Proline-Based P, N Ligands in Asymmetric Allylation and the Heck Reaction

Scott R. Gilbertson,* Dejian Xie, and Zice Fu

Department of Chemistry, Washington University, St. Louis, Missouri 63130

srg@wuchem.wustl.edu

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A series of phosphine−oxazoline ligands based on proline are reported. These ligands are synthesized from commercially available *trans*-4-hydroxy-L-proline in four steps. The ability of this type of ligand to catalyze allylic alkylation in an asymmetric fashion as well as the asymmetric Heck reaction is reported. The best of these ligands gave a palladium complex, which catalyzed the addition of dimethylmalonate to cyclopentenyl acetate in excellent yield and up to 96% ee. This same system catalyzed the Heck reaction between dihydrofuran and cyclohexene in up to 86% ee. These ligands appear to differ from the traditional phosphine−oxazoline ligands in that the stereochemistry of the stereogenic carbon next to the oxazoline is not necessarily the dominant chiral center in the induction of selectivity.

Introduction

Phosphine−oxazoline ligands have been used with success in a number of asymmetric reactions. Hayashi, Pfaltz, Helmchen, and Williams among others have used these ligands with good success in both palladium-catalyzed allylation and the Heck reaction.[1−12] The most successful ligand of this type has been based on the basic structure **1** (Figure 1). While other phosphine−oxazoline systems have been developed and tested, generally these systems have proven to be less effective than ligand **1**. In the majority of cases that have been studied, the ligands possess only one chiral center, the carbon next to the oxazoline nitrogen. Herein we report the synthesis of a series of hydroxyproline-based phosphine-oxazoline ligands (**2**). These ligands present up to three chiral centers that can be used to control the selectivity of a transition metal coordinated to them. Palladium complexes of these ligands have been tested in palladium-catalyzed allylation and the Heck reaction.[13,14]

Results and Discussion

Synthesis of Hydroxyproline-Based Phosphine−Oxazoline Ligands. The design of this system was based on the observation that ligands derived from proline often result in reasonably high stereodifferenation.[15−19] For this reason, a series of proline-based phosphine−oxazoline ligands was synthesized. The synthesis of this class of ligand begins with commercially available BOC-protected *trans*-4-hydroxy-L-proline (**3**). Either an amino acid ester or an amino alcohol is coupled to this molecule (Scheme 1). If an ester is used, the oxazoline is formed through reduction of the ester to an alcohol (**8**, **10**, **11**) and formation of a bis-mesylate by reaction with methanesulfonyl chloride. If an amino alcohol is initially coupled to proline the reduction step is not necessary. The primary mesylate then undergoes cyclization to form the oxazoline ring (**12**−**14**). After this reaction, the secondary mesylate was subjected to substitution by sodium diphenylphosphide. Following substitution, the phosphine is protected as the phosphine sulfide (**15**−**17**). The ligands are purified as the phosphine sulfides and then converted to phosphines by reduction with Raney nickel before coordination to palladium.[20,21] This route is appealing because it allows the synthesis of a wide variety of analogues. The R group on the oxazoline is easily changed by simply coupling a different amino acid

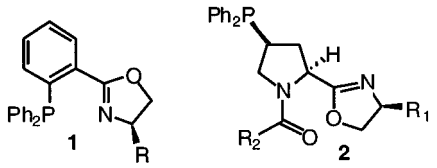

Figure 1.

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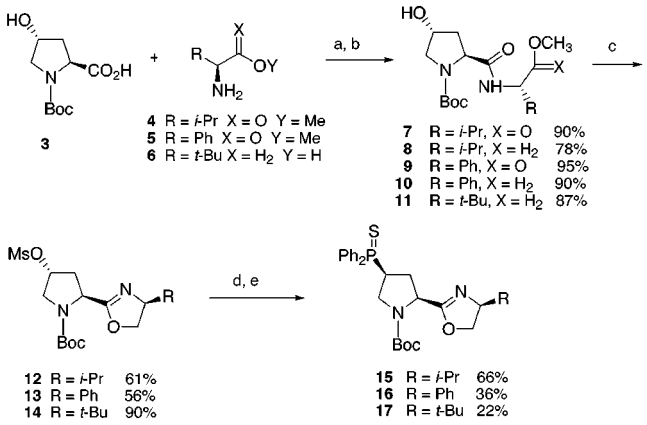
Scheme 1[a]



[a] Key: (a) EDC/HOBt, rt, CH_2Cl_2; (b) when X = O $LiBH_4$, THF, 0 °C to rt; (c) $MeSO_2Cl$, Et_3N, CH_2Cl_2, rt; (d) $Ph_2P^-Na^+$, THF, −78 °C to rt; (e) S_8, rt.

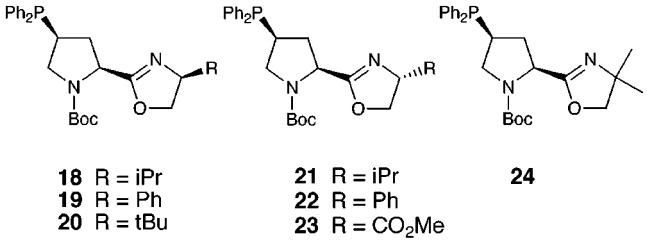


Figure 2.

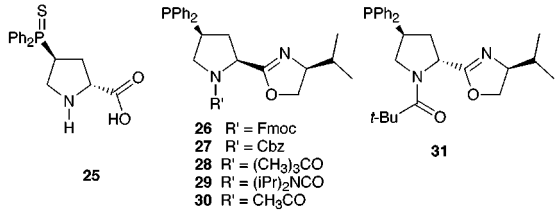


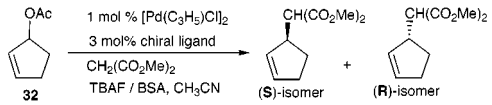
Figure 3. Phosphine−oxazoline ligands with different N-substituents.

ester to trans hydroxyproline (Figure 2). Ligands **18**−**24** have been synthesized through this approach.

In addition to being able to vary the group next to the oxazoline nitrogen, this system allows for modification of the group attached to the proline nitrogen. Our approach to these molecules takes advantage of the lability of the Boc group used to protect the nitrogen in our original example. Ligands **26**−**31** were synthesized from ligand **15** (Figure 3). Removal of the Boc group and hydrolysis of the oxazoline provided the phosphine amino acid **25**. This was converted to either a new carbamate or amide, followed by subsequent formation of the oxazoline. Compound **31**, with the oxazoline trans to diphenylphosphine group, was obtained as a diastereoisomer during the synthesis of **28**.

