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Phosphinite Thioethers Derived from Chiral Epoxides. Modular *P*,*S*-Ligands for Pd-Catalyzed Asymmetric Allylic Substitutions

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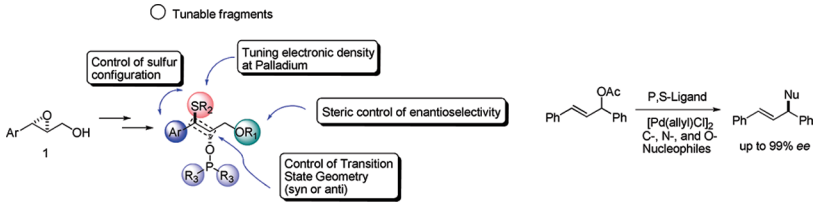

A new family of modular *P*,*S*-ligands has been prepared from enantiopure arylglycidols. These ligands have been iteratively optimized with respect to four different structural parameters for use in Pd-catalyzed allylic substitutions. As a final output, highly active and enantioselective ligands for these synthetically important transformations have been developed, and the factors controlling their catalytic behavior have been rationalized. From a methodological point of view, a convenient procedure for the regioselective ring-opening of *cis*-glycidic esters with bulky thiols to yield the corresponding *β*-alkylthio-α-hydroxy carboxylic acids has been developed.

Introduction

Metal-catalyzed asymmetric reactions have become one of the most powerful tools for the production of enantiomerically enriched compounds. Although the use of numerous chiral ligands has been reported, the design and synthesis of new types of ligands with improved performance continues to attract the interest of synthetic chemists.[1]

In general, the design of new catalysts makes use of either C_2-symmetrical ligands, resulting in catalytic systems with restricted numbers of competing diastereomeric transition states,[2] or involves ligands containing different donor atoms, able to generate electronic asymmetry on the metal. This asymmetry can be transmitted to reacting molecules bonded to the metal (for instance, through the *trans* effect)[3] and has the potential to control both the stability and reactivity of metal−substrate intermediates.

While the use of bidentate ligands with *P*,*N* coordination mode has become a mature tool in asymmetric catalysis,[4] the use of related *P*,*S*-ligands has gained considerable momentum in recent times.[5] These ligands present a key structural property that makes them very attractive in asymmetric

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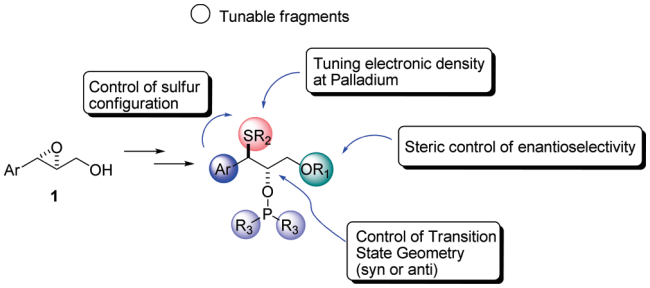


FIGURE 1. Highly modular *P*,*S*-ligands from epoxy alcohols **1**.

catalysis: the sulfur atom in dissymmetrically substituted thioethers becomes stereogenic upon coordination to the metal, thus imposing a unique asymmetric environment close to the reactive metal center.[6]

In the past several years, we have successfully developed and fine-tuned families of modular bidentate ligands (*N*/*O*,[7] *N*/*N*,[8] *S*/*N*,[9] *P*/*N*,[10] *P*/*O*−*P*[11]) for a variety of enantioselective processes starting from purely synthetic yet enantiomerically pure precursors. In the present paper, we report the synthesis of highly modular *P*,*S*-ligands from readily available enantiopure arylglycidols (Figure 1).[12] An iterative optimization process involving up to four structural parameters has allowed the identification of ligands exhibiting high catalytic activity and enantioselectivity in the asymmetric substitution of allylic substrates with a variety of C-, N-, and O-nucleophiles.

It is to be mentioned that the use of chiral epoxides as starting materials for the modular construction of enantiopure *P*,*S*-ligands has not been reported in the literature. In a related approach, Evans et al. reported the desymmetrization[13] of *meso*-cyclohexene oxide with *tert*-butyl thiol, followed by phosphinylation of the resulting alcohol as an entry to ligands for the allylic substitution[5f] and olefin hydrogenation.[5m] In the same study,[5f] the preparation of modular phosphinito thioether ligands was performed from enantiopure *N*-acyloxazolidinones through rather complex sequences starting with a highly diastereoselective electrophilic halogenation and often involving diastereomer separation, and the effect of different structural parameters on catalytic activity and enantioselectivity was analyzed (Figure 2).

Results and Discussion

Ligand Design. The general strategy for the synthesis of these thioether−phosphinite ligands is presented in Scheme 1.

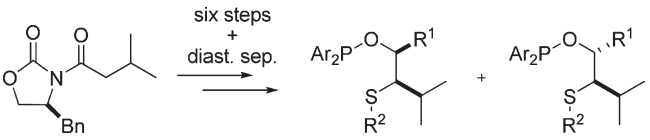
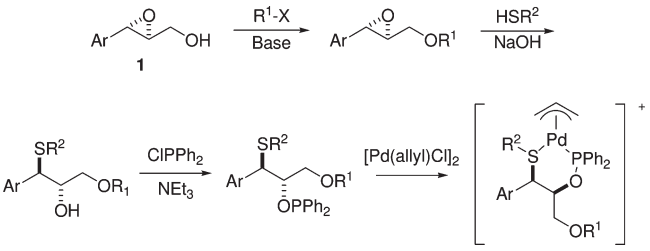
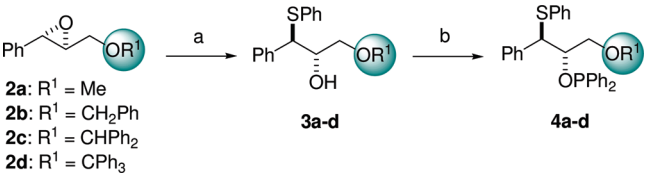


FIGURE 2. Evans' approach to modular *P*,*S*-ligands from enantiopure *N*-acyloxazolidinones.

SCHEME 1. General Procedure for the Synthesis of Chiral *P*,*S*-Ligands from Epoxy Alcohols 1



SCHEME 2. Two-Step Synthesis of Thioether−Phosphinite Ligands 4 from Epoxy Ethers 2[a]



[a]Reagents and conditions: (a) PhSH (2 equiv), NaOH (2 equiv), 65 °C, 20−120 min in dioxane/water (10:1); (b) $ClPPh_2$ (1.1 equiv), NEt_3 (1.2 equiv), 10 mol % of DMAP, 20 min in toluene, rt.

In the first step, the primary hydroxy group in the starting epoxy alcohols (**1**) is protected, and the resulting epoxy ethers are then subjected to regio- and stereoespecific ring-opening by thiolates to afford β-hydroxy sulfides. Treatment of these intermediates with chlorodiphenylphosphine and triethylamine in the presence of a 10% molar amount of 4-DMAP affords the desired ligands. Since diphenylphosphinite units show optimal performance in Pd-catalyzed allylic alkylation,[5f,q] this module was excluded from the optimization process.

For the subsequent evaluation in catalysis, the corresponding π-allylpalladium complexes were generated in situ from the corresponding *P*,*S*-ligand and metal precursor.

Ligand Optimization for the Palladium-Catalyzed Allylic Alkylation. Optimization of the Ether Moiety. We first investigated the effect of the steric bulk of the ether moiety OR^1 on the catalytic properties (activity and enantioselectivity) of the derived π-allylpalladium complexes. The steric environment at this position has proved to exert a critical influence on the catalytic activity of other chiral ligands derived from Sharpless epoxy alcohols in a variety of asymmetric reactions.[7,8,10,11]

The starting point in our optimization process was *trans*-phenylglycidol (**1a**; Ar = Ph), which is readily available in enantiopure form by Sharpless epoxidation and can be modified to incorporate a variety of OR^1 groups (Scheme 2). According to our synthetic plan, epoxy ethers bearing alcohol protecting groups of increasing sizes (**2a**−**d**) were synthesized,[7a] and then the regioselective and stereospecific ring-opening of these epoxy ethers with benzenethiol was studied.

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TABLE 1. Yields for the Synthesis of Thioether−Phosphinite Ligands 4a−d

entry	epoxy ether	yield **3** (%)	yield **4** (%)	overall yield (%)
1	**2a**	90[a]	91	82
2	**2b**	72[b]	82	59
3	**2c**	90[c]	85	77
4	**2d**	74[d]	88	65

[a]20 min. [b]60 min. [c]120 min. [d]120 min, PhSH (5 equiv), NaOH (5 equiv).

One of the most straightforward synthetic procedures for the ring-opening of epoxides with thiols takes place under basic conditions in a protic solvent.[14] Alternatively, several methods have been reported involving Lewis acid catalysis, such as the use of catalytic amounts of $InCl_3$[15a] or metal perchlorate salts in combination with thiols.[15b] Although the use of $InCl_3$ or perchlorates has been reported to induce a completely regioselective ring-opening at the benzylic position, a mixture of diastereomers was obtained in our case, probably via participation of an S_N1 mechanism.[16] Very gratifyingly, when phenylglycidyl ethers **2a−d** were treated with sodium benzenethiolate in dioxane−water,[14a] a completely regioselective and stereospecific ring-opening took place. A final phosphinylation led to thioether phosphinites **4a−d**, as shown in Scheme 2.

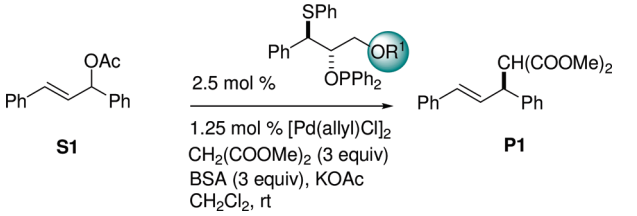
It is interesting to note that the steric effect of R^1 has some influence on the reactivity of the epoxy ethers. For instance, while the reaction of **2a** (R^1 = Me) proceeded smoothly (90% yield) in 20 min (entry 1), **2d** (R^1 = CPh_3) required a larger excess of thiol (5 equiv) and longer reaction time (2 h) to achieve a satisfactory conversion (entry 4). The obtained β-hydroxy sulfides were derivatized with chlorodiphenylphosphine in the presence of triethylamine and DMAP following a well-established procedure for related compounds.[17] The target ligands **4a−d** were obtained with overall yields ranging from 59% to 82% (Table 1) after purification by filtration through a short pad of silica gel.

Ligands **4a−d** were next evaluated in the palladium-catalyzed asymmetric allylic alkylation (AAA) of 1,3-diphenylpropenyl acetate (**S1**) with dimethyl malonate, using *N*,*O*-bis(trimethylsilyl)acetamide (BSA) as a base.[5f] The reactions were carried out in dichloromethane at room temperature in the presence of a catalyst generated in situ from 1.25 mol % of π-allylpalladium chloride dimer, 2.5 mol % of ligand, and a catalytic amount of KOAc (Table 2).

As clearly shown in Table 2, complete conversions were observed after 20 min at room temperature for ligands **4c** and **4d** and almost complete conversion for **4a** and **4b**. Unfortunately, ligands **4a−d** gave the alkylation product with poor enantioselectivities (10−12% ee) (Table 2).

Although these results were very disappointing in terms of enantioselectivity, they provided initial indication that the steric bulk of R^1 has no effect on the stereochemical outcome of the reaction. Thus, this fragment could be fixed at convenience for the optimization of the remaining modules.

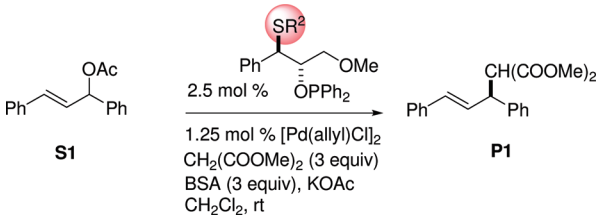
TABLE 2. Effect of the Steric Bulk in R^1 on Conversion and Enantioselectivity



ligand	R^1	conv[a] (%)	ee[b] (%)
4a	Me	92	12
4b	CH_2Ph	87	11
4c	$CHPh_2$	>99	10
4d	CPh_3	>99	12

[a]Conversion after 20 min by ^{1}H NMR of the reaction crude. [b]ee values by chiral HPLC.

TABLE 3. Effect of the Sulfur Substituent on Conversion and Enantioselectivity



entry	ligand	R^2	conv[a] (%)	ee[b] (%)
1	**4e**	3,5-dimethylphenyl	93	20
2	**4f**	2,6-dimethylphenyl	>99	43
3	**4g**	*p*-methoxyphenyl	94	9
4	**4h**	*p*-bromophenyl	>99	10
5	**4i**	*p*-*tert*-butylphenyl	>99	15
6	**4j**	2-naphthyl	88	15
7	**4k**	isopropyl	>99	66
8	**4l**	cyclohexyl	92	71
9	**4m**	*tert*-butyl	>99	71
10	**4n**	adamantyl	>99	83

[a]Conversion after 20 min by ^{1}H NMR of the reaction crude. [b]ee values by chiral HPLC.

Optimization of the Sulfur Substituent. A methyl substituent was selected as R^1 due to the favorable reactivity of the corresponding epoxy ether toward thiolate ring-opening. With this restriction, a variety of *S*-aryl derivatives with different substitution patterns on the aryl moiety (**4e−j**) and *S*-alkyl derivatives (**4k−n**) could be easily synthesized following the general synthetic strategy described above (Scheme 1). Under the standard conditions for the AAA, we studied the effect of the thioether substituent on the catalytic performance of ligands **4e−n**.

As shown in Table 3, high conversions are observed with all the studied ligands after 20 min reaction, thus indicating that the nature of the sulfur substituent does not play any role on catalytic activity. Concerning enantioselectivity, changes in the *S*-substituent showed a remarkably effect, with bulkier substituents leading to higher enantioselectivities. Thus, among the studied *S*-aryl substituents, the most notable improvement in enantioselectivity was observed

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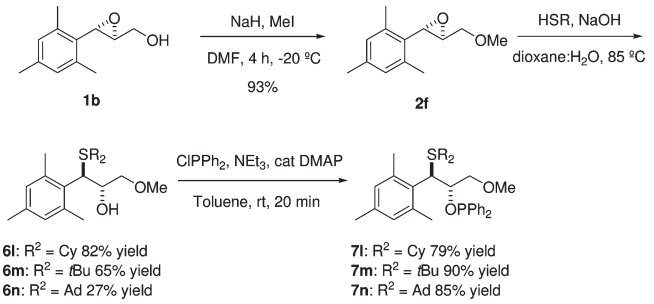
SCHEME 3. Preparation of Ligands Bearing a Mesityl Substituent



with the bulky 2,6-dimethylphenylthio group (**4f**, entry 2). These results provided an indication that bulkier alkyl thioether substituents could lead to a further increase in enantioselectivity. In fact, secondary and tertiary *S*-alkyl substituents showed a higher enantioselectivity compared to *S*-aryl ligands. A much significant increase in the asymmetric induction was observed in the case of sterically more demanding groups such as adamantyl and *tert*-butyl, which afforded the alkylation product in 83% and 71% ee, respectively (entries 9 and 10).

As already mentioned, the sulfur atom becomes stereogenic upon coordination to the metal, although control of this new chiral center is not always attainable due to its low inversion barrier (10−15 kcal/mol).[6d,18] In catalytic applications, this interconversion could have a negative influence on enantioselectivity due to the presence of competing diastereomeric complexes. We reasoned that sulfur configuration could be efficiently controlled when a bulky substituent on sulfur and a bulky aryl substituent are simultaneously present on the ligand molecule.[5f] In line with this notion, we synthesized analogues of the best ligands prepared so far but bearing a more sterically demanding mesityl substituent on the hydrocarbon chain.

Optimization of the Skeletal Aryl Substituent. Following the general synthetic strategy, ligands **7l**, **7m**, and **7n** were synthesized from the chiral epoxide **1b** bearing a mesityl substituent (Scheme 3).[19]

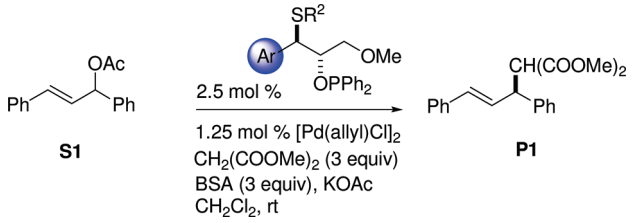
Reaction of the sodium alkoxide of **1b** with methyl iodide allowed the isolation of the expected methyl ether **2f** in 93% yield. *β*-Hydroxy sulfides **6l**−**m** were obtained by ring-opening with thiolates,[14] whereas the *β*-hydroxy sulfides **4l**−**n** (Ar = Ph) were obtained in good yields at 65−80 °C in 1 h; higher temperatures and longer reaction times (4 h for **6l** and 20 h for **6m** and **6n**) were required to achieve the ring-opening of epoxy ether **2f** (Ar = mesityl). Finally, the target ligands **7l**−**n** were readily prepared from *β*-hydroxy thioethers **6l**−**n** under the standard phosphinylation conditions (Scheme 3). Ligands **7l**−**n** were next evaluated in the AAA of **S1** (Table 4).

The incorporation of the bulkier mesityl substituent on the ligand structure provoked a small decrease in the reaction rate. Thus, nearly complete conversions were achieved in 45 min at room temperature for ligands **7m** and **7n** (entries 2, 3) and in 90 min for ligand **7l** (entry 1). For comparison, the corresponding ligands (**4l**−**n**) with Ar = phenyl afforded complete conversion in 20 min (Table 3). Interestingly, a positive effect on the enantioselectivity was observed for ligands **7l** and **7m**, affording alkylated product **P1** in 82% and 87% ee (entries 1, 2). On the other hand, with ligand **7n** the enantioselectivity decreased slightly (entry 3) compared with the parent ligand **4n** (Ar = Ph) (Table 3, entry 10).

