catalytic cycles can be considered. The first involves a carborhodation of the alkene as the key step, whereas the second involves an oxidative addition of the Rh^I catalyst to generate Rh^{III} σ-enyl intermediate. Our results suggest that both may be operative and competitive, depending on the ligands used.

The generation of the active catalyst is common to both proposed pathways. In the premixing phase, $[Rh(cod)OH]_2$ is heated in the presence of the bisphosphine ligand, and the more labile 1,5-cyclooctadiene is displaced by the chiral ligand to form **A**, which is presumably the active catalyst.[40] Upon addition of the boronic acid, fast transmetalation of the aryl moiety from boron to rhodium occurs to form **B**. Binding the alkene of substrate **1** to the Rh(I) center leads to **C**. The two proposed pathways diverge at this step.

(39) (a) Laue, C.; Schroeder, G.; Arlt, D. Eur. Pat. 749973 A1, **1996**. (b) Driesen-Holscher, B.; Kralik, J.; Agel, F.; Steffens, C.; Hu, C. *Adv. Synth. Catal.* **2004**, *346*, 979.

(40) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.

TABLE 8. Scope of Arylboronic Acids in the Rh(I)-Catalyzed Enantioselective Desymmetrization with Cl-MeO-BIPHEP[a]



entry	products	Ar	yield (%)[b]	ratio[c] 2 : 3	ee (%)[d] 2	3
1	**2b / 3b**		81	1 : 2.8	93	99
2	**2q / 3q**		89	1 : 2.3	93	99
3	**2m / 3m**		99	1 : 2.2	93	99
4	**2r / 3r**		69	1 : 2.3	94	99
5	**2s / 3s**		78	1 : 2.4	94	99
6	**2t / 3t**		66	1 : 1.3	80	99
7	**2l / 3l**		80	1 : 1.8	89	99
8	**2u / 3u**		80	1 : 2.6	91	99
9	**2v / 3v**		16	1 : 1.6	88	96
10	**2w / 3w**		31	1 : 3.5	89	99

[a]Protocol B: reactions were performed using **1a** (0.135 mmol), Rh catalyst dimer (4 mol %), (*S*)-**L16** (12 mol %) in solvent (0.47 M), under Ar; where **1a** was added at 60 °C, followed by boronic acid and base added as solids in one portion. [b]Isolated yield of mixed carbonates **2** and **3**. [c]Determined by ^{1}H NMR of purified mixture. [d]Determined by chiral HPLC analysis of deprotected alcohols **4** and **5**.

The carbo-rhodation pathway (i) shows a diastereo- and enantioselective insertion of the alkene into the Rh−Ar bond, which would generate the key intermediate **D**. Subsequent antiperiplanar β-alkoxide elimination then yields the 1,2-product **2**. This mechanism is based on our previous work for Rh-catalyzed ring opening of oxabicyclic molecules. In the present case, desymmetrization of the cyclic dicarbonate yielded exclusively the *trans* products, whereas with the previous ring-opening reaction, *cis* products were observed exclusively. The relative stereochemistry in the products is set by the carborhodation occurring on the face of the olefin *anti* to the carbonate leaving groups.

The above mechanism cannot explain the formation of the 1,4-products **3**. To account for the observed 1,4-product, we need to consider at least partial contribution from an alternative pathway.

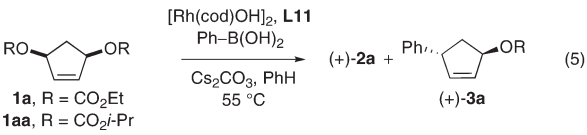
The oxidative addition pathway (ii) proceeds with an enantioselective ionization of the rhodium(I) catalyst to generate a σ-enyl rhodium(III) complex intermediate **F**. The existence of σ-enyl intermediates was demonstrated by Evans and coworkers.[13,41] They also showed that isomerization between regioisomers was slow. Once the 1,2-σ-enyl complex **F** is formed, it could reductively eliminate to yield the 1,2-substituted product **2** or equilibrate with the isomeric 1,4-σ-enyl complex **G**, from which a reductive elimination would lead to the 1,4-substituted product **3**. Accordingly, the rate of **F**/**G** isomerization versus the rate of reductive elimination would be pivotal in determining the regioselectivity of the reaction.

The regioselectivity of the reaction may therefore depend on the relative rates of three steps: k_1, k_2, and k_3/k_{-3}. Exclusive formation of the 1,2-products **2** would be observed if k_1 is much greater than k_2. Alternatively, **2** may also be formed if conditions either disfavor equilibration of **F** to **G** or force rapid reductive elimination, k_4 (e.g., by large steric demands on complex **F**). On the other hand, to obtain selectively 1,4-regiosomer **3**, k_2 must be accelerated relative to k_1 to prevent formation of **2**. For instance, factors contributing to selective formation of isomer **3** may include electron-rich phosphine ligands stabilizing ionization of the complex to Rh(III) (this seems to be what we observed in Table 7) and phosphines favoring isomerization of intermediate **F** to **G**.

We were unable to gather direct evidence for a carbo-rhodation step (the selectivity problem might simply reflect the competing formation of **F** and **G**). However, the observed ee of both regioisomers **2** and **3** should be identical since irreversible desymmetrization of the substrate takes place at k_2. Yet, as clearly shown in Tables 2, 3, 6, 7, and 8, the ee of **2** and **3** did not correlate. We therefore conclude that both pathways must occur, with the carbo-rhodation pathway potentially being less enantioselective, and therefore affording **2** with an eroded ee.

In the substitution reaction, one of the carbonates is liberated and is presumed to be ultimately trapped by boron byproducts in the alkoxyde or carbonate ionic form. Nevertheless, the potential of the alkoxide or carbonate to complex with the rhodium catalyst could not be neglected. Indeed, our substrate screening had shown that the nature of the carbonate had a strong influence on both yield and enantioselectivity.

An experiment was conducted to probe whether the alkoxide exerts a steric influence at the alkene attack or complexes to the rhodium center. Ethyl dicarbonate **1a** was submitted to the reaction conditions in the presence of 1 equiv of 2-propanol (eq 5). The results revealed that both factors are at play: the yield was 21% compared to 60%, but ee remained high (92/96% vs 93/99% ee). When the substrates bore isopropyl carbonates, the yield was poor, i.e., 20%, but enantioselectivity was the most affected parameter. In this case, ee of both products was highly eroded to 69% and 40% ee. These results suggest the released alkoxide may complex to Rh^{I} and hinder catalyst turnover. In addition, the size of the carbonate substituent may influence enantiotopic discrimination.



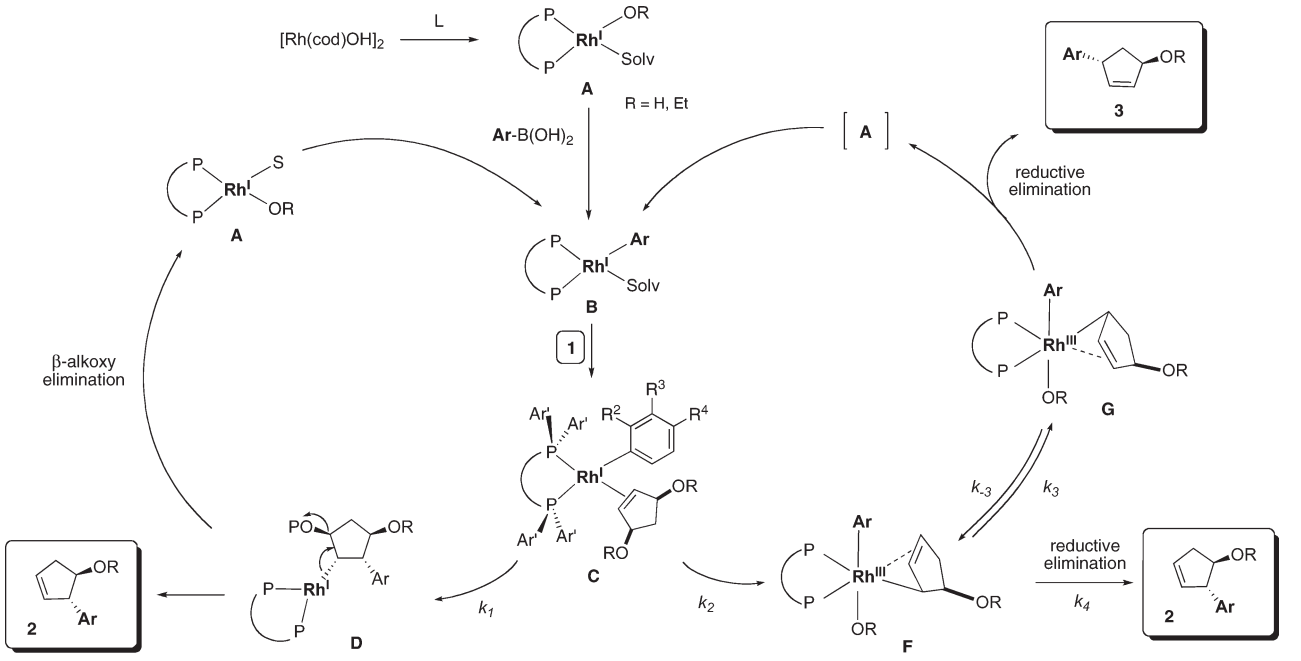
(5)