Asymmetric Allylic Substitution: Effects of Substituent on Oxazoline Ring. We first studied the allylic alkylation of cyclopentenyl acetate with dimethyl malonate, at 0 °C, using ligands **18**−**24** with different substituents on the oxazoline ring (Table 1). This reaction was chosen because there are few systems that perform this transformation with high selectivity.[22−28] In our system, the highest selectivity was achieved with ligand

Table 1. Palladium-Catalyzed Allylic Addition to Cyclopentenyl Acetate[a]



entry	ligand	yield[b] (%)	ee[c] (%)	configuration[d]
1	**18**	94	90	*S*
2	**19**	99	76	*S*
3	**20**	92	68	*S*
4	**21**	93	68	*S*
5	**22**	91	76	*S*
6	**23**	95	58	*S*
7	**24**	90	80	*S*

[a] All reactions were run at 0 °C and were complete in less than 1 h. [b] Isolated yield. [c] Enantiomeric excess was determined by [Eu(hfc)$_3$] shift reagent. [d] The absolute stereochemistry was determined by comparison to optical rotations in the literature.

18 (entry 1, Table 1). The alkyl group on the oxazoline has a considerable effect on the selectivity. Ligands with smaller groups on the oxazoline gave lower selectivity. Interestingly, when *tert*-butyl is substituted for the isopropyl group, **20** versus **18**, lower selectivity is obtained (entry 3 versus entry 1). In all of the cases presented in Table 1, the *S* enantiomer is obtained as the major product. In the phosphine−oxazoline systems reported previously, it has been shown that changing the stereochemistry of the oxazoline alkyl group alters the selectivity of the catalyst in favor of the other enantiomer. In the proline-based system there are three chiral centers (Figure 2). Ligands **18**−**20** are oxazolines that are formed from an L-amino acid. When ligand **21** from D-valine was tested, it gave lower selectivity but with the same enantiomer as the major product as with ligands **18**−**20**. This is the only case we know of where the stereochemistry of the oxazoline is overruled by other stereocenters in the molecule. Our discussion of the origin of the selectivity with this ligand system will account for this difference. Other interesting examples are the substitution of L- or D-phenylalanine (**19** or **22**) for L-valine gives the same selectivity (76% ee). Ligand **23** with a methyl ester gave a lower selectivity of 58% ee. Interestingly, ligand **24**, which does not possess a chiral center next to the oxazoline, nitrogen gives the product in 90% yield and 80% ee.

The effects of temperature and solvent on the reaction were also probed (Table 2). The ligand with the highest selectivity (**18**) was used in this study. Reduction of the temperature to −20 °C resulted in an increase in selectivity to 94% ee (entry 2, Table 2). At −35 °C, the selectivity improved to 96% ee (entry 1, Table 2). It was found that acetonitrile gives the highest selectivity with DMF and methylene chloride giving selectivities above 80% ee.

Effect of N-Substituent of Proline. This ligand system has a second position that can be varied to fine-

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Table 2. Palladium-Catalyzed Addition to Cyclopentenyl Acetate (32) Using Ligand 18[a]

entry	solvent	*T* (°C)	cation/base	time (h)	yield[b] (%)	ee[c] (%) (config)
1	CH_3CN	−35	TBAF/BSA	20	79	96 (*S*)
2	CH_3CN	−20	TBAF/BSA	6	99	94 (*S*)
3	CH_3CN	25	TBAF/BSA	0.5	95	86 (*S*)
4	CH_2Cl_2	0	TBAF/BSA	1	99	82 (*S*)
5	THF	0	TBAF/BSA	1.5	86	79 (*S*)
6	DMF	0	TBAF/BSA	2	90	85 (*S*)
7	benzene	25	TBAF/BSA	6	30	71 (*S*)
8	CH_2Cl_2	0	TBAF/NaH	24	10	68 (*S*)
9	CH_2Cl_2	0	Ce_2CO_3	6	97	87 (*S*)

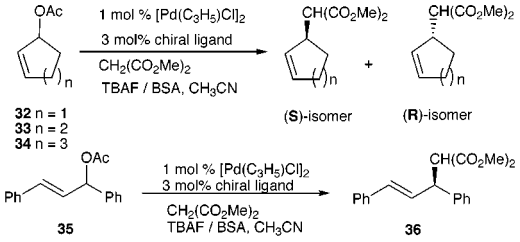
[a] Reactions were run with 2 mol % Pd to 3 mol % ligand. [b] Isolated yield. [c] Enantiomeric excess was determined by [Eu(hfc)3] shift reagent. [d] TBAF (tetrabutylammonium fluoride). [e] BSA (*N*,*O*-bis(trimethylsilyl)acetamide).

Table 3. Palladium-Catalyzed Allylic Addition to 32−35[a]

entry	substrate	ligand	*T* (°C)	time (h)	yield (%)	ee[c] (%) (config)
1	32	**18**	0	1	94	90 (*S*)
2	32	**26**	0	5	98	69 (*S*)
3	32	**27**	0	1	97	75 (*S*)
4	32	**28**	0	0.5	96	35 (*R*)
5	32	**29**	0	2	98	30 (*R*)
6	32	**30**	0	0.5	96	42 (*S*)
7	33	**18**	25	5	93	80 (*S*)
8	34	**18**	0	3	96	80 (*S*)
9	34	**28**	25	1	96	51 (*R*)
10	34	**29**	25	4	96	60 (*R*)
11	34	**30**	0	4	95	23 (*S*)
12	35	**18**	0	6	100	30 (*S*)
13	35	**28**	25	0.5	96	20 (*S*)
14	35	**29**	0	0.5	99	22 (*S*)

[a] Reactions were run with 2 mol % Pd to 3 mol % ligand. [b] Isolated yield. [c] Enantiomeric excess was determined by $[Eu(hfc)_3]$ shift reagent, and absolute stereochemistry was determined by comparison of optical rotations in the literature.

tune the selectivity of the ligand. In addition to the group on the oxazoline ring, the protecting group on nitrogen can be changed easily. Ligands **26**−**30** were examined in the allylic substitutions of cyclic substrates **32** and **34** and the linear substrate **35**, using dimethyl malonate as the nucleophile and TBAF/BSA (tetrabutylammonium fluoride/*N*,*O*-bis(trimethylsilyl)acetamide) as the base. The results are summarized in Table 3. For allylic alkylation of cyclopentenyl acetate, ligand **18** having the Boc group at nitrogen of proline turned out to be the best ligand (entry 1, Table 3). Ligand **26** (with Fmoc) and **27** (with Cbz) gave moderate selectivities of 69% ee and 75% ee, respectively (entries 2 and 3, Table 3). Ligand **30** with a sterically less demanding acetate group gave lower selectivity, 42% ee (entry 6). The six- and seven-membered ring allyl acetates also proceed in with good selectivity, 80% ee. Acyclic substrates such as **35** do not proceed with high selectivity. We believe this is due to the rather constrained nature of the pocket around the palladium.



