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Tridentate chiral NPN ligands based on bis(oxazolines) and their use in Pd-catalyzed enantioselective allylic substitution in molecular and ionic liquids

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ABSTRACT

NPN ligands based on the bis(oxazoline) skeleton can be prepared by a divergent method, which allows a high modularity both in the type of phosphorous group (phosphinite, phosphate, phosphane) and the substitution in the methylene bridge. The Pd complexes of these ligands can efficiently promote the allylic substitution both in molecular solvents and ionic liquids, with important effect of the nature of ligand, which also controls the partial recovery of the Pd catalyst in ionic liquid.

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1. Introduction

C_2-Symmetric bis(oxazolines)[1] and in general oxazoline-containing chiral ligands[2] have been extensively used in enantioselective catalysis. In spite of this, the development of new chiral ligands of this family to be used for specific applications is a matter of great interest. Phosphinooxazolines (PHOX, Fig. 1)[3] became very popular due to the success as chiral ligands for different enantioselective reactions, such as allylic substitutions, Heck coupling, or hydrogenations, and a plethora of structural variations have been described, including the presence of additional stereogenic elements (atoms, axis, planes), and the substitution of phosphane group by phosphonite, phosphite, or phosphoramidate.

However the number of tridentate ligands based on bis(oxazolines) is rather limited. Apart from the well known pyridinebis(oxazoline) (pybox) family,[4] other coordinating groups have been inserted between the two oxazoline rings, such as amine[5] or carbazole[6] to produce NNN-ligands, ether or dibenzofuran to produce NON-ligands,[7] dibenzothiophene[8] to produce NSN ligands, phenyl[9] leading to NCN ligands, and phosphine[10] or phosphite[11] to produce NPN ligands (Fig. 1). Even more scarce is the number of

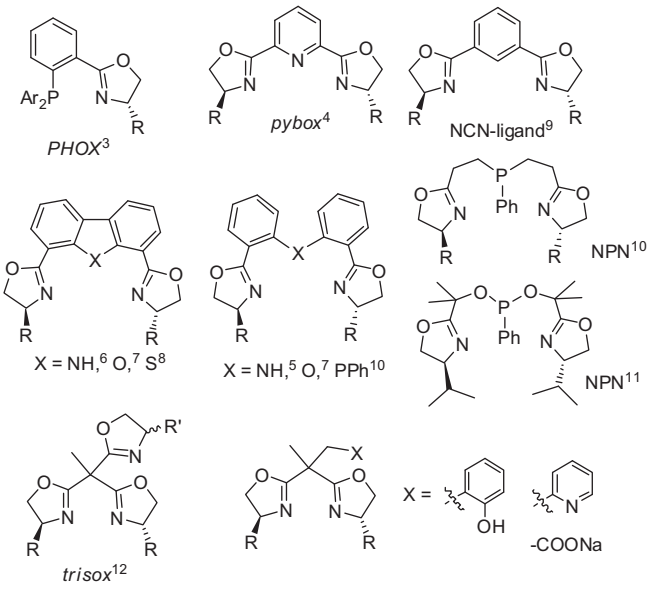

Fig. 1. Phosphinooxazolines (PHOX) and different tridentate ligands based on bis(oxazolines).

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tridentate ligands with the additional coordinating group in a sidearm of the central bridge of the bis(oxazoline) skeleton.

Tris(oxazolines)[12] can be included in this category, together with a limited number of ligands functionalized with phenol, ketone, carboxylate or pyridine groups[13] (Fig. 1). However, up to date no phosphorous-containing groups had been included in this type of sidearms tridentate ligands.

The palladium-catalyzed asymmetric allylation reaction[14] has been the subject of intense studies[15] dealing with the design, synthesis and use of a huge number of chiral non-racemic ligands. Moreover, it is used as benchmark reaction to test newly developed chiral ligands,[16] as in the case of some oxazoline-containing tridentate NNN,[17,18] NON,[7] NSN,[8] and NPN[19] ligands (Fig. 1).

One aspect still to be solved in allylic substitution is that concerning to the catalyst recovery. In the case of heterogeneous catalysts, immobilization of bidentate NN ligands onto polymeric supports leads to problems in activity, enantioselectivity, and mainly in recovery of the catalysts.[20] Better recoverability was obtained with supported tetradentate pyridylamides[21] or with a bidentate N,P-ligand.[22] Recovery of homogeneous catalysts has been carried out by modification of bis(oxazolines) with fluorinated ponytails[23] or by functionalization of a phosphite/oxazoline derived from D-glucosamine with amino groups, allowing extraction at different pH.[24] In both cases recycling problems were found either in activity or enantioselectivity.

In spite of the quick expansion in the use of ionic liquids as reaction medium,[25] their application to allylic substitution is rather scarce[26] and very few enantioselective examples are described in the literature.[27] Ferrocenyl-based diphosphines and phosphinooxazolines, as well as BINAP, were tested as ligands. First recovery was only partially successful, with similar or slightly reduced enantioselectivity and a significant drop in activity in most cases. In spite of the good results obtained in allylic substitution with simple bis(oxazoline)[28] and azabis(oxazoline)[29] ligands, their use in ionic liquids[30] leads to either no reaction at all or no enantioselectivity in case of using triphenylphosphine as additional activating agent.[31]

In this paper we describe the development of a family of highly modular tridentate NPN ligands based on bis(oxazolines) and their use to promote the Pd-catalyzed reaction between (*E*)-1,3-diphenylprop-2-enyl acetate and diethyl malonate in ionic liquids.

2. Results

2.1. Synthesis of NPN ligands based on bis(oxazolines)

The synthetic strategy is shown in Scheme 1. In the previously described methods to include an additional coordinating group as sidearm of the central methylene bridge of bis(oxazoline),[13] the inert alkyl group (methyl in the literature examples) is introduced from the starting malonate used for bis(oxazoline) synthesis, and any variation of this group would require starting the synthetic route from another substituted malonate. In an attempt to introduce higher modularity, the synthetic route was started from the easily available methylenebis(oxazoline) **1**,[32] whereas the inert alkyl group and the functionalized sidearm were sequentially introduced.