In view of these results, we decided to re-evaluate the effect of bulkiness on the alkoxy group (OR^1) on the best ligands prepared so far (**4n** and **7m**) in order to seek further improvement in enantioselectivity. To this end, we planned to prepare ligands **10a** and **10b**, conceptually derived from **4n** and **7m** and containing a much more sterically demanding trityloxy substituent ($R^1 = CPh_3$).

Unfortunately, the general synthetic strategy employed so far failed for the preparation of ligands **10a** and **10b** because ring-opening of the trityl ethers of **1a** and **1b** by the required bulky thiolates could not be accomplished. Alternatively, ligands **10a** and **10b** were prepared by a three-step sequence starting with the thiolate ring-opening of the corresponding epoxyalcohols (**1a**, **1b**). The so-prepared 3-alkylthio 1,2-diols **8a** and **8b**, were then submitted to selective protection of the primary hydroxy group with trityl chloride in pyridine at 90 °C and subsequent phosphinylation of the secondary alcohol (Scheme 4).

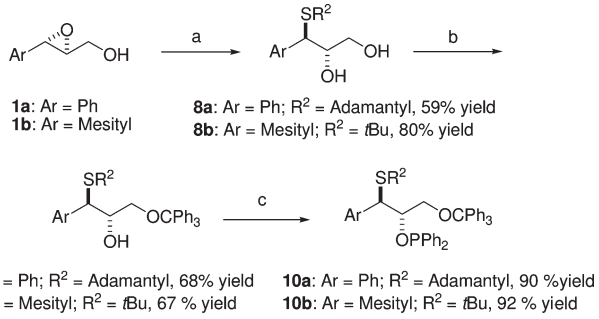
TABLE 4. Effect of the Aryl Substituent on Conversion and Enantioselectivity



entry	ligand	R^2	conv[a] (%)	ee[b] (%)
1	**7l**	cyclohexyl	96	82
2	**7m**	*tert*-butyl	97	87
3	**7n**	adamantyl	>99	80

[a]Conversion after 90 min for ligand **7l** and 45 min for ligands **7m,n** by ^{1}H NMR of the reaction crude. [b]ee values by chiral HPLC.

SCHEME 4. Synthesis of Ligands 10a and 10b[a]



[a]Reagents and conditions: (a) **1a**: AdSH (2 equiv), NaOH (2 equiv), dioxane/water, 80 °C, 120 min; **2a**: *t*-BuSH (3 equiv), NaOH (3 equiv), dioxane/water, 80 °C, 3 h; (b) $ClCPh_3$ (1.2 equiv), pyridine, 90 °C, 18 h; (c) $ClPPh_2$ (1.1 equiv), NEt_3 (1.2 equiv), 10 mol % 4-DMAP, toluene, rt, 40 min.

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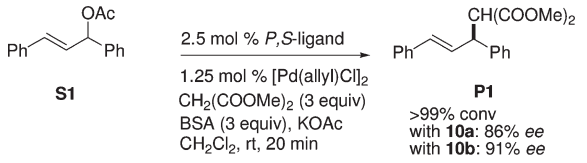
SCHEME 5. Results obtained in the Pd-catalyzed AAA of S1 with ligands 10a and 10b[a]



[a]Reaction conditions: 1.25 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 2.5 mol % of **10a**,**b**, KOAc, dimethyl malonate/BSA (3.0 equiv), CH_2Cl_2, rt.

When **10a** and **10b** were tested in the Pd-catalyzed AAA, we were pleased to find that this modification in the R^1 group had a positive influence on both catalytic activity and enantioselectivity, with **10b** leading to the highest enantioselectivity recorded over the whole optimization process (Scheme 5).

As a final element in our screening, we decided to modify the relative stereochemistry of the C2/C3 stereogenic centers in the ligand backbone (Figure 3). It was expected that this modification could lead to substantial changes in the conformational behavior of the 6-membered ring Pd chelate and, hence, to an increased discrimination between the enantiotopic faces of the π-allyl system undergoing the substitution reaction.

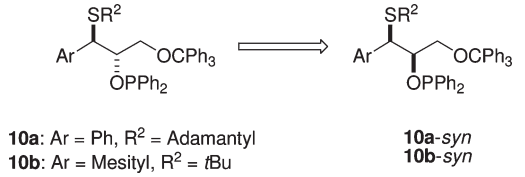


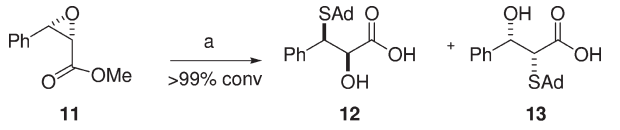
FIGURE 3. Modification of the relative stereochemistry of C2/C3.

Modification of the Relative Configuration of the Chiral Centers. The absolute and relative configurations of the two adjacent functionalized carbons present in the ring-opening products are determined by the configuration of the starting epoxide. Thus, starting from the *cis*-epoxide and following the general synthetic strategy described in Scheme 1, it should be possible to obtain the target ligands **10a**-*syn* and **10b**-*syn*; however, highly efficient and enantioselective epoxidation of *cis*-cinnamyl alcohol still remains a problem.[20−22]

As an alternative, we planned to access the enantiopure *cis*-epoxy ester through a completely stereodefined approach and to secure the target *syn* ligands through a ring-opening plus reduction sequence. For the implementation of this plan, we took advantage of the highly enantioselective catalytic dihydroxylation (ADH) of inexpensive (*E*)-methyl cinnamate. Thus, the 2,3-dihydroxy ester, obtained in high yield and with an enantiomeric excess >99%, was converted to the *cis*-glycidic ester **11** by regioselective tosylation and subsequent cyclization in basic media with an overall yield of 80%.[23]

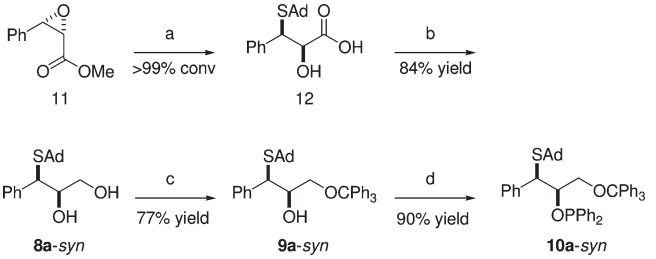
When the ring-opening of the glycidic ester **11** with adamantanethiol in the presence of sodium hydroxide was attempted, the process was poorly regioselective leading to a 2.5:1 mixture of regioisomers (Scheme 6).

SCHEME 6. Thiolate Ring-Opening of Epoxy Ester 11[a]



[a]Reagents and conditions: (a) AdSH (3 equiv), NaOH (3 equiv), dioxane/water, 80 °C, 120 min.

SCHEME 7. Synthesis of Ligand 10a-*syn*[a]



[a]Reagents and conditions: (a) AdSH (2 equiv), LiOH (2 equiv), dioxane/water, 80 °C, 60 min; (b) $BH_3 \cdot SMe_2$ (4 equiv), THF, 16 h; (c) $ClCPh_3$ (1.2 equiv), pyridine, 90 °C, 18 h; (d) $ClPPh_2$ (1.1 equiv), NEt_3 (1.2 equiv), 10 mol % 4-DMAP, toluene, rt, 40 min.

trans-Glycidic esters and amides are known to undergo regioselective and stereoespecific opening by thiols, whereas this process is less reliable with the *cis*-isomers.[24] However, after some experimentation we found that the use of lithium hydroxide instead of sodium hydroxide led to ring-opening of *cis*-glycidic ester **11** with complete regioselectivity at the C3 position and in a stereoespecific manner (Scheme 7). Interestingly, crude **12** obtained by this procedure was notably clean, so that further purification was not required. Reduction of **12** with borane−dimethyl sulfide complex in THF gave **8a**-*syn* in 85% yield which was converted uneventfully into **10a**-*syn*.

In order to rationalize the regioselectivity observed in the ring-opening reaction when lithium hydroxide was used as a base, a theoretical study was carried out for the two different pathways of the reaction (attack at C2 or C3). Taking into account that ester solvolysis likely precedes ring-opening, the studied reaction system consisted in one molecule of lithium carboxylate plus one molecule of lithium thiolate. Transition states (TSs) for the epoxide openings at C2 (TS-C2) and C3 (TS-C3) were located and characterized using DFT calculations (B3LYP/6-31G (d)). In both TSs (Figure 4), one lithium cation is simultaneously coordinated to the epoxide and to one oxygen atom of the carboxylate. The other lithium cation, in turn, is coordinated to the remaining oxygen of the carboxylate and to the attacking thiolate. Very interestingly, in the transition state corresponding to the ring-opening at C3 (TS-C3) a planar arrangement of the phenyl group respect to C3 indicates the presence of carbocationic character at that position. This should be reflected in a very high reactivity toward nucleophilic attack at C3, and accordingly, a difference of 5.5 kcal·mol^{-1} in favor of the TS leading to the C3 product was found. If the ratio of the

(20) Denis, J. N.; Greene, A. E.; Serra, A. A.; Luche, M.-J. *J. Org. Chem.* **1986**, *51*, 46.
(21) Zhang, W.; Basak, A.; Kosugi, Y.; Hoshino, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 4389.
(22) Deng, L.; Jacobsen, E. N. *J. Org. Chem.* **1992**, *57*, 4320.
(23) Wang, Z.-M.; Kolb, H. C.; Sharpless, K. B. *J. Org. Chem.* **1994**, *59*, 5104.
(24) (a) Aggarwal, V. K.; Charmant, J. P. H.; Fuentes, D.; Harvey, J. N.; Hynd, G.; Ohara, D.; Picoul, W.; Robiette, R.; Smith, C.; Vasse, J. L.; Winn, C. L. *J. Am. Chem. Soc.* **2006**, *128*, 2105. (b) Hashiyama, T.; Inoue, H.; Konda, M.; Takeda, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1725. (c) Hashiyama, T.; Inoue, H.; Takeda, M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 421.

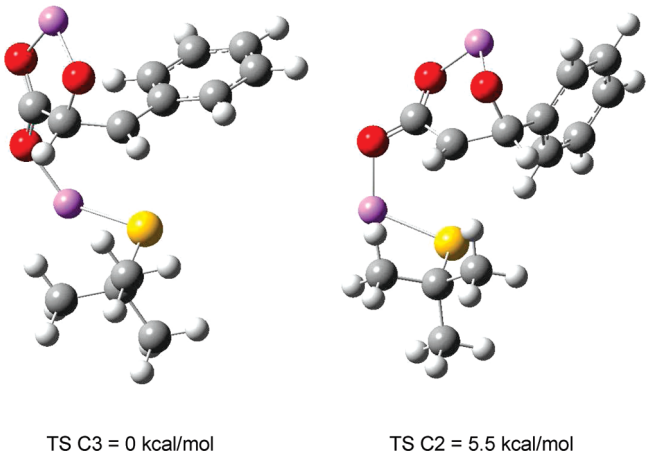
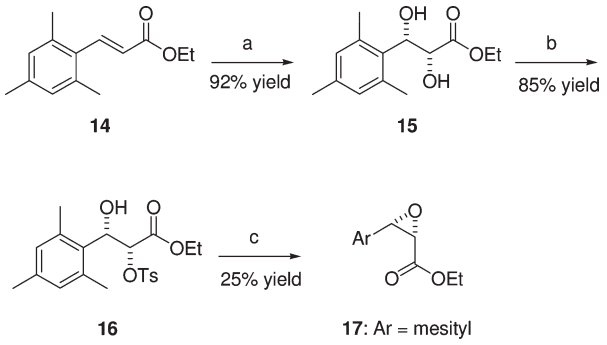


FIGURE 4. DFT-optimized transition states TS-C3 and TS-C2.

SCHEME 8. Synthesis of Epoxy Ester 17[a]



[a]Reagents and conditions: (a) see ref 25; (b) ClTs (1.02 equiv), NEt_3 (1.5 equiv), CH_2Cl_2, 0 °C, 70 h; (c) K_2CO_3 (3 equiv), H_2O (5 equiv), DMF, rt, 24 h.

products follows a Maxwell−Boltzmann distribution based on the energies of the transition states, the theoretically computed regioisomeric ratio would be higher than 99:1, in agreement with the experimental value.

Epoxyester **17**, bearing a mesityl substituent, was prepared from **14** by an analogous sequence (Scheme 8). Probably due to the presence of unfavorable steric interactions in the transition state leading to **17**, the cyclization of **16** was less efficient, and the desired epoxy ester **17** was obtained in 63% yield at 40% conversion (25% yield).

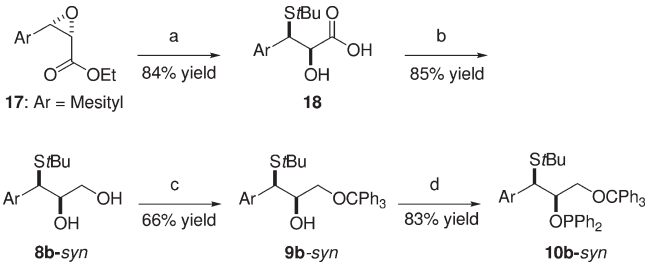
Ring-opening of the rather unreactive epoxy ester **17** could be induced by performing the reaction under microwave irradiation at 140 °C in the presence of excess of lithium *tert*-butylthiolate (Scheme 9). The resulting carboxylic acid **18** was converted to the target ligand **10b**-*syn* following the same procedure used for the preparation of **10a**-*syn*.

Ligands **10a**-*syn* and **10b**-*syn* were next evaluated in AAA of **S1** (Table 5).

Again, very high activities were observed for both ligands, and complete conversions were recorded after 20 min at rt. Interestingly, a positive effect on the enantioselectivity was observed with the *syn*-type ligands, **P1** being obtained in 94% and 96% ee with **10a**-*syn* and **10b**-*syn*, respectively. For comparison, the corresponding ligands with *anti*-configura-

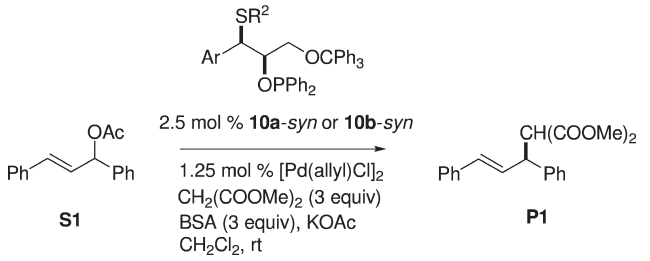
(25) Ramón, R.; Alonso, M.; Riera, A. *Tetrahedron: Asymmetry* **2007**, *18*, 2797.

SCHEME 9. Synthesis of Ligand 10b-*syn*[a]



[a]Reagents and conditions: (a) *t*-BuSH (3 equiv), LiOH (3 equiv), dioxane/water, microwave irradiation 140 °C, 3 h; (b) $BH_3 \cdot SMe_2$ (4 equiv), THF, 16 h; (c) $ClCPh_3$ (1.2 equiv), pyridine, 90 °C, 18 h; (d) $ClPPh_2$ (1.1 equiv), NEt_3 (1.2 equiv), 10 mol % of 4-DMAP, toluene, rt, 40 min.

TABLE 5. Effect of the Relative Configuration (C2/C3) on Conversion and Enantioselectivity



entry	ligand	conv[a] (%)	yield (%)	ee[b] (%)
1	**10a**-*syn*	> 99	95	94
2	**10b**-*syn*	> 99	97	96
3[c]	**10a**-*syn*	> 99	97	99

[a]Conversion after 20 min by ^{1}H NMR of the reaction crude. [b]ee values by chiral HPLC. [c]0 °C, 240 min.

tion (**10a** and **10b**, Scheme 5) afforded the alkylation product with 86% and 91% ee, respectively. Very gratifyingly, enantioselectivity increased to 99% with ligand **10a**-*syn* by simply lowering the reaction temperature to 0 °C, although a somewhat longer reaction time (240 min) was required to achieve high conversion under these conditions (entry 3).

The synthesis of **10a**-*syn* and **10b**-*syn* completed the modular optimization of the new family of *P*,*S*-ligands. Along this way, enantioselectivities in the archetypal substitution of 1,3-diphenylallyl acetate with dimethyl malonate have increased from 10 to 12% with **4a**−**d** to 99% with **10a**-*syn*, while high catalytic activities were observed over the whole series.

To compare the merits of the ligands resulting from the structural optimization with other well-established *P*,*S*-ligands, we have collected in Figure 5 the enantioselectivities in the reaction of **S1** with dimethyl malonate leading to **P1** and the corresponding reaction conditions for full conversion. It is interesting to note that the levels of catalytic activity and enantiocontrol achieved with one of our optimized ligands (**10b**-*syn*) are among the highest recorded in the considered ligand set. In particular, it is worth noting that **10b**-*syn* induces very high enantioselectivity at room temperature, where the alkylation is completed in very short reaction times.