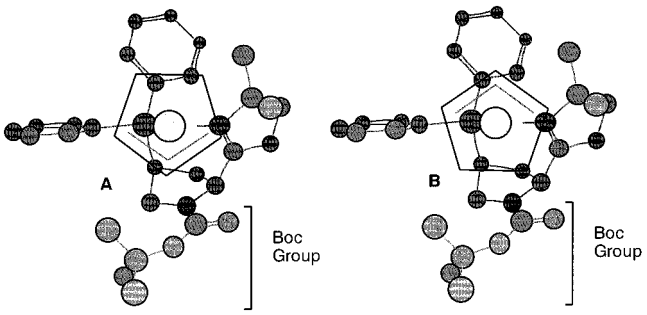


Figure 4.

Origin of Selectivity. Initially, we were surprised that the major enantiomer obtained with this ligand system was the *S* enantiomer. It has been shown by Helmchen and Pfaltz that with phosphine−oxazoline systems the nucleophile adds trans to the soft phosphine group.[9,29−31] We expected the favored conformation of the intermediate palladium π-allyl complex to be conformation **A**. It was thought that the favored conformation would be the one with the two methylenes of the five-membered ring rotated up away from the bulky Boc group. If true, the product from addition trans to the phosphine would be the *R* enantiomer. Thus, we were surprised to find that the major product is the *S* enantiomer. The *S* enantiomer comes about from preference for intermediate **B**. We feel that intermediate **B** is favored because of an interaction between the phenyl rings of the phosphine and the two methylenes of the five-membered ring (Figure 4).

To test our ideas about the preferred conformation controlling the stereochemistry of the product, we decided to replace the Boc group on nitrogen with a larger group. With such a group on nitrogen it was thought that it may be possible to turn the allyl group around such that intermediate **A** would be favored. This would result in the formation of the other enantiomer as the major product. If successful, minimally this would provide evidence for our ideas about the origin of the selectivity in this system. Optimally this could provide an approach to obtain either enantiomer of the product from two ligands that differ by only the group on the proline nitrogen. Ligands **28** and **29** where either pivalyate or diisopropylurea has been positioned on the proline nitrogen do exactly what we predicted. Both of these ligands give the *R* enantiomer, as the major product (**28**, 35% ee; **29**, 30% ee). In the case of the seven member ring allyl acetate this same effect was observed but with a greater degree of selectivity, 51% ee for **33**, and 60% ee for **34**. That the seven-member ring substrate gives better selectivity for the *R* product supports our proposed π-allyl intermediates. Since the seven-membered ring substrate has two more methylenes to interact with the bulky group on the nitrogen, one would expect a greater preference for the conformation with those methylenes away from that group.

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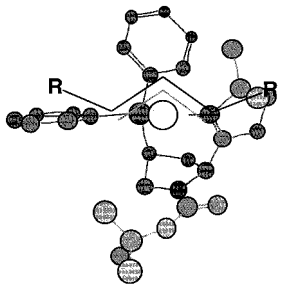
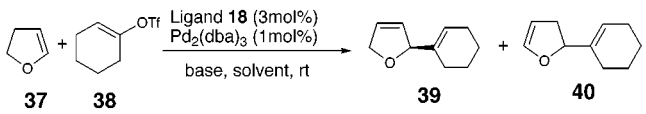


Figure 5.

To test if this ligand system is truly a bidentate ligand, compound **31** was synthesized and tested for its ability to selectively catalyze the allylation reaction. Because of the trans relationship between the phosphine and the oxazoline ring it will not be possible for this ligand to bind palladium in a bidentate manner. In the case of catalysis, with this system the product was obtained with no selectivity. We feel this system acts as a mondentate ligand and in this case that complex catalyzes the reaction with no selectivity. It is important to note that the determination of the actual catalytic species in any system like this requires considerably more work then the simple experiments laid out here. However, barring careful kinetic analysis of this system, our data is consistent with a intermediate similar to **B** being responsible for the formation of the major enantiomer.

Diphenylallyl acetate (**35**) was also examined with ligands **18**, **28**, and **30**. In all three cases, low selectivity was obtained (entries 12−14, Table 3). The "pocket" into which the allyl group must fit may be too small for the extended π-allyl complex that will form with an acyclic allyl acetate (Figure 5). Alternatively the dominant directing groups with this ligand system appear to be positioned above and below the allyl intermediate. In the case of the intermediate formed from acyclic allyl acetates one would expect there to be little or no interaction with groups positioned above or below the metal.

Intermolecular Heck Reaction. In addition to palladium-catalyzed allylation, phosphine−oxazoline ligands have been extensively used in asymmetric intermolecular Heck reactions.[3−5,10,14,32−34] With that in mind, we investigated the utility of the proline-based system in this reaction. For our initial study, we decided to use dihydrofuran (**37**) and 1-cyclohexenyltriflate (**38**) as substrates. Three ligands were studied, **18**, **20**, and **29**. Due



to its ready availability, ligand **18** was chosen to optimize the reaction conditions. Table 4 illustrates the various conditions that were tested. The choice of solvent and base can have a profound effect on the activity of these catalysts as well as on the selectivity. Good selectivity and high reactivity were observed for the reactions using benzene or dioxane as the solvent (entries 1 and 4, Table 4). High reactivity but poor selectivity was observed for NMP as solvent (entry 9, Table 4). Table 5 illustrates the result of the study where the solvent was kept constant and a variety of bases were tested. It was apparent that when diisopropylethylamine and triethylamine were employed as base, the reaction resulted in good selectivity with better yield than those using other bases. Although the reaction took less than 1 day to go to completion, Bu_4NOAc resulted in no selectivity (entry 7, Table 5). Ligands **20** and **29** were also examined but were found to give significantly lower selectivity than ligand **18** when the optimized conditions were used.

Table 4. Results of the Heck Reaction with Ligand 18 in Various Solvents Using Diisopropylethylamine as the Base

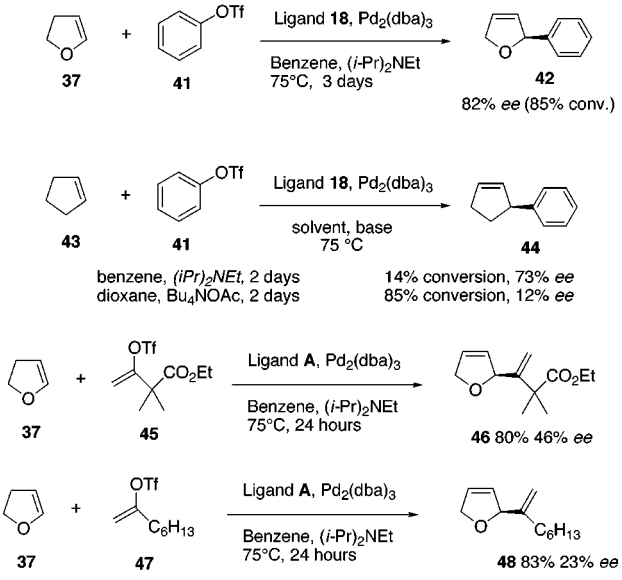
entry	solvent	time	conversion (%)	ee[a] (%)	isomer (%)
1	benzene	24 h	98	80	<2
2	toluene	2 d	84	49	4
3	benzene/hexane	5 d	99	57	1.5
4	dioxane	36 h	99	80	<2
5	dichloroethane	3 d	46	80	40
6	THF	3 d	88	70	5
7	dichloromethane	6 d	52	74	24
8	acetonitrile	3 d	52	12	33
9	NMP	20 h	99	58	5
10	DMF	2 d	80	28	4
11	DMSO	3 d	100	68	9

