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StePHOX, a new family of optically active, tunable phosphine–oxazoline ligands: syntheses and applications

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Abstract—A new class of optically active phosphine–oxazoline ligands has been synthesized wherein backbone chirality of these new ligands is installed by a Sharpless asymmetric dihydroxylation. Different backbone protecting groups as well as different substitution patterns on the oxazoline ring were studied. These ligands were tested in allylic substitution (with ee's up to 97%) and asymmetric Tsuji allylation.

1. Introduction

The phosphine–oxazoline (PHOX, Fig. 1) ligands comprise a versatile class of heterobidentate structures, which have a remarkably broad range of applications in asymmetric catalysis.[1] Several features of the PHOX ligands originally introduced by Pfaltz,[2] Helmchen,[3] and Williams,[4] are important. From an electronic perspective, the coordinating heteroatoms are sufficiently distinct that they render the reactivity of neighboring coordination sites, in a transition metal complex, nonequivalent. By altering the substitution of the aromatic backbone,[5] the electronic properties of the ligand can be fine tuned thereby leading to enhanced reactivity and selectivity for a reaction of interest. Similarly, the steric environment imposed by the ligand may be modified by altering the substituents on the oxazoline ring and on the phosphorus atom. In addition to these perturbations to the parent structure, several groups have examined alternate linkages that connect the phosphine and oxazoline groups. When these connecting elements are rendered chiral, new opportunities arise for ligand tuning and representative examples are depicted in Figure 1.[6]

To expand the tunability of the phosphine–oxazoline ligands, we have designed a new ligand class, coined StePHOX, which is depicted in Figure 2. The added control element is a dioxolane backbone, which connects the phosphine and oxazoline motifs. It was anticipated that chirality associated with the dioxolane linkage would impose itself on the ligand conformation such that the chirality on the oxazoline may not be required for asymmetric induction. Furthermore, the dioxolane offers an additional tuning element to those which are already present in the PHOX ligands. In this report, we describe an efficient synthetic route that provides members of the StePHOX ligand family. Also described, are structural studies on StePHOX–metal complexes and preliminary observations on enantioselective catalysis.

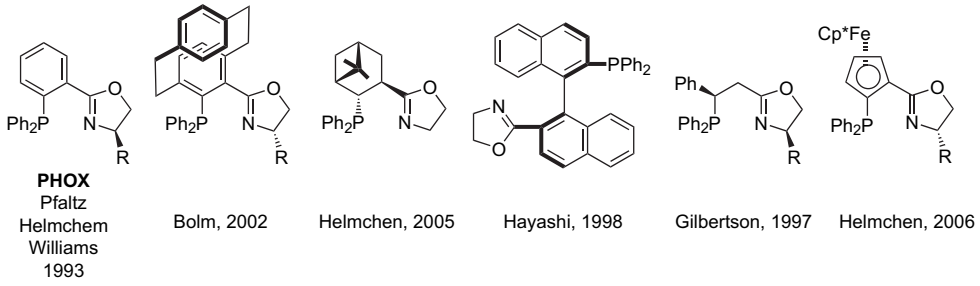

Figure 1.