As a final aspect of this research, the behavior of the optimal ligand set (**10a**,**b** and **10a**,**b**-*syn*) was studied in the alkylation of the more challenging substrates **S2** and **S3** (Table 6) and in

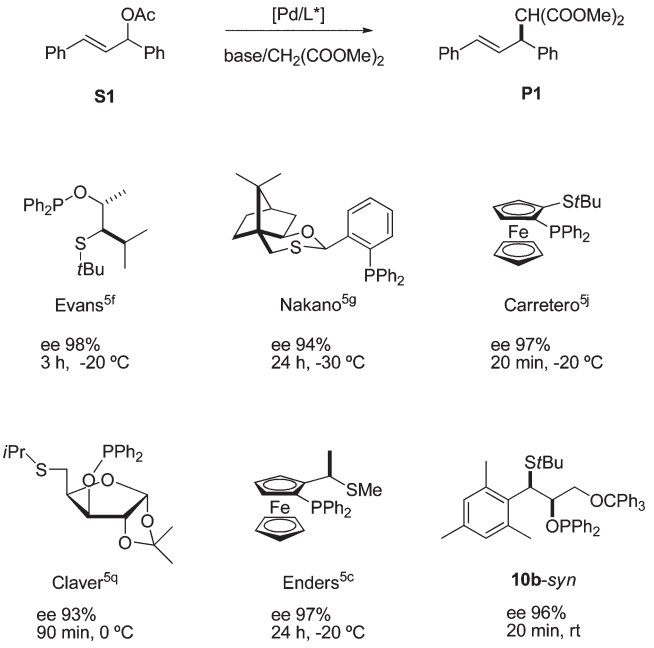
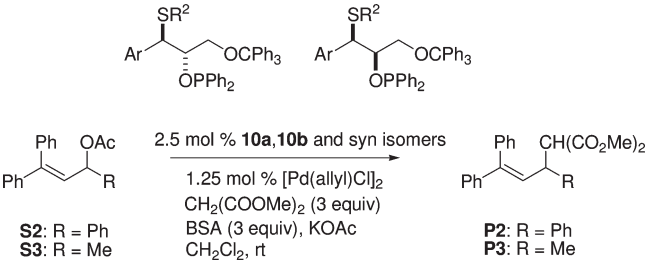


FIGURE 5. Behavior of representative *P*,*S*-ligands reported in the literature in the Pd-catalyzed allylic alkylation of 1,3-diphenylpropenyl acetate with dimethyl malonate.

TABLE 6. Enantioselective Allylic Alkylation for Substrates S2 and S3 with Dimethyl Malonate



entry	ligand	substrate	time (h)	conv[a] (%)	ee[b] (%)
1	**10a**	**S2**	16	54	97
2	**10b**	**S2**	16	46	96
3	**10a**-*syn*	**S2**	5	93	40
4	**10b**-*syn*	**S2**	5	92	70
5	**10a**	**S3**	16	45	79
6	**10b**	**S3**	16	30	82
7	**10a**-*syn*	**S3**	5	99	4
8	**10b**-*syn*	**S3**	5	99	20

[a]Conversion by ^{1}H NMR of the reaction crude. [b]ee values by chiral HPLC.

the substitution of **S1** with more challenging nucleophiles such as benzylamine and benzyl alcohol (Table 7).

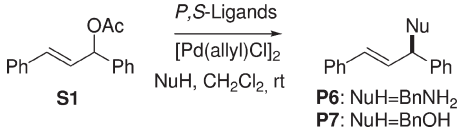
Not unexpectedly (see Table 6),[26] these trisubstituted π-allyl precursors proved to be much less reactive in front of alkylation than the 1,3-diphenyl disubstituted substrate **S1**.

At room temperature, complete conversion of **S2** and **S3** was observed over a period of 5 h using ligands **10a**,**b**-*syn*. Unfortunately, these ligands, which proved to be the most effective ones for the allylic substitution of **S1**, afforded the alkylation product in much lower enantioselectivities (entries 3, 4, 7, and 8). Presumably, this lack of enantioselectivity is derived from a different ligand structural requirement for the successful alkylation of trisubstituted π-allyl precurors compared to the disubstituted substrate **S1**. On the other hand, using ligands **10a** and **10b** under standard conditions for AAA, excellent enantioselectivities were observed for substrate **S2** (96% and 97% ee) and good asymmetric inductions for substrate **S3** (79% and 82% ee; entries 1, 2, 5 and 6). Interestingly, for substrate **S2** and using ligand **10a**, when the reaction was stopped at 54% conversion, the unreacted allylic substrate was recovered in 70% ee (entry 1), which represents a rather high selectivity for one of the substrate enantiomers.

Finally, the optimal set of ligands was also examined in the palladium-catalyzed reaction of 1,3-diphenylpropenyl acetate (**S1**) with different heteroatom nucleophiles. Benzylamine and benzyl alcohol were chosen as representative models for *N*-nucleophiles and *O*-nucleophiles, respectively, and the results obtained in these reactions are summarized in Table 7.

The catalytic system involving ligand **10b**-*syn* was found to be the most effective for the amination and etherification of **S1**. After 4 h at rt, the amination product **P6** was obtained in 97% yield and 94% ee (entry 4), whereas the analogous ligand **10b** afforded lower yield and enantioselectivity after 16 h (entry 2). Enantioselectivity increased slightly by lowering the temperature to 0 °C, but longer reaction time was required to achieve complete conversion (entry 5). Furthermore, using benzyl alcohol as a nucleophile, **10b**-*syn* was the most effective ligand for this asymmetric etherification reaction, affording the product **P7** in 96% yield and 93% ee after 3 h at rt (entry 7). The same reaction at 0 °C afforded the product in lower selectivity (86% ee) and lower yield (55% yield) after 16 h (entry 8). When the solvent was changed to toluene, the product was obtained in almost quantitative yield (96%) after 3 h with high enantioselectivity (94% ee) (entry 9). While numerous examples of enantioselective allylic amination have been reported, successful examples

TABLE 7. Effect of the Nucleophile on Conversion and Enantioselectivity



entry	ligand	NuH	time (h)	yield (%)	ee[a] (%)
1	**10a**	$BnNH_2$[b]	2	98	75
2	**10b**	$BnNH_2$[b]	16	73	73
3	**10a**-*syn*	$BnNH_2$[b]	16	65	92
4	**10b**-*syn*	$BnNH_2$[b]	4	97	94
5	**10b**-*syn*	$BnNH_2$[c]	10	95	95
6	**10a**-*syn*	BnOH[d]	3	98	90
7	**10b**-*syn*	BnOH[d]	3	96	93
8	**10b**-*syn*	BnOH[e]	16	55	86
9	**10b**-*syn*	BnOH[f]	3	96	94

[a]ee values by chiral HPLC. [b]Reaction conditions: 1.25 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 3.75 mol % of *P*,*S*-ligand, benzylamine (3 equiv), CH_2Cl_2, rt. [c]Reaction at 0 °C. [d]Reaction conditions: 2 mol % of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 4.2 mol % of *P*,*S*-ligand, benzyl alcohol (3 equiv), Cs_2CO_3 (3 equiv), CH_2Cl_2, rt. [e]Reaction at 0 °C in CH_2Cl_2. [f]Reaction at 0 °C in toluene.

(26) (a) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033. (b) Dawson, G. J.; Williams, J. M. J.; Coote, S. J. *Tetrahedron: Asymmetry* **1995**, *6*, 2535. (c) Dawson, G. J.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1995**, *36*, 461.

of asymmetric allylic etherification are very scarce. Only a recent account by Chan et al. reports high enantioselectivities in this process.[5t] When both catalytic systems are compared, it is worth mentioning that **10b**-*syn* behaves as a more active catalyst in the considered reaction while leading to similar levels of asymmetric induction.

Structural Studies. The binding mode of ligand **10a**-*syn* was established by X-ray crystallography. A suitable crystal of the $PdCl_2$ complex of **10a**-*syn* was obtained from dichloromethane/diethyl ether. Complex (**10a**-*syn*)·**PdCl$_2$** adopts a twist-boat geometry, and only one epimer of the adamantylthio substituent is observed in the crystal. In this epimer, the adamantyl group is in an *anti*-orientation with respect to the adjacent phenyl group. Furthermore, ^{1}H NMR and ^{31}P NMR studies on (**10a**-*syn*)·**PdCl$_2$** in CD_2Cl_2 at rt also showed only one diastereomeric complex, thus indicating that the sulfur inversion is blocked. In addition, the larger *trans* influence of the phosphinite is reflected in the longer Pd−Cl bond trans to the phosphorus atom (Pd−Cl_1 = 2.359 Å) compared to sulfur (Pd−Cl_2 = 2.312 Å).

Interestingly, a complementary X-ray diffraction study performed on **4m**·**PdCl$_2$** showed that changing the relative configuration of the carbons bearing the heteroatoms (C2/C3) in the ligand backbone leads to a conformational change of the 6-membered ring Pd-chelate, in agreement with previous observations by Evans.[5f] While complex (**10a**-*syn*)·**PdCl$_2$** showed a twist-boat conformation, crystals of **4m**·**PdCl$_2$** grown in dichloromethane/diethyl ether showed a half-chair conformation in the corresponding six-membered chelate ring (see Figures 1 and 2 in the Supporting Information).[27]

Origin of the Enantioselectivity. It has been generally accepted that the enantiodifferentation step in the Pd-catalyzed allylation is the substitution of π-allyl complexes with nucleophiles. Two bonds in a *trans* position compete for one metal *d*-orbital for a π-back-bond. The stronger the π-acceptor ability of the ligand is, the more electronic density is removed from the metal *d*-orbital. Through this mechanism, the electronic density at one of the allylic carbon atoms is strongly reduced by a π-acceptor in a *trans* position. Accordingly, nucleophilic attack should occur predominantly at the allyl terminus located *trans* to the best π-acceptor (P > S).

Since the (*S*) enantiomer of the alkylation product is predominantly obtained, the reaction must proceed through an M-type rather than W-type intermediate (Figure 6, top). It can be reasoned from a qualitative perspective that the M-type complex would react faster than its diastereomer W-type complex. Thus, attack of the nucleophile to the allyl terminus *trans* to phosphorus in the M-type complex will lead to a release of steric congestion between the *S*-adamantyl substituent and the proximal phenyl substituent on the allyl unit, while attack to the corresponding carbon in the W-type complex will be accompanied by an increasing steric interaction between the *S*-adamantyl group and the corresponding phenyl group on the allyl moiety as the rotation from the starting π-allyl complex to the final Pd(0)-olefin product (*R*)-**P1** proceeds (Figure 6).

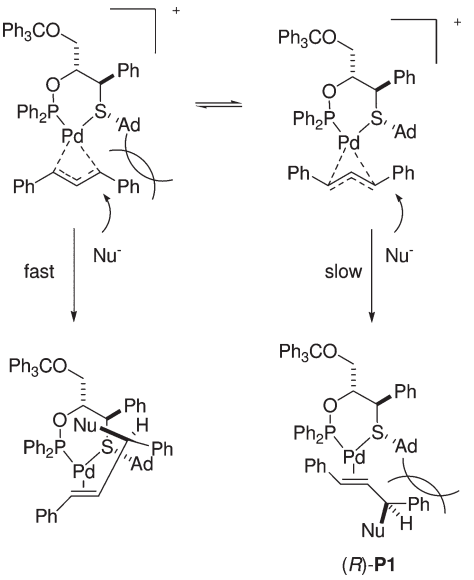


FIGURE 6. Proposed transition-state models for the asymmetric allylic substitutions.

Conclusions

In summary, a library of modularly constructed phosphinite thioether ligands derived from the ring-opening of enantiopure epoxides has been synthesized and evaluated in the Pd-catalyzed allylic substitution reactions of several substrates. These *P*,*S*-ligands have been successfully optimized by following a modular approach. Over this process, the enantioselectivity recorded in the benchmark reaction has evolved from ca. 10% in the initial ligands to 99% in the optimized structures. In general, activities and enantioselectivities are mainly controlled by the steric interactions between the substituent on sulfur, and the skeletal aryl group, and by the relative stereochemistry of the stereocenters at C2 and C3 on the ligand skeleton. Excellent enantioselectivities were obtained in the reaction of *rac*-1,3-diphenyl-2-propenylacetate with dimethyl malonate (up to 99%), benzylamine (up to 95%), and a much less common O-nucleophile, such as benzyl alcohol (up to 94%). The development of further applications of these ligands is now in progress in our laboratories.

Experimental Section

General Procedure for the Ring-Opening of Epoxides 2a−d by Thiols. To a solution of the epoxide (1 mmol) and sodium hydroxide (2 mmol) in dioxane/water (10:1 v/v) was added the corresponding thiol (2 mmol, 2 equiv). The mixture was heated at the indicated temperature, and reaction progress was monitored by TLC until disappearance of the starting epoxide

(27) Crystal data for **4 m**·**PdCl$_2$** at 100 K: $C_{26}H_{31}Cl_2O_2P_1Pd_1S_1 \times 2$ (the unit cell contains two independent molecules), 615.84 gmol^{-1}, triclinic, *P*1, a = 10.6012(5) Å, b = 12.3725(5) Å, c 12.9208(6) Å, α = 67.7560(10)°, β = 65.9300(10)°, γ = 65.8490(10)°, V = 1365.60(11) Å^3, Z = 2, ρ_{calcd} = 1.498 Mg/m^3, R_{1obs} = 0.0230 (R_{1ref} = 0.0243), wR_{2obs} = 0.0554 (wR_{2ref} = 0.0561), for 16893 reflections with $I > 2\sigma(I)$ (for 17508 reflections (R_{int}: 0.0227) with a total of 28395 measured reflections), Flack (std): −0.028(8), diffracting 2θ range: 3.58−38.13°, goodness-of-fit on F^2 = 1.015, largest diff peak (hole) = 1.437 (−0.607) e Å^{-3}. CCDC: 755742. Crystal data for (**10a**-***syn***)·**PdCl$_2$** at 100 K: $C_{50}H_{49}Cl_2O_2P_1Pd_1S_1$, 922.22 gmol^{-1}, orthorhombic, $P2_12_12_1$, a = 11.2090(5) Å, b = 12.4178(6) Å, c 31.5636(15) Å, V = 4393.4(4) Å^3, Z = 4, ρ_{calcd} = 1.394 Mg/m^3, R_{1obs} = 0.0215 (R_{1ref} = 0.0223), wR_{2obs} = 0.0547 (wR_{2ref} = 0.0550), for 24842 reflections with $I > 2\sigma(I)$ (for 25376 reflections (R_{int}: 0.0262) with a total measured of 89664 reflections), Flack (std): −0.013(6), diffracting 2θ range: 2.77−39.60°, goodness-of-fit on F^2 = 1.105, largest diff peak (hole) = 1.539 (−0.456) e Å^{-3}.CCDC: 755743. The supplementary crystallographic data for this paper can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(ca. 20−90 min). The mixture was allowed to reach room temperature. Then, 10 mL of water was added, and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried over Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by flash chromatography on silica gel, eluting with hexane/ethyl acetate mixtures to give the desired product.

(1*R*,2*S*)-3-Methoxy-1-phenyl-1-(phenylthio)propan-2-ol (3a). The following reagents were combined in the amounts indicated below, and submitted to the general procedure for the thiolate ring-opening of epoxides, by performing the reaction at 65 °C for 20 min: **2a** (130 mg, 0.79 mmol), thiophenol (165 μL, 1.58 mmol), and NaOH (63 mg, 1.58 mmol). The product was purified by flash chromatography (90% hexane, 10% ethyl acetate) to yield **3a** as a white solid (200 mg, 92% yield): mp 90−91 °C; $[\alpha]^{26}_D$ −179.4 (*c* 1.15, $CHCl_3$); IR (neat) 3372, 2891, 1583, 1493, 1481, 1453, 1438, 1348, 1189, 1091, 1073, 1059, 942, 736, 705, 687, 567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19−7.37 (m, 10H), 4.35 (d, ^3J = 6.19 Hz, 1H), 4.12−4.17 (m, 1H), 3.40−3.47 (m, 2H), 3.30 (s, 3H), 2.47 (d, ^3J = 4.27 Hz, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 134.2, 132.3, 128.9, 128.8, 128.4, 127.6, 127.4, 73.8, 71.9, 59.0, 56.2; HRMS (ES+) *m*/*z* calcd for $C_{16}H_{18}O_2SNa$: 297.0925 $[M + Na]^+$, found 297.0936.

(1*R*,2*S*)-3-(Benzyloxy)-1-phenyl-1-(phenylthio)propan-2-ol (3b). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 65 °C for 60 min: **2b** (111 mg, 0.46 mmol), thiophenol (96 μL, 0.92 mmol), and NaOH (37 mg, 0.92 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3b** as a colorless oil (117 mg, 72% yield): $[\alpha]^{26}_D$ −148.7 (*c* 0.58, $CHCl_3$); IR (neat) 3422, 3058, 3027, 2908, 2861, 1700, 1599, 1582, 1493, 1479, 1204, 1087, 1067, 1025, 736, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19−7.35 (m, 15H), 4.48 (d, ^2J = 11.8 Hz, 1H), 4.45 (d, ^2J = 11.8 Hz, 1H), 4.37 (d, ^3J = 6.15 Hz, 1H), 4.16−4.22 (m, 1H), 3.55 (dxd, ^2J = 9.6 Hz, ^3J = 2.1 Hz, 1H), 3.54 (dxd, ^2J = 9.6 Hz, ^3J = 3.3 Hz, 1H), 2.51 (d, ^3J = 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 137.8, 134.3, 132.3, 128.9, 128.4, 127.8, 127.7, 127.6, 127.3, 73.4, 72.0, 71.6, 56.3; HRMS (ES+) *m*/*z* calcd for $C_{22}H_{22}O_2NaS$ 373.1238 $[M + Na]^+$, found 373.1247.

(1*R*,2*S*)-3-(Benzhydryloxy)-1-phenyl-1-(phenylthio)propan-2-ol (3c). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 65 °C for 120 min: **2c** (250 mg, 0.79 mmol), thiophenol (165 μL, 1.58 mmol), and NaOH (63 mg, 1.58 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3c** as a white solid (305 mg, 90% yield): mp 74−75 °C; $[\alpha]^{26}_D$ −117.9 (*c* 0.51, $CHCl_3$); IR (neat) 3547, 3057, 3025, 2866, 2854, 1596, 1582, 1492, 1470, 1449, 1338, 1099, 1075, 965, 750, 737, 691, 612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18−7.33 (m, 20H), 5.3 (s, 1H), 4.41 (d, ^3J = 6.07 Hz, 1H), 4.20−4.25 (m, 1H), 3.54 (d, ^3J = 5.2 Hz, 2H), 2.51 (d, ^3J = 5.01 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 138.3, 134.5, 132.2, 128.9, 128.8, 128.4, 128.4, 128.3, 127.6, 127.5, 127.3, 126.9, 126.9, 84.3, 72.1, 70.4, 56.4; HRMS (ES+) *m*/*z* calcd for $C_{32}H_{34}O_2NaS$ 505.2177 $[M + Na]^+$, found 505.2172.

