New, Optically Active Phosphine Oxazoline (JM-Phos) Ligands: Syntheses and Applications in Allylation Reactions

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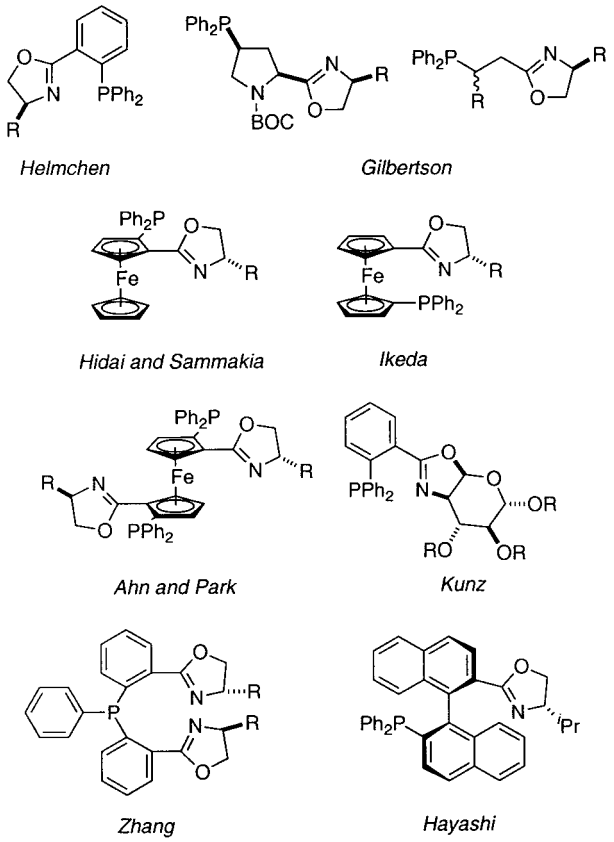
Three different syntheses of the phosphine oxazoline systems **1** are presented. Two of these approaches are divergent routes designed to involve an advanced intermediate that can be transformed into several different end-products. The third is a shorter route specifically designed to facilitate preparations of these systems on a larger scale using minimal functional group protection. Overall, eight different phosphine oxazolines were prepared. These were screened in several palladium-mediated allylation reactions. They proved to be most useful for asymmetric alkylation of 3-acetoxy-1,3-diphenylpropene and less suitable/effective for the more challenging substrates (a pentenyl derivative and a cyclohexenyl system). X-ray crystallographic analysis of the complex [(η^3-PhCHCHCHPh)Pd(**1a**)][PF_6] led to the conclusion that the origins of asymmetric induction in these systems might be indirectly attributed to interaction of the oxazoline-phenyl substituent with the palladium *and* with an allyl-phenyl substituent. Finally, data is presented for allylation of a silylenolate of an *N*-acyl oxazolidinone; excellent enantioselectivities and yields were obtained.

Some chiral ligands are clearly more useful for asymmetric syntheses than others, but no one structural class is universally ideal for all transformations. It is also impossible to confidently predict which of all of the available asymmetric ligands will be the best for a particular reaction type. Catalyst discovery and optimization therefore involves preliminary designs formulated via chemical intuition, then screening to achieve desirable results.[1−3] Consequently, even for the best ligand designs, it is desirable to have access to small focused libraries, and to have the ability to screen these efficiently.

This paper concerns chiral phosphine oxazoline ligands. Invention of the Pfaltz/Helmchen/Williams phosphine oxazoline[4−9] has inspired other groups to design similar ligands. These ligand types have been extremely useful in allylation reactions, Heck couplings, and other processes.[10] Some of these ligands are shown in Chart 1,[11−19]

Chart 1



and there are others, notably phosphite oxazolines.[20] All of the ligands shown in Chart 1 are derived from amino alcohols. The chiral pool of readily available, optically pure amino alcohols is dominated by amino acid derivatives, carbohydrate amines, and compounds such as

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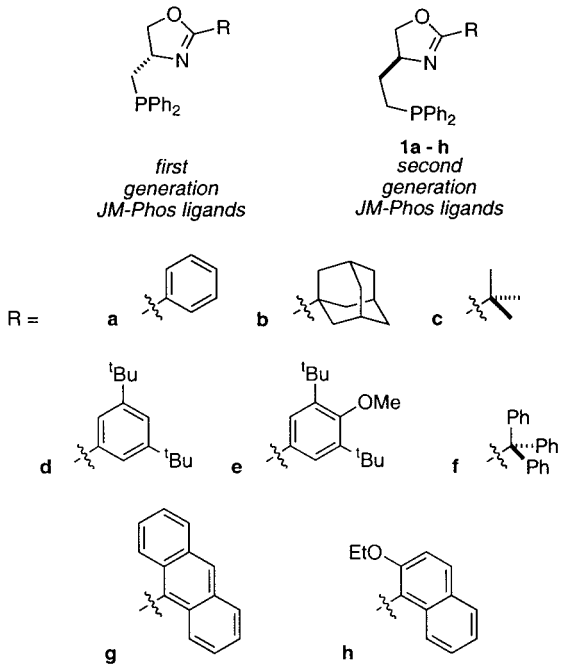
ephedrine. It does not provide a vast and diverse number of chirons for ligand syntheses.

Previous contributions from our group have commented upon the problem of obtaining libraries of catalysts for high throughput screening in catalytic reactions.[21−26] A simple approach to this problem involves generation of an advanced chiral intermediate then transformation of this into a small set of chiral coordinating compounds, i.e., a divergent ligand synthesis. Papers concerning our first generation phosphine oxazoline ligand set[24,25] and a communication on our second generation phosphine oxazoline ligand set **1**[26] have commented on potential advantages of these ligand designs over those shown above. Briefly, the salient points are that (i) the R-functionality is derived from carboxylic acids, and the pool of carboxylic acids available is much larger than for amino alcohols and includes groups with diverse steric, geometric, and electronic properties; (ii) the R-functionality is potentially conjugated with the oxazoline nitrogen so it can be used to tune the ligating properties of this atom; and (iii) the centrally placed chiral center in these ligands gives overall geometries that could be more conducive to asymmetric catalysis of some transformations and will certainly give somewhat different reactivity profiles.

This paper gives full details of the divergent synthesis previously communicated, but applied to prepare a few more ligands than were originally reported (Scheme 1a). Two alternative routes are also described; these are shorter, involve less functional-group protection, and are therefore suitable for scale-up syntheses of specific ligands that "test positive" in high-throughput screens (Scheme 1b and c). Also presented are data from screens using the ligands in four different palladium-mediated allylation reactions, including an unusual asymmetric addition of a chiral silyl enol ether to a π-allyl palladium complex (Figure 1 and reaction 1). Data from an X-ray crystallographic study of a palladium π-allyl complex is also presented.

Results and Discussion

Three Syntheses of the Ligands. Scheme 1a shows our original divergent synthesis of the second generation ligands **1**. The main advantage of this route is that the advanced intermediate **9** can be transformed into many



different phosphine oxazolines (presumably many more than the eight reported here). However, for scale-up purposes this approach is not ideal. It is relatively long, involves an inconvenient separation of isomeric oxazolidines, and protecting groups that increase the length and decrease the atom economy of the approach. Alternatives were therefore highly desirable for planned large scale syntheses of the ligands.

Scheme 1b shows the first alternative that was explored. Like the original synthesis, this begins with aspartic acid but progresses to the oxazolidinone intermediate **14** and then to the amino alcohol **9**. Chiron **9** was the key intermediate used for making a ligand set in Scheme 1a, so this approach accommodates divergence to prepare ligand libraries. This route only involves one less protecting group than the first. However, it is not significantly shorter and involves one weak step. Specifically, tosylation of the alcohol **12** was difficult to achieve selectively because the oxazolidinone was also vulnerable to addition of this reagent. Consequently, the yield of the tosylation step was only 40%, whereas all of the other transformations afforded product in 83% yield or more. We were unable to improve upon this yield or find an effective alternative to circumvent use of tosylate (brosylate, nosylate, and mesylate were tried) in the time available.

Our most direct synthesis is that shown in Scheme 1c. This involves significantly fewer steps than the other two approaches and no protecting groups at all. It is, however, ligand-specific; the R-functionality is set in the second step, but for scale-up purposes this is not a disadvantage. The experimental procedure given in this paper is for preparation of 3.7 g of ligand **1a**. There is no obvious reason why larger batches of this material should not be prepared via this third approach, though one chromatographic separation was used in the final step and this probably sets an upper limit on the scale.