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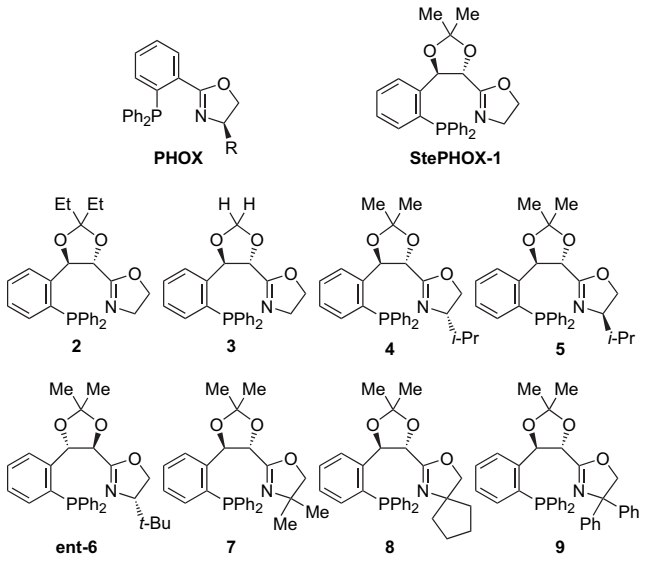
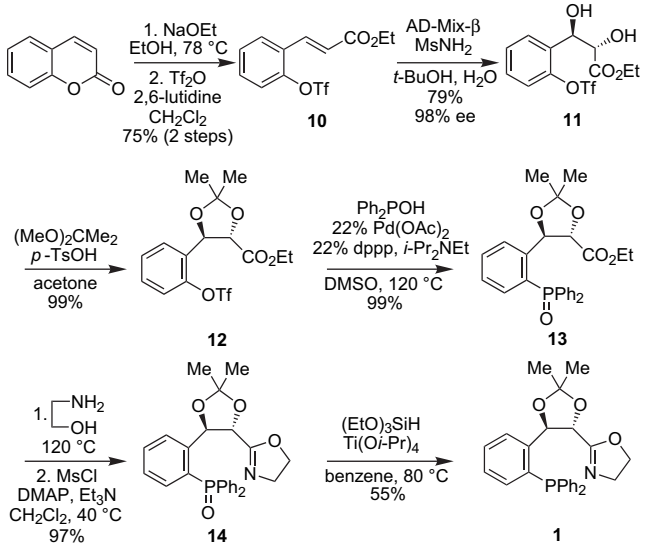


Figure 2.

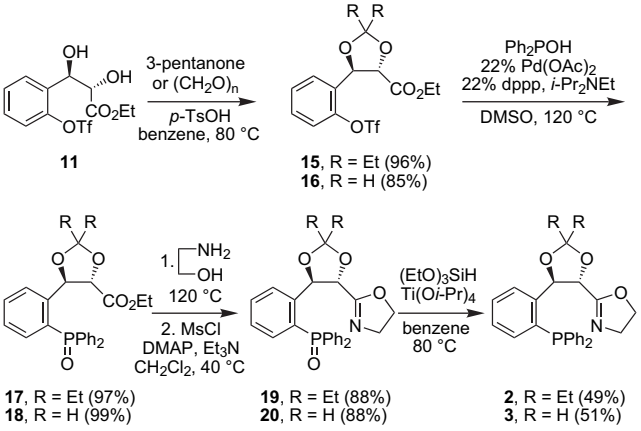
2. Results and discussion

A straightforward inexpensive route to the StePHOX family of ligands is described in Scheme 1. In this approach, inexpensive coumarin was treated with sodium ethoxide in refluxing ethanol[7] and the resulting *trans*-enoate was then converted to the derived triflate (**10**). Sharpless asymmetric dihydroxylation was then performed with AD-mix-β and methanesulfonamide to afford, in excellent enantiopurity, diol **11**.[8] After conversion of the diol to the corresponding ketal (**12**), catalytic phosphination yielded phosphine oxide **13**.[9] The ester was then condensed with ethanolamine at 120 °C in a sealed vial for 2 h to afford a hydroxyamide, which was immediately treated with MsCl, Et_3N, and catalytic DMAP to provide the oxazoline **14** in 97% yield. Finally, deoxygenation of phosphine oxide with triethoxysilane and titanium(IV) isopropoxide in refluxing benzene gave the parent ligand structure **1** in 55% yield.[10]



Scheme 1.

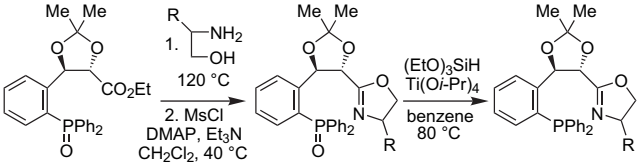
With this robust ligand synthesis in hand, several variants of the ligand structure were prepared. Using previously prepared diol **11**, two different protecting groups were introduced (Scheme 2). First, acetal **15** was prepared in 96% yield by heating diol **11** with 3-pentanone in benzene with catalytic TsOH. Alternatively, methylene acetal **16** was isolated in 85% yield after treating diol **11** with paraformaldehyde at 80 °C. Subsequently, compounds **15** and **16** were converted to **2** and **3** using a route, which is similar to that followed for the parent StePHOX ligand.



Scheme 2.