[a] Ratios were determined by GC with CHIRALDEX G-TA 30M column at 70 °C. The retention times were 24.6 min for the *S* enantiomer, 28.7 min for the *R* isomer, and 18.7 min for isomer **39**.

Table 5. Results of the Heck Reaction with Ligand 18 in Dioxane Using Various Bases

entry	base	time	conversion (%)	ee (%)	isomer (%)
1	$(^iPr)_2NEt$	36 h	98	80	<2
2	Et_3N	36 h	99	86	7
3	K_2CO_3	6 d	84	60	5
4	Proton sponge	6 d	69	71	11
5	NaOAc	5 d	39	−21	1.4
6	tBuONa	4 d	66	10	32
7	Bu_4NOAc	20 h	98	−11	
8	DBU	3 d	7	−3	
9	$Me_4NOH·5H_2O$	5 d	28	17	40
10	Et_3N/Bu_4NF (1:1)	3 d	56	2	18

Scheme 2



Additional substrates were examined to determine if this ligand system is general. Reaction of aryl triflate (**41**) and 2,3-dihydrofuran (**37**) using ligand **18** gave good selectivity and high conversion at 75 °C (Scheme 2). Reaction of aryl triflate **41** and cyclopentene **43** in the presence of diisopropylethylamine in benzene was slow

and gave moderate selectivity; the reaction with tetrabutylamoniumacetate as base in dioxane is much faster, but the selectivity is low. Reaction of dihydrofuran **37** and acyclic vinyl triflate **45** provided the product **46** with 46% ee in 80% yield. The reaction of dihydrofuran **37** and octanenyl-triflate **47** resulted in much lower selectivity (23% ee, 83% yield).

Conclusion

A proline-based phosphine−oxazoline ligand system has been developed and has been proven to be very effective in the control of the addition of dimethyl malonate to cyclic allyl acetates **32**−**34**. The results discussed above mapped out the interesting features of proline-based phosphine−oxazoline ligands. The chiral center on the oxazoline ring has moderate effect on the selectivity of catalysis, while the substituents at the proline nitrogen has pronounced and unusual influence on the stereochemistry of the product. We have shown that it is possible to reverse the selectivity of the reaction by simply changing the size of the substituent on the proline nitrogen. We are currently looking at catalysis of the addition of other nucleophiles with this system. Derivatives of this ligand are also being developed for use in other transition metal catalyzed reactions.

Experimental Section

General Methods. Melting points are uncorrected. IR spectra were recorded neat or as thin films. ^{1}H (300 or 600 MHz) and ^{13}C (75.43 or 100.57 MHz) NMR spectra were obtained in $CDCl_3$ using either TMS (for ^{1}H) or $CDCl_3$ (for ^{13}C) as the internal standard. All solvents were purchased from Aldrich and used as obtained except where noted. THF was freshly distilled from sodium benzophenone ketyl under nitrogen, methylene chloride was freshly distilled from CaH_2 under nitrogen. *n*-Butyllithium was purchased from Aldrich as a solution in hexanes, stored in a a sure seal bottle under nitrogen. All experiments were carried out under nitrogen in dried glassware, using syringe-septum cap techniques. The −78 and 0 °C external bath temperatures designated are approximate as achieved by a dry ice−acetone or ice−salt bath, respectively. Flash column chromatography was carried out using Merck Kieselgel 60 silica gel (particle size 32−63 μm).

(2*S*,2′*S*,4*R*)-*N*-*tert*-Boc-2-[[*N*-[(2′-methoxycarbonyl-2′-isopropyl)methyl]-1′-amino]carbonyl]-4-hydroxylproline (7). A mixture of *N*-*t*-Boc-L-hydroxylproline (3.50 g, 15.1 mmol), EDC (5.80 g, 30.2 mmol), and HOBt (4.10 g, 30.2 mmol) was stirred in 60 mL of dry CH_2Cl_2 at 0 °C for 5 min. In a separate flask, L-valine methyl ester hydrochloride (3.80 g, 22.7 mmol) and Et_3N (4.20 mL, 30.2 mmol) were stirred for 10 min in 60 mL of CH_2Cl_2, after which time the mixture was added to the active ester. The resulting clear solution was warmed to room temperature and stirred for 1 day. After evaporation of CH_2Cl_2, the residue was dissolved in EtOAc/H_2O (4/1, v/v). The organic layer was washed with 1 N HCl (aq), saturated $NaHCO_3$ (aq), H_2O, and brine and then dried over Na_2SO_4. The solvent was removed by evaporation, leaving a residue that was subjected to column chromatography (eluant: EtOAc/*n*-hexanes 95/5, v/v) to yield 4.68 g (90%) as a white foamy solid: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (m, 1H), 6.85 (m, 1H), 4.40 (m, 3H), 3.66 (s, 3H), 3.50−3.20 (m, 2H), 2.08 (dqq, J = 6.0, 6.8, 6.7 Hz, 1H), 1.42 (s, 9H), 0.88 (d, J = 6.8 Hz, 3H) 0.85 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 171.7, 155.5, 154.5, 80.2, 69.2, 68.6, 60.0, 58.2, 57.0, 54.6, 54.1, 51.6, 39.3, 36.2, 30.7, 27.9, 17.7, 17.6, 17.5, 17.3; IR (film) 3408.0, 3017.5, 2972.1, 1739.7, 1683.7, 1521.8, 1395.4, 1216.1, 1161.1, 745.1, 668.3 cm^{-1}; MS-FAB *m*/*z* (rel intensity) 345 (MH^+, 25), 289 (22), 245 (100); HRFAB calcd for $C_{16}H_{29}N_2O_6$ (MH^+) *m*/*e* 345.2025, measured *m*/*e* 345.2036. Anal. Calcd for $C_{16}H_{28}N_2O_6$: C, 55.80; H, 8.19. Found: C, 55.36; H, 7.87.