The treatment of the starting bis(oxazoline) **1** with equimolecular amounts of potassium *tert*-butoxide and either methyl iodide or benzyl bromide leads to the monoalkylated ligands (**2a**,**b**) in high yields. This parameter was introduced to test the effect of bulkiness in that position, given the importance observed in the case of cyclopropanation reactions with the dialkylated ligand.[33] Hydroxymethylation was performed with paraformaldehyde in the presence of triethylamine as a base,[34] leading to the intermediates **3a**,**b**.

The hydroxyl group can be easily modified with $(EtO)_2PCl$ or $^iPr_2PCl$, to obtain the corresponding phosphite (**4a**,**b**) or phosphinite (**6a**) modified bis(oxazolines), respectively, with yields over 85%. Phosphite/oxazolines bearing bulky phosphite groups have been described as excellent ligands for enantioselective allylic substitutions.[35] In view of that, the same bulky group was introduced by reaction of the hydroxymethylated bis(oxazolines) (**3a**,**b**) with the corresponding phosphorochloridite.[36] Lower yields of the final ligands (**5a**,**b**) were obtained (around 28%) probably due to the high steric hindrance introduced by this group. In all these cases, the presence of a $-CH_2-O-$ spacer between the bis(oxazoline) bridge atom and the phosphorous would lead to the formation of seven-membered chelates.

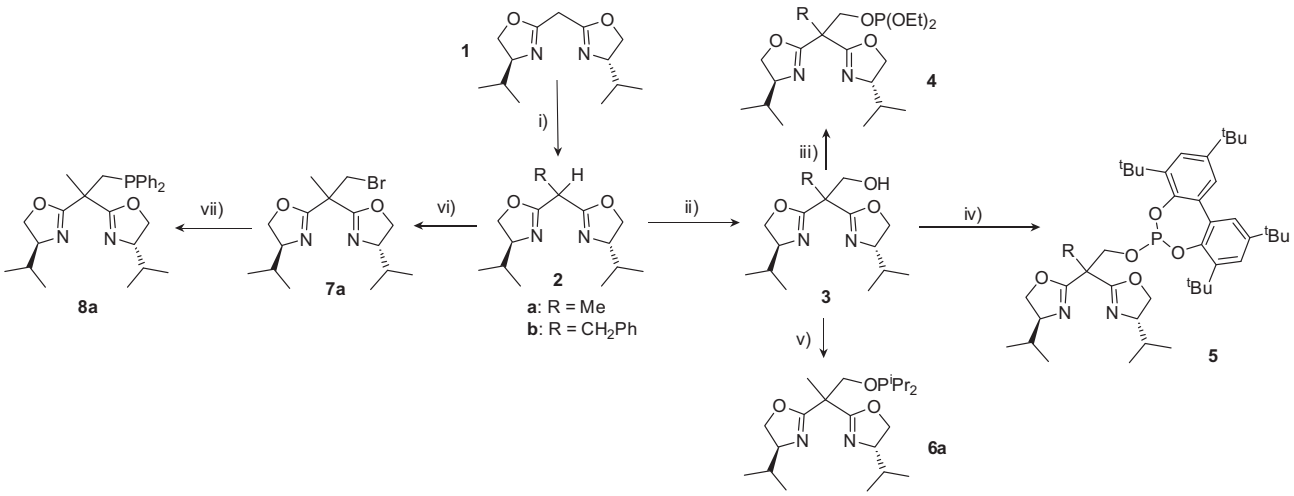
Alternatively the central bridge can be bromomethylated by reaction with dibromomethane in basic medium. The bromomethyl derivative **7a** was obtained with 94% yield, and subsequent reaction with $KPPh_2$ led to the corresponding phosphane **8a**. In this way 6-membered chelates would be possible.

2.2. Catalytic results in enantioselective allylic substitution

Benchmark reaction was that of (*E*)-1,3-diphenylprop-2-enyl acetate with diethyl malonate in dichloromethane, using *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and sodium acetate as a base, conditions suitable for comparison with most of results described in the literature. Palladium complexes were prepared in situ with ligand/Pd ratio 1.5 and results are gathered in Table 1 (entries 1–6). The presence of the phosphorus atom noticeably increased the catalytic activity, leading to total conversions after short reaction times (up to 4 h), whereas analogous bis(oxazoline) and azabis(oxazoline) required very long reaction times (typically 2–7 days[7,18,30]). It is remarkable the result obtained with **8a**, as only 15 min are required to obtain quantitative yield in dichloromethane (entry 6), in the same order than the best results described in the literature for phosphinooxazoline ligands (10 min to 24 h).[35b,37–39]

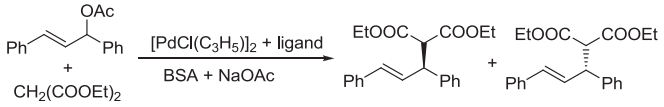
The coordination of Pd to at least one oxazoline ring is demonstrated by the obtained enantioselectivity, whose value is strongly influenced by the nature of the phosphorous group. Higher enantiomeric excess was obtained in the order phosphite (**4a**–**5a**, 52–56% ee, entries 1 and 3)<phosphinite (**6a**, 91% ee, entry 5) <phosphane (**8a**, 95% ee, entry 6). It is worthy to note that results with ligand **8a**, both in activity and selectivity, are comparable with those obtained with the classical phosphinooxazoline ligand (98% yield and 98% ee after 1 h reaction),[37] the analogous bidentate NP ligand either without (94% yield, 86% ee) or with (86% yield, 94% ee) an additional stereogenic center,[40] and the previously described NPN ligand (74% yield, 92% ee).[19] The substitution of methyl by benzyl group in the bridge between the oxazolines has a deep influence in the enantioselectivity, that increases from 52–56% ee with **4a**–**5a** to 81–83% ee with **4b**–**5b** (entries 2 and 4).