Applications of the Ligands in Allylation Reactions. Figure 1 expands upon the data previously reported for the allylation reaction shown using some of the JM-Phos ligand set.[26] Several reasonably bulky

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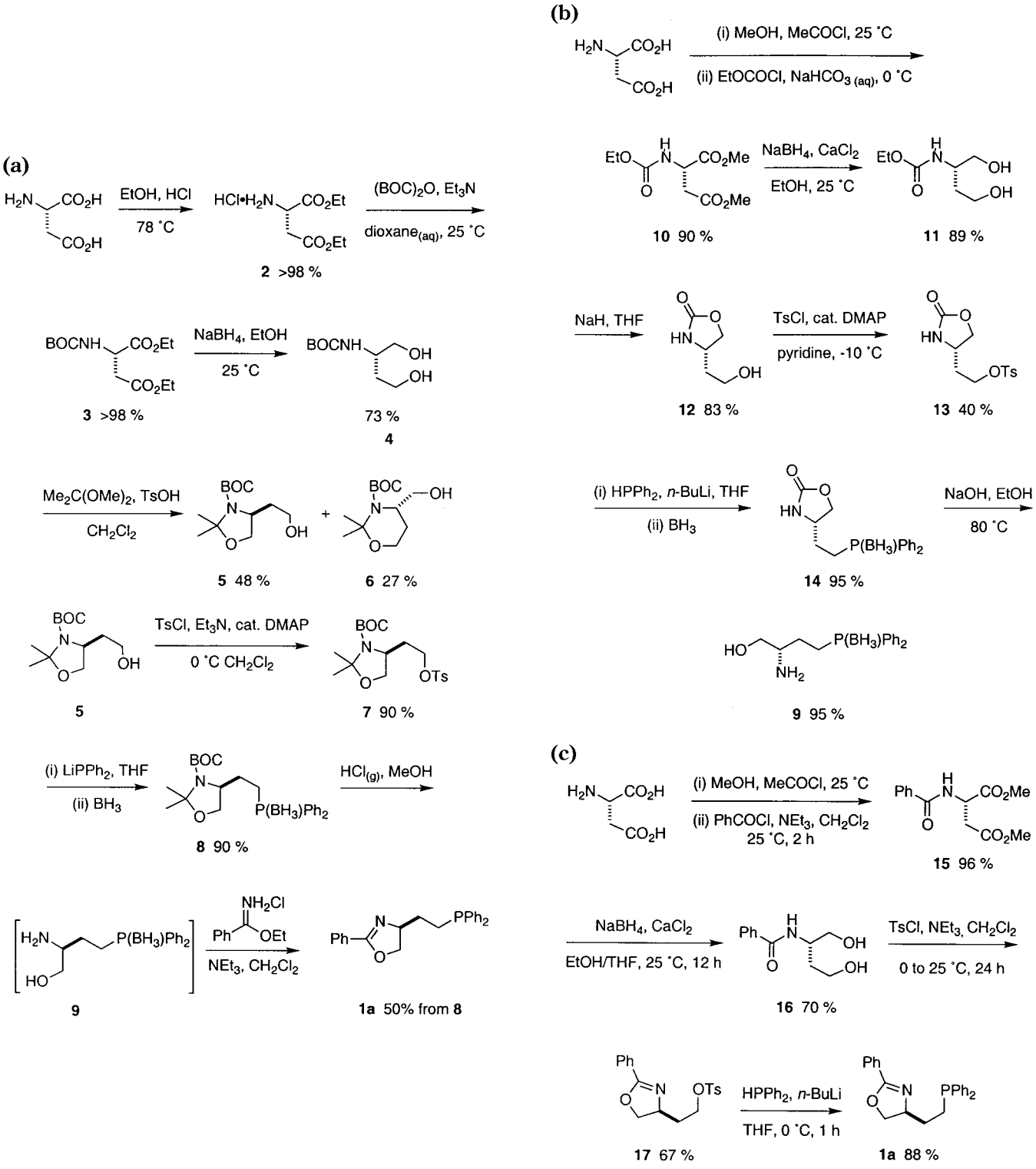
Scheme 1. (a) Original Divergent Synthesis of the JM-Phos Ligands. (b) Alternative Divergent Synthesis of the JM-Phos Ligands. (c) Shorter Synthesis of 1a Designed for Scale-Up



ligands gave excellent yields and enantioselectivities for this reaction; in most cases the minor enantiomer of the product was not detected in chiral HPLC of the crude material. The full ligand set was not tested because in three cases the enantioselectivity was perfect to within experimental error.

Ligand-to-metal ratios in this process are critical, as indicated in the communication of this work. Figure 1b shows that as the ligand-to-metal ratios are increased the enantioselectivities decrease while the yields obtained do not vary significantly. We suspect that the diminished enantioselectivities at higher ligand-to-metal ratios are a consequence of formation of a competing, catalytically active, diphosphine allyl complex that does not involve oxazoline complexation. Others have made similar observations when using the Pfaltz/Helmchen/Williams ligand to prepare catalysts in situ.[27]

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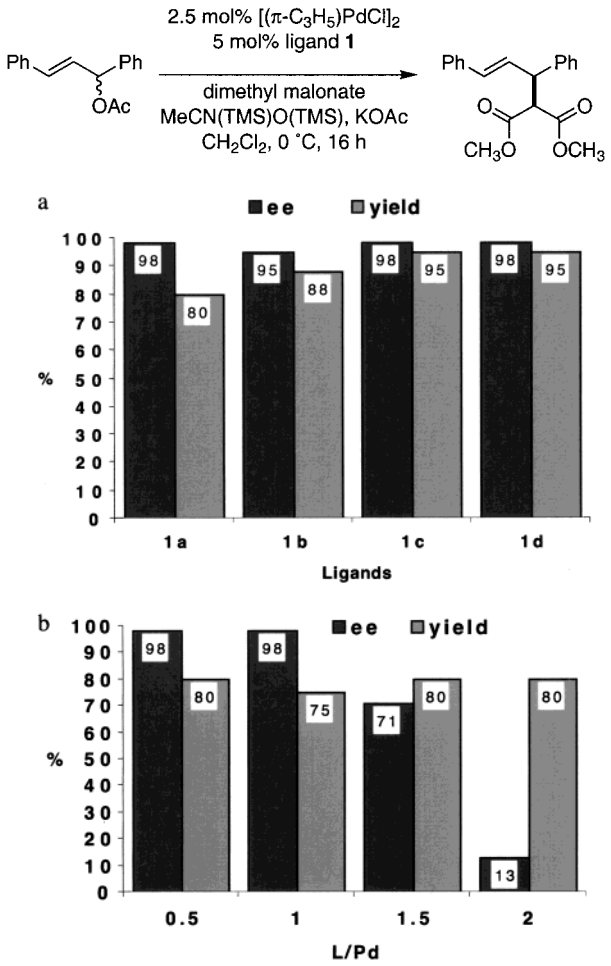

Figure 1. (a) Enantioselectivity and yield data as a function of the ligands used in the reaction shown. (b) Enantioselectivity and yield data as a function of ligand **1a**:metal ratios.

Figure 2 expands on the data set previously reported for the allylation reaction shown. The data presented in Figure 2a was obtained under essentially the same conditions as those used for the previous substrate except that a higher temperature was used (25 vs 0 °C). Ligand **1d** gave the best data (80% ee, 59% yield) in this series. However, slightly better results were obtained when the palladium catalyst precursor $[(\eta^3\text{-}C_3H_5)PdCl]_2$ was replaced with $Pd_2(dba)_3$ to give a chloride free system (Figure 2b). Screens using the full ligand set gave 80% ee and 93% yield for the catalyst from ligand **1d**, and 82% ee and 77% yield for the catalyst from **1e**. Trost[28] and then Gilbertson[11] have observed that systems with tetra-*n*-alkylammonium as the only positive counterion in the reaction can give superior results in the allylations. Figure 2c shows a small screen to probe the effects of added tetra-*n*-butylammonium fluoride. This modification, however, induced a neutral or slightly negative effect on the enantioselectivities and reduced the yields. Overall, the best data presented in Figure 2b are as good or better than that reported for every other palladium-based allylation catalyst for this substrate, with two exceptions. One of the ligand systems developed by Trost