Two control experiments were conducted to further probe the effect of free alkoxide in the reaction with BINAP as ligand (eq 6).[42] Adding 0.5 equiv of EtONa at the start of the reaction led to only 10% conversion. Similarly, adding 0.5 equiv of *t*-BuOK showed no conversion at all. These experiments suggest that the production of an alkoxide

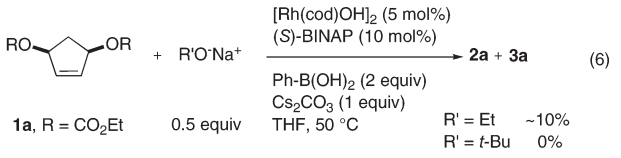
(41) (a) Evans, P. A.; Leahy, D. K. *J. Am. Chem. Soc.* **2003**, *125*, 8974. (b) Evans, P. A.; Lawler, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 8642.

(42) The reaction conditions are overall basic and may not favor decarboxylation. Nevertheless, a large amount of boron reagents and byproduct are present which may act as Lewis acids. Only a small concentration of alkoxide is required to shut down the catalytic activity.

SCHEME 2. Plausible Catalytic Cycles for the Rh-AAS Proceeding via Carborhodation and/or σ-Enyl Divergent Intermediates

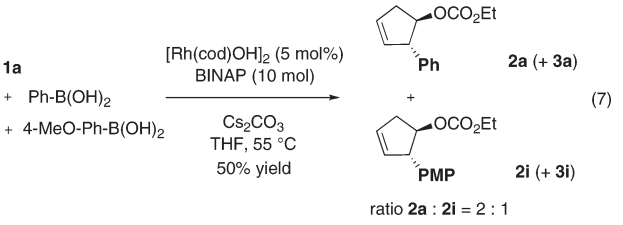


during the course of the reaction may be detrimental to the conversion. Thus, as the reaction proceeds, even if decarboxylation is slow, it may generate enough alkoxide to impede reactivity. Potential trapping agents were examined with the hope of sequestering the released ethoxide, but to no avail.[43]



(6)

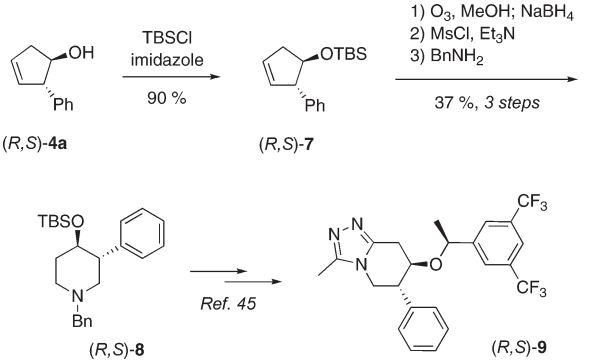
A competition experiment was performed with two different nucleophiles. When 2.0 equiv of phenylboronic acid and 2.0 equiv of 4-methoxyphenylboronic acid were added together to a reaction, the conversion achieved was only 50%, with a 2:1 ratio of products from the addition of the phenylboronic acid and 4-methoxyphenylboronic acid, respectively (highly regioselective for the 1,2-products, eq 7). These results suggest that the presence of the 4-methoxyphenylboronic acid leads to a faster deactivation of the catalyst than when only phenylboronic acid is present (where 70% conversion is otherwise achieved). A slow addition of the nucleophile was not beneficial for conversion.



(7)

Synthetic Applications. *trans*-3,4-Disubstituted piperidines are important building blocks that are present in current drug candidates.[44] In particular, many tachykinin receptor antagonists possess a triazole ring fused to a piperidine bearing a *trans*-3,4-arylhydroxy substitution motif. A specific example is illustrated by **9**, which is an analogue of Aprepitant, an NK1 inhibitor from Merck (Scheme 3).[45] Using our methodology to prepare compound (*R*,*S*)-**4a** enantioselectively would provide an alternative method to the chiral resolution reported in the patented synthesis.

SCHEME 3. Application of Methodology to the Synthesis of NK1 Inhibitor Precursors



The synthesis of the enantioenriched 3,4-*trans* disubstituted piperidine (*R*,*S*)-**8** was effected by derivatizing (*R*,*S*)-**7** to an 3-arylpiperidine in 37% yield over three steps. Piperidine **8** was obtained in 91% ee and intercepts the patented synthesis of **9**. The synthesis of the NK1 inhibitor is reported with five additional synthetic steps on the deprotected (*R*,*S*)-**8**. Notably, the stereoselective synthesis of piperidines bearing the particular substitution pattern displayed in **8** cannot

(43) The trapping agents tested included TBSCl, 4Å MS, MgO/BaO, and BF_3.

(44) (a) Humphrey, J. M. *Curr. Top. Med. Chem.* **2003**, *3*, 1423. (b) Saria, A. *Eur. J. Pharmacol.* **1999**, *375*, 51.

(45) Devita, J. R.; Young, J. R. Patent WO/2007/081897, **2007**.

be accomplished easily using traditional methods. Thus, it illustrates the value of the Rh-catalyzed AAS reaction.

Conclusions

We have reported a full study of the Rh(I)-catalyzed AAS of symmetrical allylic diols. A new catalytic method has been established to add stable sp^2 C-nucleophiles to activated alkenes. A range of chiral homoallylic alcohols can be synthesized in unprecedented enantioselectivity from simple cyclic allylic diol derivatives.

The regioselectivity of the products can be diverted by changing the bisphosphine ligand and solvent system. This work is complementary to existing methods in that it uses aryl groups as nucleophiles. The application of this methodology was demonstrated in the synthesis of enantioenriched piperidine **8**. The synthesis featured the rhodium-catalyzed AAS as a key step to establish two neighboring *trans* stereocenters. Further work will aim at expanding the method to other types of allylic diol derivatives.

Experimental Section

For general information see Supporting Information. Characterization data for **2a**−**2p**, **3a**, **3b**, **3l**, **3m**, **4a**−**4k**, **4n**−**4p**, and **5a** was reported previously.[20,46]

Rhodium-Catalyzed Desymmetrization of *cis*-Cyclopent-2-ene-1,4-diethyl Dicarbonate. Typical Preparation of the 1,2-Regioisomeric Products 2 (Procedure A). To a 1 dram vial equipped with a magnetic stir bar were added $[Rh(cod)OH]_2$ (3.7 mg, 0.0082 mmol), (*S*)-Xyl-P-PHOS[47] (14.9 mg, 0.020 mmol), and Cs_2CO_3 (53 mg, 0.164 mmol). The vial was sealed and flushed with argon. Distilled THF (0.8 mL) was added, and the mixture was stirred for 30 min on a 50−55 °C oil bath. Dicarbonate **1a** (40 mg, 0.164 mmol) and phenylboronic acid (40 mg, 0.32 mmol) were added together as a solution in distilled THF (0.8 mL). The reaction mixture was heated on a 50−55 °C oil bath. After 16 h, THF (5 mL) and hexanes (5 mL) were added to the reaction mixture, and it was concentrated with silica gel, then applied to the top of a column of silica gel, and purified by column chromatography (5−20% EtOAc/hexane as elution gradient). An inseparable mixture of the monocarbonates **2a** and **3a** was recovered as a colorless oil, 33 mg (87%). ^{1}H NMR analysis revealed an isomer ratio of 92:8 favoring the 1,2-product **2a**. The enantiomeric excess was determined on the deprotected alcohols (see Procedure C).