(2*S*,2′*S*,4*R*)-*N*-*tert*-Boc-2-[[*N*-[(2′-hydroxymethyl-2′-isopropyl)methyl]-1′-amino]carbonyl]-4-hydroxylproline (8). To a solution of (2*S*,2′*S*,4*R*)-*N*-*tert*-Boc-2-[[*N*-[(2′-methoxycarbonyl-2′-isopropyl)methyl]-1′-amino]carbonyl]-4-hydroxylproline (**7**) (4.68 g, 13.4 mmol) in 200 mL of THF was slowly added lithium borohydride solution (13.4 mL, 26.6 mmol, 2 M in THF) at 0 °C. The cooling bath was removed, and stirring was continued at room temperature for 16 h. The reaction was quenched by adding 2 N HCl, and THF was evaporated under reduced pressure. The residue was dissolved in EtOAc/H_2O (4/1, v/v), and the aqueous layer was extracted with EtOAc three times. The combined organic layers were then washed with a small amount of 1 N NaOH and brine and dried over Na_2SO_4. Evaporation of the solvent gave 3.68 g (87%) of **8** as a white foam. This material was used for the next step without further purification. The sample was judged by NMR to be at least 90% pure: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 and 6.72 (2 br s, 1H), 4.25 (m, 3H), 3.55−3.20 (m, 5H), 2.25 (m, 1H), 1.96 (m, 1H), 1.73 (m, 1H), 1.30 (m, 9H), 0.75 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ + 1 drop of DMSO-d_6) δ 173.5, 172.5, 155.7, 154.5, 80.5, 69.2, 68.6, 62.7, 62.6, 58.9, 58.8, 56.9, 56.8, 54.5, 37.1, 37.0, 28.8, 28.1, 19.3, 18.8, 18.7, 18.1; IR (film) 3410.0, 3320.0, 3055.1, 2986.6, 1675.1, 1533.3, 1420.5, 1265.2, 1163.0, 895.8, 739.7, 668.3 cm^{-1}; MS-FAB *m*/*z* (rel intensity) 317 (MH^+, 100), 303 (58); HRFAB calcd for $C_{15}H_{29}N_2O_5$ (MH^+) *m*/*e* 317.2076, measured *m*/*e* 317.2071.

(2*S*,5′*S*,4*R*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-(methylsulfonyl)oxylproline (12). A sample of **8** (3.58 g, 11.3 mmol) was dissolved in CH_2Cl_2/Et_3N (200 mL, 3/1, v/v), and the solution was cooled to 0 °C. To the solution was slowly added MsCl (3.5 mL 45.2 mmol) in 10 mL of CH_2Cl_2, with stirring through an addition funnel after which the reaction was stirred at room temperature for 16 h. This resulted in a dark-brownish solution with the precipitation of ammonium salt. The solvent was removed by evaporation, leaving a residue that was dissolved in EtOAc/H_2O (4/1, v/v). The organic solution was then washed with water twice and dried over Na_2SO_4. Evaporation of the solvent gave the crude product, which was purified by flash chromatography (eluant: EtOAc/*n*-hexanes/Et_3N, 84/15/1) to afford a brownish viscous oil in 61% yield: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.14 (m, 1H), 4.48 (dd, J = 7.3, 7.7 Hz, 1H), 4.10 (dd, J = 8.8, 8.4 Hz, 1H), 3.91−3.80 (m, 2H), 3.74−3.57 (m, 2H), 2.92 (s, 3H), 2.53−2.35 (m, 1H), 2.23−2.17 (m, 1H), 1.61 (m, 1H), 1.33 (minor) and 1.29 (major) (s, 9H), 0.79 (d, J = 6.6 Hz, 3H), 0.73 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 153.5, 80.1, 78.0, 77.6, 71.7, 71.4, 70.0, 52.9, 52.5, 52.0, 51.8, 38.3, 37.7, 36.6, 32.2, 32.0, 28.0, 18.2, 18.1, 17.6, 17.4; IR (film) 3019.4, 2970.2, 1700.2, 1690.0, 1405.1, 1368.4, 1215.1, 1173.6, 967.2, 901.7, 756.1, 668.3 cm^{-1}; MS−FAB *m*/*z* (rel intensity) 377 (MH^+, 65), 321 (100); HRFAB calcd for $C_{16}H_{29}N_2O_6S$ (MH^+) *m*/*e* 377.1746, measured *m*/*e* 377.1735.

(2*S*,5′*S*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (15). Ph_2PH (0.59 mL, 3.4 mmol) was added to a −78 °C suspension of $NaNH_2$ (0.17 g, 4.25 mmol) in degassed THF. After being stirred for 15 min, the reaction mixture was allowed to warm to room temperature and stirring was continued for 3 h. To this orange solution was added a solution of **12** (0.64 g, 1.7 mmol in 15 mL of THF), and the reaction mixture was stirred at room temperature for 12 h. Next, S_8 (0.11 g, 3.4 mmol in 15 mL of THF) was added at 0 °C, and the stirring was continued for 2 h at room temperature. After removal of solvent under reduced pressure, the residue was treated with NH_4Cl (satd) and extracted with EtOAc three times. The EtOAc solutions were combined and evaporated to give the crude phosphine that was chromatographed on silica gel with EtOAc/hexane/Et_3N (66/33/1, v/v/v) to afford 0.55 g (65%) of **15** as a white solid: R_f = 0.30 (EtOH/*n*-hexanes 2/1); mp 76−78 °C; (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.81 (m, 4H), 7.54−7.44 (m, 6H),

4.52 (dd, J_{HH} = 8.1, 8.5 Hz, 1H), 4.23 (m, 1H), 4.05 (m, 1H), 3.90 (m, 1H), 3.68 (m, 2H), 3.30 (m, 1H), 2.53 (m, 1H), 2.23 (m, 1H), 1.70 (m, 1H), 1.39 (m, 9H), 0.92 (d, J_{HH} = 6.6 Hz, 3H), 0.85 (d, J_{HH} = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 153.5, 131.8 (d, J_{CP} = 2.5 Hz), 131.1 (d, J_{CP} = 10.1 Hz), 128.8 (d, J_{CP} = 12.1 Hz), 80.2, 72.0, 70.4, 60.3, 55.3 (d, J_{CP} = 12.0 Hz), 47.4, 37.6 (d, J_{CP} = 61.4 Hz), 32.3 (d, J_{CP} = 25.1 Hz), 28.3, 18.6, 18.1; ^{31}P (120 MHz, $CDCl_3$) δ 44.12 (major) and 43.94 (minor), 44.20 (45 °C); IR (film) 3019.4, 2978.9, 1695.0, 1479.0, 1405.1, 1216.1, 1160.1, 1104.2, 758.0, 669.3 cm^{-1}; MS-FAB *m/z* (rel intensity) 499 (MH^+, 100), 399 (13), 281 (25), 219 (35); HRFAB calcd for $C_{27}H_{36}N_2O_3PS$ (MH^+) *m/e* 499.2184, measured *m/e* 499.2189. Anal. Calcd for $C_{27}H_{35}N_2O_3PS$: C, 65.04; H, 6.76. Found: C, 64.89; H. 7.07.