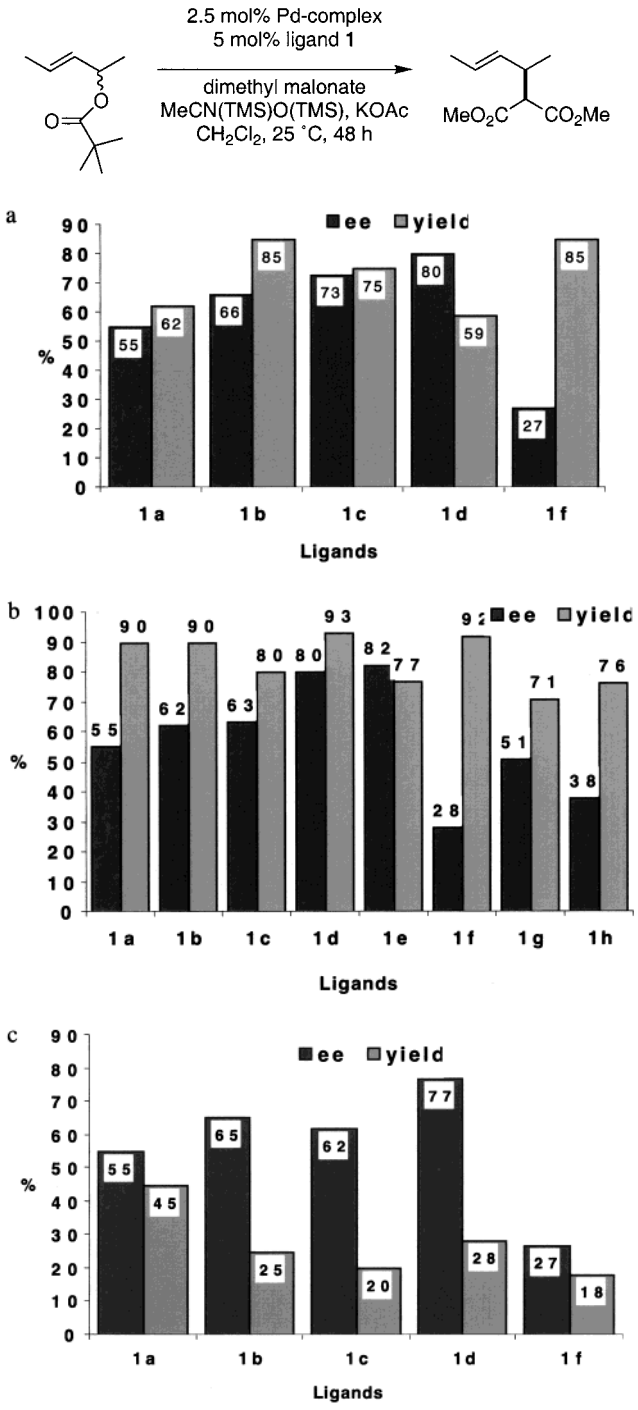

Figure 2. Enantioselectivity and yield data as a function of the ligand used in the reaction shown. (a) Using $[\eta^3\text{-allyl})\text{-}PdCl]_2$ as the palladium source. (b) Using $Pd_2(dba)_3$ as the palladium source (dba, dibenzylidene acetone). (c) Using $Pd_2(dba)_3$ as the palladium source and Bu_4NCl in place of KOAc.

gives enantioselectivies of 92% and comparable yields,[29] and Helmchen et al. have used their phosphine oxazoline in a catalyst system that gives 89.5% ee, but only 20% yield was obtained in 48 h since the reaction temperature used was −40 °C.[30]

Figure 3 shows the data obtained in a small screen using 3-acetoxycyclohexene as a substrate. Like the

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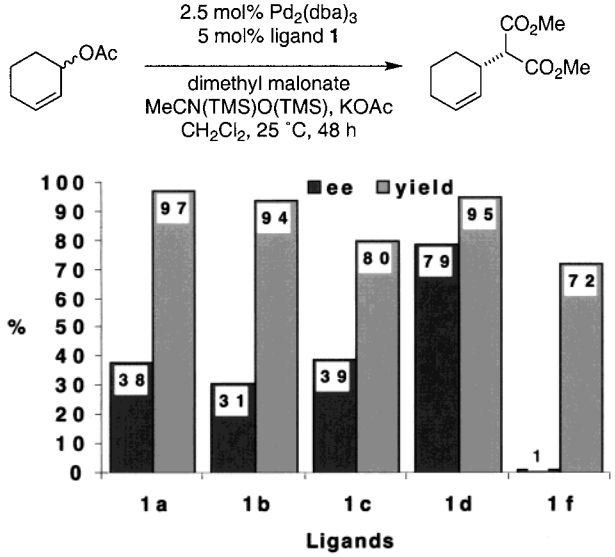


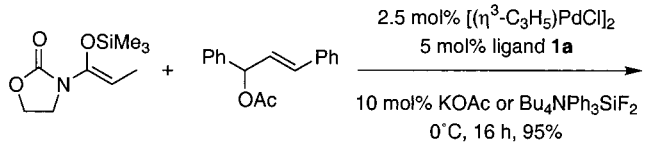
Figure 3. Enantioselectivity and yield data as a function of the ligands used in the reaction shown.

compounds featured in Figure 2, this is a challenging substrate for allylations.[31] The best data was obtained for ligand **1d** (79% ee, 95% yield). Other ligands can give superior enantioselectivities and yields in this reaction (up to approximately 98% ee),[28,32,33] but it is recognized to be more difficult to obtain high enantiomeric excesses than in some acyclic cases.[34]

The allylation reactions described above are some of those most frequently studied in this area of research. That shown in reaction 1, however, is relatively unusual. Silyl enolates in palladium-mediated allylations are not common nucleophiles, and the few literature reports in this area suggest that the yields in these reactions tend to be moderate or low.[35−40] This was not the case for the transformation shown in reaction 1. Excellent yields of product were obtained and, when potassium acetate was used as an additive, the enantiomeric excesses of the two diastereoisomers were both high. Unfortunately, the diastereoselectivity of this reaction was only 2.8:1.0 in both cases and attempts to improve this value by using TBAF·Ph_3SiF in place of potassium acetate additive reduced the enantioselectivity and had no effect on the diastereoselectivity. The relative stereochemistries of **19a** and **19b** were confirmed by taking a X-ray crystal structure of the *syn*-derivative **19a**.

X-ray Crystal Structure of a Palladium-Allyl Complex of Ligand 1a. Helmchen and co-workers have proposed a model for the origin of asymmetric induction in allylation of 1,3-diphenyl-3-acetoxypropene involving catalysts formed from their phosphine oxazoline.[30,34]

reaction 1



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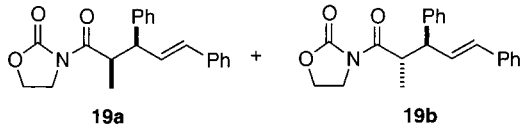

19a **19b**

additive	*syn:anti*	% *ee*, *syn*	% *ee*, *anti*
KOAc	2.8:1.0	95	95
Bu_4NF-Ph_3SiF	2.8:1.0	87	84

Their observations from crystallographic studies led them to conclude that the R-substituent on the chiral oxazoline is relatively close to the palladium and, to avoid this interaction, the ligand tilts away from the near-square planar arrangement of the metal coordinating groups. This tilt induces an edge-to-face orientation of the phenyl groups on the PPh_2 fragment, since one of them is forced to be much closer to the allyl ligand than the other. Figure 4a was produced for such a complex using coordinates obtained from The Cambridge Crystallographic database,[9] and the key interaction between the metal and the isopropyl group in this complex is indicated.

In the research reported here, a palladium complex was obtained from the same allyl ligand and the phosphine oxazoline **1a** (crystallized as hexafluorophosphate salt; Figure 4b). Direct comparisons between the two structures are of limited value because the oxazolines have different R-substituents. Palladium-to-carbon distances for the nearest C-atom of the isopropyl group in the first structure and for the oxazoline phenyl-substituent in the second structure are similar at approximately 3.5 Å. Indeed, the JM-Phos ligand in this complex is tilted away from the square plane formed by the atoms coordinated to the palladium, and this Pd-to-oxazoline-substituent interaction may play a major role in producing that tilt. It is possible, however, that this is not the only contributing factor. The main difference between the two structures is that the oxazoline phenyl-substituent in the JM-Phos complex is closer to the closest phenyl of the allyl ligand than the isopropyl group is in the first structure (approximately 3.5 and 4.1 Å between the closest C-atoms, respectively). This is true even though the oxazoline-phenyl and the relevant allyl-phenyl in the complex of ligand **1a** adopt a face-to-face orientation, i.e., they align to minimize the contacts in the solid state. Consequently, we conclude that the oxazoline substituents project more toward the allyl-phenyl groups in complexes of the JM-Phos ligands than the corresponding substituents in similar complexes of the Helmchen/Pfaltz/Williams phosphine oxazolines.

Conclusions

The synthetic procedures demonstrated in this paper enable a small library of phosphine oxazolines **1** to be prepared. These are similar to, but structurally distinct from, the well-known Pfaltz/Helmchen/Williams ligand

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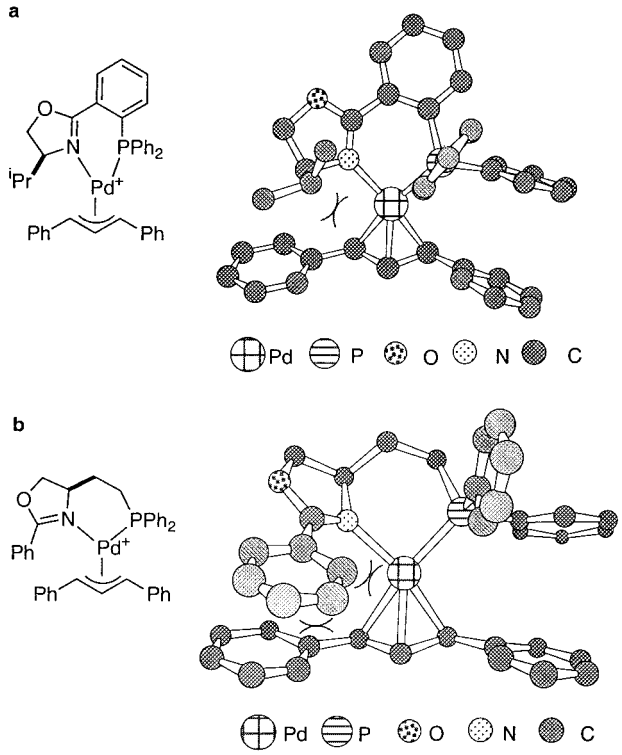

Figure 4. A Chem3D representations of the two allyl complexes shown from data collected via X-ray crystallography.

systems and many other derivatives of these. In allylation reactions the performance of some of the ligands **1** were comparable with those developed by Pfaltz, by Helmchen, and by Williams. The allylations of the silylenolate as shown in reaction 1 are encouraging, both in terms of the yields and enantioselectivities obtained; this type of transformation could be synthetically useful if a means to control the diastereoselection could be found.