Rhodium-Catalyzed Enantioselectvie Desymmetrization of *meso* Allylic Dicarbonates. (General Procedure B). Into a 13 mm × 135 mm screw-cap tube equipped with a magnetic stir bar were weighed $[Rh(cod)OH]_2$ (7.4 mg, 0.0164 mmol) and (*S*)-Cl-MeO-BIPHEP[47] (25.6 mg, 0.039 mmol). The tube was equipped with a screw-cap septum and flushed with argon. Benzene (0.30 mL) was added, and the mixture was stirred in a 60 °C oil bath for 15 min; the yellow solution turned to dark orange. Meanwhile, a solution of dicarbonate **1a** (80 mg, 0.32 mmol) in 0.40 mL of benzene was prepared. The substrate solution was canulated to the premixed complex solution at 60 °C; the reddish solution darkened. Then phenylboronic acid (80 mg, 0.64 mmol) and Cs_2CO_3 (80 mg, 0.26 mmol) were added together as solids, by rapidly opening the deep vessel (minimizing exposition to air). The tube was flushed with Ar at rt for 2−5 min, then put back to heat at 60 °C for 16 h. Reaction showed full conversion by TLC (vanillin stain). To the dark brown reaction mixture were added 5 mL of Et_2O (heavy precipitate formed) and 10 mL of saturated NH_4Cl aqueous solution. The decanted aqueous layer was extracted with 3 × 20 mL of Et_2O; the combined organic phases were dried with brine and $MgSO_4$, then filtered, and concentrated under reduced pressure. The crude residue was applied to the top of a column of silica gel and purified by column chromatography (5−25% EtOAc/hexane as elution gradient). Monocarbonates **2a** and **3a** were recovered together as a colorless oil, 62 mg (82%). ^{1}H NMR analysis revealed a **2**:**3** ratio of 1:2.8. Characterization and enantiomeric excess was determined on the deprotected alcohols (see Procedure C).

General Deprotection of Alcohols (Procedure C). The combined monocarbonate isomers **2** and **3** were dissolved in MeOH (0.02 M), and K_2CO_3 (10−14 equiv) was added. The white suspension was stirred at rt until complete conversion (typically less than 3 h).[48] One volume of saturated NH_4Cl aqueous solution was added and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield a mixture of alcohols. The 1,2- and 1,4-regioisomers **4** and **5** were separated and purified by column chromatography on silica gel (10−40% gradient of EtOAc/hexane). The yield was generally quantitative and reflected the ratio of the crude carbonates mixture. The enantioenrichment of each regioisomers was measured on the isolated products and compared to racemic samples.[49]

(1*R*,2*S*)-*trans*-2-(4′-Trifluoromethylphenyl)-cyclopent-3-enyl Ethyl Carbonate (2b)[20] and (1*R*,4*R*)-*trans*-4-(4′-Trifluoromethylphenyl)-cyclopent-2-enyl Ethyl Carbonate (3b).[20]. Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 81% yield (80 mg), showing a 1:2.8 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4b** and **5b**. *Major regioisomer* **3b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (2H, d, J = 8.2 Hz), 7.24 (2H, d, J = 8.7 Hz), 6.19−6.11 (2H, m), 5.76 (1H, ddd, J = 9.1, 4.0, 2.0 Hz), 4.25−4.16 (1H, m), 4.21 (2H, q, J = 7.1 Hz), 2.54−2.46 (1H, m), 2.11 (2H, ddd, J = 14.6, 7.1, 5.6 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(4′-Trifluoromethylphenyl)-cyclopent-3-enol (4b). Colorless oil. $[\alpha]^{28.7}_D$ = +165 (*c* 0.80, $CHCl_3$); enantiomeric ratio was 96.4:3.6, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, d, J = 8.2 Hz), 7.30 (2H, d, J = 8.1 Hz) 5.95 (1H, ddd, J = 5.9, 4.3, 2.2 Hz), 5.77 (1H, ddd, J = 6.0, 4.2, 2.1 Hz), 4.28 (1H, dt, J = 6.9, 4.3 Hz), 3.85−3.82 (1H, m), 2.82 (1H, dddd, J = 17.0, 6.8, 3.9, 2.0 Hz), 2.40 (1H, dddd, J = 17.0, 6.1, 4.3, 1.9 Hz), 1.83 (1H, br s, alcohol). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 131.4, 130.4, 127.7, 125.5 (q, J = 3.8 Hz, CF_3), 122.9, 80.8, 60.4, 41.5. ^{19}F NMR (375 MHz, $CDCl_3$): δ −63.1 (s, 3F).

(1*R*,4*R*)-*trans*-4-(4′-Trifluoromethylphenyl)-cyclopent-2-enol (5b). Colorless oil. $[\alpha]^{28.9}_D$ = +210 (*c* 1.35, $CHCl_3$); enantiomeric ratio was 99.5:0.5, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (2H, d, J = 8.0 Hz), 7.24 (2H, d, J = 8.0 Hz), 6.09 (1H, dd, J = 5.7, 2.1 Hz), 6.03 (1H, ddd, J = 7.6, 2.2, 0.6 Hz), 5.09−5.03 (1H, m), 4.29−4.18 (1H, m), 2.32 (1H, ddd, J = 14.3, 8.0, 2.7 Hz), 2.08 (1H, ddd, J = 14.1, 6.9, 5.5 Hz), 1.57 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.1 (d, J = 1.5 Hz), 138.3 (2), 135.1 (2), 128.7, 127.6 (2), 125.7 (q, J = 3.7 Hz, CF_3), 77.5, 49.9, 44.1. ^{19}F NMR (375 MHz, $CDCl_3$): δ −62.8 (s, 3F).

(46) (a) Tueting, D. R.; Echavarren, A. M.; Stille, J. K. *Tetrahedron* **1989**, *45*, 979. (b) Kobayashi, Y.; Murugesh, M. G.; Nakano, M.; Takahisa, E.; Usmani, S. B.; Ainai, T. *J. Org. Chem.* **2002**, *67*, 7110.

(47) (*S*)-Biarylphosphines ligands (BINAP, P-PHOS, and Cl-MeO-BIPHEP analogues) all lead to the (−)-enantiomers, which have the absolute stereochemistry represented in this paper. The use of the (*R*)-biarylphosphines yield the (+)-enantiomers, having the opposite stereochemistry of that represented. We arbitrarily opted to represent the (1*R*,2*S*)-**2**/**4** and (1*R*,4*R*)-**3**/**5** stereochemistry for consistency.

(48) It was verified that longer reaction times did not affect the ee (up to 48 h at rt).

(49) Racemic products were obtained following the same procedure with the achiral BIPHEP.

(1*R*,2*S*)-*trans*-2-(3′-Methoxyphenyl)-cyclopent-3-enyl Ethyl Carbonate (2l)[20] and (1*R*,4*R*)-*trans*-4-(3′-Methoxyphenyl)-cyclopent-2-enyl Ethyl Carbonate (3l).[20]. Prepared according to Procedure B. The regioisomers were obtained as a colorless oil in 80% yield (69 mg), showing a 1:1.8 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4l** and **5l**. *Major regioisomer* **3l**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80−6.65 (3H, m), 7.31−7.20 (1H, m), 6.18 (1H, dd, J = 5.6, 1.9 Hz), 6.10−6.05 (1H, m), 5.74 (1H, dd, J = 7.2, 5.2, 2.6 Hz), 4.20 (2H, q, J = 7.2 Hz), 4.16−3.98 (1H, m), 3.79 (3H, s), 2.47−2.42 (1H, m), 2.13 (1H, ddd, J = 13.0, 7.0, 5.9 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(3′-Methoxyphenyl)-cyclopent-3-enol (4l). Colorless oil. $[\alpha]^{28.2}_D$ = +160 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 94.6:5.4, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). The characterization data was fully concordant with the literature.[46] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (1H, t, J = 7.4), 6.70−6.62 (3H, m) 5.80 (1H, ddd, J = 6.0, 4.4, 2.2 Hz), 5.67 (1H, ddd, J = 6.1, 4.1, 2.1 Hz), 4.18 (1H, dt, J = 6.7, 4.2 Hz), 3.70 (3H, s), 3.64 (1H, sp, J = 1.9 Hz), 2.70 (1H, dddd, J = 16.9, 6.7, 3.9, 2.1 Hz), 2.27 (1H, dd, J = 16.9, 2.1 Hz), 1.80 (1H, br s, alcohol). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.1, 144.3, 132.2, 129.8, 128.7, 120.1, 113.2, 112.1, 81.2, 60.8, 55.3, 41.6. IR (NaCl, neat film): 3323 (br), 3055, 3023, 2909, 2842, 1588, 1484, 1406, 1073, 1010 cm^{-1}. MS *m*/*z* (rel intensity): 190 (M^+, 100), 172 (20), 162 (50), 147 (41), 134 (63), 129 (27), 121 (38), 115 (32), 91 (32).

(1*R*,4*R*)-*trans*-4-(3′-Methoxyphenyl)-cyclopent-2-enol (5l). Colorless oil. $[\alpha]^{28.8}_D$ = +220 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 99.4:0.6, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (2H, t, J = 7.9 Hz), 6.77−6.67 (3H, m) 6.06−6.01 (2H, m), 5.08−5.02 (1H, m), 4.15−4.10 (1H, m), 3.79 (3H, s), 2.28 (1H, ddd, J = 14.1, 8.0, 2.8 Hz), 2.11 (1H, ddd, J = 14.1, 6.9, 6.0 Hz), 1.48 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 146.5, 138.9, 134.1, 129.6, 119.5, 112.9, 111.5, 77.5, 55.2, 49.9, 44.0. IR (NaCl, neat film): 3333 (br), 3055, 3001, 2963, 2939, 2839, 1604, 1489, 1458, 1435, 1319, 1265, 1157, 1041, 1026, 771 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 190.1 (M^+, 30), 172 (100), 157 (47), 129 (33), 128 (38), 127 (29), 115 (18), 85 (21), 84 (30). HRMS (EI$^+$) calcd for $C_{12}H_{14}O_2$ [M^+]: 190.0994, found 190.0991.