When the reaction was carried out in an ionic liquid, [bmim][PF_6], reaction times required for total conversion were similar to those required in the molecular solvent, with the only exception of **8a**, that required 2.5 h (entry 17) instead of the 15 min in CH_2Cl_2. It is worth noting that the activating role of phosphorous was much higher than that showed by PPh_3 in the experiments with the same P/Pd ratio (1.5).[30,31] With regard to enantioselectivity, the effect of the nature of the phosphorous group follows the same trend: phosphite (**4a**–**5a**, 13–34% ee, entries 7 and 11)<phosphinite (**6a**, 68% ee, entry 15)<phosphane (**8a**, 92% ee, entry 17). As can be seen enantioselectivity is in general lower than that obtained in dichloromethane. The inclusion of a benzyl substituent in the bridge also improves enantioselectivity 37 (**4b**, entry 9) versus 13% ee (**4a**, entry 7) and 57 (**5b**, entry 13) versus 34% ee (**5a**, entry 11). To sum up the best ligand in dichloromethane, **8a**, is also the best one in ionic liquid with almost the same enantioselectivity (92% ee, entry 17). This overall result improves the best one described in the literature with ionic liquids (31% yield and 92% ee after 5 h with ^{i}Pr-Phosferrox).[27b]



Scheme 1. Synthesis of NPN ligands based on bis(oxazolines). Reagents and conditions: (i) *t*-BuOK/THF+MeI (or benzyl bromide), reflux, 4 h; (ii) paraformaldehyde/CH_2Cl_2+dioxane+H_2O+Et_3N/THF, rt, 3 days; (iii) MS 4 Å/toluene rt, 8 h; 4-dimethylaminopyridine+$(EtO)_2PCl$, rt, 18 h; (iv) 4-dimethylaminopyridine/toluene+(3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphorochloridite, rt, overnight; (v) MS 4 Å/toluene rt, 8 h; 4-dimethylaminopyridine+$^iPr_2PCl$, rt, 18 h; (vi) *n*-BuLi/THF+CH_2Br_2, reflux, 4 h; (vii) $KPPh_2$/THF, 0 °C, 1 h.

Table 1
Results of allylic substitution with NPN ligands based on bis(oxazolines) in molecular solvents and ionic liquids



Entry	Ligand[a]	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	**4a**	CH_2Cl_2	3	100	52
2	**4b**	CH_2Cl_2	3	100	83
3	**5a**	CH_2Cl_2	1.5	100	56
4	**5b**	CH_2Cl_2	4	100	81
5	**6a**	CH_2Cl_2	3	100	91
6	**8a**	CH_2Cl_2	0.25	100	95
7	**4a**	[bmim][PF_6]	4	100	13
8		Reuse	168	50	8
9	**4b**	[bmim][PF_6]	3	100	37
10		Reuse	17	100	29
11	**5a**	[bmim][PF_6]	1.5	100	34
12		Reuse	144	<10	4
13	**5b**	[bmim][PF_6]	4.5	100	57
14		Reuse	168	30	56
15	**6a**	[bmim][PF_6]	3	100	68
16		Reuse	12	100	32
17	**8a**	[bmim][PF_6]	2.5	100	92
18		Reuse	240	80	54

[a] Ligand/Pd ratio=1.5.
[b] Determined by NMR.
[c] Determined by HPLC. The major product has *S* configuration.

Unfortunately full recovery of catalytic performance of the ionic liquid solutions was not possible. In all cases the catalytic activity was reduced, and as a consequence lower yields were obtained (entries 8, 12, and 14) or much longer reaction times were required for total conversion (entries 10 and 16). A drop in enantioselectivity was also observed, with the only exception of **5b** (entry 14), but again the general trend was phosphite (**4a**–**5a**, 4–8% ee, entries 8 and 12)<phosphinite (**6a**, 32% ee, entry 16)<phosphane (**8a**, 54% ee, entry 18).

3. Discussion

In the series of type **a** ligands, the bis(oxazoline) backbone is identical in all cases, and only the phosphorous arm is changed. The electronic properties of this arm can be represented by the Pd–P bond length in model complexes with analogous monodentate phosphine ligands[41] (Fig. 2). The obtained enantiomeric ratio fits quite well (r=0.981) with this parameter (Fig. 3), showing that electronic properties of phosphorous group are more important than the size of substituents, as demonstrated by the similar result of **4a** and **5a**, or the PPdN chelate size (7 in **6a**, 6 in **8a**), which has only marginal influence. The same correlation (r=0.967) with the same slope can be found for enantioselectivity obtained in ionic liquid (Fig. 3). Hence we can argue that the same electronic effects are controlling the enantioselectivity in both types of solvent, and that the change of solvent affects in the same way to all the complexes. In contrast with other steric features, the substitution of methyl by benzyl group in the bridge between the oxazolines has a deep influence, probably due to conformational changes in the oxazoline moiety. The double benzyl substitution had shown a slightly positive effect in bis(oxazolines)[18] that contrasts with the negative effect on copper catalyzed enantioselective cyclopropanation.[32]

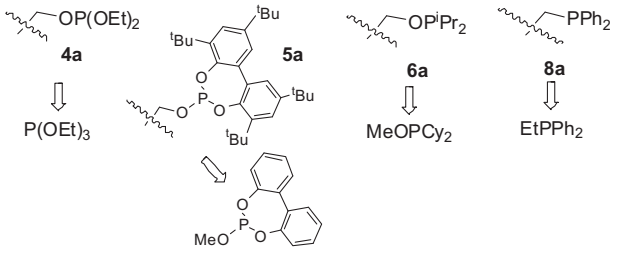


Fig. 2. Model monodentate phosphines.