Experimental Section

General Procedures. High field NMR spectra were recorded on Varian XL-200E (^{1}H at 200 MHz and ^{13}C at 50 MHz) and Unity Plus 300 (^{1}H at 300 MHz, ^{13}C at 75 MHz, and ^{31}P at 121 MHz) spectrometers. Chemical shifts of ^{1}H and ^{13}C spectra are referenced to the NMR solvents; ^{31}P spectra are referenced to H_3PO_4 (85%) external standard (0 ppm). Melting points are uncorrected. Optical rotations were measured on Jasco DIP-360 digital polarimeter. Flash chromatography was performed using silica gel (230−600 mesh). Thin-layer chromatography was performed on glass plates coated with silica gel 60 F254 (E. Merck, Darmstadt, Germany). Dichloromethane was distilled over CaH_2, and THF over Na/benzophenone. Other solvents were purchased from commercial supplier and were used without further purification. L-Aspartic acid, 1,1-dimethoxypropane, acetyl chloride, triethylamine, di-*tert*-butyl dicarbonate, ethyl chloroformate, and *p*-toluenesulfonic acid monohydrate were purchased from Aldrich. 1,3-Dimethylpropenyl pivalate,[6] cyclohex-2-enyl acetate,[41] and the compounds **10**−**12** were synthesized following literature procedures.[42,43]

(*S*)-*N*-*tert*-Butoxycarbonyl Aspartic Acid Diethyl Ester 3. Absolute EtOH (420 mL) was cooled in ice and acetyl chloride (71.4 mL, 1.03 mol) was added dropwise to generate HCl in situ. After the addition, the reaction was stirred for an additional 30 min. L-Aspartic acid (33.27 g, 0.25 mol) was added in one portion and the solution was heated slowly to reflux. Refluxing was continued until the reaction was complete (TLC); this took approximately 4 h. The reaction mixture was then cooled to 25 °C and the solvent was removed under reduced pressure. Further drying under vacuum gave crude diethyl L-aspartate hydrochloride **2** as a viscous oil that crystallized on standing to a white solid, yield 60 g (100%). This material was used without further purification. Spectral data for this sample were consistent with those given in the literature:[44,45] ^{13}C NMR (75 MHz, d_6-DMSO) δ 169.1, 168.2, 70.0, 60.9, 48.5, 34.2, 14.9 and 13.9.

A sample of the diethyl L-aspartate hydrochloride **2** (57.5 g, 0.273 mol) was dissolved in water (59 mL) and dioxane (149 mL) and then cooled to 0 °C. Triethylamine (74 mL, 0.53 mol) and then di-*tert*-butyl dicarbonate (74.99 g, 0.34 mol) were added with stirring. The reaction mixture was then heated at 50 °C for 14 h after which TLC (EtOAc/EtOH 1:1) indicated complete consumption of the starting material. The solvent was removed under vacuum, and aqueous citric acid (150 mL, 10% w/v) was added to adjust the pH to 2−3. The aqueous solution was extracted with ether (4 × 250 mL), and the combined organic extracts were washed with brine (100 mL), dried over Na_2SO_4, andconcentrated under vacuum to give **3** (78.8 g, 99%) as a light yellow oil, which was used without further purification. Spectral data for this sample were consistent with those given in the literature:[46] ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (1H), 4.49 (m, 1H), 4.12 (m, 4H), 2.90 (dd, J = 16.8 Hz, J = 4.6 Hz), 2.76 (d, J = 4.88 Hz, 1H), 1.46 (s, 9H), 1.21 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 170.8, 155.4, 79.8, 61.6, 60.9, 49.9, 36.7, 28.2, 14.0 and 13.9.

(*S*)-2-(*tert*-Butoxycarbonylamino)-1,4-butanediol 4. A stirred solution of (*S*)-*N*-BOC diethyl l-asparate **3** (47.41 g, 0.16 mol) in absolute EtOH (770 mL) was cooled in an ice−water bath, and then sodium borohydride (60.8 g, 1.6 mol) was added in 10 g portions. The cooling bath was removed when the reaction subsided, and the reaction mixture was heated slowly to reflux for 1 h; after this time TLC (EtOAc/EtOH 3:1) analysis indicated complete consumption of the starting material. The reaction mixture was cooled to 25 °C, and the lumps that formed were broken up to give a slurry that was poured into brine (450 mL). The mixture was filtered, and the filtrate was concentrated in a vacuum to ca. 100 mL and extracted with ether (6 × 300 mL). The insoluble solid material was extracted by stirring in ether (4 × 1L) for 2 h. The combined ether extracts were dried over $MgSO_4$, filtered, and concentrated to give **4** as a colorless oil (24.4 g, 73%), which crystallized on standing. Spectral data for this sample were consistent with those given in the literature:[46] ^{1}H NMR (200 MHz, d_6-DMSO) δ 6.45 (d, J = 8.4 Hz, 1H), 4.57 (t, J = 5.6 Hz, 1H), 4.35 (t, J = 5.1 Hz, 1H), 3.40 (m, 4H), 3.23 (m, 1H), 1.62 (m, 1H), 1.40 (m, 1H), 1.36 (s, 9H); ^{13}C NMR (50 MHz, d_6-DMSO) δ 155.5, 77.4, 63.5, 58.0, 49.6, 34.4, 28.3.

(*S*)-*N*-*tert*-Butoxycarbonyl-4-(2-hydroxy)ethyl-2,2-dimethyloxazolidine 5. 1,1-Dimethoxypropane (87 mL, 0.707 mol) and *p*-toluenesulfonic acid monohydrate (1.33 g, 7 mmol) were added to a stirred solution of the diol **4** (14.39 g, 70 mmol) in CH_2Cl_2 (319 mL) at 25 °C. The reaction was monitored by TLC (EtOAc/hexanes 2:1) until complete (36 h). The reaction mixture was then washed with aqueous $NaHCO_3$ (5%, 2 × 50 mL) and brine (50 mL), dried ($MgSO_4$) ,and concentrated to form a colorless oil, which crystallized upon standing. The ratio of the desired five-membered ring product **5** to the undesired six-membered ring product **6** was 6.4:3.6. Recrystallization from heptane gave **5** as colorless needles (8.2 g, 48%). Spectral data for this sample were consistent with those given in the

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literature:[47] ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.17 (m, 1H), 3.97 (m, 1H), 3.86−3.42 (m, 3H), 3.33 (br, 1H), 1.76 (m, 2H), 1.5 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (50 MHz,, $CDCl_3$) δ 153.9, 93.6, 80.9, 68.2, 58.6, 53.9, 37.7, 27.7, 26.3, 24.3.

The minor product (*S*)-*N*-*tert*-butoxycarbonyl-2,2-dimethyl-4-hydroxymethyl-1,3-oxazine **6** was isolated as a colorless oil via flash chromatography using EtOAc/hexanes (3:1 v/v) as eluant: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.37−3.77 (m, 5H), 1.62 (m, 2H), 1.35 (s, 9H), 1.24 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (50 MHz,, $CDCl_3$) δ 155.0, 101.2, 79.1, 63.8, 57.9, 48.5, 35.7, 28.3, 24.7, 24.6.

(*S*)-*N*-2-*tert*-Butoxycarbonyl-4-(4-toluenesulfonyloxyethyl)-2,2-dimethyloxazolidine 7. Dry, freshly crystallized *p*-toluenesulfonyl chloride (1.86 g, 9.8 mmol) and 4-(dimethylamino)pyridine (10 mg, 0.082 mmol) were added to a solution of alcohol **5** (2.00 g, 8.15 mmol) in triethylamine (2.6 mL, 18.75 mmol) and CH_2Cl_2 (20 mL) at 5 °C with stirring. The resulting solution was protected from moisture and kept at 5 °C until all of the starting material **5** had reacted (33 h, TLC). A colorless solid, presumably triethylamine hydrochloride, crystallized out of the reaction and was filtered away. The filtrate was diluted with CH_2Cl_2 to a volume of 90 mL, washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated to give the crude tosylate **7** as a white solid. This material was purified by dissolving in ether (ca. 330 mL) and filtering through Celite 545 on a wad of cotton to give 2.95 g (90%) of **7** as a colorless solid. This material was found to decompose on standing at room temperature so only limited characterization data was obtained: $[\alpha]^{24}_D$ +3.1 (c = 1.5, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78 (m, 2H), 7.35 (d, 2H), 4.09 (m, 2H), 4.09 (m, 2H), 3.90 (m, 2H), 3.73 (m, 1H), 2.95 (m, 2H), 1.51 (s, 6H), 1.44 (s, 9H).