A second set of ligand structures was prepared, which possess substitution on the oxazoline ring. Accordingly, phosphine oxide **13** was condensed with an appropriate aminoalcohol at 120 °C for 2 h and the resulting hydroxyamide was then treated with MsCl, Et_3N, and catalytic DMAP to afford phosphine oxides **21**–**26** in good to excellent yields (Table 1). Deoxygenation was then performed as usual with

Table 1. Synthesis of ligands **4**–**9**

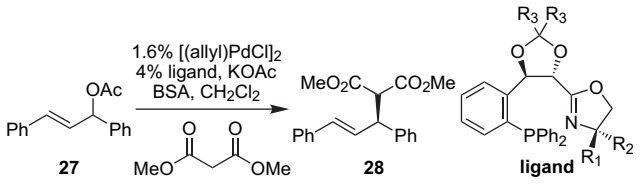


Aminoalcohol	Intermediate	Yield (%)	Ligand	Yield (%)
i-Pr, NH$_2$, OH	**21**	92	**4**	45
i-Pr, NH$_2$, OH	**22**	91	**5**	54
t-Bu, NH$_2$, OH	*ent*-**23**	84	*ent*-**6**	27
Me, Me, NH$_2$, OH	**24**	66	**7**	50
NH$_2$, OH	**25**	84	**8**	45
Ph, Ph, NH$_2$, OH	**26**	57	**9**	65

triethoxysilane and titanium(IV) isopropoxide in refluxing benzene to yield target ligands **4**–**9**. *tert*-Butyl substituted ligand *ent*-**6** was prepared starting from (*S*)-*tert*-leucinol, but employed *ent*-**13** as starting material.

The effectiveness of the StePHOX class of ligands was first assessed by employing them in an enantioselective Pd-catalyzed allylic alkylation reaction.[11,12] The parent StePHOX ligand **1** was examined first, using acetate **27** and dimethyl malonate (Table 2). This ligand, which possesses chirality solely on the backbone of the structure, provided the product **28** in 62% enantiomeric excess and favored the (*S*)-enantiomer. As can be seen in Table 1, replacement of the backbone dioxolane methyl groups, with either hydrogen atoms or ethyl groups (ligand **2** and **3**), leads to a slight decrease in enantioselection. In contrast to backbone modification, modification of the oxazoline group leads to much larger changes in selectivity. While attachment of an α-configured substituent (ligand **4**) leads to a only minor diminution in selectivity (62→48% ee), when the ligand bears a β-substituent (ligand **5**), a significant enhancement in enantioselection results (62→97% ee). This enhancement appears to be maximal with a β-isopropyl group, the corresponding ligand with a *tert*-butyl substituent exhibits diminished selectivity. Since ligand **5** exhibits significantly improved enantioselection, whereas epimeric ligand **4** exhibits only a moderate diminution in selectivity relative to **1**, it seemed reasonable to expect enhanced selectivity with geminally substituted ligands. Ligands **7**–**9** are all accessible from commercially available inexpensive aminoalcohols and the selectivity rivals were achieved with valinol derived **5**.

Table 2. StePHOX used in allylic substitution with compound **27**



Ligand	R_1	R_2	R_3	Yield (%)	ee **28** (%)
1	H	H	Me	64	62
2	H	H	Et	71	48
3	H	H	H	58	58
4	H	*i*-Pr	Me	61	46
5	*i*-Pr	H	Me	88	97
ent-**6**	*t*-Bu	H	Me	71	−79
7	Me	Me	Me	80	89
8	$CH_2CH_2CH_2CH_2$		Me	86	95
9	Ph	Ph	Me	79	75

To learn about the structure of the StePHOX ligands bound to a transition metal center, parent structure StePHOX **1** was treated with $(CH_3CN)_2PdCl_2$ and the resulting complex was crystallized from CH_2Cl_2. As can be observed in X-ray analysis depicted in Figure 3, the phosphine and oxazoline occupy cis coordination sites on the palladium center with the oxazoline ring oriented orthogonal to the palladium square plane and roughly parallel to a pseudo axial phenyl group on phosphorus.[13] Notably, the benzylic hydrogen on the ligand backbone resides 2.315 Å from the palladium atom. This example of preagostic bonding results in