Attempts to crystallize the catalyst precursor **8a**/Pd(allyl) were unsuccessful. However the ^1H NMR spectrum of this species (Fig. 4) shows a total split of the signals of both oxazolines, one at higher and the other one to lower field. This seems to indicate the coordination of Pd to only one oxazoline ring, as well as to the phosphane group, as shown by the ^{31}P NMR chemical shift from −23 ppm in **8a** to 23 ppm in the complex. This result is in agreement with the precedent with an NPN ligand based on oxazolines,[19] in which the tridentate ligand acted as bidentate with the formation of a six-membered chelate. Ligands can only act as tridentate when they are compatible with the planar–square geometry of Pd,

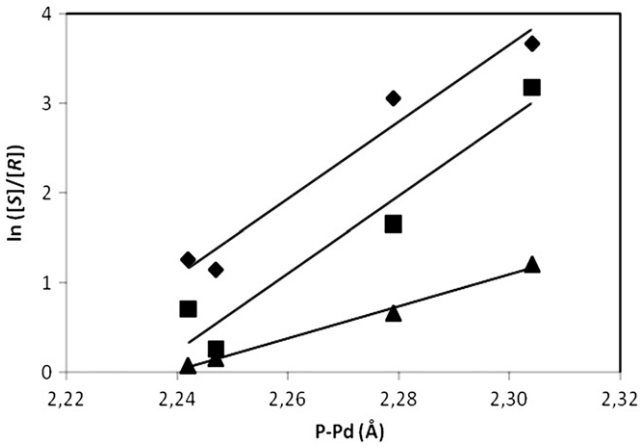


Fig. 3. Relationship between enantiomeric ratio obtained in allylic substitution and P-Pd bond distance in model compounds. Reactions in: (◆) dichloromethane; (■) [bmim][PF_6]; (▲) recovered in [bmim][PF_6].

as in the case of pybox[42] or pyridinebis(oxazolidines),[43] whereas in this case the tridentate ligand allows only the *fac*-coordination. Analogous NON, NSN, and NNN tridentate ligands,[13] including tris(oxazolines),[18] did not reach κ^3 coordination with Re, Fe, Cu, or Pd, forming only the box chelate.

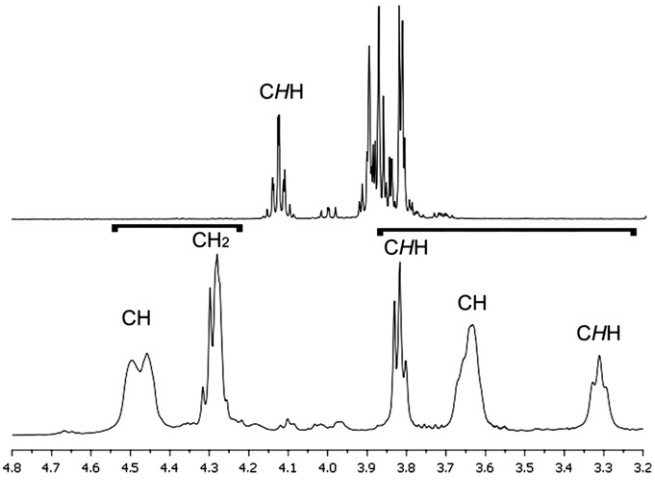


Fig. 4. Comparison of the ^{1}H NMR spectra of ligand **8a** (top) and the **8a**–Pd complex (bottom).

With any of the ligands described in this work, PN chelation will generate an additional stereogenic center on the quaternary carbon at the bridge between the two oxazoline rings (Fig. 5). A similar feature on phosphorous atom was produced in the previously described NPN ligand (Fig. 5),[19] or with the axial chirality in unfixed biphenyl-phosphinooxazoline.[16c] The possible formation of diastereomers might account for the poorly resolved NMR signals and the impossibility to crystallize the complex, although in the other two mentioned cases Pd complexation led to only one of the possible diastereomers. The importance of the presence of an additional stereogenic center has been demonstrated by the match-mismatch problem found with related phosphinooxazoline ligands (Fig. 5),[40] and the control of the absolute configuration of the final product in phosphinooxazoline ligands with chiral backbone between the chelating groups, such as phosphanorbornadiene,[44] substituted ferrocene with planar chirality,[45] P-stereogenic atom,[46] or 1,3-dioxolane[47] (Fig. 5).

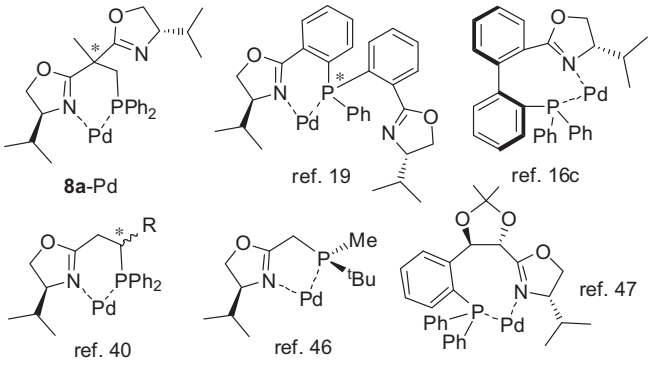


Fig. 5. Possible NPN–Pd complexes, with the new stereogenic centers created, and the simpler analogous NP–Pd complex.

The loss of catalytic performance after recovery may be ascribed to two different causes. On the one hand the partial extraction of full complex due to its solubility in the extracting solvent or to the existence of an equilibrium of complex formation, as already shown in the case of bis(oxazoline)–copper complexes in ionic liquids,[48] allowing the extraction of free ligand, which in this case it is highly detrimental for both catalytic activity and enantioselectivity in the recovered ionic liquid phase. On the other hand the formation of Pd black particles is observed, which may also reduce the concentration of active species. The correlation between the enantiomeric ratio obtained in the recovered ionic liquid phase and the P–Pd bond distance (Fig. 3, r=0.997) shows that the electronic properties of the phosphorous group also control this aspect of catalysis.

Studies about the coordination ability of this kind of ligands with different metals, as well as the catalytic activity of the metal complexes are currently under development.

4. Conclusion

Highly modular NPN ligands based on bis(oxazoline) skeleton has been developed. Any type of phosphorous-containing group can be introduced, including phophinite, phosphite or phosphane, with different possible substitutions (methyl and benzyl have been used) at the methylene bridge between both oxazoline rings.

Pd coordination seems to take place through the phosphorous-containing group and one oxazoline ring, as the possible *fac*-coordination cannot be reached with Pd. This type of ligands can be more active and enantioselective than simpler analogues for allylic substitution in dichloromethane, and it is able to promote the same reaction in ionic liquids. The efficiency of the catalyst depends mainly on the donor character of the phosphorous group, with additional role of the substitution at the methylene bridge. Catalysts are not fully recoverable in ionic liquids, showing that the stability of the complex is a key issue to reach this goal.