(1*R*,2*S*)-*trans*-2-(3′-Methylphenyl)-cyclopent-3-enyl Ethyl Carbonate (2m)[20] and (1*R*,4*R*)-*trans*-4-(3′-Methylphenyl)-cyclopent-2-enyl Ethyl Carbonate (3m).[20]. Prepared according to Procedure B. The regioisomers were obtained as a colorless oil in 99% yield (81 mg), showing a 1:2.2 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4m** and **5m**. *Major regioisomer* **3m**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22−7.16 (1H, m), 7.07−7.00 (2H, m), 6.92 (1H, d, J = 6.9 Hz), 6.18 (1H, dd, J = 5.6, 1.9 Hz), 6.07 (1H, ddd, J = 5.0, 4.8, 2.3 Hz), 5.79−5.75 (1H, m), 4.20 (2H, q, J = 7.1 Hz), 4.15−4.08 (1H, m), 2.46 (1H, ddd, J = 14.7, 7.7, 2.3 Hz), 2.33 (3H, s), 2.12 (1H, ddd, J = 14.6, 7.1, 5.9 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(3′-Methylphenyl)-cyclopent-3-enol (4m). Colorless oil. $[\alpha]^{27.5}_D$ = +197 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 96.4:3.6, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). The characterization data was fully concordant with previous reports from the literature.[46] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (1H, t, J = 7.5 Hz), 7.06−6.97 (3H, m), 5.89 (1H, ddd, J = 5.0, 4.4, 2.2 Hz), 5.77 (1H, ddd, J = 6.0, 4.2, 2.1 Hz), 4.31−4.26 (1H, m), 3.73 (1H, sp, J = 1.9 Hz), 2.81 (1H, dddd, J = 16.9, 6.5, 4.1, 2.0 Hz), 2.37 (1H, dddd, J = 16.9, 6.3, 4.1, 2.0 Hz), 2.34 (3H, s), 1.88 (1H, br s, alcohol). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 138.2, 132.4, 129.4, 128.5, 128.1, 127.4, 124.4, 81.0, 60.7, 41.3. IR (NaCl, neat film): 3323 (br), 3336 (br), 3056, 3022, 2921, 2863, 1650, 1607, 1490, 1456, 1272, 1161, 1054 cm^{-1}. MS *m*/*z* (rel intensity): 174 (M^+, 93), 156 (25), 146 (55), 131 (69), 128 (47), 118 (100), 115 (41), 105 (50), 91 (42). HRMS (ESI)$^+$ calcd for $C_{12}H_{14}O$ [M^+]: 174.104465, found 174.104256.

(1*R*,4*R*)-*trans*-4-(3′-Methylphenyl)-cyclopent-2-enol (5m). Colorless oil. $[\alpha]^{28.1}_D$ = +172 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 99.5:0.5, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (1H, t, J = 8.2 Hz), 7.01 (1H, d, J = 7.7 Hz), 6.95−6.92 (2H, m) 6.06−6.01 (2H, m), 5.07−5.03 (1H, m), 4.13−4.08 (1H, m), 2.33 (3H, s), 2.27 (1H, ddd, J = 14.1, 8.0, 2.6 Hz), 2.10 (1H, ddd, J = 14.1, 7.0, 5.5 Hz), 1.56 (1H, br s, alcohol). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 139.3, 138.2, 133.9, 128.5, 127.8, 127.1, 124.1, 77.5, 49.8, 44.1, 21.4. IR (NaCl, neat film): 3348 (br), 3055, 3024, 2962, 2924, 1705, 1604, 1589, 1489, 1435, 1257, 1172, 1111, 1026, 779, 702 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 174.1 (M^+, 22), 156 (100), 141 (52), 128 (33), 115 (49), 91 (11), 84 (16). HRMS (EI$^+$) calcd for $C_{12}H_{14}O$ [M^+]: 174.1045, found 174.1046.

(1*R*,2*S*)-*trans*-2-(3′-Bromophenyl)-cyclopent-3-enyl Ethyl Carbonate (2q) and (1*R*,4*R*)-*trans*-4-(3′-Bromophenyl)-cyclopent-2-enyl Ethyl Carbonate (3q). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 89% yield (89 mg), showing a 1:2.3 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4q** and **5q**. *Minor regioisomer* **2q**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.03 (4H, m), 5.96 (1H, ddd, J = 5.8, 4.0, 2.0 Hz), 5.80−5.75 (1H, m), 5.00 (1H, ddd, J = 6.6, 2.6, 3.1 Hz), 4.20 (2H, q, J = 7.1 Hz), 3.96 (1H, brs), 2.54−2.45 (1H, m), 2.91 (1H, dddd, J = 17.8, 6.3, 3.9, 2.1 Hz), 1.31 (3H, t, J = 7.1 Hz). *Major regioisomer* **3q**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.03 (4H, m), 6.15 (1H, dd, J = 5.6, 1.7 Hz), 6.10 (1H, ddd, J = 7.7, 5.6, 2.2 Hz), 5.77−5.72 (1H, m), 4.20 (2H, q, J = 7.1 Hz), 4.15−4.08 (1H, m), 2.46 (1H, dt, J = 6.8, 2.2 Hz), 2.10 (1H, ddd, J = 14.7, 7.1, 5.9 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(3′-Bromophenyl)-cyclopent-3-enol (4q). Colorless oil. $[\alpha]^{26.3}_D$ = +146 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 96.8:3.2, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.28 (2H, m), 7.15 (1H, t, J = 7.6 Hz), 7.09 (1H, dd, J = 7.6, 1.4 Hz), 5.90 (1H, ddd, J = 6.1, 4.3, 2.2 Hz), 5.71 (1H, ddd, J = 6.1, 4.1, 2.0 Hz), 4.28−4.19 (1H, m), 3.74−3.66 (1H, m), 2.77 (1H, ddd, J = 17.0, 3.0, 1.8 Hz), 2.34 (1H, ddd, J = 17.0, 3.9, 1.8 Hz), 2.08 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 131.2, 130.0, 129.9, 129.8, 129.4, 125.8, 122.5, 81.4, 61.3, 42.8. IR (NaCl, neat film): 3331 (br), 3057, 2906, 2843, 1592, 1564, 1475, 1426, 1287, 1265, 1163, 1072, 1052, 996, 950, 780, 720 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 240 (M^+, 14), 238 (17), 222 (33), 184 (40), 182 (44), 141 (65), 131 (75), 128 (44), 115 (100), 91 (14). HRMS (EI$^+$) calcd for $C_{11}H_{11}BrO$ [M^+]: 237.9993, found 237.9996.

(1*R*,4*R*)-*trans*-4-(3′-Bromophenyl)-cyclopent-2-enol (5q). Colorless oil. $[\alpha]^{27.0}_D$ = +181 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 99.5:0.5, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (1H, dd, J = 6.1, 1.2 Hz), 7.26 (1H, t, J = 2.2 Hz), 7.15 (1H, t, J = 7.8 Hz), 7.05 (1H, dd, J = 7.6, 1.2 Hz), 6.08−6.05 (1H, m), 6.01 (1H, dd, J = 4.7, 2.0 Hz), 5.12−5.01 (1H, m), 4.16−4.08 (1H, m), 2.28 (1H, ddd, J = 14.1, 8.0, 2.6 Hz), 2.07 (1H, ddd, J = 14.0, 7.0, 5.4 Hz), 1.57 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 137.8, 134.3, 129.8, 129.7, 129.1, 125.6, 122.5, 77.9, 50.8, 45.2. IR (NaCl, neat film): 3328 (br), 3057, 2963, 2930, 2876, 1592, 1476, 1424, 1350, 1110, 1072, 1052, 937, 791, 778, 743, 692 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 240 (M^+, 6), 238 (16), 222 (72), 141 (100), 139 (23), 115 (67), 86 (22), 84 (27). HRMS (EI$^+$) calcd for $C_{11}H_{11}BrO$ [M^+]: 237.9993, found 237.9990.