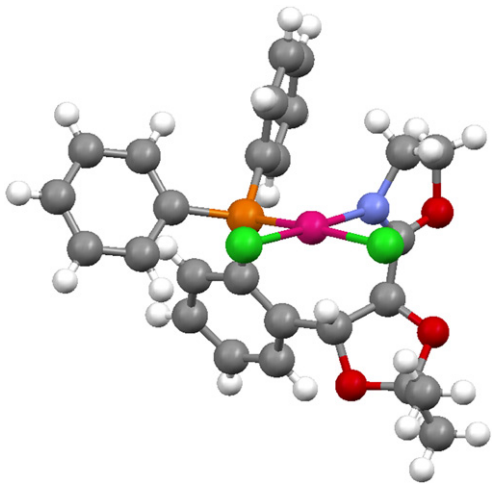


Figure 3. X-ray structure of **1**·$PdCl_2$.

significant downfield shifting of the hydrogen atom relative to the uncomplexed ligand structure in the ^{1}H NMR spectrum (6.03→9.42 ppm, vide infra).[14] The geminal methyl groups on the dioxolane ring are directed underneath the palladium square plane suggesting that, while tuning these elements did not substantially alter the selectivity in the allylic substitution reaction, they may have a significant impact on stereoselection in other catalytic transformations. In a similar fashion, elements attached to the oxazoline backbone and phosphorus atom, appear well positioned to impact reaction outcome.

On the basis of the X-ray analysis of **1**·$PdCl_2$ and the known requirements for selectivity in allylic substitution with PHOX complexes, it is not too surprising that ligand **1** does not provide high selectivity. Seminal studies by Helmchen[15] and Brown[16] suggest that electronic differentiation of the allylic termini in Pd–allyl complexes derived from P,N ligands, favors addition of nucleophiles to the carbon, which is *trans* to phosphorus.[17] Effective ligands are generally those that perturb the ratio of *endo*/*exo* π-allyl palladium complexes in favor of the *exo* isomer, and this ratio often determines the product enantioselection. In a symmetric allyl fragment, such as the one used here, the ratio of *exo*/*endo* isomer should dictate the ultimate ratio of product enantiomers.[18] Since the pseudo equatorial phenyl group on phosphorus in ligand **1** nearly bisects the palladium square plane, one would expect little bias in the conformer ratio and therefore, little selectivity. It is more surprising that ligand **4** does not lead to a selective reaction and clearly more detailed structural studies are required to understand these phenomena.

The significant enhancement in enantioselection that results from a β-configured substituent versus an α-substituent appears to arise from a difference in ligand conformation. As mentioned above, when StePHOX **1** is coordinated to $PdCl_2$, the benzylic hydrogen is shifted downfield as a result of an agostic interaction. This same agostic interaction is present in the Pd complex of ligand **4**, as determined by ^{1}H NMR analysis (Fig. 4). In contrast, when ligand **5** is treated with $PdCl_2$, a much smaller perturbation in the benzylic hydrogen resonance is observed (6.13→7.67 ppm) thereby

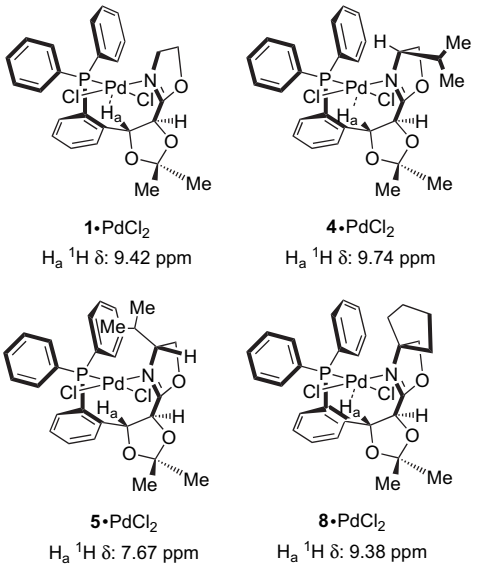
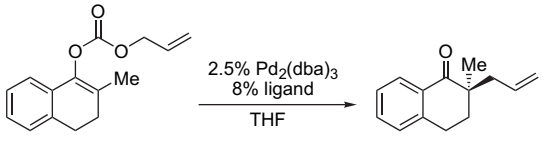


Figure 4.

suggesting that this hydrogen atom is in a different environment than in the corresponding complex of **1** and **4**. On the basis of the X-ray structure in Figure 3, one might expect that with a β-configured isopropyl group, steric interactions between the isopropyl group and the pseudo axial aryl ring are likely too severe (see **5**·$PdCl_2$ representation, Fig. 4) for the ligand to adopt the same conformation as StePHOX **1** or **4**. Contrary to our expectations, ligand **8** exhibits agostic bonding that is similar to **1** and **4** when coordinated to palladium, yet exhibits selectivity comparable to ligand **5**. It is tenable that conformational similarities between **5** and **8** arise in the context of a palladium allyl, but not in a palladium dichloride complex.