5. Experimental section

5.1. General methods

All manipulations were carried out with exclusion of air by using standard Schlenk techniques or in an argon-filled MBraun drybox. Solvents were obtained from a Solvent Purification System (MBraun). Deuterated solvents were dried with appropriate drying agents and degassed with argon prior to use. CHN analyses were carried out in a Perkin–Elmer 2400 CHNS/O analyzer. ESI MS were obtained in a Bruker Microtof-Q mass spectrometer. Infrared

spectra were recorded in KBr using an FT-IR Perkin–Elmer Spectrum One spectrometer. NMR spectra were recorded in $CDCl_3$ at rt on Bruker Avance 500 or 400 MHz spectrometers. ^1H (500.13 or 400.13 MHz) and ^{13}C (125.8 or 100.6 MHz) NMR chemical shifts were measured relative to the partially deuterated solvent peak but are reported in parts per million relative to TMS. ^{31}P (202.5 or 162.0 MHz) chemical shifts were measured relative to H_3PO_4 (85%). Coupling constants, *J*, are given in hertz. In general, NMR spectral assignments were achieved through ^1H COSY, ^1H NOESY, ^{13}C APT, $^1H/^{13}C$ HSQC and $^1H/^{13}C$ HMBC experiments.

5.2. Synthesis of ligands

*5.2.1. 2,2′-Ethylidenebis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**2a**).* *t*-BuOK (480.7 mg, 4.2 mmol) was added to a solution of 2,2′-methylenebis[(4*S*)-4-isopropyl-4,5-dihydro-oxazole] (**1**) (1 g, 4.2 mmol) in THF (20 ml) at rt and the mixture was stirred for 1 h. Methyl iodide (264.1 μl, 4.2 mmol) was added and the reaction was heated under reflux for 4 h. The solvent was evaporated under reduced pressure, brine (15 ml) was added to the crude and the aqueous phase was extracted with ethyl acetate (3×20 ml). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under vacuum. Yield: 984 mg (93%) as a yellow oil. IR (ν cm^{-1}): 1608 (C=N). Elemental analysis ($C_{14}H_{24}N_2O_2$): theoretical C 66.63, H 9.59, N 11.10: experimental C 66.72, H 9.57, N 11.18. *m*/*z* (ESI): $[M+H]^+$=253.1. ^1H NMR: 4.20 (dd, *J*=9.6, *J*=8.0 Hz, 2H; CH_2 oxazole), 3.96 (dd, *J*=11.6, *J*=7.6, 2H; CH_2 oxazole), 3.93 (m, 2H; CH oxazole), 3.50 (c, *J*=7.2, 1H; C*H*CH_3 ethylidene), 1.75 (m, 2H; C*H*CH_3), 1,45 (d, *J*=7.2, 3H; CHC*H*$_3$ ethylidene), 0.91 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.90 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.83 (d, *J*=6.8, 6H; CHC*H*$_3$). ^{13}C NMR: 165.52, 165.36 (2×s, C=N), 71.75, 71.68 (2×s, CH oxazole), 70.12, 70.07 (2×s, CH_2 oxazole), 33.94 (s, *C*HCH$_3$ ethylidene), 32.29, 32.27 (2×s, *C*HCH$_3$), 18.59, 18.55, 17.69, 17.58 (4×s, CHCH$_3$), 15.27 (s, CH*C*H$_3$ ethylidene).

*5.2.2. 2,2′-(2-Phenylethylidene)bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**2b**).* *t*-BuOK (240.4 mg, 2.1 mmol) was added to a solution of 2,2′-methylenebis[(4*S*)-4-isopropyl-4,5-dihydro-oxazole] (**1**) (500 mg, 2.1 mmol) in THF (20 ml) at rt and the mixture was stirred for 1 h. Benzyl bromide (254.8 μl, 2.1 mmol) was added and the reaction was heated under reflux for 4 h. The solvent was evaporated under reduced pressure, brine (15 ml) was added to the crude and the aqueous phase was extracted with ethyl acetate (3×20 ml). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under vacuum. The yellow oil was purified by column chromatography on neutral alumina (hexane/ethyl acetate=65:35, 1% NEt_3). Yield: 558 mg (81%). IR (ν cm^{-1}): 1613 (C=N). Elemental analysis ($C_{20}H_{28}N_2O_2$): theoretical C 73.13, H 8.59, N 8.53; experimental C 72.99, H 8.65, N 8.46. *m*/*z* (ESI): $[M+H]^+$=329.1 ^1H NMR: 7.20–7.09 (m, 5H; CH_{Ph}), 4.15–4.13 (m, 2H; CH_2 oxazole), 3.93–3.80 (m, 4H; CH_2 and CH oxazole), 3.75–3.10 (ABX: δ_X=3.71, δ_A=3.22, δ_B=3.14, J_{AB}=13.6, J_{AX}=8.3, J_{BX}=8.7, 3H; *CHCH*$_2$Ph), 1.65 (m, 1H; C*H*CH_3), 1.55 (m, 1H; C*H*CH_3), 0.82 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.75 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.73 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.68 (d, *J*=6.8, 3H; CHC*H*$_3$). ^{13}C NMR: 163.86, 163.76 (2×s, C=N), 138.07 (s, $C_{ipso-Ph}$), 128.94, 128.20, 126.42 (3×s, $C_{o\text{-}m\text{-}p\text{-}Ph}$), 71.79, 71.77 (2×s, CH oxazole), 70.07, 70.02 (2×s, CH_2 oxazole), 41.24 (s, *C*H$_2$Ph), 35.76 (s, CH*C*H$_2$Ph), 32.29, 32.15 (2×s, *C*HCH$_3$), 18.51, 18.41, 17.72, 17.65 (4×s, CH*C*H$_3$).