(1*R*,2*S*)-*trans*-2-(4′-Fluoro-3-methylphenyl)-cyclopent-3-enyl Ethyl Carbonate (2r) and (1*R*,4*R*)-*trans*-4-(4′-Fluoro-3-methylphenyl)-cyclopent-2-enyl Ethyl Carbonate (3r). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 69% yield (60 mg), showing a 1:2.3 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4r** and **5r**. *Minor regioisomer* **2r**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03−6.96 (1H, m), 6.95−6.88 (2H,

m), 5.93 (1H, ddd, J = 5.9, 4.2, 2.1 Hz), 5.78 (1H, dd, J = 4.3, 2.2 Hz), 4.99 (1H, dt, J = 6.6, 2.7 Hz), 4.20 (2H, q, J = 7.1 Hz), 3.40 (1H, brs), 2.90 (1H, dddd, J = 17.8, 6.6, 4.0, 1.8 Hz), 2.51−2.44 (1H, m), 2.24 (3H, s), 1.31 (3H, t, J = 7.1 Hz). *Major regioisomer* **3r**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03−6.96 (1H, m), 6.95−6.88 (2H, m), 6.14 (1H, dd, J = 5.6, 2.0 Hz), 6.07 (1H, dt, J = 5.6, 2.3 Hz), 5.74 (1H, dd, J = 6.9, 4.0, 2.1 Hz), 4.20 (2H, q, J = 7.1 Hz), 4.09 (1H, dddd, J = 7.8, 5.7, 4.2, 2.1 Hz), 2.45 (1H, ddd, J = 14.6, 7.9, 2.1 Hz), 2.24 (3H, s), 2.08 (1H, ddd, J = 14.6, 7.1, 1.3 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(4′-Fluoro-3′-methylphenyl)-cyclopent-3-enol (4r). Colorless oil. $[\alpha]^{28.2}_D$ = +187 (*c* 0.50, $CHCl_3$); enantiomeric ratio was 97.1:2.9, as determined by HPLC analysis (Chiralcel OD-H; 215 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96 (1H, d, J = 8.0 Hz), 6.94−6.86 (2H, m), 5.87 (1H, dd, J = 5.9, 2.3 Hz), 5.71 (1H, dd, J = 6.0, 2.0 Hz), 4.20 (1H, dt, J = 6.6, 4.1 Hz), 3.70−3.64 (1H, m), 3.76 (1H, ddd, J = 16.9, 6.7, 2.0 Hz), 3.34 (1H, ddd, J = 16.8, 4.1, 2.1 Hz), 2.23 (3H, d, J = 2.0 Hz), 2.04 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0 (d, J = 243.1 Hz), 138.1 (d. J = 3.8 Hz), 132.4, 130.5 (d, J = 5.2 Hz), 129.7, 126.1 (d, J = 7.9 Hz), 125.0 (d, J = 17.2 Hz), 115.1 (d, J = 22.1 Hz), 81.2, 60.1, 41.5, 14.7. ^{19}F NMR (375 MHz, $CDCl_3$): δ −121.4 (dd, J = 7.6, 1.9 Hz, 1F). IR (NaCl, neat film): 3337 (br), 3056, 3017, 2962, 2844, 1501, 1252, 1236, 1207 1118, 1051, 949, 819, 756 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 192.1 (M^+, 47), 174 (51), 159 (43), 146 (48), 136 (100), 133 (44), 123 (30), 109 (30). HRMS (EI$^+$) calcd for $C_{12}H_{13}OF$ [M^+]: 192.0950, found 192.0950.

(1*R*,4*R*)-*trans*-4-(4′-Fluoro-3′-methylphenyl)-cyclopent-2-enol (5r). Colorless oil. $[\alpha]^{28.1}_D$ = +204 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 99.3:0.7, as determined by HPLC analysis (Chiralcel OD-H; 215 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95−6.86 (3H, m), 6.06−5.98 (2H, m), 5.09−5.00 (1H, m), 4.14−4.06 (1H, m), 2.27 (1H, ddd, J = 14.1, 8.0, 2.6 Hz), 2.24 (3H, d, J = 2.0 Hz) 2.05 (1H, ddd, J = 14.2, 6.8, 5.5 Hz), 1.58 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7 (d, J = 243.1 Hz), 140.3 (d. J = 3.7 Hz), 139.3, 134.2, 130.1 (d, J = 5.9 Hz), 125.9, 125.8, 115.1 (d, J = 22.4 Hz), 77.6, 49.3, 44.4, 14.7 (d, J = 3.8). ^{19}F NMR (375 MHz, $CDCl_3$): δ −121.7 (dd, J = 13.3, 5.7 Hz, 1F). IR (NaCl, neat film): 3326 (br), 3055, 3018, 2962, 2927, 2891, 1501, 1325, 1245, 1205, 1118, 1028, 882, 790, 756 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 192.1 (M^+, 5), 175 (15), 174 (100), 159 (82), 146 (29), 133 (54), 109 (11). HRMS (EI$^+$) calcd for $C_{12}H_{13}OF$ [M^+]: 192.0950, found 192.0949.

(1*R*,2*S*)-*trans*-2-(3′-Fluoro-5′-methoxyphenyl)-cyclopent-3-enyl Ethyl Carbonate (2s) and (1*R*,4*R*)-*trans*-4-(3′-Fluoro-5′-methoxyphenyl)-cyclopent-2-enyl Ethyl Carbonate (3s). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 78% yield (72 mg), showing a 1:2.4 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4s** and **5s**. *Minor regioisomer* **2s**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59−6.40 (3H, m), 5.95 (1H, ddd, J = 5.9, 4.1, 2.1 Hz), 5.79−5.73 (1H, m), 5.02 (1H, dt, J = 6.6, 2.7 Hz), 4.20 (2H, q, J = 7.1 Hz), 3.94 (1H, brs), 3.77 (3H, s), 2.90 (1H, dddd, J = 17.8, 6.6, 3.9, 1.8 Hz), 2.52−2.43 (1H, m), 1.31 (3H, t, J = 7.1 Hz). *Major regioisomer* **3s**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.59−6.40 (3H, m), 6.15 (1H, dd, J = 5.6, 1.8 Hz), 6.09 (1H, ddd, J = 5.6, 3.2, 2.2 Hz), 5.76−5.71 (1H, m), 4.20 (2H, q, J = 7.1 Hz), 4.13−4.05 (1H, m), 3.77 (3H, s), 2.45 (1H, ddd, J = 14.6, 7.8, 2.2 Hz), 2.11 (1H, ddd, J = 14.6, 7.1, 5.8 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(3′-Fluoro-5′-methoxyphenyl)-cyclopent-3-enol (4s). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.55−6.43 (3H, m), 5.91 (1H, ddd, J = 12.2, 5.8, 2.4 Hz), 5.73 (1H, ddd, J = 8.0, 6.1, 1.9 Hz), 4.25 (1H, ddd, J = 8.2, 6.6, 3.1 Hz), 3.77 (3H, s), 3.74−3.68 (1H, m), 2.79 (1H, ddd, J = 17.0, 6.9, 2.1 Hz), 2.36 (1H, ddd, J = 17.0, 4.1, 2.2 Hz), 1.98 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, J = 245.0 Hz), 161.0 (d. J = 11.4 Hz), 145.8 (d, J = 8.9 Hz), 131.5, 130.2, 109.0 (d, J = 2.6 Hz), 106.4 (d, J = 21.7 Hz), 99.6 (d, J = 25.7 Hz), 80.7, 60.6 (d, J = 2.0 Hz), 55.5, 41.4. ^{19}F NMR (375 MHz, $CDCl_3$): δ −112.2 (t, J = 9.8 Hz, 1F). IR (NaCl, neat film): 3332 (br), 3055, 3010, 2963, 2938, 28340, 1604, 1502, 1457, 1318, 1255, 1229, 1045, 1024, 821, 765 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 208.1 (M^+, 97), 190 (99), 180 (100), 175 (33), 152 (35), 146 (50), 139 (32), 86 (27), 84 (45). HRMS (EI$^+$) calcd for $C_{12}H_{13}O_2F$ [M^+]: 208.0900, found 208.0905.

(1*R*,4*R*)-*trans*-4-(3′-Fluoro-5′-methoxyphenyl)-cyclopent-2-enol (5s). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.42−6.34 (3H, m), 5.97 (1H, ddd, J = 5.5, 3.3, 2.1 Hz), 5.93 (1H, dd, J = 5.5, 2.0 Hz), 4.97 (1H, ddd, J = 7.0, 4.6, 2.1 Hz), 4.06−3.97 (1H, m), 3.70 (3H, s), 2.19 (1H, ddd, J = 14.1, 8.1, 2.7 Hz), 2.00 (1H, ddd, J = 14.1, 8.7, 5.4 Hz), 1.62 (1H, br s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (d, J = 244.8 Hz), 161.0 (d. J = 11.4 Hz), 148.1 (d. J = 8.8 Hz), 138.2, 134.7, 108.9 (d, J = 2.6 Hz), 106.1 (d, J = 21.7 Hz), 99.3 (d, J = 25.3 Hz), 77.3, 55.5, 49.9 (d, J = 2.1 Hz), 43.8. ^{19}F NMR (375 MHz, $CDCl_3$): δ −112.2 (t, J = 9.7 Hz, 1F). IR (NaCl, neat film): 3334 (br), 3053, 3010, 2959, 2843, 1601, 1499, 1254, 1237, 1116, 1052, 949, 789 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 208.1 (M^+, 7), 190 (100), 175 (23), 147 (20), 146 (51), 133 (17), 127 (13), 86 (14), 84 (28). HRMS (EI$^+$) calcd for $C_{12}H_{13}O_2F$ [M^+]: 208.0900, found 208.0903.