To further examine the usefulness of the StePHOX ligand class, the asymmetric Tsuji allylation was performed on compound **29** (Table 3).[19,20] The reactions were performed by premixing the appropriate ligand with tris(dibenzylideneacetone)dipalladium and then adding compound **29**. Compound **30** was isolated in good to excellent yield. Although the results with respect to enantioselectivity were less impressive than the previous example, the ligands showed encouraging levels of asymmetric induction. Again, it appears that substitution on the β-face of the ligand is important

Table 3. StePHOX used in Tsuji allylation with compound **29**



29 **30**

Entry	Ligand	Yield **30** (%)	ee **30** (%)
1	**1**	95	5
2	**4**	97	22
3	**5**	94	59
4	*ent*-**6**	86	−58
5	**7**	98	29
6	**8**	80	30

(entries 3 and 4) and it is relatively inconsequential on the α-face (entry 2). *gem*-Dialkyl substituted ligands **7** and **8** did not provide similarly high levels of selectivity as in the allylic substitution described above.

3. Conclusion

In summary, we have designed and synthesized a new highly tunable family of phosphine–oxazoline ligands that shows good to excellent enantioselectivities (ee's up to 97%) in the Pd-catalyzed allylic substitution and good enantioselectivities (ee's up to 59%) in the asymmetric Tsuji allylation. Current experiments are aiming to further improve the enantioselectivity and to develop new applications of this class of ligands.

4. Experimental

4.1. Synthesis of 10

Finely cut pieces of sodium (3.93 g, 0.17 mol) were added to a cooled (0 °C) solution of absolute EtOH (90 mL). The solution was stirred and allowed to warm to room temperature. A solution of coumarin (5.0 g in 47 mL, 34.2 mmol) was then added. The resulting yellow mixture was stirred at reflux for 16 h, cooled to room temperature, and the mixture was then concentrated under reduced pressure. A saturated aqueous solution of NH_4Cl (200 mL) was added to the crude reaction mixture and it was extracted with EtOAc (3×100 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was dissolved in 1/1 hexane/EtOAc (100 mL) and filtered through a pad of silica gel and the filtrate was then concentrated under reduced pressure to give the desired product (5.57 g) as an off-white solid. This material (4.15 g, 21.6 mmol) was dissolved in CH_2Cl_2 (70 mL) and 2,6-lutidine (3.8 mL, 32.4 mmol) was added. The solution was cooled to −78 °C and a solution of trifluoromethanesulfonic anhydride (4.5 mL, 27.0 mmol) in CH_2Cl_2 (38 mL) was added via canula. The reaction mixture was stirred for 0.5 h at −78 °C, 0.5 h at 0 °C, and 2 h at room temperature. Saturated aqueous NH_4Cl (100 mL) was then added and the mixture was extracted with CH_2Cl_2 (3×100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (1/0 to 9/1 hexane/EtOAc) to give triflate **10** (8.28 g, 75% over two steps) as a yellow oil. IR (thin film, ν cm^{-1}): 2987, 1717, 1642, 1424, 1214, 1140. ^1H NMR: δ 7.85 (1H, d, J=16.0 Hz), 7.68 (1H, dd, J=7.8, 1.7 Hz), 7.47–7.33 (3H, m), 6.48 (1H, d, J=16.0 Hz), 4.26 (2H, q, J=7.1 Hz), 1.32 (3H, t, J=7.1 Hz). ^{13}C NMR: δ 165.8, 147.6, 135.7, 131.5, 128.6, 128.2, 128.0, 122.6, 122.2, 117.0, 60.8, 14.1. MS (ESI) $(M+H)^+$: 325.1. HRMS (ESI) $(M+Na)^+$ calcd for $C_{12}H_{11}F_3O_5SNa$: 347.0171. Found: 347.0178.