*5.2.3. 2,2′-(1-Hydroxymethylethylidene)bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**3a**).* To a stirred suspension of **2a** (1 g, 3.96 mmol) and paraformaldehyde (148.5 mg, 4.95 mmol) in dichloromethane (6 ml) were added 1,4-dioxane (1 ml) and water (0.2 ml). A solution of NEt_3 (0.8 ml) in THF (3 ml) was added dropwise for 3 h and the solid was gradually dissolved. The resulting solution was stirred for 3 days at rt. The solvent was evaporated under reduced pressure, the crude was redissolved in dichloromethane (5 ml), washed with water (3×4 ml), dried over $MgSO_4$, filtered and concentrated under vacuum. Yield: 838 mg (75%). IR (ν cm^{-1}): 3237 (O–H), 1651 (C=N). Elemental analysis ($C_{15}H_{26}N_2O_3$): theoretical C 63.80, H 9.28, N 9.92; experimental C 63.70, H 9.23, N 9.85. *m*/*z* (ESI): $[M+H]^+$=283.1. ^1H NMR: 4.23 (ABX, δ_A=3.85, δ_B=3.80, δ_X=4.60, J_{AB}=11.0, J_{AX}=6.4, J_{BX}=7.4; 3H; C(CH_3)CH_2OH), 4.24–4.20 (m, 2H; CH_2 oxazole), 4.02–3.92 (m, 4H; CH_2 and CH oxazole), 1.81–1.69 (m, 2H; C*H*CH_3), 1.44 (s, 3H; C(C*H*$_3$)CH_2OH), 0.91 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.90 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.86 (d, *J*=6.8, 3H; CHC*H*$_3$), 0.85 (d, *J*=6.8, 3H; CHC*H*$_3$). ^{13}C NMR: 167.30, 167.01 (2×s, C=N), 71.44, 71.38 (2×s, CH oxazole), 70.02, 69.95 (2×s, CH_2 oxazole), 67.71 (s, C(CH_3)CH_2OH), 44.28 (s, *C*(CH_3)CH_2OH), 32.42, 32.31 (2×s, *C*HCH$_3$), 18.65 (s, C(*C*H$_3$)CH_2OH), 18.47, 18.33, 17.92, 17.79 (4×s, CHCH$_3$).

*5.2.4. 2,2′-(1-Hydroxymethyl-2-phenylethylidene)bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**3b**).* From **2b** (800 mg) following the previous method. Yield: 733 mg (84%). IR (ν cm^{-1}): 3250 (O–H), 1647 (C=N). Elemental analysis ($C_{21}H_{30}N_2O_3$): theoretical C 70.36, H 8.43, N 7.82; experimental C 70.44, H 8.45, N 7.89. *m*/*z* (ESI): $[M+H]^+$=358.9. ^1H NMR: 7.27–7.22 (m, 5H; CH_{Ph}), 4.31–4.26 (m, 2H; CH_2 oxazole, 1H; C(CH_2Ph)CH_2O*H*), 4.08 (m, 1H; CH_2 oxazole), 4.03–3.90 (m, 1H; CH_2 oxazole, 2H; CH oxazole, 2H; C(CH_2Ph)CH_2OH), 3.31 (AB: δ_A=3.33, δ_B=3.29, J_{AB}=13.6, 2H; C(C*H*$_2$Ph)CH_2OH), 1.78 (m, 1H; C*H*CH_3), 1.67 (m, 1H; C*H*CH_3), 0.96 (d, *J*=6.7, 3H; CHC*H*$_3$), 0.90 (d, *J*=6.7, 3H; CHC*H*$_3$), 0.89 (d, *J*=6.7, 3H; CHC*H*$_3$), 0.84 (d, *J*=6.7, 3H; CHC*H*$_3$). ^{13}C NMR: 166.05, 166.04 (2×s, C=N), 135.90 (s, $C_{ipso-Ph}$), 130.47, 128.00, 126.78 (3×s, $C_{o\text{-}m\text{-}p\text{-}Ph}$), 71.72, 71.46 (2×s, CH oxazole), 70.01, 69.80 (2×s, CH_2 oxazole), 64.67 (s, C(CH_2Ph)CH_2OH), 48.93 (s, *C*(CH_2Ph)CH_2OH), 38.08 (s, C(*C*H$_2$Ph)CH_2OH), 32.50, 32.38 (2×s, *C*HCH$_3$), 18.56 (s, 2C; CHCH$_3$), 18.18, 17.94 (2×s, CHCH$_3$).

*5.2.5. 2,2′-(1-Bromomethylethylidene)bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**7a**).* To a solution of **2a** (1 g, 3.9 mmol) in THF (20 ml) at −78 °C was added *n*-BuLi (2.5 ml 1.6 M in hexanes, 4 mmol) and the mixture was stirred for 1 h. Then dibromomethane (278 μl, 3.9 mmol) was added and the reaction mixture was heated under reflux for 4 h. The solvent was evaporated under reduced pressure, brine (15 ml) was added to the crude and the aqueous phase was extracted with ethyl acetate (3×20 ml). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under vacuum. Yield: 1.24 g (94%) as a yellow oil. IR (ν cm^{-1}): 1648 (C=N). Elemental analysis ($C_{15}H_{25}N_2O_2Br$): theoretical C 52.18, H 7.29, N 8.11; experimental C 52.08, H 7.20, N 8.21. *m*/*z* (ESI): $[M+H]^+$=345.1. ^1H NMR: 4.24–4.18 (m, 2H; CH_2 oxazole), 4.02–3.92 (m, 2H; CH_2 oxazole, 2H; CH oxazole), 3.82 (AB: δ_A=3.86, δ_B=3.83, J_{AB}=10.3, 2H; CCH_3CH_2Br), 1.83–1.74 (m, 2H; *CH*CH_3), 1.61 (s, 3H; C*C*H$_3$CH$_2$Br), 0.91 (d, *J*=7.0, 3H; CHC*H*$_3$), 0.89 (d, *J*=7.0, 3H; CHC*H*$_3$), 0.86 (d, *J*=6.4, 3H; CHC*H*$_3$), 0.84 (d, *J*=6.4, 3H; CHC*H*$_3$). ^{13}C NMR: 165.40, 165.31 (2×s, C=N), 71.93, 71.61 (2×s, CH oxazole), 70.22, 70.10 (2×s, CH_2 oxazole), 43.47 (s, *C*CH_3CH_2Br), 37.42 (s, CCH_3CH_2Br), 32.21, 32.16 (2×s, *C*HCH$_3$), 21.16 (s, C*C*H$_3$CH$_2$Br), 18.64, 18.44, 17.73, 17.45 (4×s, CHCH$_3$).