Detailed procedures for **16**, **17**, **21**, **22**, **23**, and **24** are provided in the Supporting Information.

(2*S*,5′*S*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-phenyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (16): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92−7.82 (m, 4H), 7.55−7.43 (m, 6H), 7.32−7.20 (m, 5H), 5.20 (dd, J_{HH} = 9.8, 8.3 Hz, 1H), 4.62 (J_{HH} = 8.5, 8.6 Hz, 1H), 4.17 (m, 2H), 3.86−3.58 (m, 2H), 3.36 (m, 1H), 2.65 (m, 1H), 2.34 (m, 1H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 143.4, 141.9, 131.8 (d, J_{CP} = 3.0 Hz), 131.0 (d, J_{CP} = 10.1 Hz), 128.7 (d, J_{CP} = 12.0 Hz), 128.6 (d, J_{CP} = 7.6 Hz), 127.5, 126.6, 126.4, 80.2, 75.0, 69.4, 55.2 (d, J_{CP} = 11.0 Hz), 47.3, 37.6 (d, J_{CP} = 60.1 Hz), 31.9 (d, J_{CP} = 47.1 Hz), 28,2, 28.1; ^{31}P (120 MHz, $CDCl_3$) δ 44.3 (major), 44.1 (minor); IR (film) 3019.4, 2980.8, 1695.3, 1404.1, 1216.1, 1160.1, 755.1, 668.3 cm^{-1}; MS-FAB *m/z* (rel intensity) 539 (MLi^+, 49), 439 (90), 294 (20); HRFAB Calcd for $C_{30}H_{33}N_2O_3PSLi$ (MLi^+) *m/e* 539.2109, measured *m/e* 539.2115. Anal. Calcd for $C_{30}H_{33}N_2O_3PS$: C, 67.52; H, 6.42. Found: C, 67.67; H. 6.21.

(2*S*,5′*S*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-*tert*-butyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (17): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.80 (m, 4H), 7.51−7.30 (m, 6H), 4.56 (dd, J_{HH} = 7.8, 9.3 Hz, 1H), 4.20−4.12 (m, 2H). 3.84 (m, 1H), 3.65 (m, 2H), 3.30 (m, 1H), 2.50 (m, 1H), 2.24 (m, 1H), 1.40 (s, 9H), 0.85 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 153.4, 131.7 (d, J_{CP} = 3 Hz), 131.0 (d, J_{CP} = 9.8 Hz), 128.74 (d, J_{CP} = 12.0 Hz), 128.67 (d, J_{CP} = 12.0 Hz), 80.1, 75.5, 68.9, 55.3 (d, J_{CP} = 12.0 Hz), 47.3, 37.4 (d, J_{CP} = 60.2 Hz), 33.5, 32.0, 28.2, 25.6; ^{31}P (120 MHz, $CDCl_3$) δ 44.11 (major), 43.89 (minor); IR (film) 2977.0, 2905.6, 2865.0, 1693.4, 1478.4, 1404.1, 1367.5, 1246.0, 1161.1, 1104.2, 999.1, 960.0, 909.4, 731.0, 649.0 cm^{-1}; MS−FAB *m/z* (rel intensity) 513 (MH^+, 100), 413 (20), 295 (25); HRFAB calcd for $C_{28}H_{38}N_2O_3PS$ (MH^+) *m/e* 513.2341, measured *m/e* 513.2322.

(2*S*,5′*R*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (the phosphine sulfide of 21): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.81 (m, 4H), 7.51−7.44 (m, 6H), 4.53 (dd, J_{HH} = 8.1, 8.0 Hz, 1H), 4.33 (dd, J_{HH} = 8.5, 8.3 Hz, 1H), 3.90 (dd, J_{HH} = 8.8, 8.1 Hz, 1H), 3.84−3.62 (m, 4H), 3.27 (m, 1H), 2.50 (m, 1H), 2.30 (m, 1H), 1.70 (m, 1H), 1.42 (s, 9H), 1.27 (d, J_{HH} = 6.1 Hz, 3H), 1.01 (d, J_{HH} = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 153.5, 131.8 (d, J_{CP} = 3.0 Hz), 131.8 (d, J_{CP} = 3.0 Hz),131.1 (d, J_{CP} = 10.0 Hz), 128.8 (d, J_{CP} = 12.0 Hz), 128.7 (d, J_{CP} = 12.0 Hz),-80.3, 72.8, 71.2, 62.2, 54.9 (d, J_{CP} = 11.0 Hz), 47.5, 37.8 (d, J_{CP} = 61.0 Hz), 32.4 (d, J_{CP} = 51.5 Hz), 28.3, 19.4, 18.8; ^{31}P (120 MHz, $CDCl_3$) δ 44.2; IR (film) 3054.1, 2984.7, 1696.3, 1400.2, 1265.2, 1160.1, 738.7 cm^{-1}; MS-FAB *m/z* (rel intensity) 505 (MLi^+, 37), 405 (66), 294 (21), 160 (100); HRFAB calcd for $C_{27}H_{36}N_2O_3PSLi$ (MLi^+) *m/e* 505.2266, measured *m/e* 505.2274. Anal. Calcd for $C_{27}H_{35}N_2O_3PS$: C, 65.04; H, 6.76. Found: C, 64.58; H. 6.87.

(2*S*,5′*R*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-phenyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (the phosphine sulfide of 22): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91−7.82 (m, 4H), 7.50−7.45 (m, 6H), 7.32−7.20 (m, 5H), 5.20 (dd, J_{HH} = 9.0, 9.0 Hz, 1H), 4.62 (dd, J_{HH} = 8.1, 8.6 Hz, 2H), 4.16 (m, 1H), 3.75 (m. 2H), 3.38 (m, 1H), 2.70 (m, 1H), 2.33 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 153.4, 141.9, 131.8 (d, J_{CP} = 3.0 Hz), 131.0 (d, J_{CP} = 10.0 Hz), 128.8 (d, J_{CP} = 12.1 Hz), 128.7 (d, J_{CP} = 7.0 Hz), 127.5, 126.7, 126.4, 80.3, 75.0, 69.4, 54.3 (d, J_{CP} = 145.2 Hz), 47.3, 37.6 (d, J_{CP} = 59.6 Hz), 31.9 (d, J_{CP} = 47.6 Hz), 28.2; ^{31}P (120 MHz, $CDCl_3$) δ 44.3 (major), 44.1 (minor); IR (film) 3019.4, 2980.8, 1695.3, 1405.1, 1216.1, 1160.1, 756.1, 668.3 cm^{-1}; MS-FAB *m/z* (rel intensity) 533 (MH^+, 100), 433 (30), 315 (25), 259 (27), 219 (30), 154 (25); HRFAB calcd for $C_{30}H_{34}N_2O_3PS$ (MH^+) *m/e* 533.2028, measured *m/e* 533.2032.