4.2. Synthesis of 11

To a stirred solution of triflate **10** (8.11 g, 25.0 mmol) in *t*-BuOH (125 mL) and H_2O (125 mL) were added methanesulfonamide (2.38 g, 25.0 mmol) and AD-mix-β (35 g). The mixture was stirred at room temperature for 48 h and

then sodium sulfite (7.57 g, 60.0 mmol) was added. The resulting mixture was stirred for 0.5 h and then H_2O (200 mL) was added. The mixture was extracted with CH_2Cl_2 (3×150 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was recrystallized from hexane (100 mL) to give the first crop of white needles (2.51 g). The mother liquor was purified by flash chromatography (9/1 to 0/1 hexane/EtOAc) to give the desired product (5.8 g), which was recrystallized in hexane to give the second crop of white needles (2.42 g). Mother liquor was recrystallized a third time to give another crop of pure diol **11** (2.13 g, total=7.06 g, 79%). $[\alpha]_D^{25}$ −10.5 (*c* 1.25, $CHCl_3$). IR (thin film, ν cm^{-1}): 3398, 2989, 1740, 1424, 1214, 1140. ^1H NMR: δ 7.71–7.69 (1H, m), 7.44–7.37 (2H, m), 7.31–7.28 (1H, m), 5.37 (1H, dd, *J*=7.5, 2.4 Hz), 4.34 (1H, dd, *J*=5.6, 2.5 Hz), 4.29 (2H, q, *J*=7.2 Hz), 3.29 (1H, d, *J*=5.6 Hz), 2.92 (1H, d, *J*=7.5 Hz), 1.29 (3H, t, *J*=7.2 Hz). ^{13}C NMR: δ 172.2, 146.1, 133.0, 129.8, 129.3, 128.5, 121.1, 119.0, 73.1, 68.5, 62.6, 13.9. MS (ESI) $(M+H)^+$: 359.1; $(M+Na)^+$: 381.2. HRMS (ESI) $(M+Na)^+$ calcd for $C_{12}H_{13}F_3O_7SNa$: 381.0226. Found: 381.0232. Chiral HPLC analysis performed on Chiralcel OD-H, Daicel, 5% *i*-PrOH in hexane, 1.0 mL min^{-1}, wavelength: 220 nm.

4.3. Synthesis of 12

To a stirred solution of diol **11** (0.99 g, 2.76 mmol) in acetone (5.3 mL) were added 2,2-dimethoxypropane (2.1 mL) and *p*-toluenesulfonic acid (26 mg, 0.14 mmol). The solution was stirred at room temperature for 16 h and then Et_3N was added to neutralize the acid and the solvent was then removed. The crude product was extracted with Et_2O (3×10 mL) and saturated with aqueous $NaHCO_3$. The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (9/1 hexane/EtOAc) to give acetonide **12** (1.00 g, 91%) as a colorless oil. $[\alpha]_D^{25}$ −4.7 (*c* 1.35, $CHCl_3$). IR (thin film, ν cm^{-1}): 2993, 2943, 1760, 1424, 1216, 1142. ^1H NMR: δ 7.68–7.65 (1H, m), 7.46–7.39 (2H, m), 7.32–7.30 (1H, m), 5.44 (1H, d, *J*=7.6 Hz), 4.30 (1H, d, *J*=7.6 Hz), 4.20 (2H, tt, *J*=14.3, 7.2 Hz), 1.60 (3H, s), 1.55 (3H, s), 1.22 (3H, t, *J*=7.2 Hz). ^{13}C NMR: δ 169.3, 147.5, 130.3, 128.9, 128.8, 121.2, 120.1, 117.0, 112.2, 81.0, 74.5, 61.8, 26.8, 25.6, 13.8. MS (ESI) $(M+H)^+$: 399.1. HRMS (ESI) $(M+Na)^+$ calcd for $C_{15}H_{17}F_3O_7SNa$: 421.0539. Found: 421.0548.