(1*R*,2*S*)-*trans*-2-(4′-Methoxy-3′-methylphenyl)-cyclopent-3-enyl Ethyl Carbonate (2t) and (1*R*,4*R*)-*trans*-4-(4′-Methoxy-3′-methylphenyl)-cyclopent-2-enyl Ethyl Carbonate (3t). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 66% yield (60 mg), showing a 1:1.3 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4t** and **5t**. *Major regioisomer* **3t**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03−6.97 (1H, m), 6.94−6.88 (1H, m), 6.74 (1H, d, J = 6.7 Hz), 6.16 (1H, dd, J = 5.6, 2.0 Hz), 6.05 (1H, dt, J = 5.6, 2.3 Hz), 5.72 (1H, ddd, J = 6.9, 3.8, 2.1 Hz), 4.20 (2H, q, J = 7.1 Hz), 4.10−4.04 (1H, m), 3.81 (3H, s), 2.45 (1H, ddd, J = 14.5, 7.8, 2.0 Hz), 2.20 (3H, m), 2.10 (1H, ddd, J = 14.6, 7.1, 5.8 Hz), 1.31 (3H, t, J = 7.1 Hz). *Minor regioisomer* **2t**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03−6.97 (1H, m), 6.94−6.88 (1H, m), 6.76 (1H, d, J = 3.8 Hz), 5.90 (1H, ddd, J = 5.9, 4.1, 2.1 Hz), 5.81−5.76 (1H, m), 5.00 (1H, ddd, J = 6.6, 3.7, 2.7 Hz), 4.16 (2H, q, J = 7.1 Hz), 3.92 (1H, brs), 3.81 (3H, s), 2.91 (1H, dddd, J = 17.7, 6.6, 4.0, 1.8 Hz), 2.49−2.43 (1H, m), 2.20 (3H, s), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(4′-Methoxy-3′-methylphenyl)-cyclopent-3-enol (4t). Colorless oil. $[\alpha]^{28.5}_D$ = +172 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 89.7:10.3, as determined by HPLC analysis (Chiralcel OD-H; 235 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93−6.85 (2H, m), 6.69 (1H, d, J = 7.9 Hz), 5.78 (1H, ddd, J = 5.9, 4.4, 2.2 Hz), 5.68 (1H, ddd, J = 5.9, 4.1, 2.1 Hz), 4.22−4.14 (1H, m), 3.74 (3H, s), 3.63−3.59 (1H, m), 2.71 (1H, dddd, J = 23.6, 6.7, 3.9, 1.8 Hz), 2.27 (1H, ddt, J = 16.8, 4.1, 2.0 Hz), 2.13 (3H, s), 1.75 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 134.1, 132.7, 129.7, 129.1, 126.8, 125.4, 110.0, 81.1, 59.9, 55.4, 41.2, 16.2. IR (NaCl, neat film): 3348 (br), 3055, 2993, 2916, 2839, 1612, 1504, 1465, 1257, 1219, 1134, 1033, 949, 810 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 204.1 (M^+, 14), 172 (8), 161 (35), 148 (100), 128 (49), 115 (43), 91 (23), 71 (22). HRMS (EI$^+$) calcd for $C_{13}H_{16}O_2$ [M^+]: 204.1150, found 204.1147.

(1*R*,4*R*)-*trans*-4-(4′-Methoxy-3′-methylphenyl)-cyclopent-2-enol (5t). Colorless oil. $[\alpha]^{28.6}_D$ = +228 (*c* 1.00, $CHCl_3$); enantiomeric ratio was 99.6:0.4, as determined by HPLC analysis (Chiralcel OD-H; 225 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95−6.86 (2H, m), 6.74 (1H, d, J = 8.2 Hz), 6.05−5.96 (2H, m), 5.04 (1H, ddd, J = 7.0, 3.7, 2.2 Hz), 4.09−4.03 (1H, m), 3.80 (3H, s), 2.25 (1H, ddd, J = 14.1, 8.1, 2.6 Hz), 2.19 (3H, s), 2.07 (1H, ddd, J = 14.2, 7.0, 5.6 Hz), 1.69 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 139.9, 136.6, 133.7, 129.6, 126.9, 125.3, 110.2, 77.7, 55.6, 49.3, 44.5, 16.4. IR (NaCl, neat film): 3348 (br), 3055, 2993, 2947, 2831, 1705 (w), 1612, 1504, 1465, 1249, 1219, 1134, 1111, 1033, 910, 810 cm^{-1}. MS (EI$^+$) *m*/*z* (rel intensity): 204.1 (M^+, 22), 186 (88), 171 (100), 127 (11), 115 (45), 84 (5). HRMS (EI$^+$) calcd for $C_{13}H_{16}O_2$ [M^+]: 204.1150, found 204.1154.

(1*R*,2*S*)-*trans*-2-(4′-Methylsulfanylphenyl)-cyclopent-3-enyl Ethyl Carbonate (2u) and (1*R*,4*R*)-*trans*-4-(4′-Methylsulfanylphenyl)-cyclopent-2-enyl Ethyl Carbonate (3u). Prepared according to *Procedure B*. The inseparable regioisomers were obtained as a colorless oil in 80% yield (72 mg), showing a 1:2.6 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4u** and **5u**. *Minor regioisomer* **2u**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (2H, dd, J = 5.6, 3.3 Hz), 7.05 (2H, dd, J = 8.3, 1.8 Hz), 5.93 (1H, ddd, J = 5.8, 4.1, 2.1 Hz), 5.80 (1H, dd, J = 4.3, 2.1 Hz), 5.00 (1H, dt, J = 6.6, 2.7 Hz), 4.20 (2H, q, J = 7.1 Hz), 3.96 (1H, brs), 2.89 (1H, dddd, J = 17.7, 6.6, 3.9, 1.8 Hz), 2.46 (3H, s), 2.52−2.48 (1H, m), 1.31 (3H, t, J = 7.1 Hz). *Major regioisomer* **3u**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (2H, dd, J = 11.4, 1.6 Hz), 7.14 (2H, dd, J = 8.4, 1.8 Hz), 6.16 (1H, dd, J = 5.6, 1.9 Hz), 6.08 (1H, ddd, J = 5.5, 3.1, 2.3 Hz), 5.75 (1H, ddd, J = 7.0, 3.9, 2.1 Hz), 4.20 (2H, q, J = 7.1 Hz), 4.15−4.08 (1H, m), 2.46 (3H, s), 2.48−2.42 (1H, m), 2.09 (1H, ddd, J = 14.6, 7.1, 5.9 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(4′-Methylsulfanylphenyl)-cyclopent-3-enol (4u). Colorless oil. $[\alpha]^{28.9}_D$ = +205 (c 1.00, $CHCl_3$); enantiomeric ratio was 95.6:4.4, as determined by HPLC analysis (Chiralcel OD-H; 262 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (2H, ddd, J = 8.4, 4.3, 2.2 Hz), 7.11 (1H, ddd, J = 8.2, 4.1, 2.2 Hz), 5.90 (1H, ddd, J = 5.8, 2.4, 2.2 Hz), 5.75 (1H, ddd, J = 5.9, 2.2, 2.0 Hz), 4.24 (1H, ddd, J = 6.6, 5.8, 4.3 Hz), 3.74−3.72 (1H, m), 2.80 (1H, dddd, J = 15.3, 6.8, 3.9, 2.2 Hz), 2.47 (3H, s), 2.37 (1H, dddd, J = 17.0, 6.1, 4.1, 2.0 Hz), 1.81 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 136.6, 132.3, 129.9, 128.1 (2C), 127.4 (2C), 81.2, 60.4, 41.6, 16.4. IR (NaCl, neat film): 3348 (br), 3055, 3016, 2962, 2916, 2839, 1489, 1435, 1404, 1319, 1049, 949, 817, 732 cm^{-1}. MS (EI$^+$) m/z (rel intensity): 206.1 (M$^+$, 25), 188 (8), 150 (100), 129 (34), 128 (53), 116 (39), 115 (51), 91 (17), 89 (9). HRMS (EI$^+$) calcd for $C_{12}H_{14}OS$ [M$^+$]: 206.0765, found 206.0760.