(2*S*,5′*R*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-methoxylcarbonyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (the phosphine sulfide of 23): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.82 (m, 4H), 7.52−7.43 (m, 6H), 4.75−4.68 (m, 1H), 4.61−4.45 (m, 3H), 3.77 (s, 3H), 3.76 (m, 2H), 3.34 (m, 1H), 2.65−2.45 (m, 1H), 2.27−2.19 (m, 1H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ170.9, 169.7, 153.5, 140.0 (d, J_{CP} = 10.1 Hz), 131.8, 131.7, 128.7 (d, J_{CP} = 12.0 Hz), 80.5, 69.4, 68.0, 54.8 (d, J_{CP} = 11.5 Hz), 52.4, 47.3 (d, J_{CP} = 6.0 Hz), 37.5 (d, J_{CP} = 60.1 Hz), 32.3, 28.0; ^{31}P (120 MHz, $CDCl_3$) δ 44.3; IR (film) 3054.4, 2987.1, 1742.5, 1696.3, 1551.9, 1421.9, 1265.0, 1159.3, 896.0, 737.0, 703.7; MS-FAB *m/z* (rel intensity 515 (MH^+, 100), 415 (53), 219 (65); HRFAB calcd for $C_{26}H_{32}N_2O_6PS$ (MH^+) *m/e* 515.1769, found 515.1767.

(2*S*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′,5′-dimethyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (phosphine sulfide of 24): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, CDCl3) δ 7.94−7.81 (m, 4H), 7.51−7.42 (m, 6H), 4.50 (dd, J_{HH} = 8.3, 8.3 Hz, 1H), 4.02 (d, J_{HH} = 8.1 Hz, 1H), 3.91 (d, J_{HH} = 8.1 Hz, 1H), 3.70 (m, 2H), 3.30 (m, 1H), 2.55 (m, 1H), 2.22 (m, 1H), 1.42 (s, 9H), 1.31 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 153.5, 131.8 (d, J_{CP} = 3.0 Hz), 131.1 (d, J_{CP} = 10.1 Hz), 128.8 (d, J_{CP} = 12.1 Hz), 128.5 (d, J_{CP} = 27.5 Hz), 80.3, 79.4, 67.1, 55.0 (d, J_{CP} = 11.1 Hz), 47.4 (d, J_{CP} = 6.1 Hz), 37.6 (d, J_{CP} = 60.0 Hz), 33.2, 28.3, 28.1; ^{31}P (120 MHz, $CDCl_3$) δ 44.1; IR (film) 3019.4, 2977.0, 1695.3, 1404.1, 1216.1, 1160.1, 758.0, 668.3 cm^{-1}; MS-FAB *m/z* (rel intensity) 485 (MH^+, 100), 368 (48), 267 (15); HRFAB calcd for $C_{26}H_{33}N_2O_3PS$ (M^+) *m/e* 484.1949, measured *m/e* 484.1949.

Sample Procedure for Raney Nickel Reduction. (2*S*,5′*S*,4*S*)-*N*-*tert*-Boc-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazole-2′-yl)-4-diphenylphosphinoproline (18). Phosphine sulfide **15** (50 mg, 0.1 mmol) was added to Raney nickel (0.5 g), in CH_3CN (6 mL), that had been washed with methanol (three times), ether (three times), and degassed CH_3CN (three times). The reaction mixture was stirred at room temperature for 8 h, by which time the ^{31}P NMR spectrum indicated the complete reduction of the phosphine sulfide to the phosphine. The Raney nickel was then filtrated through a syringe filter. Evaporation of solvent afforded 40 mg (86%) of **18** as a white solid that was ready to use for catalysis: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.20 (m, 10H), 4.39 (dd, J = 7.8, 8.4 Hz, 1H), 4.13 (m, 1H), 3.94−3.83 (m, 2H), 3.64 (m, 1H), 3.29 (m, 1H), 2.80 (m, 1H), 2.26 (m, 1H), 1.92 (m, 1H), 1.64 (m, 1H), 1.33 (s, 9H), 0.84 (d, J = 6.3 Hz, 3H), 0.77 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 153.6, 133.33 (J_{CP} = 11.6 Hz), 133.0 (J_{CP} = 19.1 Hz), 129.1, 128.6 (J_{CP} = 6.8 Hz), 79.9, 71.9, 70.2, 55.64 (d, J_{CP} = 8.0 Hz), 50.7 (d, J_{CP} = 28.0 Hz), 36.3 (d, J_{CP} = 20.0 Hz), 35.2 (d, J_{CP} = 9.0 Hz), 32.5, 28.3, 18.6, 17.9; ^{31}P (120 MHz, $CDCl_3$) δ −9.24 (major) and −10.0 (minor); MS-FAB *m/z* (rel intensity) 467 (MH^+, 100), 411 (30), 254 (37), 185 (50); HRFAB calcd for $C_{27}H_{36}N_2O_3P$ (MH^+) *m/e* 467.2463, measured *m/e* 467.2471.

(2*S*,5′*R*,4*S*)-*N*-Fmoc-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline sulfide (26): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90−7.16 (m, 18 H), 4.91−3.61 (m, 8H), 3.35 (m, 1H), 2.57 (m, 1H), 2.30 (m, 1H), 1.66 (m, 1H), 1.30 (m, 1H), 0.90−0.79 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 165.3, 154.2, 153.9, 143.9, 143.8, 143.6, 143.4, 141.0, 131.8, 131.7, 131.0, 130.8, 128.7 (d, J_{CP} = 12.0 Hz),

127.5, 126.8, 125.0, 124.8, 119.7; ^{31}P (120 MHz, $CDCl_3$) δ 44.3; IR (film) 3054.4, 2986.9, 1705.6, 1421.7, 1353.8, 1264.6, 1165.8, 1104.3, 896.1, 747.3; MS−FAB *m/z* (rel intensity) 621 (MH^+, 100), 403 (30); HRFAB calcd for $C_{37}H_{38}N_2O_3PS$ (MH^+) *m/e* 621.2341, found 621.2337.