4.4. Synthesis of 13

To a stirred solution of acetonide **12** (1.32 g, 3.31 mmol) in DMSO (66 mL) were added diphenylphosphine oxide (1.43 g, 7.06 mmol), palladium(II) acetate (164 mg, 0.73 mmol), 1,3-bis(diphenylphosphino)propane (0.30 g, 0.73 mmol), and *N*,*N*-diisopropylethylamine (1.15 mL, 6.63 mmol). The orange solution was stirred at 120 °C for 3 h. The resulting dark red mixture was then cooled to room temperature and 5% aqueous HCl (400 mL) was added. The mixture was extracted with CH_2Cl_2 (3×100 mL). The combined organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (1/1 hexane/EtOAc) to give phosphine oxide **13** (1.48 g, 99%) as a yellow foam. $[\alpha]_D^{25}$ +33.7 (*c* 0.76, $CHCl_3$). IR (thin film, ν cm^{-1}): 2989, 1756, 1437, 1194, 1104. ^1H NMR: δ 7.81 (1H, dd, *J*=7.6, 3.9 Hz), 7.68–7.57 (5H, m), 7.54–7.39 (6H, m), 7.28–7.24 (1H, m), 7.05 (1H, dd, *J*=13.9, 7.7 Hz), 6.06 (1H, d, *J*=7.3 Hz), 4.43 (1H, d, *J*=7.7 Hz), 4.26–4.12 (2H, m), 1.51 (3H, s), 1.26 (3H, s), 1.19 (3H, t, *J*=7.1 Hz). ^{13}C NMR: δ 169.0, 142.2 (d, J_{PC}=6.7 Hz), 133.3 (d, J_{PC}=102.9 Hz), 132.8 (d, J_{PC}=12.4 Hz), 132.4 (d, J_{PC}=104.5 Hz), 132.1 (d, J_{PC}=2.5 Hz), 131.9 (d, J_{PC}=9.6 Hz), 131.8 (d, J_{PC}=102.2 Hz), 131.5 (d, J_{PC}=2.7 Hz), 131.4 (d, J_{PC}=9.8 Hz), 131.3 (d, J_{PC}=4.7 Hz), 128.8 (d, J_{PC}=9.5 Hz), 128.1 (d, J_{PC}=12.2 Hz), 127.5 (d, J_{PC}=12.4 Hz), 111.0, 81.7, 76.6 (d, J_{PC}=5.4 Hz), 60.9, 26.7, 25.1, 13.6. ^{31}P NMR: δ 32.9. MS (ESI) $(M+H)^+$: 451.0. HRMS (ESI) $(M+H)^+$ calcd for $C_{26}H_{28}O_5P$: 451.1669. Found: 451.1672. $(M+Na)^+$ calcd for $C_{26}H_{27}O_5PNa$: 473.1488. Found: 473.1491.

4.5. Synthesis of 14

In a vial were added phosphine oxide **13** (1.95 g, 4.32 mmol) and ethanolamine (1.31 mL, 21.6 mmol). The vial was sealed with a screw cap and heated in an oil bath at 120 °C for 2 h. The resulting orange solution was diluted with brine and extracted with EtOAc (2×10 mL) and then with CH_2Cl_2 (2×10 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude hydroxyamide (1.94 g, 97%) obtained was used in the next step without further purification. To the hydroxyamide (1.91 g, 4.10 mmol) were added CH_2Cl_2 (53 mL), Et_3N (1.14 mL, 8.21 mmol), and DMAP (5 mg, 0.04 mmol). The solution was cooled to 0 °C and methanesulfonyl chloride (0.64 mL, 8.21 mmol) was then added dropwise. The resulting solution was stirred for 1 h at 0 °C where TLC showed complete disappearance of the starting material. Another portion of Et_3N (5.15 mL, 36.9 mmol) was then added and the solution was stirred under reflux for 16 h. After cooling the solution, saturated aqueous NH_4Cl was added and the mixture was extracted with CH_2Cl_2 (3×50 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (1/1 to 0/1 hexane/EtOAc) to give oxazoline **14** (1.78 g, 97%) as a white foam. $[\alpha]_D^{25}$ +31.6 (*c* 0.34, $CHCl_3$). IR (thin film, ν cm^{-1}): 3421, 3058, 2987, 2937, 1669, 1437, 1372, 1250, 1194. ^1H NMR: δ 7.79 (1H, dd, *J*=7.9, 4.0 Hz), 7.63–7.54 (5H, m), 7.52–7.46 (2H, m), 7.45–7.38 (4H, m), 7.25–7.20 (1H, m), 7.00 (1H, ddd, *J*=8.8, 8.2, 1.0 Hz), 6.07 (1H, d, *J*=8.2 Hz), 4.55 (1H, d, *J*=8.2 Hz), 4.24–4.17 (2H, m), 3.78–3.63 (2H, m), 1.49 (3H, s), 1.26 (3H, s). ^{13}C NMR: δ 164.1, 142.1 (d, J_{PC}=5.0 Hz), 133.0 (d, J_{PC}=94.3 Hz), 132.9 (d, J_{PC}=98.0 Hz), 132.4 (d, J_{PC}=4.9 Hz), 132.2 (d, J_{PC}=100.2 Hz), 132.2 (d, J_{PC}=9.6 Hz), 131.7 (d, J_{PC}=9.7 Hz), 131.6 (d, J_{PC}=3.2 Hz), 131.6 (d, J_{PC}=4.9 Hz), 129.3 (d, J_{PC}=9.6 Hz), 128.4 (d, J_{PC}=5.1 Hz), 128.3 (d, J_{PC}=5.0 Hz), 127.8 (d, J_{PC}=12.6 Hz), 110.9, 78.9, 76.7, 67.9, 54.4, 26.9, 25.6. ^{31}P NMR: δ 33.3. MS (ESI) $(M+H)^+$: 448.0. HRMS (ESI) $(M+H)^+$ calcd for $C_{26}H_{27}NO_4P$: 448.1672. Found: 448.1677. $(M+Na)^+$ calcd for $C_{26}H_{26}NO_4PNa$: 470.1492. Found: 470.1503.