(1*R*,2*S*)-1-Phenyl-1-(phenylthio)-3-(trityloxy)propan-2-ol (3d). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 65 °C for 120 min: **2d** (310 mg, 0.79 mmol), thiophenol (165 μL, 3.95 mmol, 5 equiv), and NaOH (158 mg, 3.95 mmol, 5 equiv). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3d** as a white solid (293 mg, 74% yield): mp 91−92 °C; $[\alpha]^{26}_D$ −70.0 (*c* 0.65, $CHCl_3$); IR (neat) 3424, 3057, 3026, 2922, 2851, 1596, 1582, 1490, 1448, 1069, 1027, 899,743, 695, 632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.39 (m, 6H), 7.18−7.29 (m, 19 H), 4.44 (d, ^3J = 5.7 Hz, 1H), 4.11−4.17 (m, 1H), 3.28 (dxd, ^2J = 9.53 Hz, ^3J = 5.76 Hz, 1H), 3.18 (dxd, ^2J = 9.53 Hz, ^3J = 5.40 Hz, 1H), 2.39 (d, ^3J = 5.12 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 137.9, 134.6, 131.9, 128.9, 128.8, 128.6, 128.3, 127.8, 127.4, 127.2, 127.1, 87.0, 72.3, 64.9, 56.4; HRMS (ES+) *m*/*z* calcd for $C_{34}H_{30}O_2NaS$ 525.1864 $[M + Na]^+$, found 525.1857.

(1*R*,2*S*)-1-(3,5-Dimethylphenylthio)-3-methoxy-1-phenylpropan-2-ol (3e). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 20 min: **2a** (177 mg, 1.078 mmol), 3,5-dimethylbenzenethiol (326 μL, 2.156 mmol), and NaOH (86.2 mg, 2.156 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3e** as an oil (270 mg, 83% yield): $[\alpha]^{26}_D$ −204.4 (*c* 0.7, $CHCl_3$); IR (neat) 3438, 2914, 1599, 1579, 1491, 1451, 1190, 1120, 1074, 962, 847, 748, 699, 686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24−7.38 (m, 5H), 6.97 (s, 2H), 6.85 (s, 1H), 4.33 (d, ^3J = 5.85 Hz, 1H), 4.11−4.16 (m, 1H), 3.45 (dxd, ^2J = 9.6 Hz, ^3J = 4.1 Hz, 1H), 3.4 (dxd, ^2J = 9.6 Hz, ^3J = 6.1 Hz, 1H), 3.3 (s, 3H), 2.56 (d, ^3J = 4.1 Hz, 1H, OH), 2.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.3, 133.5, 129.9, 129.3, 128.8, 128.4, 127.5, 73.9, 71.7, 59.0, 56.1, 21.1; HRMS (ES+) *m*/*z* calcd for $C_{18}H_{22}O_2NaS$ 325.1238 $[M + Na]^+$, found 325.1222.

(1*R*,2*S*)-1-(2,6-Dimethylphenylthio)-3-methoxy-1-phenylpropan-2-ol (3f). The following reagents were combined in the amounts indicated according to the general procedure fo the thiolate ring-opening of epoxides and heated at 65 °C for 40 min: **2a** (177 mg, 1.078 mmol), 2,6-dimethylbenzenethiol (326 μL, 2.156 mmol), and NaOH (86.2 mg, 2.156 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3f** as a white solid (227 mg, 70% yield): mp 83−84 °C; $[\alpha]^{26}_D$ −248.9 (*c* 0.61, $CHCl_3$); IR (neat) 3457, 2918, 2898, 2888, 2820, 1493, 1457, 1437, 1078, 1063, 1030, 876, 775, 731, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19−7.25 (m, 5H), 7.01−7.1 (m, 3H), 4.14−4.19 (m, 1H), 3.96 (d, ^3J = 6.7 Hz, 1H), 3.51 (dxd, ^2J = 9.6 Hz, ^3J = 3.8 Hz, 1H), 3.46 (dxd, ^2J = 9.6 Hz, ^3J = 6.1 Hz, 1H), 3.31 (s, 3H), 2.44 (d, ^3J = 4.1 Hz, 1H; OH), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 138.8, 132.0, 128.6, 128.5, 128.3, 128.1, 127.5, 74.2, 72.1, 59.0, 55.7, 21.9; HRMS (ES+) *m*/*z* calcd for $C_{18}H_{22}O_2NaS$ 325.1238 $[M + Na]^+$, found 325.1231.

(1*R*,2*S*)-3-Methoxy-1-(4-methoxyphenylthio)-1-phenylpropan-2-ol (3g). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 20 min: **2a** (115 mg, 0.7 mmol), 4-methoxybenzenethiol (178 μL, 1.4 mmol), and NaOH (56 mg, 1.4 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3g** as an oil (190 mg, 89% yield): $[\alpha]^{26}_D$ −202.8 (*c* 0.77, $CHCl_3$); IR (neat) 3434, 3060, 2925, 2895, 2835, 1591, 1570, 1492, 1452, 1284, 1243, 1173, 1120, 1028, 1120, 1028, 960, 827, 699, 640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21−7.29 (m, 7H), 6.76−6.78 (br t, 1H), 6.74−6.75 (br t, 1H), 4.16 (d, ^3J = 6.2 Hz, 1H), 4.09−4.14 (m, 1H), 3.76 (s, 3H), 3.47 (dxd, ^2J = 9.6 Hz, ^3J = 3.8 Hz, 1H), 3.42 (dxd, ^2J = 9.6 Hz, ^3J = 6.14 Hz, 1H), 3.3 (s, 3H), 2.53 (d, ^3J = 3 .8 Hz, 1H; OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 138.3, 135.7, 128.9, 128.4, 127.5, 124.1, 114.5, 74.1, 71.4, 59.1, 57.5, 55.3; HRMS (ES+) *m*/*z* calcd for $C_{17}H_{20}O_3NaS$: 327.1031 $[M + Na]^+$, found 327.1044.

(1*R*,2*S*)-1-(4-Bromophenylthio)-3-methoxy-1-phenylpropan-2-ol (3h). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 30 min: **2a** (200 mg, 1.218 mmol), 4-bromobenzenethiol (485 mg, 2.436 mmol), and NaOH (97.4 mg, 2.436 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3h** as a white solid (350 mg, 81% yield): mp 70−71 °C; $[\alpha]^{26}_D$ −207.9

(*c* 0.81, $CHCl_3$); IR (neat) 3387, 2942, 2904, 2841, 1491, 1468, 1452, 1384, 1371, 1260, 1189, 1091, 1079, 1062, 1007, 994, 944, 875, 817, 790, 732, 727, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23−7.35 (m, 7H), 7.16 (br s, 1H), 7.14 (br s, 1H), 4.32 (d, ^3J = 6.14 Hz, 1H), 4.14 (br m, 1H), 3.39−3.46 (m, 2H), 3.3 (s, 3H), 2.46 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 133.6, 133.5, 131.9, 128.8, 128.5, 127.8, 121.5, 73.7, 72.0, 59.0, 56.2; HRMS (ES+) *m*/*z* calcd for $C_{16}H_{17}O_2NaSBr$ 375.0030 $[M + Na]^+$, found 375.0042.

(1*R*,2*S*)-1-(4-*tert*-Butylphenylthio)-3-methoxy-1-phenylpropan-2-ol (3i). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 20 min: **2a** (200 mg, 1.218 mmol), 4-*tert*-butylbenzenethiol (433 μL, 2.436 mmol), and NaOH (97.4 mg, 2.436 mmol). The product was purified by flash chromatography (90% hexane, 10% ethyl acetate) to yield **3i** as a white solid (342 mg, 85% yield): mp 71−72 °C; $[\alpha]^{27}_D$ −190.5 (*c* 0.63, $CHCl_3$); IR (neat) 3363, 2951, 2866, 2833, 1493, 1358, 1270, 1195, 1107, 1093, 916, 878, 810, 703, 683 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24−7.37 (m, 9H), 4.3 (d, ^3J = 6.7 Hz, 1H), 4.09−4.14 (m, 1H), 3.42 (dxd, ^2J = 9.6 Hz, ^3J = 4.1 Hz, 1H), 3.38 (dxd, ^2J = 9.6 Hz, ^3J = 6 Hz, 1H), 3.28 (s, 3H), 2.56 (d, ^3J = 4.1 Hz, OH, 1H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.83, 138.3, 132.29, 130.61, 128.84, 128.4, 127.6, 126.0, 73.9, 71.7, 59.0, 56.5, 34.5, 31.2; HRMS (ES+) *m*/*z* calcd for $C_{20}H_{26}O_2S$ 330.1654 [M], found 330.1656.

(1*R*,2*S*)-3-Methoxy-1-(naphthalen-2-ylthio)-1-phenylpropan-2-ol (3j). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 20 min: **2a** (200 mg, 1.218 mmol), 2-naphthalenethiol (394 mg, 2.436 mmol), and NaOH (97.4 mg, 2.436 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3j** as a white solid (352 mg, 89% yield): mp 85−86 °C; $[\alpha]^{27}_D$ −247.3 (*c* 0.49, $CHCl_3$); IR (neat) 3443, 2924, 2900, 1493, 1469, 1454, 1121, 1105, 1078, 1063, 990, 942, 866, 816, 751, 730, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (br, 1H), 7.74−7.77 (m, 1H), 7.67−7.70 (m, 2H), 7.38−7.47 (m, 5H), 7.22−7.32 (m, 2H), 4.47 (d, ^3J = 6.1 Hz, 1H), 4.16−4.31 (m, 1H), 3.47 (dxd, ^2J = 9.67 Hz, ^3J = 4.4 Hz, 1H), 3.44 (dxd, ^2J = 9.67 Hz, ^3J = 5.9 Hz, 1H), 3.28 (s, 3H), 2.53 (d, ^3J = 4.4 Hz, 1H; OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 133.5, 132.3, 131.7, 130.9, 129.4, 128.8, 128.5, 128.4, 127.7, 127.6, 127.3, 126.4, 126.2, 73.8, 72.0, 59.0, 56.1; HRMS (ES+) *m*/*z* calcd for $C_{20}H_{20}O_2NaS$ 347.1082 $[M + Na]^+$, found 347.1085.

(1*R*,2*S*)-1-(isopropylthio)-3-methoxy-1-phenylpropan-2-ol (3k). The following reagents were combined in the amounts indicated according to the general procedure for the thiolate ring-opening of epoxides and heated at 65 °C for 30 min: **2a** (215 mg, 1.31 mmol), 2-propanethiol (250 μL, 2.62 mmol) and NaOH (105 mg, 2.62 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3k** as a white solid (253 mg, 83% yield). Mp 72−73 °C; $[\alpha]^{26}_D$ −172.1 (*c* 0.6, $CHCl_3$); IR (neat) 3438, 2958, 2890, 2862, 2837, 1490, 1462, 1453, 1444, 1246, 1152, 1120, 1062, 1050, 992, 942, 749, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.41 (m, 2H), 7.31−7.35 (m, 2H), 7.24−7.28 (m, 1H), 4.04−4.09 (m, 1H), 4.02 (d, ^3J = 6.4 Hz, 1H), 3.48 (dxd, ^2J = 9.6 Hz, ^3J = 3.8 Hz, 1H), 3.42 (dxd, ^2J = 9.6 Hz, ^3J = 6.3 Hz, 1H), 3.36 (s, 3H), 2.66 (sept, ^3J = 6.7 Hz, 1H), 2.41 (br s, 1H, OH), 1.24 (d, ^3J = 6.7 Hz, 3H), 1.16 (d, ^3J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 128.8, 128.5, 127.4, 74.1, 72.7, 59.1, 51.6, 34.7, 23.5, 23.2; HRMS (ES+) *m*/*z* calcd for $C_{13}H_{20}O_2NaS$: 263.1082 $[M + Na]^+$, found 263.1084.

(1*R*,2*S*)-1-(cyclohexylthio)-3-methoxy-1-phenylpropan-2-ol (3l). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 65 °C for 20 min: **2a** (146 mg, 0.89 mmol), cyclohexylthiol (224 μL, 1.78 mmol) and NaOH (71 mg, 1.78 mmol). The product was purified by flash chromatography (90% hexane,10% ethyl acetate) to yield **3l** as a white solid (180 mg, 72% yield). Mp 68−69 °C; $[\alpha]^{26}_D$ −178.4 (*c* 0.84, $CHCl_3$); IR (neat) 3422, 3056, 3028, 2915, 2892, 2847, 2812, 1491, 1449, 1111, 1095, 1074, 1061, 981, 946, 698, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23−7.39 (m, 5H), 4.03−4.09 (m, 2H), 3.46 (dxd, ^2J = 9.6 Hz, ^3J = 3.6 Hz, 1H), 3.41 (dxd, ^2J = 9.6 Hz, ^3J = 5.8 Hz, 1H), 3.35 (s, 3H), 2.43−2.50 (m, 2H), 1.93−1.97 (br d, 1H), 1.54−1.80 (m, 4H), 1.13−1.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 128.7, 128.4, 127.4, 74.1, 72.7, 59.1, 51.1, 43.3, 33.7, 33.5, 25.9, 25.8, 25.7; HRMS (ES+) *m*/*z* calcd for $C_{16}H_{24}O_2NaS$: 303.1395 $[M + Na]^+$, found 303.1377.

(1*R*,2*S*)-1-(tert-butylthio)-3-methoxy-1-phenylpropan-2-ol (3m). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 75 °C for 1 h: **2a** (110 mg, 0.67 mmol), *tert*-butylthiol (148 μL, 1.34 mmol) and NaOH (53.6 mg, 1.34 mmol). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **3m** as a white solid (115 mg, 71% yield). Mp 74−75 °C; $[\alpha]^{26}_D$ −179.9 (*c* 0.75, $CHCl_3$); IR (neat) 3445, 2962, 2937, 2908, 2860, 2819, 1601, 1490, 1453, 1363, 1264, 1191, 1157, 1117, 1100, 1076, 1062, 986, 940, 743, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.42 (m, 2H), 7.29−7.33 (m, 2H), 7.22−7.26 (m, 1H), 3.99−4.05 (m, 2H), 3.36−3.43 (m, 2H), 3.34 (s, 3H), 2.42 (d, ^3J = 4.68, 1H, OH), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 128.8, 128.4, 127.1, 73.8, 73.6, 59.0, 50.7, 44.2, 31.4; HRMS (ES+) *m*/*z* calcd for $C_{14}H_{22}O_2NaS$: 277.1238 $[M + Na]^+$, found 277.1233.

(1*R*,2*S*)-1-(adamantylthio)-3-methoxy-1-phenylpropan-2-ol (3n). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 80 °C for 60 min: **2a** (61 mg, 0.37 mmol), adamanthanethiol (263 mg, 1.48 mmol, 4 equiv) and NaOH (59.4 mg, 1.48 mmol, 4 equiv). The product was purified by flash chromatography (90% hexane,10% ethyl acetate) to yield **3n** as a white solid (80 mg, 64% yield). Mp 73−74 °C; $[\alpha]^{26}_D$ −176.8 (*c* 0.96, $CHCl_3$); IR (neat) 3443, 3058, 3025, 2901, 2847, 1599, 1491, 1450, 1342, 1299, 1189, 1120, 1042, 963, 747, 698, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.41 (m, 2H), 7.28−7.32 (m, 2H), 7.21−7.26 (m, 1H), 4.11 (d, ^3J = 5.97 Hz, 1H), 3.98−4.03 (m, 1H), 3.35−3.41 (m. 2H), 3.32 (s, 3H), 2.50 (d, ^3J = 4.68, 1H, OH), 1.98 (br s, 3H), 1.75−1.82 (br m, 6H), 1.59−1.67 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 128.7, 128.3, 127.0, 73.9, 73.7, 59.0, 48.1, 46.5, 43.8, 36.2, 29.7; HRMS (ES+) *m*/*z* calcd for $C_{20}H_{28}O_2NaS$: 355.1708 $[M + Na]^+$, found 355.1703.

(2*S*,3*R*)-3-(adamantylthio)-3-phenylpropane-1,2-diol (8a). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 80 °C for 120 min: **1a** (200 mg, 1.33 mmol), adamanthanethiol (475 mg, 2.66 mmol) and NaOH (106 mg, 2.66 mmol). The product was purified by flash chromatography (80% hexane, 20% ethyl acetate) to yield **8a** as a white solid (250 mg, 59% yield). Mp 69−70 °C; $[\alpha]^{26}_D$ −201.9 (*c* 0.9, $CHCl_3$); IR (neat) 3402, 2901, 2847, 1598, 1498, 1449, 1341, 1300, 1076, 1042, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22−7.42 (m, 5H), 4.11 (d, ^3J = 6.9 Hz, 1H), 3.86−3.91 (m, 1H), 3.64−3.7 (m. 1H), 3.55−3.6 (m, 1H), 2.37(d, ^3J = 5.83 Hz, 1H, OH), 2.04−2.07 (m, 1H, OH), 1.98 (br s, 3H), 1.73−1.85 (br m, 6H), 1.59−1.67 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 128.6, 128.6, 127.2, 74.9, 64.0, 48.2, 46.7, 43.8, 36.1, 29.7; HRMS (ES+) *m*/*z* calcd for $C_{19}H_{27}O_2S$: 319.1732 $[M + H]^+$, found 319.1726.