*5.2.6. 2,2′-[1-(Diethoxyphosphinooxymethyl)ethylidene]-bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**4a**).* To a solution of **3a** (360 mg, 1.27 mmol) in toluene (10 ml) was added 4 Å molecular sieves and the suspension was stirred for 8 h. The solution was transferred to another Schlenk, 4-dimethylaminopyridine (171 mg, 1.40 mmol) was added and stirred until complete dissolution. Chlorodiethylphosphite (220.6 μl, 1.46 mmol) was added dropwise and the mixture was stirred for 18 h. The solution was filtered via cannula, the resulting solution was evaporated under reduced

pressure, hexane was added to the crude and the solid was filtered off. The final solution was concentrated under vacuum to obtain **4a** as an oil Yield: 450 mg (87%). IR (ν cm^{-1}): 1649 (C=N). Elemental analysis ($C_{19}H_{35}N_2O_5P$): theoretical C 56.70, H 8.76, N 6.96; experimental C 56.63; H 8.81; N 6.92. *m/z* (ESI): $[M+H]^+$=403.2. ^{1}H NMR: 4.23–4.11 (m, 2H; C(CH_3)CH_2OP(OCH_2CH_3)$_2$, 2H; CH_2 oxazole), 3.99–3.91 (m, 2H; CH_2 oxazole, 2H; CH oxazole), 3.88–3.81 (m, 4H; OP(OC$H_2$$CH_3$)$_2$), 1.81–1.73 (m, 2H; C$H$$CH_3$ oxazole), 1.57 (s, 3H; C(CH_3)CH_2OP(OEt)$_2$), 1.23 (t, J=7.0, 6H; OP(OCH_2CH_3)$_2$), 0.90 (d, J=6.8, 3H; CHCH_3), 0.89 (d, J=6.6, 3H; CHCH_3), 0.84 (d, J=6.8, 3H; CHCH_3), 0.83 (d, J=6.8, 3H; CHCH_3). ^{13}C NMR: 165.67, 166.65 (2×s, C=N), 71.85, 71.63 (2×s, CH oxazole), 69.80, 69.61 (2×s, CH_2 oxazole), 65.19 (d, $J_{(C-P)}$=11.4, C(CH_3)CH_2OP(OEt)$_2$), 58.09 (d, $J_{(C-P)}$=10.9, OP(OC$H_2$$CH_3$)$_2$), 43.72 (d, $J_{(C-P)}$=5.5, C(CH_3)CH_2OP(OEt)$_2$), 32.25, 32.15 (2×s, C$H$$CH_3$), 19.60 (s, C(C$H_3$)$CH_2$OP(OEt)$_2$), 18.60, 18.51, 17.56, 17.35 (4×s, CHCH_3), 16.87 (d, $J_{(C-P)}$=4.9, OP(OCH_2CH_3)$_2$). ^{31}P NMR: 138.87 (s).

*5.2.7. 2,2′-[1-(Diethoxyphosphinooxymethyl)-2-phenyl ethylidene]-bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**4b**).* From **3b** (240 mg, 0.67 mmol) following the previous procedure. Yield: 285 mg (89%). IR (ν cm^{-1}): 1650 (C=N). Elemental analysis ($C_{25}H_{39}N_2O_5P$): theoretical C 62.74, H 8.21, N 5.85; experimental C 62.77, H 8.24, N 5.80. *m/z* (ESI): $[M+H]^+$=479.2. ^{1}H NMR: 7.17–7.11 (m, 5H; CH_{Ph}), 4.17–4.08 (m, 2H; CH_2 oxazole), 4.05 (ABX, δ_A=4.09, δ_B=4.00, J_{AB}=10.8, J_{AX}=5.9, J_{BX}=5.4; 2H; C(CH_2Ph)CH_2OP(OEt)$_2$), 3.92–3.80 (m, 2H; CH_2 oxazole, 4H; OP(OC$H_2$$CH_3$)$_2$, 2H; CH oxazole), 3.37 (AB: δ_A=3.40, δ_B=3.35, J_{AB}=13.6, 2H; C(CH_2Ph)CH_2OP(OEt)$_2$), 1.70 (m, 1H; C$H$$CH_3$), 1.61 (m, 1H; C$H$$CH_3$), 1.96 (t, J=7.0, 6H; OP(OCH_2CH_3)$_2$), 0.85 (d, J=6.8, 3H; CHCH_3), 0.78 (d, J=6.6, 3H; CHCH_3), 0.76 (d, J=6.8, 3H; CHCH_3), 0.71 (d, J=6.8, 3H; CHCH_3). ^{13}C NMR: 165.26, 164.20 (2×s, C=N), 136.36 (s, $C_{ipso-Ph}$), 130.49, 127.97, 126.60 (s, $C_{o\text{-}m\text{-}p\text{-}Ph}$), 72.14, 71.98 (2×s, CH oxazole), 69.65, 69.46 (2×s, CH_2 oxazole), 61.17 (d, $J_{(C-P)}$=12.8, C(CH_2Ph)CH_2OP(OEt)$_2$), 58.09 (d, $J_{(C-P)}$=10.5, OP(OC$H_2$$CH_3$)$_2$), 58.00 (d, $J_{(C-P)}$=9.9, OP(OC$H_2$$CH_3$)$_2$), 48.18 (d, $J_{(C-P)}$=6.3, C(CH_2Ph)CH_2OP(OEt)$_2$), 36.21 (s, C(CH_2Ph)CH_2OP(OEt)$_2$), 32.36, 32.29 (2×s, C$H$$CH_3$), 18.79 18.70, 17.76, 17.61 (4×s, CHCH_3), 16.92 (d, $J_{(C-P)}$=4.8, OP(OCH_2CH_3)$_2$). ^{31}P NMR: 138.80 (s).