4.6. Synthesis of 1

To a stirred solution of oxazoline **14** (0.56 g, 1.25 mmol) in benzene (63 mL) were added triethoxysilane (1.25 mL,

6.76 mmol) and titanium(IV) isopropoxide (0.20 mL, 0.69 mmol). The solution was stirred under reflux for 4 h. More triethoxysilane (0.23 mL, 1.25 mmol) and titanium(IV) isopropoxide (0.20 mL, 0.31 mmol) were added and the black solution was stirred under reflux for 1 h. After cooling to room temperature, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (8/2 to 1/1 hexane/EtOAc) to give P,N-ligand **1** (0.26 g, 49%) as a white foam. The product was recrystallized in hexane/Et_2O to give white cubic crystals (0.18 g, 32%). $[\alpha]_D^{25}$ −39.0 (*c* 0.65, $CHCl_3$). IR (thin film, ν cm^{-1}): 3056, 2987, 1669, 1436, 1245, 1216, 1077. ^1H NMR: δ 7.68 (1H, dd, J=6.9, 3.1 Hz), 7.41 (1H, td, J=7.9, 1.2 Hz), 7.31–7.28 (6H, m), 7.26–7.15 (5H, m), 6.94 (1H, ddd, J=7.7, 4.1, 1.3 Hz), 6.15 (1H, t, J=7.9 Hz), 4.52 (1H, d, J=8.3 Hz), 4.07–4.00 (1H, m), 3.94–3.87 (1H, m), 3.64–3.55 (1H, m), 3.39–3.31 (1H, m), 1.59 (3H, s), 1.53 (3H, s). ^{13}C NMR: δ 164.0, 141.7 (d, J_{PC}=24.0 Hz), 137.2 (d, J_{PC}=11.3 Hz), 136.9 (d, J_{PC}=11.8 Hz), 136.0 (d, J_{PC}=17.1 Hz), 134.7 (d, J_{PC}=1.1 Hz), 133.6 (d, J_{PC}=17.6 Hz), 133.4 (d, J_{PC}=16.7 Hz), 129.9, 128.8, 128.7, 128.5 (d, J_{PC}=7.1 Hz), 128.4, 128.3, 127.1 (d, J_{PC}=6.0 Hz), 111.0, 77.9 (d, J_{PC}=148.1 Hz), 77.9 (d, J_{PC}=29.6 Hz), 67.9, 54.3, 27.1, 26.2. ^{31}P NMR: δ −17.7. MS (ESI) $(M+H)^+$: 432.1. HRMS (ESI) $(M+H)^+$ calcd for $C_{26}H_{27}NO_3P$: 432.1723. Found: 432.1726.

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Supplementary data

The supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.05.043.

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