(*S*)-*N*-*tert*-Butoxycarbonyl-4-ethylenediphenylphosphinoborane-2,2-dimethyloxazolidine 8. *n*-Butyllithium in hexanes (1.6 M, 17.1 mL, 27.4 mmol) was added to a solution of diphenylphosphine (4.52 g, 24.3 mmol) in THF (100 mL) at 0 °C. The orange-red solution was stirred at 0 °C for 30 min. A solution of tosylate **7** (8.44 g, 21.1 mmol) in THF (60 mL) was then added dropwise to the solution of the diphenylphosphide anion at 0 °C. The reaction mixture was stirred for another 30 min. Borane−THF complex (1 M, 26 mL, 26 mmol) was added to the solution at 0 °C and stirred for an additional 20 min. The solvent was removed, and the remaining material was dissolved in EtOAc (600 mL), washed with 1 M $HCl_{(aq)}$ (100 mL), saturated $NaHCO_3$ (100 mL), and brine (100 mL), dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure. The residue was further purified by column chromatography on silica gel using EtOAc/hexane eluant (3:7 v/v) to give 8.1 g (18.9 mmol, 90%) of a colorless oil, which crystallized upon standing at 25 °C: mp 95.0−96.5 °C; R_f 0.81 (EtOAc/hexane, 1:1 v/v); $[\alpha]^{24}_D$ +34.0 (c = 10.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.63 (m, 4H), 7.43 (m, 6H), 3.92 (m, 2H), 3.67 (m, 1H), 2.17 (m, 2H), 1.83 (m, 2H), 1.60 (s, 3H), 1.54 (s, 9H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.9, 131.9−132.1, 131.2, 128.9, 128.8, 94.0, 19.9, 67.0, 57.4, 28.3, 26.7, 22.9, 22.3, 21.8; ^{31}P NMR ($CDCl_3$, 121 MHz) δ 16.76 (br); HRMS (M + Na^+) m/z calcd for $C_{24}H_{35}NO_3$PBNa 450.23453, found 450.23672

(*S*)-2-Phenyl-4-[(diphenylphosphino)ethyl]oxazoline 1a. The protected phosphine **8** (500 mg, 1.17 mmol) was dissolved in 8 mL of MeOH and cooled to 0 °C. Gaseous HCl was bubbled through the reaction for 5−10 min. The MeOH was removed under vacuum and the residue was redissolved in 8 mL of 1,2-dichloroethane. Triethylamine (1.5 mL, 9.3 mmol) and benzimidic acid ethyl ester hydrochloride[48] (230 mg, 1.24 mmol) were added to the solution, and the reaction was heated to reflux for 6 h. The solvent was removed, and the crude product was further purified by column chromatography on silica gel using EtOAc/hexane eluant (2:8 v/v) to afford oxazoline **1a** (210 mg, 0.58 mmol, 50% yield) as a colorless solid: mp 52.5−54 0.0 °C; R_f 0.76 (EtOAc/hexane, 3:7 v/v). $[\alpha]^{24}_D$ −72.7 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.93 (d, J = 7 Hz), 7.29−7.49 (m, 13H), 4.34−4.49 (m, 4H), 4.00 (dd, J = 7.5 Hz, J = 7.5 Hz), 2.24−2.34 (m, 2H), 2.07−2.15 (m, 2H), 1.67−1.85 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.7, 138.6, 138.3, 132.8, 132.6, 128.6, 128.5−128.2, 127.7, 72.2, 67.5 (d, J = 13.5 Hz), 32.1(d, J = 16.5 Hz), 24.1(d, J = 11.5 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.81; HRMS (M^+ + 1) m/z calcd for $C_{23}H_{23}$NOP 360.15170, found 360.15147.

General Procedure for Preparation of Oxazolines 1b−h. (*S*)-2-(1-Admantyl)-4-[(diphenylphosphino)ethyl]oxazoline 1b. The protected phosphine **8** (500 mg, 1.17 mmol) was dissolved in 8 mL of MeOH and cooled to 0 °C. Gaseous HCl was bubbled through the reaction for 5−10 min, and the MeOH was removed under vacuum. The residue was redissolved in 8 mL of 1,2-dichloroethane. Triethylamine (0.44 mL, 4.1 mmol), catalytic 4-(dimethylamino)pyridine (2 mg), and 1-admantanecarbonyl chloride (256 mg, 1.28 mmol) were added to the solution and stirred for 12 h at room temperature. Subsequently, borane−THF (1 M, 2 mL, 2 mmol) was added to the reaction mixture at 0 °C, and stirred for another 10 min. The reaction mixture was diluted with 15 mL of CH_2Cl_2, washed with $HCl_{(aq)}$ (0.5 M, 10 mL × 2) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated. 1,4-Diazobicyclo-[2.2.2]octane (656 mg, 5.85 mmol) was added to the flask, and THF (8 mL) was added. This reaction mixture was cooled to 0 °C and methanesulfonyl chloride (86 μL, 1.28 mmol) was added. The reaction was stirred at 25 °C for 4 h then heated to 50 °C for another 4 h. The resulting slurry was filtered and then concentrated at reduced pressure. The crude product was purified by flash chromatography (SiO_2) using EtOAc/hexane eluant (2:8 v/v) to give 370 mg (0.89 mmol, 75%) of the product **1b** as a colorless oil: R_f 0.76 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −47.7 (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.48 (m, 4H), 7.34−7.41 (m, 6H), 4.14−4.23 (m, 2H), 3.81 (m, 1H), 2.18−2.24 (m, 1H), 2.03−2.08 (m, 3H), 1.90 (m, 3H), 1.64−1.83 (m, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.5, 138.6, 138.2, 132.9, 132.7, 132.4, 128.6−128.3, 71.5, 66.4 (d, J = 13.5 Hz), 39.6, 36.5, 35.1, 32.1(d, J = 16.5 Hz), 28.1, 23.6 (d, J = 11.5 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.81; HRMS (M^+ + 1) m/z calcd for $C_{27}H_{33}$NOP 418.22998, found 418.22583.

(*S*)-2-*tert*-Butyl-4-[(diphenylphosphino)ethyl]oxazoline 1c. This compound was prepared via the same method used for compound **1b**, but beginning with 500 mg (1.17 mmol) of **8**, 117 mg (0.34 mmol, 30%) of the oxazoline **1c** was produced as a colorless oil: R_f 0.68 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −46.9 (c = 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (s, 2H), 7.38−7.56 (m, 5H), 7.26−7.34 (m, 6H), 4.33−4.47 (m, 2H), 3.97 (t, J = 7 Hz, 1H), 2.14−2.27 (m, 1H), 2.04−2.12 (m, 1H), 1.70−1.84 (m, 1H), 1.65−1.70 (m, 1H), 1.33 (s, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.0, 138.6, 138.2, 132.7, 132.4, 132.1, 128.6−128.3, 72.0, 66.6 (d, J = 13.5 Hz), 33.2, 32.1(d, J = 16.5 Hz), 27.8, 23.6 (d, J = 11.5 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.37; HRMS (M^+ + 1) m/z calcd for $C_{21}H_{27}$NOP 340.18303, found 340.18281.

(*S*)-2-(3,5-Di-*tert*-butylphenyl)-4-[(diphenylphosphino)-ethyl]oxazoline 1d. This compound was prepared via the same method used to prepare **1b**. Beginning with 500 mg (1.17 mmol) of **8**, 227 mg (0.48 mmol, 41%) of the oxazoline **1d** was produced as a colorless oil: R_f 0.77 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −39.5 (c = 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.44 (m, 4H), 7.27−7.37 (m, 6H), 4.21 (m, 1H), 4.12 (m, 1H), 3.80 (dd, J = 6.3 Hz, J = 7.8 Hz), 2.14 (m, 1H), 2.01 (m, 1H), 1.60 (m, 2H), 1.57 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.4, 150.9, 138.5, 138.3, 132.9, 132.8, 132.6, 128.7−128.4, 127.0, 125.6, 122.5, 72.0, 67.5 (d, J = 13.5 Hz), 34.9, 32.1(d, J = 16.5 Hz), 31.4, 24.0 (d, J = 12.0 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.20; HRMS (M^+ + 1) m/z calcd for $C_{31}H_{39}$NOP 472.27693, found 472.27524.

(*S*)-2-(3,5-Di-*tert*-butyl-4-methoxyphenyl)-4-[(diphenylphosphino)ethyl]oxazoline 1e. This compound was prepared via the same method used to prepare **1b**. Beginning with 278 mg (0.65 mmol) of **8**, 130 mg (0.26 mmol, 40%) of the oxazoline **1e** was produced as a colorless oil: R_f 0.61 (EtOAc/hexane, 2:8 v/v); $[\alpha]^{24}_D$ −34.8 (c = 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$,

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300 MHz) δ 7.81 (s, 2H), 7.40 (m, 4H), 7.30 (m, 6H), 4.40 (m, 2H), 4.00 (m, 1H), 3.67 (s, 3H), 2.25 (m, 1H), 2.10 (m, 1H), 1.83 (m, 1H), 1.67 (m, 1H), 1.42 (s, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.0, 162.5, 143.9, 138.4, 132.9, 132.6, 128.7−128.4, 126.8, 122.0, 72.0, 67.5 (d, J = 14 Hz), 64.4, 35.8, 32.1(d, J = 16.5 Hz), 31.9, 24.0 (d, J = 12.0 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.20; HRMS ($M^+ + 1$) m/z calcd for $C_{32}H_{41}NOP$ 502.28749, found 502.28731.