(2*S*,5′*R*,4*S*)-*N*-Cbz-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (27): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.82 (m, 4H), 7.48 (m, 6H), 7.30 (m, 5H), 5.26−4.95 (m, 2H), 4.62 (dd, J = 7.8, 8.7 Hz, 1H), 4.21−3.65 (m, 5H), 3.35 (m, 1H), 2.54 (m, 1H), 2.25 (m, 1H), 1.70−1.57 (m, 1H), 0.87−0.77 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 154.0, 136.4, 131.8, 131.7, 131.0, 130.9, 128.7 (d, J_{CP} = 12.0 Hz), 128.2, 127.8, 71.8, 70.3, 55.3 (d, J_{CP} = 11.0 Hz), 55.1 (d, J_{CP} = 11.0 Hz), 47.9, 47.3, 38.3 (d, J_{CP} = 61.1 Hz), 37.6 (d, J_{CP} = 60.2 Hz), 32.2, 32.1, 31.2, 18.5, 17.9; ^{31}P (120 MHz, $CDCl_3$) δ 44.0; IR 3054.4, 2987.1, 1705.3, 1603.7, 1551.9, 1437.0, 1421.8, 1359.3, 1262.9, 1170.4, 896.1, 743.0; MS-FAB *m/z* (rel intensity) 532 (MH^+, 77), 315 (28), 154 (100); HRFAB calcd for $C_{30}H_{33}N_2O_3PS$ (MH^+) *m/e* 532.1949, found 532.1940.

(2*S*,5′*R*,4*S*)-*N*-Piv-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (28) and (2*R*,5′*R*,4*S*)-*N*-Piv-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (31). Compound 28: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90−7.77 (m, 4H), 7.53−7.41 (m, 6H), 4.81 (dd, J = 8.4, 8.4 Hz, 1H), 4.18−4.09 (m, 1H), 3.96−3.80 (m, 4H), 3.36−3.23 (m, 1H), 2.39−2.14 (m, 2H), 1.71−1.60 (m, 1H), 1.12 (s, 9H), 0.86 (d, J = 6.9 Hz, 3H), 0.79 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ176.1, 166.2, 131.94 (d, J_{CP} = 6.0 Hz), 311.90 (d, J_{CP} = 6.0 Hz), 131.1, 131.0, 130.8, 128.9 (d, J_{CP} = 12.0 Hz), 128.8 (d, J_{CP} = 12.0 Hz), 71.7, 70.2, 56.4 (d, J_{CP} = 11.0 Hz), 48.7 (d, J_{CP} = 6.5 Hz), 39.4 (d, J_{CP} = 60.2 Hz), 38.7, 32.4, 29.7, 27.3, 18.6, 18.0; ^{31}P (120 MHz, $CDCl_3$) δ 43.0; IR 3054.4, 2987.1, 1670.4, 1625.9, 1548.1, 1440.0, 1421.9, 1264.9, 896.0, 739.9, 710.0; MS-FAB *m/z* (rel intensity) 483 (MH^+, 100), 265 (175), 152 (43); HRFAB calcd for $C_{27}H_{36}N_2O_2PS$ (MH^+) *m/e* 483.2235, found 483.2233.

Compound 31: (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93−7.81 (m, 4H), 7.53−7.42 (m, 6H), 4.92 (d, J = 8.7 Hz, 1H), 4.30−4.22 (m, 1H), 4.05−3.85 (m, 5H), 2.48 (br s, 1H), 1.82−1.76 (m, 2H), 1.20 (s, 9H), 0.92 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ176.2, 167.2, 131.9 (d, J_{CP} = 7.0 Hz), 131.8 (d, J_{CP} = 7.0 Hz), 131.2, 131.0, 130.9, 128.9 (d, J_{CP} = 13.5 Hz), 128.7 (d, J_{CP} = 12.2 Hz), 71.6, 70.0, 56.2, 47.9, 38.9, 38.0, 32.2, 29.6, 27.4, 18.6, 17.6; ^{31}P (120 MHz, $CDCl_3$) δ 45.8; IR (film) 3054.5, 2986.9, 1675.3, 1640.0, 1532.2, 1421.9, 1265.1, 896.0, 736.8, 705.1; MS-FAB *m/z* (rel intensity) 483 (MH^+, 100), 256 (40), 219 (30), 152 (43); HRFAB calcd for $C_{27}H_{36}N_2O_2PS$ (MH^+) *m/e* 483.2235, found 483.2231.

(2*S*,5′*R*,4*S*)-*N*-Acetyl-2-(4′,5′-dihydro-5′-isopropyl-1′,3′-oxazol-2′-yl)-4-diphenylphosphinothioylproline (30): (*NMR spectra are reported for a mixture of two rotamers*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.76 (m, 4H), 7.50−7.39 (m, 6H), 4.66−4.55 (m, 1H), 4.26−4.11 (m, 1H), 4.05−3.84 (m, 3H), 3.60−3.18 (m, 2H), 2.71−2.15 (m, 2H), 1.95 and 1.94 (s, 3H), 1.71−1.60 (m, 1H), 0.89−0.76 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) d169.6, 168.7, 165.4, 132.1−131.7 (m), 131.1−130.8 (m), 129.0−128.7 (m), 72.0, 71.7, 70.8, 70.2, 55.7 (d, J_{CP} = 11.0 Hz) 48.6, 46.9, 38.4 (d, J_{CP} = 60.1 Hz), 37.1 (d, J_{CP} = 59.6 Hz), 32.4, 32.2, 30.9, 22.5, 21.7, 18.6, 18.5, 18.1, 17.8; ^{31}P (120 MHz, $CDCl_3$) d 44.5 and 43.9; IR (film) 3054.1, 2986.7, 1650.9, 1551.1, 1436.4, 1421.9, 1265.0, 1102.1, 909.0, 947.9, 650.7; MS-FAB *m/z* (rel intensity) 441 (MH^+, 100), 328 (10), 218 (32); HRFAB calcd for $C_{24}H_{30}N_2O_2PS$ (MH^+) *m/e* 441.1766, found *m/e* 441.1777.

Procedure for π-Allylation. The phosphine−oxazoline ligand was mixed with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in degassed solvent, followed by addition of the cyclic allylic acetate. To this mixture a solution containing dimethyl malonate (3 equiv), TBAF (3 equiv), and BSA (3 equiv) was added slowly through an addition funnel (30 min). After the reaction was complete, water was added to quench the reaction, and the organic solvent was removed by evaporation. The water layer was then extracted with diethyl ether twice and the ether solution was washed with saturated $NaHCO_3$, brine and dried over Na_2SO_4. Evaporation of solvent gave a residue that was chromatographed by using EtOAc/*n*-hexanes (10/90, v/v) as an eluant to afford a colorless oil.

Procedure for the Heck Reaction. A mixture of triflate, alkene (5 mol equiv), base (3 equiv), $Pd_2(dba)_3$ (1.5 mol %), and ligand (3 mol %) in degassed solvent was stirred at the reaction temperature. The progress of the reaction was monitored by GC and TLC. Upon completion, the mixture was diluted with additional diethyl ether and washed with water and brine, dried, and evaporated. Crude product was purified by chromatography on a silica gel column using hexane as the eluant.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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