Selective Protection of the Primary Hydroxyl Group in 8a as a Trityl Ether. (1*R*,2*S*)-1-phenyl-1-(adamantylthio)-3-(trityloxy)-propan-2-ol (9a). A solution of **8a** (235 mg, 0.74 mmol) and triphenylmethyl chloride (252 mg, 0.89 mmol) in pyridine (6 mL) was heated at 90 °C for 18 h under N_2. The solvent was removed *in vacuo*, and the residual oil was chromatographed using hexane:Et_2O (9:1) as eluent to give 283 mg (68%) of **9a** as a white solid. Mp 77−78 °C; $[\alpha]^{26}_D$ −79.5 (*c* 0.9, $CHCl_3$); IR (neat)

3448, 3083, 3056, 3023, 2901, 2847, 1597, 1490, 1448, 1342, 1299, 1218, 1072, 1042, 1031, 761, 745, 632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.43 (m, 6H), 7.14−7.29 (m, 14H), 4.2 (d, ^3J = 5.33 Hz, 1H), 4.02−4.07 (m, 1H), 3.14 (dxd, ^2J = 9.39 Hz, ^3J = 5.57 Hz, 1H), 3.04 (dxd, ^2J = 9.39 Hz, ^3J = 5.57 Hz, 1H), 2.42 (d, ^3J = 6.16, 1H, OH), 1.98 (br s, 3H), 1.72−1.82 (br m, 6H), 1.59−1.68 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 140.9, 128.8, 128.7, 128.1, 127.7, 127.0, 126.7, 86.9, 74.5, 64.9, 48.0, 46.3, 43.9, 36.2, 29.7; HRMS (ES+) m/z calcd for $C_{38}H_{40}O_2NaS$: 583.2647 $[M + Na]^+$, found 583.2631.

Protection of epoxyalcohol 1b as a Methyl Ether. (2*S*,3*S*)-2-mesityl-3-(methoxymethyl)oxirane (2f). A solution of **1b** (300 mg, 1.56 mmol) in DMF (3 mL) was added *via canula* to a suspension of sodium hydride (44 mg, 1.81 mmol) in DMF (2 mL) at −20 °C under N_2. The mixture was stirred for 20 min, and methyl iodide (126 μL, 2.03 mmol) was syringed into the mixture. After being stirred for 4 h at −20 °C, the mixture was allowed to reach room temperature and stirred for another hour. MeOH (10 mL) and brine (10 mL) were added. The aqueous solution was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried and concentrated *in vacuo*. The residual oil was chromatographed using hexane: Et_2O (9:1−7:3) as eluent to give 300 mg (93%) of the epoxyether (**2f**) as an oil. $[\alpha_D]^{27}$ −13.4 (*c* 0.44, $CHCl_3$); IR (neat) 2977, 2887, 1729, 1615, 1453, 1374, 1315, 1199, 954, 850, 816, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 2H), 3.88 (dxd, ^2J = 11.4 Hz, ^3J = 2.9 Hz, 1H), 3.81 (d, ^3J = 2.3 Hz, 1H), 3.56 (dxd, ^2J = 11.4 Hz, ^3J = 5.3 Hz, 1H), 3.46 (s, 3H), 3.13−3.16 (m, 1H), 2.35 (s, 6H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 137.0, 130.3, 128.6, 72.6, 59.3, 58.3, 54.4, 20.8, 19.6; HRMS (ES+) m/z calcd for $C_{13}H_{18}O_2Na$: 229.1204 $[M + Na]^+$, found 229.1205.

(1*R*,2*S*)-1-(*tert*-Butylthio)-1-mesityl-3-methoxypropan-2-ol (6m). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 85 °C for 20 h: **2f** (21 mg, 0.1 mmol), *tert*-butylthiol (98 μL, 0.91 mmol, 9 equiv), and NaOH (37 mg, 0.91 mmol, 9 equiv). The product was purified by flash chromatography (90% hexane,10% ethyl acetate) to yield **6m** as a white solid (20 mg, 65% yield): mp 85−86 °C; $[\alpha]^{26}_D$ −102.7 (*c* 0.64, $CHCl_3$); IR (neat) 3444, 2959, 2921, 2896, 2862, 1611, 1456, 1364, 1161, 1120, 1093, 1061, 931, 850, 823, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 1H), 6.79 (s, 1H), 4.42 (d, ^3J = 10.2 Hz, 1H), 4.04−4.09 (m, 1H), 3.81 (dxd, ^2J = 9.6 Hz, ^3J = 2.5 Hz, 1H), 3.73 (dxd, ^2J = 9.6 Hz, ^3J = 4.9 Hz, 1H), 3.43 (s, 3H), 2.46 (s, 3H), 2.42 (s, 3H), 2.33 (s, 3H), 1.98 (d, ^3J = 3.8 Hz, 1H, OH), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 136.4, 136.2, 134.8, 131.3, 129.2, 73.9, 72.3, 59.1, 44.3, 43.6, 31.4, 21.5, 20.8; HRMS (ES+) m/z calcd for $C_{17}H_{28}O_2NaS$ 319.1708 $[M + Na]^+$, found 319.1719.

(1*R*,2*S*)-1-(Cyclohexylthio)-1-mesityl-3-methoxypropan-2-ol (6l). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 85 °C for 4 h: **2f** (39 mg, 0.19 mmol), cyclohexylthiol (119 μL, 0.95 mmol, 5 equiv), and NaOH (38 mg, 0.95 mmol, 5 equiv). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **6l** as a white solid (50 mg, 82% yield): mp 89−90 °C; $[\alpha]^{27}_D$ −146.8 (*c* 0.49, $CHCl_3$); IR (neat) 3447, 2923, 2850, 1447, 1376, 1262, 1195, 1121, 1094, 1063, 851, 643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 1H), 6.81 (s, 1H), 4.44 (d, ^3J = 10.3 Hz, 1H), 4.16−4.22 (m, 1H), 3.82 (dxd, ^2J = 9.7 Hz, ^3J = 2.3 Hz, 1H), 3.72 (dxd, ^2J = 9.7 Hz, ^3J = 5 Hz, 1H), 2.52−2.59 (m, 1H), 3.45 (s, 3H), 2.46 (s, 3H), 2.35 (s, 3H), 2.24 (s, 3H), 2−2.07 (m, 1H), 1.94 (d, ^3J = 3.9 Hz, 1H, OH), 1.55−1.86 (m, 4H), 1.19−1.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 136.9, 136.4, 133.7, 131.3, 129.1, 74.2, 72.4, 59.1, 45.0, 44.7, 34.2, 34.0, 26.1, 26.0, 25.7, 21.6, 21.1, 20.7; HRMS (ES+) m/z calcd for $C_{19}H_{30}O_2NaS$ 345.1864 $[M + Na]^+$, found 345.1864.

(1*R*,2*S*)-1-(Adamanthylthio)-1-mesityl-3-methoxypropan-2-ol (6n). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 90 °C for 24 h: **2f** (100 mg, 0.48 mmol), adamanthanethiol (773 mg, 4.4 mmol, 9 equiv), and NaOH (175 mg, 4.4 mmol, 9 equiv). The product was purified by flash chromatography (95% hexane, 5% ethyl acetate) to yield **6n** as a white solid (50 mg, 27% yield):mp 87−88 °C; $[\alpha]^{27}_D$ −149.1 (*c* 0.58, $CHCl_3$); IR (neat) 3433, 2902, 2848, 1448, 1230, 1113, 1082, 1071, 1043, 948, 899, 851, 608 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.79 (s, 1H), 4.45 (d, ^3J = 10.1 Hz, 1H), 4.02−4.08 (m, 1H), 3.82 (dxd, ^2J = 9.7 Hz, ^3J = 2.6 Hz, 1H), 3.69 (dxd, ^2J = 9.7 Hz, ^3J = 5.4 Hz, 1H), 3.43 (s, 3H), 2.45 (s, 3H), 2.43 (s, 3H), 2.23 (s, 3H), 2 (br s, 4H), 1.61−1.86 (m, 16H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 136.2, 136.1, 135.2, 131.2, 129.2, 74.0, 72.3, 59.1, 46.5, 43.8, 40.8, 36.2, 29.7, 21.7, 21.52, 20.8; HRMS (ES+) m/z calcd for $C_{23}H_{34}O_2NaS$ 397.2177 $[M + Na]^+$, found 397.2177.

(2*S*,3*R*)-3-(*tert*-Butylthio)-3-mesitylpropane-1,2-diol (8b). The following reagents were combined in the amounts indicated according to the general thiolate ring-opening of epoxides procedure and heated at 80 °C for 3 h: **1b** (196 mg, 1.02 mmol), *tert*-butylthiol (338 μL, 3.06 mmol, 3 equiv), and NaOH (122 mg, 3.06 mmol, 3 equiv). The product was purified by flash chromatography (hexane/ethyl acetate, 7:3−6:4) to yield **8b** as a white solid (230 mg, 80% yield): mp 103−104 °C; $[\alpha]^{27}_D$ −141.3 (*c* 0.57, $CHCl_3$); IR (neat) 3347, 2965, 2920, 2861, 1609, 1456, 1363, 1276, 1216, 1162, 1091, 1030, 1012, 918, 878, 849 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.82 (s, 1H), 4.43 (d, ^3J = 10.2 Hz, 1H), 3.97−4.04 (m, 2H), 3.88−3.95 (m, 1H), 2.46 (s, 3H), 2.42 (s, 3H), 2.25 (s, 3H), 2.17−2.22 (br s, 1H, OH), 1.73 (br s, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 136.8, 136.7, 134.0, 131.5, 129.4, 73.2, 63.7, 44.9, 31.4, 21.5, 21.5, 20.7; HRMS (ES+) m/z calcd for $C_{16}H_{26}O_2NaS$ 305.1551 $[M + Na]^+$, found 305.1563.

(1*R*,2*S*)-1-(*tert*-Butylthio)-1-mesityl-3-(trityloxy)propan-2-ol (9b). A solution of **8b** (282 mg, 1 mmol) and triphenylmethyl chloride (369 mg, 1.3 mmol) in pyridine (7 mL) was heated at 90 °C for 18 h under N_2. The solvent was removed in vacuo, and the residual oil was chromatographed using hexane/Et_2O (9:1−7:1) as eluent to give 350 mg (67%) of **9b** as a white solid: mp 109−110 °C; $[\alpha]^{27}_D$ −51.7 (*c* 0.58, $CHCl_3$); IR (neat) 3539, 3057, 3022, 2958, 2921, 1489, 1447, 1363, 1219, 1158, 1091, 1031, 928, 899, 852, 758, 75, 698, 640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.5 (m, 5H), 7.22−7.32 (m, 10H), 6.8 (s, 1H), 6.79 (s, 1H), 4.34 (d, ^3J = 10 Hz, 1H), 3.99−4.04 (m, 1H), 3.72 (dxd, ^2J = 9.7 Hz, ^3J = 2.8 Hz, 1H), 3.36 (dxd, ^2J = 9.7 Hz, ^3J = 5.5 Hz, 1H), 2.43 (s, 3H), 2.39 (s, 3H), 2.23 (s, 3H), 2.12 (d, ^3J = 3.8 Hz, 1H, OH), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 137.5, 136.1, 135.0, 131.2, 129.1, 128.8, 127.8, 127.1, 87.0, 72.6, 65.9, 44.0, 44.0, 31.4, 21.7, 21.5, 20.7; HRMS (ES+) m/z calcd for $C_{35}H_{40}O_2NaS$ 547.2647 $[M + Na]^+$, found 547.2663.

(2*R*,3*R*)-3-(Adamantylthio)-2-hydroxy-3-phenylpropanoic acid (12). A mixture of **11** (200 mg, 1.12 mmol), adamanthanethiol (398 mg, 2.24 mmol, 2 equiv), and lithium hydroxide (53.8 mg, 2.24 mmol, 2 equiv) in a mixture of dioxane/H_2O, 10:1 (4.5 mL) was stirred at 80 °C for 1 h. Then 10 mL of water was added, and the mixture was extracted with CH_2Cl_2 to remove the excess thiol. The aqueous phase was acidified with HCl 1 M and extracted with AcOEt (3 × 10 mL). The combined organic phases were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The solid obtained was used without further purification: mp 197−198 °C; $[\alpha]^{26}_D$ −141.27 (*c* 0.52, $CHCl_3$); IR (neat) 3435, 3350, 3239, 2922, 2846, 1731, 1692, 1448, 1340, 1096, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.32−7.36 (m, 2H), 7.24−7.28 (m, 1H), 4.47 (d, ^3J = 3.3 Hz, 1H), 4.42 (d, ^3J = 3.3 Hz, 1H), 3.11 (s, 1H, OH), 1.98 (br s, 2H), 1.71−1.83 (br m, 6H), 1.59−1.67 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 141.7, 128.5, 128.3, 127.4, 73.8, 47.9, 46.3, 43.7, 36.1, 29.7;

HRMS (ES+) m/z calcd for $C_{19}H_{24}O_3NaS$ 355.1344 $[M + Na]^+$, found 355.1357.

(2*R*,3*R*)-3-(Adamantylthio)-3-phenylpropane-1,2-diol (8a-*syn*). To a solution of **12** (372 mg, 1.12 mmol) in THF (7 mL) at 0 °C was added dropwise the complex borane−dimethyl sulfide (425 μL, 4.48 mmol, 4 equiv), and the mixture was stirred at rt for 16 h. MeOH was added slowly followed by water. The mixture was extracted with CH_2Cl_2 (2 × 15 mL) and once with 15 mL of EtOAc. The combined organic phases were dried with $MgSO_4$ and filtered. The solvent was removed in vacuo to yield **8a-*syn*** as a white solid (302 mg, 84% yield). The solid obtained was used without further purification: mp 95−96 °C; $[\alpha]^{26}_D$ −240.6 (*c* 0.32, $CHCl_3$); IR (neat) 3499, 3208, 3053, 2898, 2847, 1594, 1108, 1084, 868, 746, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.2 (m, 5H), 4.07 (d, ^3J = 9.6 Hz, 1H), 3.63−3.55 (m, 2H), 3.45 (s. 1H, OH), 3.31−3.26 (m, 1H), 2.1 (br s, 1H, OH), 2.0 (br s, 3H), 1.77−1.88 (br m, 6H), 1.61−1.69 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 128.6, 128.0, 127.1, 73.7, 62.8, 49.4, 47.1, 43.9, 36.1, 29.7; HRMS (ES+) calcd for $C_{19}H_{26}O_2NaS$ 341.1551 $[M + Na]^+$, found 341.1548.

(1*R*,2*R*)-1-(Adamantylthio)-1-phenyl-3-(trityloxy)propan-2-ol (9a-*syn*). A solution of **8a-*syn*** (220 mg, 0.7 mmol) and triphenylmethyl chloride (235 mg, 0.83 mmol) in pyridine (10 mL) was heated at 90 °C for 18 h under N_2. The solvent was removed in vacuo, and the residual oil was chromatographed using hexane/Et_2O (9:1−7:1) as eluent to give 300 mg (77%) of **9a-*syn*** as a white solid: mp 113−114 °C; $[\alpha]^{28}_D$ −101.84 (*c* 0.91, $CHCl_3$); IR (neat) 3461, 2903, 2848, 1489, 1448, 1083, 746, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.44 (m, 6H), 7.09−7.27 (m, 14H), 4.3 (d, ^3J = 8.5 Hz, 1H), 3.68−3.73 (m, 1H), 3.31 (dxd, ^2J = 9.7 Hz, ^3J = 3.36 Hz, 1H), 3.16 (d, ^3J = 1.75, 1H, OH), 2.72 (dxd, ^2J = 9.7 Hz, ^3J = 4.1 Hz, 1H), 2.01 (br s, 3H), 1.79−1.9 (br m, 6H), 1.62−1.7 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.99, 142.8, 128.66, 128.2, 128.09, 127.69, 126.87, 126.61, 86.4, 73.77, 63.79, 49.14, 46.75, 44, 36.19, 29.77; HRMS (ES+) m/z calcd for $C_{38}H_{40}O_2NaS$ 583.2647 $[M + Na]^+$, found 583.2635.

(1*R*,2*S*)-1-(Ethoxycarbonyl)-2-hydroxy-2-mesitylethyl 4-Methylbenzenesulfonate (16). To a stirred solution of **15** (2.58 g, 10.22 mmol) in 70 mL of DCM at 0 °C under argon was added triethylamine (2.14 mL, 15.33 mmol, 1.5 equiv) followed by *p*-toluenesulfonyl chloride (2 g, 10.43 mmol, 1.02 equiv). After being stirred for 70 h at 0 °C, the reaction mixture was diluted with ethyl acetate, and the crude was purified by silica gel chromatography hexane/AcOEt (7:3) to give **16** as a white solid (3.53 g, 85% yield): mp 81−82 °C; $[\alpha]^{26}_D$ +17.0 (*c* 0.22, $CHCl_3$); IR (neat) 3452, 2961, 1704, 1598, 1371, 1310, 1174, 1017, 873, 854 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 6.74 (s, 2H), 5.38 (dxd, ^3J = 7.9 Hz, ^3J = 3.8 Hz, 1H), 5.25 (d, ^3J = 7.9 Hz, 1H), 3.74−3.86 (m, 2H), 2.47 (d, ^3J = 3.8 Hz, 1H, OH), 2.44 (s, 3H), 2.32 (br s, 6H), 2.2 (s, 3H), 0.84 (t, ^3J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 145.2, 138.1, 137.2, 132.7, 130.2, 129.7, 129.1, 126.2, 80.2, 70.9, 61.6, 21.7, 20.8, 20.6, 13.3; HRMS (ES+) m/z calcd for $C_{21}H_{26}O_6NaS$ 429.1348 $[M + Na]^+$, found 429.1337.