(1*R*,4*R*)-*trans*-4-(4′-Methylsulfanylphenyl)-cyclopent-2-enol (5u). Colorless oil. $[\alpha]^{28.1}_D$ = +298 (c 1.00, $CHCl_3$); enantiomeric ratio was 99.5:0.5, as determined by HPLC analysis (Chiralcel OD-H; 262 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (2H, dd, J = 9.4, 1.8 Hz), 7.05 (2H, dd, J = 8.2, 1.8 Hz), 6.06−5.97 (2H, m), 5.08−5.01 (1H, m), 4.15−4.05 (1H, m), 2.46 (3H, s), 2.27 (1H, ddd, J = 14.0, 8.0, 2.8 Hz), 2.06 (1H, ddd, J = 14.2, 7.2, 4.6 Hz), 1.66 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 139.2, 136.2, 134.4, 127.8 (2C), 127.4 (2C), 77.6, 49.6, 44.3, 16.5. IR (NaCl, neat film): 3333 (br), 3055, 3016, 2962, 2931, 2885, 1489, 1435, 1411, 1319, 1026, 817, 732 cm^{-1}. MS (EI$^+$) m/z (rel intensity): 206.1 (M$^+$, 5), 150 (15), 142 (41), 128 (40), 115 (100), 102 (31), 89 (42), 63 (41). HRMS (EI$^+$) calcd for $C_{12}H_{14}OS$ [M$^+$]: 206.0765, found 206.0766.

(1*R*,2*S*)-*trans*-2-(2′-Fluorophenyl)-cyclopent-3-enyl Ethyl Carbonate (2v) and (1*R*,4*R*)-*trans*-4-(2′-Fluorophenyl)-cyclopent-2-enyl Ethyl Carbonate (3v). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 16% yield (13 mg), showing a 1:1.3 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols **4v** and **5v**. *Minor regioisomer* **2v**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24−7.16 (1H, m), 7.10−6.98 (3H, m), 5.93 (1H, ddd, J = 5.9, 4.3, 2.2 Hz), 5.77 (1H, dd, J = 4.1, 2.2 Hz), 5.16 (1H, dt, J = 6.8, 2.9 Hz), 4.28 (1H, brs.), 4.20 (2H, q, J = 7.1 Hz), 2.96 (1H, dddd, J = 17.9, 6.8, 4.0, 2.1 Hz), 2.55−2.49 (1H, m), 1.31 (3H, t, J = 7.1 Hz). *Major regioisomer* **3v**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24−7.16 (1H, m), 7.10−6.98 (3H, m), 6.18 (1H, dd, J = 5.6, 2.0 Hz), 6.10 (1H, ddd, J = 5.6, 3.2, 2.4 Hz), 5.74 (1H, ddd, J = 7.9, 4.4, 2.3 Hz), 4.44 (1H, dddd, J = 13.7, 7.9, 4.3, 2.2 Hz), 4.20 (2H, q, J = 7.1 Hz), 2.53−2.47 (1H, m), 2.14 (1H, ddd, J = 14.6, 7.2, 5.8 Hz), 1.31 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(2′-Fluorophenyl)-cyclopent-3-enol (4v). Colorless oil. $[\alpha]^{28.8}_D$ = +150 (c 0.30, $CHCl_3$); enantiomeric ratio was 94.1:5.9, as determined by HPLC analysis (Chiralcel OD-H; 215 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23−7.17 (1H, m), 7.10−7.02 (3H, m), 5.95 (1H, ddd, J = 5.9, 4.4, 2.2 Hz), 5.75 (1H, ddd, J = 5.9, 4.3, 2.2 Hz), 4.35 (1H, dt, J = 6.6, 3.3 Hz), 4.10 (1H, brs), 2.80 (1H, dddd, J = 17.2, 6.7, 4.1, 2.1 Hz), 2.39 (1H, ddt, J = 17.2, 3.6, 2.0 Hz), 1.97 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2 (d, J = 245.0 Hz), 130.7 (d, J = 9.7 Hz), 129.4 (d, J = 15.0 Hz), 128.4 (d, J = 4.5 Hz), 128.3 (d, J = 8.2 Hz), 124.3 (d, J = 3.4 Hz), 115.6, 115.4, 79.8, 54.1 (d, J = 1.5 Hz), 41.5. ^{19}F NMR (375 MHz, $CDCl_3$): δ −118.3 (d, J = 8.6 Hz, F). IR (NaCl, neat film): 3348 (br), 3055, 2993, 2924, 2847, 1720 (w), 1581, 1489, 1450, 1226, 1041, 949, 864, 756 cm^{-1}. MS (EI$^+$) m/z (rel intensity): 178.1 (M$^+$, 3), 146 (21), 135 (44), 133 (51), 122 (100), 115 (14), 109 (45), 75 (30), 63 (24). HRMS (EI$^+$) calcd for $C_{11}H_{11}FO$ [M$^+$]: 178.0794, found 178.0800.

(1*R*,4*R*)-*trans*-4-(2′-Fluorophenyl)-cyclopent-2-enol (5v). Colorless oil. $[\alpha]^{28.5}_D$ = +98 (c 0.82, $CHCl_3$); enantiomeric ratio was 98.2:1.8, as determined by HPLC analysis (Chiralcel OD-H; 215 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22−7.14 (1H, m), 7.10−6.97 (3H, m), 6.09−6.00 (2H, m), 5.08−5.01 (1H, m), 4.48−4.40 (1H, m), 2.31 (1H, ddd, J = 14.1, 8.1, 2.8 Hz), 2.11 (1H, ddd, J = 13.8, 6.8, 5.5 Hz), 1.58 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0 (d, J = 245.3 Hz), 137.7, 134.8, 131.7 (d, J = 14.7 Hz), 128.1 (d, J = 2.6 Hz), 128.0, 124.4 (d, J = 3.3 Hz), 115.6, 115.4, 77.3, 42.8 (d, J = 2.6 Hz), 42.7. ^{19}F NMR (375 MHz, $CDCl_3$): δ −119.0 to −119.1 (m, rotamers). IR (NaCl, neat film): 3317 (br), 3063, 2963, 2931, 1581, 1489, 1450, 1350, 1226, 1111, 1026, 756 cm^{-1}. MS (EI$^+$) m/z (rel intensity): 178.1 (M$^+$, 20), 160 (100), 159 (72), 133 (75), 122 (19), 109 (34), 86 (24), 84 (44). HRMS (EI$^+$) calcd for $C_{11}H_{11}FO$ [M$^+$]: 178.0794, found 178.0791.

(1*R*,2*S*)-*trans*-2-(Thiophen-3′-yl)-cyclopent-3-enyl Ethyl Carbonate (2w) and (1*R*,4*R*)-*trans*-4-(Thiophen-3′-yl)-cyclopent-2-enyl Ethyl Carbonate (3w). Prepared according to Procedure B. The inseparable regioisomers were obtained as a colorless oil in 31% yield (24 mg), showing a 1:3.5 ratio of **2**:**3** by ^{1}H NMR spectroscopy. The regioisomers were characterized as the free alcohols. *Minor regioisomer* **2w**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23−7.18 (1H, m), 6.97−6.91 (2H, m), 5.85−5.76 (2H, m), 4.99 (1H, dt, J = 6.5, 2.3 Hz), 4.13 (2H, q, J = 7.1 Hz), 4.00 (1H, brs), 2.82 (1H, dddd, J = 17.8, 6.5, 3.8, 1.8 Hz), 2.45−2.36 (1H, m), 1.24 (3H, t, J = 7.1 Hz). *Major regioisomer* **3w**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22−6.98 (1H, m), 6.89−6.86 (1H, m), 6.81 (1H, dd, J = 4.9, 1.1 Hz), 6.14 (1H, dd, J = 5.6, 2.0 Hz), 5.96 (1H, dt, J = 5.6, 2.3 Hz), 5.67 (1H, ddd, J = 7.1, 4.1, 2.1 Hz), 4.21−4.14 (1H. m), 4.13 (2H, q, J = 7.1 Hz), 2.37 (1H, dd, J = 14.5, 7.8, 2.4 Hz), 2.10 (1H, ddd, J = 14.1, 7.1, 5.7 Hz), 1.24 (3H, t, J = 7.1 Hz).