(*S*)-2-Triphenylmethyl-4-[(diphenylphosphino)ethyl]-oxazoline 1f. This compound was prepared via the same method for compound **1b**. Beginning with 500 mg (1.17 mmol) of **8**, 191 mg (0.36 mmol, 31%) of the oxazoline **1f** was produced as a colorless oil: R_f 0.71 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −46.6 (c = 2.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25−7.50 (m, 25H), 4.35 (m, 2H), 4.02 (m, 1H), 2.21 (m, 1H), 2.10 (m, 1H), 1.77 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.6, 143.4, 138.4, 138.2, 132.9, 132.6, 132.4, 130.1−126.5, 71.9, 66.8 (d, J = 13.5 Hz), 61.4, 31.8 (d, J = 16.5 Hz), 23.7 (d, J = 11.5 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.51; HRMS ($M^+ + 1$) m/z calcd for $C_{36}H_{33}NOP$ 526.22998, found 526.22938.

(*S*)-2-(9-Anthryl)-4-[(diphenylphosphino)ethyl]oxazoline 1g. This compound was prepared via the same method for compound **11b**. Beginning with 500 mg of **8** (1.17 mmol), 27 mg (0.059 mmol, 5%) of the oxazoline **1g** was produced as a light yellow oil: R_f 0.62 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −40.3 (c = 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.52 (s, 1H), 8.11 (m, 2H), 7.99 (m, 2H), 7.58−7.31 (m, 14H), 4.70 (m, 2H), 4.25 (m, 1H), 2.52 (m, 1H), 2.30 (m, 1H), 1.99 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.2, 138.6, 138.4, 138.1, 132.9−132.5, 130.9, 130.0, 129.5, 128.7−128.4, 126.7, 125.3, 125.2, 122.7, 72.5, 68.4 (d, J = 13.5 Hz), 32.7 (d, J = 17.0 Hz), 24.5 (d, J = 12.0 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.37; HRMS ($M^+ + 1$) m/z calcd for $C_{31}H_{27}NOP$ 460.18303, found 460.18362.

(*S*)-2-[1-(2-Ethoxy)naphthyl]-4-[(diphenylphosphino)-ethyl]oxazoline 1h. This compound was prepared via the same method for compound **1b**. Beginning with 500 mg of **8** (1.17 mmol), 26 mg (0.059 mmol, 5%) of the oxazoline **1h** was produced as a colorless oil: R_f 0.42 (EtOAc/hexane, 3:7 v/v); $[\alpha]^{24}_D$ −36.0 (c = 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.87−7.73 (m, 4H), 7.48−7.21 (m, 12H), 4.53 (m, 2H), 4.15 (q, J = 7.2 Hz, 2H), 4.10 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.9, 155.2, 138.5, 138.3, 132.9−131.6, 128.6−127.3, 123.9, 114.4, 112.9, 72.0, 67.9 (d, J = 14.0 Hz), 65.3, 32.4 (d, J = 16.6 Hz), 24.1 (d, J = 11.0 Hz), 14.9; ^{31}P NMR ($CDCl_3$, 121 MHz) δ −15.11; HRMS ($M^+ + 1$) m/z calcd for $C_{29}H_{29}NO_2P$ 454.19359, found 454.19542.

(*S*)-*N*-Ethoxycarbonyl-Aspartic Acid Dimethyl Ester 10. MeOH (600 mL) was cooled in ice and acetyl chloride (110 mL, 1.54 mol) was added dropwise to generate HCl in situ. After the addition, L-aspartic acid (64.3 g, 0.48 mol) was added to the solution at 0 °C and then the solution was slowly warmed to reflux. The refluxing was continued for 3 h and the reaction mixture was cooled to room temperature during overnight. The solvent was removed under reduced pressure to give the crude dimethyl L-aspartate hydrochloride as viscous oil. This crude product was further diluted with water (1.6 L) and cooled in an ice−water bath, and sodium bicarbonate (210 g, 2.5 mol) was added to the solution carefully. Ethyl chloroformate was added to the solution dropwise at 0 °C. After the addition, the solution was stirred at 25 °C for another 4 h and the product was formed during this period as colorless oil in the bottom of the flask. The organic layer was separated and the aqueous solution was further extracted with EtOAc (200 mL × 4). The combined organic solution was washed with water, saturated $NaCl_{(aq)}$, dried over Na_2SO_4, filtered ,and concentrated to give **10** (101.5 g, 0.44mol, 90%) as a colorless oil: $[\alpha]^{24}_D$ +41.6° (c = 4.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.62 (d, J = 8 Hz, 1H), 4.59 (m, 1H), 4.09 (q, J = 7 Hz, 2H), 3.73 (s, 3H), 3.66 (s, 3H), 2.99 (dd, J = 9 Hz, J = 4 Hz, 1H), 2.82 (dd, J = 9 Hz, J = 4 Hz, 1H), 1.22 (t, J = 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.2, 171.1, 156.1, 61.2, 52.7, 51.9, 50.2, 36.4, 14.4; HRMS ($M^+ + 1$) m/z calcd for $C_9H_{16}NO_6$ 234.09776, found 234.09784.

(*S*)-2-(Ethoxycarbonylamino)-1,4-butanediol 11. Calcium chloride (35 g, 0.63mol) was added to a solution of **10** (35.5 g, 0.15 mol) in absolute EtOH (300 mL) and THF (150 mL). Then sodium borohydride (28.8 g, 0.76 mol) was added to the solution portionwise at 25 °C. When the reaction became vigorously, the reaction flask was put into an ice−water bath. After being stirred at room temperature for 12 h, the reaction mixture was poured into aqueous citric acid (1 M, 600 mL) at 0 °C and then the solution was extracted with EtOAc (150 mL × 4). The organic solution was washed with saturated $NaCl_{(aq)}$, dried over Na_2SO_4, filtered, and concentrated to give the diol **11** (23.9 g, 89%) as a white solid: $[\alpha]^{24}_D$ −26.4° (c = 3.04, CH_3OH); ^{1}H NMR (d_6-DMSO, 300 MHz) δ 6.76 (d, J = 8 Hz, 1H), 3.93 (q, J = 7 Hz, 2H), 3.58−3.25 (m, 4H), 1.67 (m, 1H), 1.63, (m, 1H), 1.14, (t, J = 7 Hz, 3H); ^{13}C NMR (d_6-DMSO, 75 MHz) δ 156.1, 63.5, 59.5, 57.9, 49.9, 34.3, 14.7; HRMS ($M^+ + 1$) m/z calcd for $C_7H_{16}NO_4$ 178.10793, found 178.10789.

(*S*)-4-(2-Hydroxyethyl)-2-oxazolidinone 12. Butanediol **11** (19.46 g, 0.11 mol) was dissolved in anhydrous THF (270 mL). Sodium hydride (5.4 g, 0.225 mol) was added to the solution at 0 °C. The reaction was stirred at 25 °C for 2 h and refluxed for another 2 h. After being cooled to room temperature, the solution was neutralized with 1 M $HCl_{(aq)}$ and the solvent was removed under vacuum. The residue was redissolved in MeOH (400 mL), dried over Na_2SO_4, filtered, and evaporated to dryness. The crude **12** (11.4 g, 79%) was obtained as a white solid: $[\alpha]^{24}_D$ −11.6° (c = 2.03, CH_3OH); ^{1}H NMR (d_6-DMSO, 300 MHz) δ 7.69 (br, 1H), 4.40 (br, 1H), 4.35 (m, 1H), 3.92 (m, 1H), 3.47 (m, 1H), 3.47 (m, 2H), 1.60 (m, 2H); ^{13}C NMR (d_6-DMSO, 75 MHz) δ 158.9, 69.5, 57.4, 49.8, 38.0.

(*S*)-4-[2-(4-Toluenesulfonyloxy)ethyl]-2-oxazolidinone 13. Dry, freshly crystallized *p*-toluenesulfonyl chloride (1.6 g, 8.4 mmol) and 4-(dimethylamino)pyridine (20 mg, 0.16 mmol) were added to a solution of alcohol **12** (1.0 g, 7.6 mmol) and pyridine (15 mL, 0.185 mol) at −10 °C. The resulting solution was gradually warmed to 25 °C during 12 h. The reaction mixture was acidified with 2 M HCl (100 mL), extracted with CH_2Cl_2 (50 mL × 3), washed with saturated $NaHCO_{3(aq)}$ and $NaCl_{(aq)}$, dried over Na_2SO_4, and evaporated. The crude product was recrystallized twice in EtOAc/hexanes to give **13** (0.75 g, 40%) as a light yellow solid: $[\alpha]^{24}_D$ −12.5° (c = 3.82, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76 (dd, J = 7 Hz, J = 2 Hz, 2H), 7.35 (dd, J = 7 Hz, J = 2 Hz, 2H), 6.08 (s, 1H), 4.46 (m, 1H), 4.10 (m, 2H), 3.98 (m, 2H), 2.43 (s, 3H), 1.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.6, 145.3, 130.0, 128.9, 127.8, 69.9, 66.9, 49.8, 34.4, 21.6; HRMS ($M^+ + 1$) m/z calcd for $C_{12}H_{16}NO_5S$ 286.07492, found 286.07627.