(2*S*,3*S*)-Ethyl 3-Mesityloxirane-2-carboxylate (17). A solution of **16** (3.5 g, 8.61 mmol) and 0.78 mL (43.1 mmol, 5 equiv) of water in 45 mL of DMF at rt was treated with potassium carbonate (3.57 g, 25.8 mmol, 3 equiv). After being stirred for 24 h at rt, the reaction mixture was processed with ether in the usual way, and the crude product was purified by silica gel chromatography with 10% ether in hexane to provide 0.51 g (25% yield) of the desired epoxide: $[\alpha]^{27}_D$ −13.6 (*c* 0.42, $CHCl_3$); IR (neat) 2977, 2923, 1755, 1727, 1613, 1442, 1288, 1188, 1107, 1049, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.76 (s, 2H), 4.22 (d, ^3J = 4.4 Hz, 1H), 3.87−4.02 (m, 2H), 3.81 (d, ^3J = 4.4 Hz, 1H), 2.34 (br s, 6H), 2.23 (s, 3H), 0.91 (t, ^3J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 137.3, 136.8, 128.6, 126.9, 61.0, 57.0, 53.4, 20.9, 19.6, 13.6; HRMS (ES+) m/z calcd for $C_{14}H_{18}O_3Na$ 257.1154 $[M + Na]^+$, found 257.1151.

(2*R*,3*R*)-3-(*tert*-Butylthio)-2-hydroxy-3-mesitylpropanoic acid (18). In a sealed microwave tube were placed the epoxy ester **17** (250 mg, 1.21 mmol), LiOH (87 mg, 3.64 mmol, 3 equiv), and *tert*-butylthiol (414 μL, 3.64 mmol) dissolved in 5.5 mL of dioxane/H_2O (10:1). The mixture was stirred at 140 °C under microwave irradiation for 3 h, 25 mL of water was added, and the mixture was extracted with CH_2Cl_2 to remove the excess thiol. The aqueous phase was acidified with HCl 1 M and was extracted with AcOEt (3 × 25 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvent was removed in vacuo. ^1H NMR spectrum of the resulting crude showed complete conversion and only one regioisomer. The solid obtained (288 mg, 80% yield) was used without further purification:mp 127−128 °C; $[\alpha]^{26}_D$ −156.13 (*c* 0.25, $CHCl_3$); IR (neat) 3547, 2961, 1758, 1702, 1456, 1362, 1162, 1101, 929, 852 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 1H), 6.8 (s, 1H), 4.62 (d, ^3J = 6.8 Hz, 1H), 4.31 (m, 1H), 3.81 (d, ^3J = 6.8 Hz, 1H), 2.41 (s, 3H), 2.4 (s, 3H), 2.23 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 137.3, 136.8, 134.8, 134.5, 131.3, 129.3, 72.2, 47.4, 44.8, 31.4, 21.7, 21.1, 20.8; HRMS (ES−) m/z calcd for $C_{16}H_{23}O_3S$ 295.1368 $[M - H]^-$, found 295.1374.

(2*R*,3*R*)-3-(*tert*-Butylthio)-3-mesitylpropane-1,2-diol (8b-*syn*). To a solution of **18** (504 mg, 1.7 mmol) in THF (10 mL) at 0 °C was added dropwise 646 μL (44.8 mmol, 4 equiv) of the complex borane−dimethyl sulfide. The reaction was stirred at rt for 24 h. Then MeOH was added slowly followed by water. The mixture was extracted with CH_2Cl_2 (2 × 20 mL) and once with 25 mL of EtOAc. The combined organic phases were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude was purified by silica gel chromatography (hexane/EtOAc) (3:1) to afford **8b-*syn*** (410 mg, 85% yield) as an oil: $[\alpha]^{26}_D$ −192.9 (*c* 0.67, $CHCl_3$); IR (neat) 3398, 2959, 2920, 1612, 1457, 1365, 1270, 1160, 1093, 1039, 920, 875, 852, 817, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 2H), 4.4 (d, ^3J = 10.2 Hz, 1H), 3.77−3.82 (m, 2H), 3.62−3.66 (m, 2H), 3.25−3.31 (m, 1H), 2.46 (s, 3H), 2.34 (s, 3H), 2.23 (s, 3H), 2.12−2.15 (m, 1H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 136.4, 135.4, 134.7, 131.1, 129.3, 71.4, 62.7, 47.0, 44.8, 31.6, 21.6, 21.2, 20.7; HRMS (ES+) m/z calcd for $C_{16}H_{26}O_2NaS$ 305.1551 $[M + Na]^+$, found 305.1541.

(1*R*,2*R*)-1-(*tert*-Butylthio)-1-mesityl-3-(trityloxy)propan-2-ol (9b-*syn*). A solution of **8b-*syn*** (430 mg, 1.52 mmol) and triphenylmethyl chloride (519 mg, 1.83 mmol) in pyridine (15 mL) was heated at 90 °C for 24 h under N_2. The solvent was removed in vacuo, and the residual oil was chromatographed using hexane/Et_2O (9:1−7:1) as eluent to give 530 mg (66%) of **9b-*syn*** as a white solid: mp 117−118 °C; $[\alpha]^{27}_D$ −110.4 (*c* 1.01, $CHCl_3$); IR (neat) 3483, 3084, 2959, 1596, 1407, 1112, 929, 852 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.36 (m, 6H), 7.15−7.23 (m, 9H), 6.71 (s, 1H), 6.6 (s, 1H), 4.27 (d, ^3J = 9.6 Hz, 1H), 3.95−4 (m, 1H), 3.48 (s, 1H), 3.11 (dxd, ^2J = 9.8 Hz, ^3J = 3.4 Hz, 1H), 2.92 (dxd, ^2J = 9.8 Hz, ^3J = 5.1 Hz, 1H), 2.28 (s, 3H), 2.18 (s, 3H), 2.13 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 136.7, 135.9, 135.2, 134.7, 131.0, 129.0, 128.7, 127.6, 126.8, 86.9, 71.6, 65.5, 48.1, 44.4, 31.7, 21.7, 21.4, 20.7; HRMS (ES+) m/z calcd for $C_{35}H_{40}O_2NaS$ 547.2647 $[M + Na]^+$, found 547.2671.

General Procedure for the Phosphinite Incorporation. To a Schlenk flask containing β-hydroxy sulfide (0.55 mmol) and DMAP (0.055 mmol, 0.1 equiv) in toluene (0.28 M) at rt were added NEt_3 (0.66 mmol, 1.2 equiv) and chlorodiphenylphosphine (0.55 mmol, 1.01 equiv) via syringe. The reaction was stirred for 20 min. The solvent was removed in vacuo, and the reaction crude was diluted with 95:5 hexane−ethyl acetate mixture (0.5 mL, dried over molecular sieves, and degassed with argon). The resulting slurry was loaded onto a plug of silica and

purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate).

((1*R*,2*S*)-3-Methoxy-1-phenyl-1-(phenylthio)propan-2-yloxy)-diphenylphosphine (4a). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3a** (151 mg, 0.55 mmol), DMAP (6.7 mg. 0.055 mmol), NEt_3 (92 μL, 0.66 mmol), and chlorodiphenylphosphine (101.1 μL, 0.55 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4a** as an oil (230 mg, 91% yield): $[\alpha]^{26}_D$ −130.0 (*c* 0.63, $CHCl_3$); IR (neat) 3067, 2890, 1582, 1492, 1480, 1434, 1127, 1089, 1069, 1024, 998, 965, 953, 739, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.09−7.37 (m, 20H), 4.41−4.46 (m, 2H), 3.37 (dxd, ^2J = 9.9 Hz, ^3J = 4.44 Hz, 1H), 3.28 (dxd, ^2J = 9.9 Hz, ^3J = 4.78 Hz, 1H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1 (d, *J* = 18.9 Hz), 142.1 (d, *J* = 14.5 Hz), 138.6, 134.9, 132.2, 130.6, 130.4, 130.4, 130.1, 129.3, 129.0, 128.9, 128.7, 128.1, 128.0, 128.0, 127.9, 127.3, 127.1, 81.5 (d, *J* = 19.7 Hz), 73.2 (d, *J* = 3,3 Hz), 58.5, 55.6 (d, *J* = 6.6 Hz); ^{31}P NMR δ 119.6; HRMS (ES+) *m*/*z* calcd for $C_{28}H_{27}O_2NaPS$ 481.1367 $[M + Na]^+$, found 481.1386.

((1*R*,2*S*)-3-(Benzyloxy)-1-phenyl-1-(phenylthio)propan-2-yloxy)-diphenylphosphine (4b). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3b** (36 mg, 0.1 mmol), DMAP (1.3 mg, 0.01 mmol), NEt_3 (17.2 μL, 0.12 mmol), and chlorodiphenylphosphine (19 μL, 0.1 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4b** as an oil (45 mg, 82% yield): $[\alpha]^{26}_D$ −117.9 (*c* 0.51, $CHCl_3$); IR (neat) 3055, 3027, 3002, 2898, 2857, 1582, 1493, 1479, 1434, 1116, 1092, 1070, 1051, 1024, 998, 736, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.43 (m, 2H), 7.13−7.33 (m, 23H), 4.53−4.6 (m, 2H), 4.25 (d, ^2J = 11.9 Hz, 1H), 4.21 (d, ^2J = 11.9 Hz, 1H), 3.58−3.62 (m, 1H), 3.45−3.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0 (d, *J* = 18.4 Hz), 142.1 (d, *J* = 14.7 Hz), 138.6, 137.9, 135.0, 132.1, 130.7, 130.5, 130.4, 129.4, 129.0, 128.9, 128.7, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.7, 127.5, 127.3, 127.0, 81.6 (d, *J* = 19.7 Hz), 73.1, 71.0 (d, *J* = 3,6 Hz), 55.7; ^{31}P NMR δ 119.1. HRMS (ES+) *m*/*z* calcd for $C_{34}H_{32}O_2PS$ 535.1861 $[M + H]^+$, found 535.1853.

((1*R*,2*S*)-3-(Benzhydryloxy)-1-phenyl-1-(phenylthio)propan-2yloxy)diphenylphosphine (4c): $[\alpha]^{27}_D$ −59.13 (*c* 0.44, $CHCl_3$); IR (neat) 3055, 3027, 3003, 2916, 2857, 1583, 1492, 1479, 1435, 1091, 1071, 1047, 1025, 1000, 923, 740, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.30 (m, 2H), 7.06−7.19 (m, 28H), 5.02 (s, 1H), 4.46−4.55 (m, 2H), 3.54 (dxd, ^2J = 10.2 Hz, ^3J = 4.8 Hz, 1H), 3.40 (dxd, ^2J = 10.2 Hz, ^3J = 5.16 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8 (d, *J* = 18.3 Hz), 142 (d, *J* = 15.23 Hz), 141.94, 141.91, 138.6, 134.99, 132.03, 130.68, 130.47, 130.38, 130.16, 129.4, 129.97, 128.93, 128.72, 128.25, 128.2, 128.08, 128.03, 128.0, 127.98, 127.91, 127.34, 127.27, 127.21, 126.98, 126.87, 84.15, 81.73 (d, *J* = 19.81 Hz), 69.63 (d, *J* = 3,78 Hz), 58.56, 57.72 (d, *J* = 6.03 Hz); ^{31}P NMR (162, MHz, $CDCl_3$) δ 118.38; HRMS (ES+) *m*/*z* calcd for $C_{40}H_{35}O_2NaSP$: 633.1993 $[M + Na]^+$, found 633.2010.

Diphenyl((1*R*,2*S*)-1-phenyl-1-(phenylthio)-3-(trityloxy)propan-2-yloxy)phosphine (4d). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3d** (85.6 mg, 0.17 mmol), DMAP (2.1 mg, 0.017 mmol), NEt_3 (29 μL, 0.2 mmol), and chlorodiphenylphosphine (31.5 μL, 0.17 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4d** as an oil (103 mg, 88% yield): $[\alpha]^{25}_D$ −56.7 (*c* 0.67, $CHCl_3$); IR (neat) 3056, 3025, 3004, 2922, 2872, 2852, 1583, 1491, 1480, 1448, 1436, 1218, 1072, 1026, 1000, 747, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01−7.30 (m, 35H), 4.50 (d, ^3J = 4.98 Hz, 1H), 4.39−4.45 (m, 1H), 3.14 (dxd, ^2J = 9.8 Hz, ^3J = 5.7 Hz, 1H), 3.06 (dxd, ^2J = 9.8 Hz, ^3J = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 142.8 (d, *J* = 18.5 Hz), 142.1 (d, *J* = 15.5 Hz), 138.0, 135.5, 131.6, 130.8, 130.6, 130.4, 130.2, 129.4, 129.0, 128.9, 128.7, 128.6, 128.0, 128.0, 127.9, 127.9, 127.7, 127.2, 126.9, 126.8, 87.1, 82.1 (d, *J* = 19.4 Hz), 64.6 (d, *J* = 4.2 Hz), 56.1 (d, *J* = 5.2 Hz); ^{31}P NMR (162, MHz, $CDCl_3$) δ 118.8; HRMS (ES+) *m*/*z* calcd for $C_{46}H_{39}O_2NaSP$ 709.2306 $[M + Na]^+$, found 709.2307.

((1*R*,2*S*)-1-(3,5-Dimethylphenylthio)-3-methoxy-1-phenylpropan-2-yloxy)diphenylphosphine (4e). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3e** (81.7 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **3a** as an oil (115 mg, 87% yield): $[\alpha]^{27}_D$ −119.8 (*c* 0.66, $CHCl_3$); IR (neat) 3052, 3027, 2916, 2893, 1599, 1580, 1492, 1480, 1466, 1453, 1434, 1129, 1094, 1074, 1026, 967, 848, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.46 (m, 2H), 7.36−7.38 (m, 2H), 7.21−7.33 (m, 11H), 6.91 (s, 2H), 6.81 (s, 1H), 4.47−4.54 (m, 2H), 3.46 (dxd, ^2J = 9.9 Hz, ^3J = 4.4 Hz, 1H), 3.38 (dxd, ^2J = 9.9 Hz, ^3J = 4.4 Hz, 1H), 3.06 (s, 3H), 2.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3 (d, *J* = 18.5 Hz), 142.2 (d, *J* = 14.6 Hz), 138.8, 138.2, 134.3, 130.5 (d, *J* = 22.0 Hz), 130.2 (d, *J* = 22.0 Hz), 129.7, 129.3, 129.0, 128.9, 128.8, 128.1, 128.0, 127.9 (d, *J* = 7.3 Hz), 127.2, 81.5 (d, *J* = 19.7 Hz), 73.2 (d, *J* = 3,7 Hz), 58.5, 55.3 (d, *J* = 6.5 Hz), 21.1; ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.3; HRMS (ES+) *m*/*z* calcd for $C_{30}H_{31}O_2NaPS$ 509.1680 $[M + Na]^+$, found 509.1688.

((1*R*,2*S*)-1-(2,6-Dimethylphenylthio)-3-methoxy-1-phenylpropan-2-yloxy)diphenylphosphine (4f). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3f** (87.6 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4f** as an oil (110 mg, 80% yield): $[\alpha]^{28}_D$ −174.4 (*c* 0.62, $CHCl_3$); IR (neat) 3052, 2921, 2891, 2859, 2807, 1478, 1457, 1433, 1124, 1106, 1095, 1076, 1060, 1009, 947, 876, 777, 736, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.45 (m, 2H), 7.28−7.32 (m, 3H), 7.11−7.20 (m, 10H), 7.02−7.06 (m, 2H), 6.97−6.99 (m, 2H), 4.59−4.66 (m, 1H), 4.15 (d, ^3J = 6.7 Hz, 1H), 3.49 (dxd, ^2J = 10 Hz, ^3J = 4.98 Hz, 1H), 3.43 (dxd, ^2J = 10 Hz, ^3J = 4.4 Hz, 1H), 3.03 (s, 3H), 2.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 143.2 (d, *J* = 19 Hz), 142.1 (d, *J* = 14 Hz), 139.5, 132.6, 130.4 (d, *J* = 19.1 Hz), 130.2 (d, *J* = 18 Hz), 129.0, 129.0, 128.6, 128.3, 128.1, 128.0 (d, *J* = 7.3 Hz), 128.0, 127.8 (d, *J* = 7 Hz), 127.0, 82.4 (d, *J* = 19.7 Hz), 73.6 (d, *J* = 2.93 Hz), 58.4, 55.4 (d, *J* = 6.56 Hz), 21.9; ^{31}P NMR (162, MHz, $CDCl_3$) δ 120.4; HRMS (ES+) *m*/*z* calcd for $C_{30}H_{31}O_2NaPS$ 509.1680 $[M + Na]^+$, found 509.1683.

((1*R*,2*S*)-3-Methoxy-1-(4-methoxyphenylthio)-1-phenylpropan-2-yloxy)diphenylphosphine (4g). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3g** (82.2 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **3a** as an oil (112 mg, 85% yield): $[\alpha]^{27}_D$ −93.7 (*c* 0.65, $CHCl_3$); IR (neat) 2924, 2893, 2835, 1591, 1571, 1493, 1454, 1438, 1285, 1246, 1181, 1126, 1104, 1072, 720, 640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.37 (m, 2H), 7.12−7.22 (m, 15H), 6.64−6.66 (m, 2H), 4.38−4.44 (m, 1H), 4.26 (d, ^3J = 5.85 Hz, 1H), 3.68 (s, 3H), 3.38 (dxd, ^2J = 9.8 Hz, ^3J = 5.26 Hz, 1H), 3.31 (dxd, ^2J = 9.8 Hz, ^3J = 4.82 Hz, 1H), 2.97 (s, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 159.6, 143.3 (d, J = 19 Hz), 142.3 (d, J = 14 Hz), 138.8, 135.6, 130.5, 130.4, 130.3, 130.2, 129.4, 129.0, 128.8, 128.1, 128.0, 128.0, 127.9, 127.9, 127.1, 124.9, 114.3, 81.2 (d, J = 19.3 Hz), 73.4 (d, J = 3 Hz), 58.5, 56.9 (d, J = 6.56 Hz), 52.2; ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.4; HRMS (ES+) m/z calcd for $C_{29}H_{30}O_3PS$ 489.1653 $[M + H]^+$, found 489.1652.