(1*R*,2*S*)-*trans*-2-(Thiophen-3′-yl)-cyclopent-3-enol (4w). Colorless oil. $[\alpha]^{27.6}_D$ = +108 (c 0.40, $CHCl_3$); enantiomeric ratio was 94.4:5.6, as determined by HPLC analysis (Chiralcel OD-H; 235 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (1H, dd, J = 4.9, 3.0 Hz), 6.99−6.96 (1H, m), 6.95 (1H, dd, J = 4.1, 1.2 Hz), 5.87 (1H, ddd, J = 5.9, 4.1, 2.0 Hz), 5.82 (1H, ddd, J = 5.9, 4.0, 2.0 Hz), 4.31 (1H, dt, J = 6.9, 3.7 Hz), 3.89−3.84 (1H, m), 2.80 (1H, ddd, J = 6.5, 3.6, 1.8 Hz), 2.35 (1H, ddt, J = 17.0, 3.7, 1.8 Hz), 1.84 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 133.2, 129.8, 127.3, 126.1, 120.3, 80.0, 56.1, 41.5. IR (NaCl, neat film): 3333 (br), 3101, 3055, 2916, 2847, 1527, 1411, 1319, 1257, 1157, 1049, 940, 841, 779, 748, 640 cm^{-1}. MS (EI$^+$) m/z (rel intensity): 166.0 (M$^+$, 37), 148 (27), 147 (53), 138 (38), 135 (42), 123 (54), 110 (100), 97 (58), 91 (19), 84 (30), 77 (17). HRMS (EI$^+$) calcd for $C_9H_{10}OS$ [M$^+$]: 166.0452, found 166.0452.

(1*R*,4*R*)-*trans*-4-(Thiophen-3′-yl)-cyclopent-2-enol (5w). Colorless oil. $[\alpha]^{27.8}_D$ = +269 (c 0.50, $CHCl_3$); enantiomeric ratio was 99.6:0.4, as determined by HPLC analysis (Chiralcel OD-H; 235 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.20 (1H, m), 6.97−6.82 (2H, m), 6.07 (1H, brs), 5.99 (1H, brs), 5.02 (1H, brs), 4.22 (1H, brs), 2.30−2.08 (2H, m), 1.58 (1H, brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 138.9, 133.9, 127.1, 126.1, 119.6, 77.5, 45.2, 43.2. IR (NaCl, neat film): 3317 (br), 3101, 3055, 2962,

2931, 2893, 1527, 1411, 1319, 1157, 1111, 1026, 779 cm^{-1}. MS (EI^+) *m*/*z* (rel intensity): 166.0 (M^+, 32), 148 (99), 147 (91), 135 (21), 123 (23), 121 (52), 115 (100), 97 (29), 63 (30). HRMS (EI^+) calcd for $C_9H_{10}OS$ [M^+]: 166.0452, found 166.0451.

***tert*-Butyldimethyl((1*R*,2*S*)-2-phenylcyclopent-3-enyloxy)silane (7).** On the basis of a literature protocol,[50] a solution of **4a** (100 mg, 0.62 mmol) in dry DCM (10 mL) was stirred at 0 °C under N_2. *tert*-Butyldimethylsilyl chloride (207 mg, 1.37 mmol) and imidazole (127 mg, 1.87 mmol) were added. The reaction was allowed to stir overnight at room temperature. Water (5 mL) was added, and the layers were decanted. The aqueous layer was extracted with DCM (3 × 15 mL), the combined organic layers were washed with brine, dried with $MgSO_4$, and filtered, and the solvent was removed under reduced pressure to give an oil. The product was purified by column chromatography (10% EtOAc/Hex) to afford a colorless oil (152 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.43−7.28 (m, 5H), 5.90 (ddd, 1H, J = 6.1, 4.0, 2.1 Hz), 5.84 (ddd, 1H, J = 6.0, 4.0, 2.0 Hz), 4.35−4.31 (m, 1H), 3.86−3.83 (m, 1H), 2.82 (dddd, 1H, J = 16.2, 9.4, 7.0, 2.4 Hz), 2.47 (dddd, 1H, J = 16.4, 7.6, 5.5, 2.4 Hz), 0.96 (s, 9H), 0.14 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.7, 132.7, 129.6, 127.8, 127.7, 126.6, 82.6, 60.6, 26.1, 26.0, 18.3, −4.7 ppm. IR ($CHCl_3$) υ: 3060, 3029, 2956, 2929, 2857, 1471, 1361, 1252, 1113, 897 cm^{-1}. HRMS (EI^+) calcd for $C_{13}H_{17}OSi$ [M^+]: 217.1049; found: 217.1051.

3-(*tert*-Butyldimethylsilyloxy)-2-phenylpentane-1,5-diol. According to a modified literature protocol,[51] cyclopentene **7** (162 mg, 1.12 mmol) was dissolved in dry DCM (36 mL) and MeOH (40 mL) and cooled down to −78 °C. A stream of ozone was bubbled through until solution turned blue, and then N_2 was bubbled through until all blue color disappeared. Sodium borohydride (212 mg, 5.6 mmol) was added in four equal portions every 15 min for the duration of 1 h, while maintaining the temperature at −78 °C. The reaction was left to stir at room temperature until complete by TLC analysis. The solvent was removed under reduced pressure; the residue was retaken in EtOAc (25 mL) and was washed with brine. The aqueous wash was extracted with EtOAc (5 × 25 mL), the combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure to give an oil, which was purified using column chromatography (50−100% EtOAc/Hex, then 5% MeOH/DCM) to give the diol as a white solid (100 mg, 55%). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.27−7.17 (m, 5H), 4.14 (ddd, 1H, J = 9.8, 5.1, 1.6 Hz), 4.03 (dd, 1H, J = 10.9, 7.4 Hz), 3.86 (dd, 1H, J = 10.9, 7.4 Hz), 3.60 (td, 2H, J = 7.4, 1.4 Hz), 3.01 (ddd, 1H, J = 11.6, 7.3, 4.4 Hz), 0.084 (s, 9H), 0.03 (s, 6H) ppm. ^{13}CNMR (75 MHz, $CDCl_3$) δ: 143.9, 133.8, 133.2, 131.7, 77.3, 68.2, 64.5, 57.4, 40.4, 30.6, 22.7, −0.5 ppm. IR ($CHCl_3$) υ: 3338, 2956, 2925, 2883, 2852, 1473, 1251, 1098, 1031, 915 cm^{-1}. HRMS (EI^+) calcd for $C_{13}H_{19}O_2Si$ [M-75]$^+$: 235.1154; found 235.1165.

3-(*tert*-butyldimethylsilyloxy)-2-phenylpentane-1,5-diyl dimethanesulfonate. Following a literature protocol,[52] the above diol (55 mg, 0.31 mmol) was dissolved in dry DCM (8 mL) under N_2 at 0 °C. Triethylamine (0.18 mL 1.3 mmol) and methanesulfonyl chloride (0.05 mL. 0.67 mmol) were added to the flask and the reaction was allowed to warm up to room temperature and stirred for 16 h. Water (30 mL) was added to quench the reaction, and the aqueous layer was extracted with DCM (5 × 20 mL). The combined organic layers were dried with $MgSO_4$, filtered, and the solvent was removed under reduced pressure to give the desired bissulfonate as a brown oil (135 mg, 100%), which was used without further purification in the next step.

1-Benzyl-4-(*tert*-butyldimethylsilyloxy)-3-phenylpiperidine (8). The above bissulfonate (135 mg, 0.29 mmol) was dissolved in dry dioxane (15 mL). Benzylamine (0.473 mL, 4.34 mmol) and triethylamine (0.081 mL, 0.58 mmol) were added and the reaction was allowed to stir at 80 °C overnight. The reaction was washed with H_2O (20 mL) and 3 M NaOH (2 mL). The aqueous layer was extracted with Et_2O (3 × 25 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, and filtered, and the solvent was removed under reduced pressure to give a red oil, which was purified using column chromatography (40% EtOAc/Hex) to give piperidine **8** as a red oil (35 mg, 32%). ^1H NMR (300 MHz, $CDCl_3$) δ: 7.84−7.64 (m, 10H), 4.12 (td, 1H, J = 9.8, 4.8 Hz), 4.04 (d, 2H, J = 2.8 Hz), 3.44 (dt, 2H, J = 11.4, 1.7 Hz), 3.32−3.24 (m, 2H), 2.78−2.60 (m, 2H), 2.43−2.19 (m, 2H), 1.18 (s, 9H), 0.33 (s, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 147.8, 134.6, 134.2, 133.8, 133.6, 132.6, 132.0, 80.0, 68.3, 64.0, 57.8, 56.7, 40.8, 31.2, 23.4, 0.9 ppm. IR ($CHCl_3$) υ: 3029, 2627, 2855, 2801, 1495, 1472, 1361, 1252, 1108, 835 cm^{-1}. HRMS (EI^+) calcd for $C_{24}H_{35}NOSi$ [M]$^+$: 381.2488, found 381.2469.

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Supporting Information Available: General experimental methods, reaction procedures, complete characterization data, and copies of ^1H and ^{13}C NMR spectra for compounds **1**, **1a**, **1aa**, **2a**, **2b**, **2l**, **2m**, **2q**−**2w**, **3a**, **3b**, **3l**, **3m**, **3q**−**3w**, **4a**, **4b**, **4l**, **4m**, **4q**−**4w**, **5a**, **5b**, **5l**, **5m**, **5q**−**5w**, **7**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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