(*S*)-4-[2-(Diphenylphosphinoborane)ethyl]-2-oxazolidinone 14. *n*-Butyllithium in hexanes (1.6 M, 17.1 mL, 27.4 mmol) was added to a solution of diphenylphosphine (2.56 g, 13.7 mmol) in THF (120 mL) at 0 °C. The orange-red solution was stirred at 0 °C for 30 min. The tosylate **13** (3.74 g, 13.1 mmol) dissolved in THF (50 mL) was added to the solution of phosphide at 0 °C. The resulting solution was stirred at 0 °C for 1 h. Borane−THF complex (1 M, 14 mL, 14 mmol) was added to the solution and stirred for another 30 min. The reaction was quenched with water (10 mL) and then the solution was neutralized with 1 M $HCl_{(aq)}$, diluted with ether (200 mL), washed with saturated $NaHCO_{3(aq)}$ and $NaCl_{(aq)}$, dried over Na_2SO_4, and evaporated to yield the oily product **14** (3.9 g, 12.4 mmol, 95%): $[\alpha]^{24}_D$ −22.0° (c = 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.65 (m, 4H), 7.40 (m, 6H), 6.93 (s, 1H), 4.42 (m, 1H), 3.87 (m, 2H), 2.36 (m, 1H), 2,12 (m, 1H), 1.82 (m, 1H), 1.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.1, 132.1−131.4, 128.9−128.6, 69.6, 52.8 (d, J = 15 Hz), 28.7, 21.2 (d, J = 38 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ 16.3; HRMS ($M^+ - 1$) m/z calcd for $C_{17}H_{20}NO_2BP$ 312.13247, found 312.13248.

(*S*)-2-Amino-4-diphenylphosphinoborane-1-butanol 9. Oxazolidinone **14** (1.0 g, 3.2 mmol) was dissolved in EtOH (10 mL) and $NaOH_{(aq)}$ (1 N, 10 mL). The solution was refluxed for 2.5 h. The reaction mixture was diluted with ether (100 mL), washed with saturated $NH_4Cl_{(aq)}$ (20 mL), $NaCl_{(aq)}$ (20 mL), dried over Na_2SO_4, filtered and evaporated to give **9** as a colorless oil (0.92 g, 99%): $[\alpha]^{24}_D$ 1.6° (c = 2.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (m, 4H), 7.42 (m, 6H), 6.08 (s, 1H), 3.49 (m, 1H), 3.25 (m, 1H), 2.81 (m, 1H), 2.45 (br, 3H) 2.31 (m, 1H), 2.21 (m, 1H), 1.62 (m, 1H), 1.42 (m, 1H); ^{13}C NMR

($CDCl_3$, 75 MHz) δ 132.1, 131.5, 131.2, 129.0, 66.2, 53.5 (d, J = 14 Hz), 27.4, 22.2 (d, J = 38 Hz); ^{31}P NMR ($CDCl_3$, 121 MHz) δ 16.9; HRMS ($M^+ + 1$) m/z calcd for $C_{16}H_{24}NOPB$ 288.16886, found 288.16995.

(*S*)-*N*-Benzoyl-Aspartic Acid Dimethyl Ester 15. Dimethyl L-aspartate hydrochloride[43] **2** (10.0 g, 50 mmol) was dissolved in CH_2Cl_2 (150 mL) and triethylamine (20.2 g, 200 mmol). Benzoyl chloride (7.38 g, 52.5 mmol) was added to the reaction dropwise at 25 °C. After the addition, the reaction was stirred at 25 °C for another 2 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with $HCl_{(aq)}$ (1 N, 100 mL), saturated $NaHCO_{3(aq)}$ (100 mL), and $NaCl_{(aq)}$ (80 mL), dried over Na_2SO_4, filtered, and evaporated to afford **15** (13.0 g, 98%) as a white solid: $[\alpha]^{24}_D$ −31.7° (c = 1.67, CH_3OH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80 (m, 2H), 7.50−7.41 (m, 3H), 7.22 (d, J = 8 Hz, 1H), 5.03 (m, 1H), 3.76 (s, 3H), 3.67 (s, 3H), 3.12 (dd, J = 17 Hz, 4 Hz, 1H), 2.95 (dd, J = 17 Hz, 4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.7, 171.2, 166.8, 133.5, 131.8, 128.5, 127.1, 52.9, 52.0, 48.8, 36.0; HRMS ($M^+ + 1$) m/z calcd for $C_{13}H_{16}NO_5$ 266.10285, found 266.10219.

(*S*)-2-(Benzoylamino)-1,4-butanediol 16. Diester **15** (17.54 g, 66 mmol) and calcium chloride (14.65 g, 13 mmol) were dissolved in EtOH (150 mL) and THF (75 mL). Sodium borohydride (9.90 g, 264 mmol) was added to the solution in several portions at 25 °C. The reaction was exothermic and kept below 40 °C by an ice−water bath if necessary. After the addition, the reaction was stirred for another 12 h at room temperature. The solution was poured into aqueous citric acid (1 M, 200 mL), extracted with EtOAc (150 mL × 3), washed with saturated $NaCl_{(aq)}$ (80 mL), dried over Na_2SO_4, filtered and evaporated to afford **16** (7.41 g, 53%) as a viscous oil: $[\alpha]^{24}_D$ −27.7 (c = 3.14, CH_3OH); ^{1}H NMR (d_6-DMSO, 300 MHz) δ 8.07 (d, J = 8 Hz, 1H), 7.85 (d, J = 7 Hz, 2H), 7.49 (m, 2H), 7.33 (d, J = 6 Hz, 1H), 5.18 (br, 1H), 4.72 (br, 1H), 4.04 (m, 1H), 3.47 (m, 4H), 1.81 (m, 1H), 1.77 (m, 1H); ^{13}C NMR (d_6-DMSO, 75 MHz) δ 166.3, 131.0, 128.1, 127.3, 126.6, 63.3, 62.9, 49.0, 34.0; HRMS ($M^+ + 1$) m/z calcd for $C_{11}H_{16}NO_3$ 210.11302, found 210.11289.

(*S*)-2-Phenyl-4-[2-(*p*-toluenesulfonyl)ethyl]oxazoline 17. Diol **16** (105 mg, 0.50 mmol) was dissolved in CH_2Cl_2 (4 mL) and triethylamine (0.42 mL, 3.0 mmol) and cooled to 0 °C. *p*-Toluenesulfonyl chloride (287 mg, 1.51 mmol) was added to the solution in one portion at 0 °C. The reaction was stirred for 20 h and slowly warmed to room temperature. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with $HCl_{(aq)}$ (1 N, 10 mL), saturated $NaHCO_{3(aq)}$ (10 mL), and $NaCl_{(aq)}$ (10 mL), dried over Na_2SO_4, filtered, and evaporated to afford the crude tosylate. The crude product was recrystallized in EtOAc/hexane to give **17** (115 mg, 67%) as a yellow solid: $[\alpha]^{24}_D$ −59.2 (c = 2.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.85 (d, J = 7 Hz, 2H), 7.77 (d, J = 7 Hz, 2H), 7.45−7.28 (m, 5H), 4.45 (dd, J = 8 Hz, J = 8 Hz, 1H), 4.31 (m, 1H), 4.22 (m, 2H), 4.00 (dd, J = 8 Hz, J = 8 Hz, 1H), 2.40 (s, 3H), 1.97 (dt, J = 8 Hz, J = 8 Hz, 2H); ^{13}C NMR (d_6-DMSO, 75 MHz) δ 245.2, 164.0, 144.8, 131.4, 129.8, 128.3, 128.2, 128.2, 127.9, 72.3, 67.9. 63.5, 35.1, 21.6; HRMS ($M^+ + 1$) m/z calcd for $C_{18}H_{20}NO_4S$ 346.11310, found 346.11091.

(*S*)-2-Phenyl-4-[(diphenylphosphino)ethyl]oxazoline 1a. *n*-Butyllithium (1.6 M in hexanes, 11 mL, 17.6 mmol) was added to a solution of diphenyl phosphine (2.21 g, 11.87 mmol) in THF (120 mL) at 0 °C. The solution of the phosphide anion was cannulated to a solution of tosylate **17** (4.06 g, 11.75 mmol)/THF (120 mL) at 0 °C. The reaction was kept at 0 °C for another 1 h. The reaction was then quenched with saturated NH_4Cl(aq) (5 mL), diluted with ether (100 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified further by flash chromatography on silica gel using 20% EtOAc/hexanes eluant to afford the title compound **1a** 3.70 g (88%).