((1*R*,2*S*)-1-(4-Bromophenylthio)-3-methoxy-1-phenylpropan-2-yloxy)diphenylphosphine (4h). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3h** (95.4 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4h** as an oil (129 mg, 89% yield): $[\alpha]^{27}_D$ −100.6 (*c* 0.31, $CHCl_3$); IR (neat) 3053, 2891, 1492, 1472, 1453, 1385, 1231, 1190, 1129, 1091, 1070, 1026, 1009, 887, 741, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.36 (m, 2H), 7.14−7.27 (m, 15H), 7.01−7.05 (m, 2H), 4.34−4.44 (m, 2H), 3.36 (dxd, ^2J = 9.8 Hz, ^3J = 4.5 Hz, 1H), 3.23 (dxd, ^2J = 9.8 Hz, ^3J = 5.11 Hz, 1H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0 (d, J = 18.9 Hz), 142.0 (d, J = 15.5 Hz), 138.1, 134.1, 133.6, 131.8, 130.7, 130.5, 130.3, 130.1, 129.4, 129.1, 129.0, 128.2, 128.1, 128.1, 128.1, 128.0, 127.5, 121.3, 81.2 (d, J = 19.7 Hz), 73.0 (d, J = 3,6 Hz), 58.6, 55.7 (d, J = 5.9 Hz); ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.4; HRMS (ES+) m/z calcd for $C_{28}H_{27}O_2PBrS$ 537.0653 $[M + H]^+$, found 537.0634.

((1*R*,2*S*)-1-(4-*tert*-Butylphenylthio)-3-methoxy-1-phenylpropan-2-yloxy)diphenylphosphine (4i). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3i** (86 mg, 0.26 mmol), DMAP (3.2 mg, 0.026 mmol), NEt_3 (44 μL, 0.31 mmol), and chlorodiphenylphosphine (48 μL, 0.26 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4i** as an oil (107 mg, 80% yield): $[\alpha]^{26}_D$ −103.6 (*c* 0.61, $CHCl_3$); IR (neat) 3053, 2959, 1491, 1481, 1452, 1434, 1394, 1362, 1190, 1128, 1120, 1073, 741, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.44 (m, 19H), 4.45−4.53 (m, 2H), 3.42 (dxd, ^2J = 9.9 Hz, ^3J = 5.3 Hz, 1H), 3.35 (dxd, ^2J = 9.9 Hz, ^3J = 4.84 Hz, 1H), 3.02 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 143.2 (d, J = 18.3 Hz), 142.2 (d, J = 14.3 Hz), 138.9, 132.2, 131.4, 130.6, 130.4, 130.4, 130.2, 129.3, 129.0, 128.5, 128.1, 128.1, 128.0, 128.0, 127.9, 127.2, 125.8, 81.5 (d, J = 19.6 Hz), 73.3 (d, J = 3,1 Hz), 58.5, 55.8 (d, J = 6.7 Hz), 34.5, 31.2; ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.3; HRMS (ES+) m/z calcd for $C_{32}H_{35}O_2NaSP$ 537.1993 $[M + Na]^+$, found 537.2002.

((1*R*,2*S*)-3-Methoxy-1-(naphthalen-2-ylthio)-1-phenylpropan-2-yloxy)diphenylphosphine (4j). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3j** (87.6 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4j** as an oil (110 mg, 80% yield): $[\alpha]^{27}_D$ −52.2 (*c* 0.42, $CHCl_3$); IR (neat) 3053, 2922, 2890, 2858, 1588, 1493, 1453, 1437, 1227, 1194, 1125, 1114, 965, 943, 744, 728, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.78 (m, 2H), 7.65−7.69 (m, 2H), 7.20−7.47 (m, 18H), 4.68 (d, ^3J = 5.9 Hz, 1H), 4.54−4.60 (m, 1H), 3.50 (dxd, ^2J = 9.9 Hz, ^3J = 5.5 Hz, 1H), 3.4 (dxd, ^2J = 9.9 Hz, ^3J = 5.3 Hz, 1H), 3.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1 (d, J = 18.3 Hz), 142.1 (d, J = 14.6 Hz), 138.5, 133.6, 132.4, 132.2, 130.7, 130.5, 130.3, 130.1, 129.4, 129.4, 129.0, 129.0, 128.2, 128.2, 128.1, 128.0, 128.0, 127.9, 127.6, 127.4, 127.4, 126.3, 126.0, 81.4 (d, J = 19.76 Hz), 73.1 (d, J = 3,7 Hz), 58.6, 55.4 (d, J = 6.2 Hz); ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.6; HRMS (ES+) m/z calcd for $C_{32}H_{29}O_2NaPS$ 531.1524 $[M + Na]^+$, found 531.1523.

((1*R*,2*S*)-1-(Isopropylthio)-3-methoxy-1-phenylpropan-2-yloxy)-diphenylphosphine (4k). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3k** (64.9 mg, 0.27 mmol), DMAP (3.3 mg, 0.027 mmol), NEt_3 (45 μL, 0.32 mmol), and chlorodiphenylphosphine (50 μL, 0.27 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4k** as an oil (99 mg, 86% yield): $[\alpha]^{28}_D$ −106.9 (*c* 0.58, $CHCl_3$); IR (neat) 3160, 3139, 3125, 2957, 1738, 1492, 1480, 1453, 1434, 1381, 1365, 1230, 1216, 1200, 1130, 1095, 1073, 1054, 1026, 760, 741, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.48 (m, 4H), 7.16−7.34 (m, 11H), 4.41−4.48 (m, 1H), 4.24 (d, ^3J = 6.7 Hz, 1H), 3.55 (dxd, ^2J = 10.23 Hz, ^3J = 4.97 Hz, 1H), 3.47 (dxd, ^2J = 10.23 Hz, ^3J = 4.38 Hz, 1H), 3.17 (s, 3H), 2.63−2.73 (sept, ^3J = 6.7 Hz, 1H), 1.24 (d, ^3J = 6.7 Hz, 3H), 1.16 (d, ^3J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2 (d, J = 19 Hz), 142.1 (d, J = 14 Hz), 140.0, 130.5, 130.4, 130.3, 130.2, 129.2, 128.9, 128.7, 128.1, 128.0, 128.0, 127.8, 127.8, 127.0, 82.4 (d, J = 19 Hz), 73.3 (d, J = 3,42 Hz), 58.6, 50.6 (d, J = 5.8 Hz), 34.7, 23.4, 23.2; ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.2; HRMS (ES+) m/z calcd for $C_{25}H_{29}O_2PNaS$ 447.1524 $[M + Na]^+$, found 447.1517.

((1*R*,2*S*)-1-(Cyclohexylthio)-3-methoxy-1-phenylpropan-2-yloxy)-diphenylphosphine (4l). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3l** (31 mg, 0.11 mmol), DMAP (1.4 mg, 0.011 mmol), NEt_3 (19 μL, 0.13 mmol), and chlorodiphenylphosphine (20 μL, 0.11 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4l** as an oil (35 mg, 68% yield): $[\alpha]^{28}_D$ −104.9 (*c* 0.54, $CHCl_3$); IR (neat) 2924, 2850, 1492, 1480, 1449, 1435, 1129, 1096, 1070, 927, 885, 741, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14−7.46 (m, 15H), 4.38−4.44 (m, 1H), 4.23 (d, ^3J = 6.72 Hz, 1H), 3.54 (dxd, ^2J = 10 Hz, ^3J = 6.72 Hz, 1H), 3.44 (dxd, ^2J = 10 Hz, ^3J = 4.4 Hz, 1H), 3.14 (s, 3H), 2.42−2.50 (m, 1H), 1.92−1.95 (br d, 1H), 1.63−1.79 (m, 4H), 1.14−1.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2 (d, J = 18.3 Hz), 142.1 (d, J = 14.54 Hz), 140.2, 130.5, 130.4, 130.3, 130.2, 129.1, 129.0, 128.7, 128.2, 128.0, 128.0, 127.9, 127.8, 127.0, 82.6 (d, J = 19 Hz), 73.4 (d, J = 3,3 Hz), 58.6, 50.0 (d, J = 6.6 Hz), 43.3, 33.5, 29.7, 26.0, 25.8, 25.8; ^{31}P NMR (162, MHz, $CDCl_3$) δ 119.0; HRMS (ES+) m/z calcd for $C_{28}H_{33}O_2NaPS$ 487.1837 $[M + Na]^+$, found 487.1830.

((1*R*,2*S*)-1-(*tert*-Butylthio)-3-methoxy-1-phenylpropan-2-yloxy)-diphenylphosphine (4m). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3m** (53.4 mg, 0.21 mmol), DMAP (2.6 mg, 0.021 mmol), NEt_3 (35 μL, 0.25 mmol), and chlorodiphenylphosphine (39 μL, 0.21 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4m** as an oil (84 mg, 91% yield): $[\alpha]^{27}_D$ −116.6 (*c* 0.63, $CHCl_3$); IR (neat) 3056, 3000, 2960, 2938, 2895, 1492, 1480, 1471, 1453, 1437, 1364, 1189, 1127, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.44 (m, 15H), 4.32−4.39 (m, 1H), 4.19 (d, ^3J = 6.4 Hz, 1H), 3.49 (dxd, ^2J = 9.7 Hz, ^3J = 4.97 Hz, 1H), 3.32 (dxd, ^2J = 9.7 Hz, ^3J = 5.1 Hz, 1H), 3.13 (s, 3H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3 (d, J = 19 Hz), 142.1 (d, J = 14 Hz), 141.9, 130.5 (d, J = 13.8 Hz), 130.355 (d, J = 15 Hz), 129.452, 129.0, 128.7, 128.0, 128.0, 127.8 (d, J = 6.8 Hz), 126.7, 83.3 (d, J = 19 Hz), 73.0 (d, J = 3.75 Hz), 58.5, 49.2 (d, J = 5.8 Hz), 44.2, 31.3; ^{31}P NMR (162, MHz, $CDCl_3$) δ 118.7; HRMS (ES+) m/z calcd for $C_{26}H_{31}O_2PNaS$ 461.1680 $[M + Na]^+$, found 461.1682.

4m·PdCl$_2$. To a Schlenk flask containing the thiophosphinite ligand **4m** (2.02 mg, 0.0046 mmol) in CH_2Cl_2 (0.1 mL) was added $(MeCN)_2PdCl_2$ (1.19 mg 0.0046 mmol), and the reaction was stirred for 30 min. The solution was concentrated in vacuo, and the residue diluted with CH_2Cl_2 (0.1 mL). Et_2O (1.1 mL)

was then added rapidly with stirring to precipitate **4m·PdCl$_2$**, which was filtered and dried in vacuo overnight. An X-ray quality crystal was obtained by slow diffusion of Et_2O into a solution of **4m·PdCl$_2$** in CH_2Cl_2.

((1*R*,2*S*)-1-(Adamantylthio)-3-methoxy-1-phenylpropan-2-yloxy)-diphenylphosphine (4n). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **3n** (37 mg, 0.11 mmol), DMAP (1.3 mg, 0.011 mmol), NEt_3 (19 μL, 0.13 mmol), and chlorodiphenylphosphine (20 μL, 0.11 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **4n** as an oil (45 mg, 78% yield): $[\alpha]^{28}_D$ −129.7 (*c* 0.49, $CHCl_3$); IR (neat) 2901, 2847, 1492, 1480, 1450, 1434, 1343, 1300, 1128, 1095, 1071, 966, 945, 924, 751, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.44 (m, 4H), 7.14−7.31 (m, 14H), 4.30−4.36 (m, 1H), 4.26 (d, ^3J = 6.31 Hz, 1H), 3.50 (dxd, ^2J = 9.8 Hz, ^3J = 5.01 Hz, 1H), 3.33 (dxd, ^2J = 9.8 Hz, ^3J = 5.02 Hz, 1H), 3.12 (s, 3H), 1.94 (br s, 3H), 1.71−1.81 (br m, 6H), 1.57−1.64 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3 (d, *J* = 19.3 Hz), 142.4, 142.2 (d, *J* = 13.9 Hz), 130.6, 130.5, 130.4, 130.2, 129.3, 129.0, 128.7, 128.0, 128.0, 128.0, 127.8, 126.6, 83.6 (d, *J* = 19 Hz), 73.1 (d, *J* = 3,3 Hz), 58.5, 46.5 (d, *J* = 6.5 Hz), 43.7, 43.7, 36.2, 29.7; ^{31}P NMR (162, MHz, $CDCl_3$) δ 118.7; HRMS (ES+) *m*/*z* calcd for $C_{32}H_{38}O_2PS$: 517.2330 $[M + H]^+$, found 517.2302.

((1*R*,2*S*)-1-(Adamantylthio)-1-phenyl-3-(trityloxy)propan-2-yloxy)diphenylphosphine (10a). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **9a** (100 mg, 0.18 mmol), DMAP (2.2 mg, 0.018 mmol), NEt_3 (30 μL, 0.21 mmol), and chlorodiphenylphosphine (33 μL, 0.18 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **10a** as an oil (120 mg, 90% yield): $[\alpha]^{26}_D$ −88.5 (*c* 0.39, $CHCl_3$); IR (neat) 3054, 2901, 2847, 1738, 1490, 1448, 1434, 1350, 1299, 1217, 1155, 1071, 1029, 977, 924, 898, 849, 742, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06−7.43 (m, 30H), 4.37−4.43 (m, 1H), 4.35 (d, ^3J = 4.31 Hz, 1H), 3.20 (dxd, ^2J = 9.8 Hz, ^3J = 5.7 Hz, 1H), 2.96 (dxd, ^2J = 9.8 Hz, ^3J = 6.3 Hz, 1H), 1.93 (br s, 3H), 1.56−1.78 (br m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 143.0 (d, *J* = 19.8 Hz), 142.2 (d, *J* = 14.61 Hz), 141.1, 130.7 (d, *J* = 21.3 Hz), 130.5 (d, *J* = 22.0 Hz), 129.5, 128.9, 128.8, 128.6, 128.0 (d, *J* = 6.0 Hz), 127.9 (d, *J* = 6.0 Hz), 127.7, 127.7, 126.9, 126.4, 87.0, 84.4 (d, *J* = 19 Hz), 64.6 (d, *J* = 3.8 Hz), 46.9 (d, *J* = 5.7 Hz), 46.3, 43.7, 36.2, 29.7; ^{31}P NMR (162, MHz, $CDCl_3$) δ 117.7; HRMS (ES+) *m*/*z* calcd for $C_{50}H_{50}O_2PS$ 745.3269 $[M + H]^+$, found 745.3264.

((1*R*,2*S*)-1-(Cyclohexylthio)-1-mesityl-3-methoxypropan-2-yloxy)diphenylphosphine (7l). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **6l** (38 mg, 0.1 mmol), DMAP (1.2 mg, 0.01 mmol), NEt_3 (17 μL, 0.12 mmol), and chlorodiphenylphosphine (19 μL, 0.1 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **7l** as an oil (41 mg, 79% yield): $[\alpha]^{27}_D$ −41.0 (*c* 0.36, $CHCl_3$); IR (neat) 2924, 2851, 1738, 1435, 1375, 1217, 1094, 1052, 946, 738, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.42 (m, 1H), 7.23−7.30 (m, 3H), 7.1−7.13 (m, 1H), 6.97−7.01 (m, 2H), 6.64−6.67 (m, 4H), 4.62 (d, ^3J = 10.9 Hz, 1H), 4.48−4.54 (m, 1H), 3.82 (s, 1H), 3.81 (s, 1H), 3.18 (s, 3H), 2.57−2.64 (m, 1H), 2.38 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H), 2−2.04 (m, 1H), 1.86−1.91 (m, 1H), 1.66−1.78 (m, 2H), 1.52−1.58 (m, 1H), 1.17−1.37 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, (d, *J* = 17.6 Hz), 142.2 (d, *J* = 14.7 Hz), 136.8, 136.5, 135.7, 134.9, 131.0, 130.0 (d, *J* = 21.6 Hz), 130.0 (d, *J* = 21.9 Hz), 128.9, 128.7, 128.2, 127.9 (d, *J* = 6.6 Hz), 127.4 (d, *J* = 7.1 Hz), 82.1 (d, *J* = 19.1 Hz), 73.7 (d, *J* = 3.1 Hz), 58.5, 45.1, 43.9 (d, *J* = 5.9 Hz), 34.3, 33.8, 26.2, 26.1, 25.8, 21.7, 21.3 (d, *J* = 2.2 Hz), 20.8; ^{31}P NMR (162, MHz, $CDCl_3$) δ 117.3; HRMS (ES+) *m*/*z* calcd for $C_{31}H_{40}O_2PS$: 507.2487 $[M + H]^+$, found 507.2506.

((1*R*,2*S*)-1-(*tert*-Butylthio)-1-mesityl-3-methoxypropan-2-yloxy)-diphenylphosphine (7m). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **6m** (26.7 mg, 0.09 mmol), DMAP (1.1 mg, 0.009 mmol), NEt_3 (15 μL, 0.11 mmol), and chlorodiphenylphosphine (17 μL, 0.09 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **7m** as an oil (39 mg, 90% yield): $[\alpha]^{25}_D$ = −23.4 (*c* 0.58, $CHCl_3$); IR (neat) 2920, 2894, 2861, 1479, 1470, 1457, 1435, 1126, 1093, 1068, 1054, 1028, 1000, 967, 947, 739, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.44 (m, 2H), 7.25−7.31 (m, 3H), 7.09−7.13 (m, 1H), 6.96−7 (m, 2H), 6−6.64 (m, 4H), 4.6 (d, ^3J = 11 Hz, 1H), 4.33−4 (m, 1H), 3.8−3.86 (m, 2H), 3.14 (s, 3H), 2.37 (s, 3H), 2.36 (s, 3H), 2.20 (s, 3H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, (d, *J* = 18.3 Hz), 142.2 (d, *J* = 13.2 Hz), 137.0, 136.2, 136.2, 135.4, 131.0, 130.0 (d, *J* = 22 Hz), 128.9, 128.7, 128.2, 127.9 (d, *J* = 7.0 Hz), 127.4 (d, *J* = 6.6 Hz), 81.9 (d, *J* = 19.8 Hz), 73.3 (d, *J* = 2.85 Hz), 58.4, 44.6, 42.7 (d, *J* = 6.5 Hz), 31.3, 21.5 (d, *J* = 2.7 Hz), 20.8; ^{31}P NMR (162, MHz, $CDCl_3$) δ 117.8; HRMS (ES+) *m*/*z* calcd for $C_{29}H_{38}O_2PS$ 481.2330 $[M + H]^+$, found 481.2314.

((1*R*,2*S*)-1-(Adamantylthio)-1-mesityl-3-methoxypropan-2-yloxy)diphenylphosphine (7n). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **6n** (26 mg, 0.07 mmol), DMAP (0.8 mg, 0.007 mmol), NEt_3 (12 μL, 0.08 mmol), and chlorodiphenylphosphine (13 μL, 0.07 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **7n** as an oil (33 mg, 85% yield): $[\alpha]^{26}_D$ −45.7 (*c* 0.42, $CHCl_3$); IR (neat) 2903, 2848, 1479, 1450, 1434, 1376, 1343, 1300, 1254, 1126, 1093, 1053, 946, 909, 888, 737, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.44 (m, 1H), 7.23−7.30 (m, 3H), 7.09−7.12 (m, 1H), 6.96−7 (m, 2H), 6.59−6.63 (m, 4H), 4.62 (d, ^3J = 11.1 Hz, 1H), 4.33−4.40 (m, 1H), 3.86 (dxd, ^2J = 10 Hz, ^3J = 2.1 Hz, 1H), 3.80 (dxd, ^2J = 10 Hz, ^3J = 4.4 Hz, 1H), 3.14 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H), 2.2 (s, 3H), 1.98 (br s, 3H), 1.59−1.87 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9 (d, *J* = 18 Hz), 142.3 (d, *J* = 13.9 Hz), 137.0, 136.6, 135.8, 135.3, 131.9, 130.0 (d, *J* = 22 Hz), 130.0 (d, *J* = 22 Hz), 128.9, 128.6, 128.1, 127.8 (d, *J* = 7 Hz), 127.4 (d, *J* = 6.6 Hz), 82.0 (d, *J* = 19.6 Hz), 73.5 (d, *J* = 2.7 Hz), 58.4, 43.7, 40.0 (d, *J* = 6.4 Hz), 36.2, 29.7, 21.8, 21.5 (d, *J* = 2.2 Hz), 20.8; ^{31}P NMR (162, MHz, $CDCl_3$) δ 117.8; HRMS (ES+) *m*/*z* calcd for $C_{35}H_{43}O_2NaPS$ 581.2619 $[M + Na]^+$, found 581.2620.

((1*R*,2*S*)-1-(*tert*-Butylthio)-1-mesityl-3-(trityloxy)propan-2-yloxy)diphenylphosphine (10b). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **9b** (79 mg, 0.15 mmol), DMAP (1.9 mg, 0.015 mmol), NEt_3 (25 μL, 0.18 mmol), and chlorodiphenylphosphine (28 μL, 0.15 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **10b** as an oil (98 mg, 92% yield): $[\alpha]^{26}_D$ +13.1 (*c* 0.33, $CHCl_3$); IR (neat) 3056, 2958, 2917, 1738, 1596, 1488, 1447, 1363, 1261, 1219, 1157, 1083, 1048, 1022, 998, 966, 943, 913, 807, 740, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−7.30 (m, 21H), 6.9−6.94 (m, 2H), 6.72−6.75 (m, 2H), 6.45 (s, 1H), 6.38 (s, 1H), 4.4−4.47 (m, 1H), 4.21 (d, ^3J = 11 Hz, 1H), 3.99 (dxd, ^2J = 10 Hz, ^3J = 1.5 Hz, 1H), 3.22 (dxd, ^2J = 10 Hz, ^3J = 6.5 Hz, 1H), 2.24 (s, 3H), 2.22 (s, 3H), 2.05 (s, 3H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0,

143.6 (d, J = 16 Hz), 142.4 (d, J = 16.8 Hz), 137.1, 135.7, 135.5, 135.4, 131.0, 130.4 (, d, J = 24 Hz), 129.7 (d, J = 21.67 Hz), 128.9, 128.9, 128.3, 127.8 (d, J = 6.6 Hz), 127.5, 127.3 (d, J = 7.4 Hz), 126.7, 87.2, 82.9 (d, J = 20.4 Hz), 67.2 (d, J = 2.32 Hz), 44.1, 43.6 (d, J = 5.2 Hz), 31.2, 21.7 (d, J = 3.1 Hz), 20.7; ^{31}P NMR (162, MHz, $CDCl_3$) δ 116.8; HRMS (ES+) m/z calcd for $C_{47}H_{50}O_2PS$ 709.3269 $[M + Na]^+$, found 709.3268.

((1*R*,2*R*)-1-(Adamantylthio)-1-phenyl-3-(trityloxy)propan-2-yloxy)diphenylphosphine (10a-*syn*). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **9a-*syn*** (100 mg, 0.18 mmol), DMAP (2.2 mg, 0.018 mmol), NEt_3 (30 μL, 0.21 mmol), and chlorodiphenylphosphine (33 μL, 0.18 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **10a-*syn*** as a white solid (120 mg, 90% yield): $[\alpha]^{27}_D$ −73.1 (c 0.51, $CHCl_3$); IR (neat) 3054, 2901, 1597, 1490, 1447, 1434, 1342, 1071, 741, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.41 (m, 4H), 7.32−7.35 (m, 6H), 7.27−7.29 (m, 3H), 7.18−7.24 (m, 14H), 7.08−7.1 (m, 3H), 4.22−4.28 (m, 1H), 3.36 (dxd, ^2J = 9.5 Hz, ^3J = 5.4 Hz, 1H), 3.16 (dxd, ^2J = 10.4 Hz, ^3J = 5.4 Hz, 1H), 1.88 (br s, 3H), 1.51−1.69 (br m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 142.8 (d, J = 19.2 Hz), 142.9, 142.2 (d, J = 15.9 Hz), 131.0 (d, J = 22.7 Hz), 130.5 (d, J = 22.2 Hz), 129.0, 128.9, 128.8, 128.7, 128.0 (d, J = 7.3 Hz), 128.0 (d, J = 7.3 Hz), 127.8, 127.7, 126.8, 126.5, 86.1, 84.6 (d, J = 18.3 Hz), 65.3 (d, J = 4.3 Hz), 47.6 (d, J = 5.2 Hz), 45.7, 43.7, 36.2, 29.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 117.2; HRMS (ES+) m/z calcd for $C_{50}H_{49}O_2PSNa$ 767.3089 [M], found 767.3052.

((1*R*,2*R*)-1-(*tert*-Butylthio)-1-phenyl-3-(trityloxy)propan-2-yloxy)diphenylphosphine (10b-*syn*). The following reagents were combined in the amounts indicated according to the general procedure for the phosphinite incorporation: **9b-*syn*** (100 mg, 0.19 mmol), DMAP (2.4 mg, 0.019 mmol), NEt_3 (32 μL, 0.23 mmol), and chlorodiphenylphosphine (35 μL, 0.19 mmol). The resulting slurry was loaded onto a plug of silica and purified by flash chromatography (1 × 3 cm, 95% hexane, 5% ethyl acetate) to yield **10b-*syn*** as a white solid (112 mg, 83% yield): $[\alpha]^{27}_D$ −52.5 (c 0.51, $CHCl_3$); IR (neat) 3057, 2959, 2914, 2860, 1597, 1448, 1260, 1064, 984, 926, 799, 739, 693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.63 (m, 4H), 7.07−7.32 (m, 21H), 6.62 (s, 1H), 6.57 (s, 1H), 4.54−4.62 (m, 1H), 4.24 (d, ^3J = 8.9 Hz, 1H), 2.96−3.05 (m, 2H), 2.33 (s, 3H), 2.17 (s, 3H), 2.15 (s, 3H), 0.95 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 143.1 (d, J = 17.6 Hz), 142.7 (d, J = 16.1 Hz), 137.2, 135.8, 135.5, 134.2, 132.1 (d, J = 22.7 Hz), 131.4, 130.4 (d, J = 22.3 Hz), 129.0, 128.9, 128.6, 127.9 (d, J = 6.9 Hz), 127.7 (d, J = 7.3 Hz), 127.4, 126.6, 87.1, 84.0 (d, J = 19.7 Hz), 66.4 (d, J = 2.9 Hz), 46.8 (d, J = 4.4 Hz), 43.83, 31.1, 22.2, 21.5, 20.7; ^{31}P NMR (162, MHz, $CDCl_3$) δ 118.6; HRMS (ES+) m/z calcd for $C_{47}H_{50}O_2PS$ 709.3269 $[M - H]^-$, found 709.3250.

((1*R*,2*R*)-1-(Adamantylthio)-1-phenyl-3-(trityloxy)propan-2-yloxy)diphenylphosphinepalladium(II) Chloride (10a-*syn*)·PdCl$_2$. To a Schlenk flask containing the thiophosphinite ligand **10a-*syn*** (34.3 mg, 0.046 mmol) in CH_2Cl_2 (1 mL) was added $(MeCN)_2PdCl_2$ (11.9 mg 0.046 mmol), and the reaction was stirred for 40 min. The solution was concentrated in vacuo, and the residue was diluted with CH_2Cl_2 (0.6) mL. Then Et_2O (10 mL) was added rapidly with stirring to precipitate **PdCl$_2$-10a-*syn***, which was filtered and dried in vacuo overnight (42 mg, 99% yield): mp >200 °C; $[\alpha]^{27}_D$ −108.2 (c 0.54, CH_2Cl_2); IR (neat) 3054, 2901, 1597, 1490, 1447, 1434, 1342, 1071, 741, 694 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.28−8.33 (m, 2H), 7.81−7.86 (m, 2H), 7.60−7.65 (m, 1H), 7.52−7. 57 (m, 2H), 7.40−7.43 (m, 1H), 7.08−7.33 (m, 22H), 4.41 (d, J^3 = 10.6 Hz, 1H), 3.82−3.88 (m, 1H), 2.85 (dxd, ^2J = 10.6 Hz, ^3J = 2.2 Hz, 1H), 2.39 (dxd, ^2J = 10.6 Hz, ^3J = 2.2 Hz, 1H), 2.22 (br d, 3H), 1.99 (br s, 6H), 1.55−1.64 (br m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3 (d, J = 26.6 Hz), 147.3 (d, J = 27 Hz), 143.4, 136.7, 134.5 (d, J = 13 Hz), 133.1, 133.2, 129.9, 129.6, 129.2 (d, J = 12.2 Hz), 128.8 (d, J = 17.8 Hz), 128.7, 128.6, 128.5, 128.2, 127.6, 87.1, 80.6, 62.9 (d, J = 6.8 Hz), 60.6, 47.6 (d, J = 5.2 Hz), 44.3, 42.7, 35.8, 30.8; ^{31}P NMR (162 MHz, CD_2Cl_2) δ 110.8. X-ray quality crystals were grown by slow vapor diffusion of Et_2O into a solution of **PdCl$_2$-10a-*syn*** in CH_2Cl_2 to yield orthorhombic crystals. A suitable crystal (0.15 × 0.15 × 0.06 mm) was chosen for X-ray diffraction analysis; see the Supporting Information.

General Procedure for the Palladium-Catalyzed Allylic Alkylation Reaction. To a Schlenck flask containing ligand **10b-*syn*** (4.215 mg, 0.006 mmol) and $[(C_3H_5)PdCl]_2$ (1.088 mg, 0.006 mmol Pd) was added CH_2Cl_2 (0.6 mL). After 1 h of stirring at rt, 1,3-diphenylpropenyl acetate (60 mg, 0.238 mmol) dissolved in CH_2Cl_2 (0.6 mL) was added, followed by dimethyl malonate (82 μL, 0.71 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (177 μL, 0.71 mmol), and a pinch of KOAc. The mixture was stirred at room temperature for 20 min and then was diluted with diethyl ether and washed with saturated $NH_4Cl_{(aq)}$. The organic layers were dried over $MgSO_4$ and filtered, and the solvents were evaporated in vacuo. The residue was purified by flash chromatrography (85% hexane, 15% EtOAc) to afford **(*S*,*E*)-dimethyl 2-(1,3-diphenylallyl)malonate** as a colorless oil. The absolute configuration of the product was assigned by comparing the sign of its specific rotation with literature data.[5j] HPLC analysis (Chiralcel-AD-H, hexane/2-propanol 95:5, 1 mL/min, 254 nm, t_R = 21 min, t_S = 24 min) showed the ee to be 96%.

(*S*)-Methyl 2-Carbomethoxy-3,5,5-triphenylpent-4-enoate (P2). The following reagents were combined in the amounts indicated according to the general procedure for the allylic alkylation with dimethyl malonate: **9a-*syn*** (2.48 mg, 0.003 mmol), $[(C_3H_5)PdCl]_2$ (0.54 mg, 0.003 mmol), 1,3,3-triphenylpropenyl acetate (**S2**) (39 mg, 0.12 mmol), dimethyl malonate (41 μL, 0.36 mmol), BSA (88 μL, 0.36 mmol), and a pinch of potassium acetate. The product was purified by flash chromatography (9:1 hexane/ethyl acetate) to yield **P3** as an oil (26 mg, 54% yield). The absolute configuration of the product was assigned by comparing the sign of its specific rotation with literature data. $[\alpha]^{25}_D$ = −182 (c 0.3, CH_2Cl_2); $[\alpha]^{25}_D$ = −186 (c 0.44, CH_2Cl_2) for optically pure **P2**. HPLC analysis (AD-H column, 0.3 mL/min *n*-hexane/2-propanol 97:3: t_R = 44.7 min, t_S = 46.7 min) showed the ee to be 97%.

(*S*)-Methyl 2-Carbomethoxy-3-methyl-5,5-diphenylpent-4-enoate (P3). The following reagents were combined in the amounts indicated according to the general procedure for the allylic alkylation with dimethyl malonate: **9a** (5.3 mg, 0.007 mmol), $[(C_3H_5)PdCl]_2$ (1.08 mg, 0.006 mmol), 4,4-diphenylbutenyl-2-acetate (**S3**) (63 mg, 0.24 mmol), dimethyl malonate (82 μL, 0.71 mmol), BSA (177 μL, 0.71 mmol), and a pinch of potassium acetate. The product was purified by flash chromatography (9:1 hexane/ethyl acetate) to yield **P3** as an oil (33 mg, 40% yield). HPLC analysis (OD-H column, 1 mL/min *n*-hexane/2-propanol 99:1: t_R = 9.1 min, t_S = 10.6 min) showed the ee to be 82%.

General Procedure for the Palladium-Catalyzed Allylic Amination Reaction. To a Schlenk flask containing ligand **10b-*syn*** (4.215 mg, 0.006 mmol) and $[(C_3H_5)PdCl]_2$ (0.725 mg, 0.004 mmol Pd) was added CH_2Cl_2 (0.5 mL). After 1 h of stirring at rt, 1,3-diphenylpropenyl acetate (40 mg, 0.16 mmol) dissolved in CH_2Cl_2 (0.5 mL) was added, followed by benzylamine (52 μL, 0.476 mmol). The mixture was stirred at room temperature for 4 h. Then the mixture was diluted with diethyl ether and washed with saturated NH_4Cl_{aq}. The organic layers were dried over $MgSO_4$ and filtered and the solvents were evaporated *in vacuo*. The residue was purified by flash chromatrography (87% hexane, 13% EtOAc) to afford **(*R*,*E*)-*N*-benzyl-1,3-diphenylprop-2-en-1-amine** (97% yield) as a colorless oil. The absolute configuration of the product was assigned by comparing the sign

of its specific rotation with literature data.[5j] HPLC analysis (Chiralcel-OJ, hexane/2-propanol 87:13, 0.5 mL/min, 254 nm, t_S = 14.2 min, t_R = 17.5 min) showed the ee to be 94%.

General Procedure for the Palladium-Catalyzed Allylic Etherification Reaction. To a Schlenk flask containing ligand **10b-*syn*** (3.717 mg, 0.005 mmol) and $[(C_3H_5)PdCl]_2$ (0.914 mg, 0.005 mmol Pd) was added toluene (0.6 mL). After 1 h of stirring at rt, 1,3-diphenylpropenyl acetate (31.5 mg, 0.125 mmol) dissolved in CH_2Cl_2 (0.5 mL) was added, followed by cesium carbonate (122 mg, 0.375 mmol) and benzyl alcohol (39 μL, 0.375 mmol). The mixture was stirred at 0 °C for 3 h, and then the mixture was diluted with ethyl acetate and washed with saturated NH_4Cl_{aq}. The organic layers were dried over $MgSO_4$ and filtered, and the solvents were evaporated under vacuum. The residue was purified by flash chromatography (95% hexane, 5% Et_2O) to afford (***R*,*E*)-(3-(benzyloxy)prop-1-ene-1,3-diyl)dibenzene** (96% yield) as a colorless oil. The absolute configuration of the product was assigned by comparing the sign of its specific rotation with literature data.[5t] HPLC analysis (Chiralcel-OJ-H, hexane/2-propanol 98:2, 0.75 mL/min, 254 nm, t_S = 27.9 min, t_R = 34 min) showed the ee to be 94%.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra. Crystallographic data for (**10a-*syn*)·$PdCl_2$** and **4 m·$PdCl_2$** (CIF). Cartesian coordinates and energies of TS C2 and TS C3 calculated at the BLYP/6-31G (d) level. This material is available free of charge via the Internet at http://pubs.acs.org.