Typical Procedure for the Enantioselective Allylation. Methyl (*R*)-(*E*)-2-Methoxycarbonyl-3,5-diphenylpent-4-enoate. In a nitrogen atmosphere, allylpalladium chloride dimer (1.8 mg, 0.0049 mmol), the ligand **1a** (3.2 mg, 0.009 mmol), and solid potassium acetate (2 mg, 0.02 mmol) were weighed into a half-dram vial equipped with a small glass bead to enhance agitation. CH_2Cl_2 (800 μL) was added to the vial, and the solution was cooled to 0 °C and allowed to equilibrate for 0.5 h. Neat dimethyl malonate (46 μL, 0.4 mmol) was added, followed by *N*,*O*-bis(trimethylsilyl)acetamide (100 μL, 0.4 mmol) and a 0.2 M stock solution of 1,3-diphenylpropenyl acetate (1 mL, 0.2 mmol). The reaction was agitated for 12 h at 0 °C. The solvent was removed, and the residue was passed through a short silica plug (20% EtOAc/hexanes). The reaction mixture was analyzed via HPLC (ChiralCel OD analytical column; eluting with 99:1 hexanes/2-propanol, flow rate 0.5 mL/min, 254 nm, t_1 = 20.5 min, t_2 = 21.4 min). The HPLC separation was calibrated using racemic material. The optical rotation of the product was compared with the literature rotation to assign absolute configuration (*R*).[8]

Methyl (*R*)-(*E*)-2-Methoxycarbonyl-3,5-dimethylpent-4-enoate. In a nitrogen atmosphere, allylpalladium chloride dimer (1.8 mg, 0.0049 mmol), the ligand **1a** (3.2 mg, 0.009 mmol), and solid potassium acetate (2 mg, 0.02 mmol) were weighed into a half-dram vial equipped with a small glass bead to enhance agitation. CH_2Cl_2 (800 μL) was added to the vial and allowed to equilibrate for 0.5 h at 25 °C. Neat dimethyl malonate (46 μL, 0.4 mmol) was added, followed by *N*,*O*-bis(trimethylsilyl)acetamide (100 μL, 0.4 mmol), and a 0.2 M stock solution of 1,3-dimethylpropenyl pivalate (1 mL, 0.2 mmol). The reaction was agitated for 48 h at 25 °C. The solvent was removed, and the residue was passed through a short silica plug (20% EtOAc/hexanes). Then the reaction mixture was analyzed via GC (70 °C; retention time, t_1 = 71.7 min, t_2 = 72.9 min; the chiral column was prepared by Vigh et al.;[49] 30.7 m × 0.25 mm, 30% *tert*-butyldimethylsilyl cyclodextrin derivative in OV-1701-vi of 0.25 μm film thickness). The GC separation was calibrated using racemic material. The optical rotation of the product was compared with the literature rotation to assign absolute configuration(*R*).[50]

(*S*)-Cyclohexene 3-(2′-Propane-1′,3′-dioic acid dimethyl ester). In a nitrogen atmosphere, allylpalladium chloride dimer (1.8 mg, 0.0049 mmol), the ligand **1a** (3.2 mg, 0.009 mmol), and solid potassium acetate (2 mg, 0.02 mmol) were weighed into a half-dram vial equipped with a small glass bead to enhance agitation. Dichloromethane (800 μL) was added to the vial and allowed to equilibrate for 0.5 h at 25 °C. Neat dimethyl malonate (46 μL, 0.4 mmol) was added, followed by *N*,*O*-bis(trimethylsilyl)acetamide (100 μL, 0.4 mmol), and a 0.2 M stock solution of cyclohex-2-enyl acetate(1 mL, 0.2 mmol). The reaction was agitated for 60 h at 25 °C. The solvent was removed, and the residue was passed through a short silica plug (20% EtOAc/hexanes). Then the reaction mixture was analyzed via GC (120 °C; retention time, t_1 = 23.7 min, t_2 = 24.4 min; the chiral column was prepared by Vigh et al.;[49] 30.7 m × 0.25 mm, 30% β-*tert*-butyldimethylsilyl cyclodextrin derivative in OV-1701-vi of 0.25 μm film thickness). The GC separation was calibrated using racemic material. The optical rotation of the product was compared with the literature rotation to assign absolute configuration (*S*).[28,51]

3-((*Z*)-1-Trimethylsilyloxypro-1-enyl)-2-oxazolidone (18). Sodium bis(trimethylsilyl)amide (1 M in THF, 1.54 mL, 1.54 mmol) was added to the solution of 3-propionyl-oxazolidin-2-one[52] (200 mg, 1.40 mmol) in THF (4 mL) at −78 °C. Then trimethylsilyl chloride (250 μL, 1.96 mmol) was added to the solution at −78 °C and the reaction was slowly warmed to room temperature in 5 h. The solvent was removed in a vacuum and the residue was dissolved in CH_2Cl_2 (10 mL). The resulting solution was filtered through a short silica plug, concentrated to give **18** as a colorless oil (231 mg, 1.07 mmol, 77%). Spectral data for this compound were consistent with those given in the literature.[53]

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Allylic Alkylation of 1,3-Diphenylpropenyl Acetate with 3-((*Z*)-1-Trimethylsilyloxypro-1-enyl)-2-oxazolidone (18). In a nitrogen atmosphere, allylpalladium chloride dimer (1.8 mg, 0.0049 mmol), the ligand **1a** (3.2 mg, 0.009 mmol), and solid potassium acetate (2 mg, 0.02 mmol) were weighed into a 5-mL flask equipped with a stir bar. Dichloromethane (500 μL) was added to the vial and allowed to equilibrate for 0.5 h at 0 °C. A solution of 1,3-diphenylpropenyl acetate (51 mg, 0.2 mmol) and 3-((*Z*)-1-trimethylsilyloxypro-1-enyl)-2-oxazolidone (64.6 mg, 0.3 mmol) in CH_2Cl_2 (500 μL) was added to the flask by syringe at 0 °C. The reaction was stirred at 0 °C for 16 h. The solvent was removed, and the residue was passed through a short silica plug (30% EtOAc/hexanes) to give a mixture of **19a** and **19b** (65.4 mg, 95%). These two diastereomers were further separated by flash column chromatography. **19a**: R_f 0.51 (EtOAc/hexane, 3:7 v/v); **19b**: R_f 0.40 (EtOAc/hexane, 3:7 v/v). The syn-*E*-relative configuration of **19a** was determined by X-ray crystallography. The absolute configuration was tentatively assigned as shown on the basis of the similar allylation described in Figure 1a. The enantioselectivity of this reaction was analyzed via HPLC (Chiralcel OD analytical column; flow rate 1.0 mL/min, 254 nm, eluting with programmed hexanes/2-propanol: 0−20 min, 1% of 2-propanol; 20−45 min, ramp 1−10% of 2-propanol; 45−55 min, 10% of 2-propanol; 55−65 min, ramp 10−15%; 65−70 min, 15% of 2-propanol; 70−80 min, ramp 15−1% of 2-propanol; syn isomer (**19a**) t_1 = 42.4 min, t_2 = 45.3 min; anti isomer (**19b**) t_1 = 43.2 min, t_2 = 66.1 min). This HPLC separation was calibrated using racemic material. Spectroscopic data of **19a** (syn): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.16 (m, 10H), 6.40 (dd, J = 3 Hz, J = 2 Hz, 1H), 6.39 (d, J = 2 Hz) 4.52 (ddd, J = 10.6 Hz, J = 6 Hz, J = 2.4 Hz, 1H, CHCON), 4.22 (m, 1H, CH_2(oxazolidone)), 4.02 (m, 1H, CH_2-(oxazolidone)), 3.98 (m, 1H, CH_2(oxazolidone)), 3.79 (m, 1H, CH_2(oxazolidone)), 3.55 (m, 1H, CHPh), 1.01 (d, J = 6 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 245.2, 176.4, 141.3, 136.9, 131.3, 130.5, 128.8, 128.5, 128.1,127.4, 126.8, 126.1, 61.7, 54.7, 42.6, 42.3, 15.7; HRMS (M + Na^+) m/z calcd for $C_{21}H_{21}NO_3Na$ 358.14191, found 358.14272. Spectroscopic data of **19b** (anti): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.16 (m, 10H), 6.49 (d, J = 15 Hz, J = Hz, 1H), 6.32 (dd, J = 15 Hz, J = 7 Hz) 4.44 (m, 1H, CHCON), 4.24 (m, 1H, CH_2(oxazolidone)), 3.98 (m, 1H, CH_2(oxazolidone)), 3.80 (m, 1H, CH_2(oxazolidone)), 3.69 (m, 1H, CH_2(oxazolidone)), 3.52 (m, 1H, CHPh), 1.27 (d, J = 7 Hz, 3H, Me); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 245.2, 176.1, 142.5, 137.0, 131.9, 130.3, 128.5, 128.0, 127.7, 127.4, 126.6, 126.3, 61.7, 53.6, 42.6, 42.0, 16.0.

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Supporting Information Available: Crystallographic data for the two X-ray structural analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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