*5.2.8. (3,3′,5,5′-Tetra-tert-butyl-1,1′-biphenyl-2,2′-diyl)-{2,2-bis[(4S)-4-isopropyl-4,5-dihydro-oxazol-2-yl]propyl}-phosphite (**5a**).* A solution of **3a** (142 mg, 0.5 mmol) and dimethylaminopyridine (0.5 mmol, 61 mg, azeotropically pre-dried over toluene (3×1 mL)), in dry degassed toluene (10 mL) and cooled to 0 °C, was slowly added to a solution of (3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphorochloridite[36] (0.6 mmol, 285 mg) in dry degassed toluene (2 mL). The mixture was allowed to warm to rt and stirred overnight. The mixture was then filtered to eliminate the pyridine salts, and the filtrate was concentrated to dryness. The white foam obtained was purified by flash chromatography over nitrogen. Yield: 100 mg (28%). Elemental analysis ($C_{43}H_{65}N_2O_5P$): theoretical C 71.64, H 9.09, N 3.89; experimental C 71.60, H 9.20, N 3.87. *m/z* (ESI): $[M+H]^+$=721.4. ^{1}H NMR: 7.42–7.41 (m, 2H; CH_{Ph}), 7.17–7.16 (m, 2H; CH_{Ph}), 4.13–4.02 (m, 2H; C(CH_3)CH_2OP(OR)$_2$, 2H; CH_2 oxazole), 3.94–3.84 (m, 2H; CH_2 oxazole, 2H; CH oxazole), 1.75–1.68 (m, 2H; C$H$$CH_3$), 1.53 (s, 3H; C(C$H_3$)$CH_2$OP(OR)$_2$), 1.48 (s, 18H; C($CH_3$)$_3$), 1.34 (s, 18H, C($CH_3$)$_3$), 0.85 (d, J_{HH}=6.8, 3H; CHCH_3), 0.84 (d, J_{HH}=6.8, 3H; CHCH_3), 0.79 (d, J_{HH}=6.8, 6H; CHCH_3). ^{13}C NMR: 165.33, 166.32 (2×s, C=N), 146.35 (d, J_{CP}=4.0; C_{ipso}-OP), 139.73 (d, J_{CP}=2.7; C_{ipso}–*t*-Bu), 132.66 (d, J_{CP}=1.2; C_{ipso}–C_{ipso}), 132.63 (d, J_{CP}=1.2; C_{ipso}–*t*-Bu), 126.49, 124.15 (2×s, CH_{Ph}), 71.61, 71.51 (2×s, CH oxazole), 69.60 (s, CH_2 oxazole), 66.11 (s, C(CH_3)CH_2OP(OR)$_2$), 43.65 (d, J_{CP}=4.3; C(CH_3)CH_2OP(OR)$_2$), 35.29, 35.26, 34.60 (3×s, C(CH_3)$_3$), 32.13, 31.99 (2×s, C$H$$CH_3$ oxazole), 31.48, 30.92, 30.90, 30.86, 30.83 (5×s, C(CH_3)$_3$), 19.81 (s, C(CH_3)CH_2OP(OR)$_2$), 18.49, 18.45, 17.45, 17.41 (4×s, CHCH_3). ^{31}P NMR: 135.15 (s).

*5.2.9. (3,3′,5,5′-Tetra-tert-butyl-1,1′-biphenyl-2,2′-diyl)-{2,2-bis[(4S)-4-isopropyl-4,5-dihydro-oxazol-2-yl]-3-phenyl-propyl}-phosphite (**5b**).* From **3b** (179 mg, 0.5 mmol) and (3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diyl)phosphorochloridite[36] following the previous procedure. Yield: 110 mg (28%). Elemental analysis ($C_{49}H_{69}N_2O_5P$): theoretical C 73.84, H 8.73, N 3.52; experimental C 73.70, H 8.90, N 3.48. *m/z* (ESI): $[M+H]^+$=797.5. ^{1}H NMR: 7.45–7.43 (m, 2H; CH_{Ph}), 7.20–7.18 (m, 2H; CH_{Ph}), 7.15–7.09 (m, 5H; CH_{Ph}), 4.23 (ABX: δ_A=4.26, δ_B=4.21, J_{AB}=10.8, J_{AX}=6.0, J_{BX}=5.2; 2H; C(CH_2Ph)CH_2OP(OR)$_2$), 4.13 (m, 1H; CH_2 oxazole), 4.05 (m, 1H; CH_2 oxazole), 3.89 (m, 1H; CH_2 oxazole), 3.87–3.78 (m, 2H; CH oxazole, 1H; CH_2 oxazole), 3.40 (AB: δ_A=3.42, δ_B=3.35, J_{AB}=13.6, 2H; C(CH_2Ph)CH_2OP(OR)$_2$), 1.65 (m, 1H; C$H$$CH_3$), 1.55 (m, 1H; C$H$$CH_3$), 1.49 (s, 18H; C($CH_3$)$_3$), 1.37(s, 18H; C($CH_3$)$_3$), 0.83 (d, J_{HH}=6.0, 3H; CHCH_3), 0.80 (d, J_{HH}=6.0, 3H; CHCH_3), 0.76 (d, J_{HH}=6.8, 3H; CHCH_3), 0.75 (d, J_{HH}=6.8, 3H; CHCH_3). ^{13}C NMR: 164.05, 163.96 (2×s, C=N), 146.47–124.21, 72.11, 71.99 (2×s, CH oxazole), 69.86, 69.62 (2×s, CH_2 oxazole), 63.74 (d, $J_{(C-P)}$=8.4; C(CH_2Ph)CH_2OP(OR)$_2$), 48.47 (d, J_{CP}=5.3; C(CH_2Ph)CH_2OP(OR)$_2$), 36.77 (C(CH_2Ph)CH_2OP(OR)$_2$), 35.56, 35.55, 34.85 (3×s, C(CH_3)$_3$), 32.54, 32.29 (2×s, C$H$$CH_3$), 31.75, 31.36, 31.29, 31.26, 31.25 (5×s, C(CH_3)$_3$), 19.04, 18.83, 17.96, 17.79 (4×s, CHCH_3). ^{31}P NMR: 145.3 (s).

*5.2.10. 2,2′-[1-(Diisopropylphosphinooxymethyl)ethylidene]-bis[(4S)-4-isopropyl-4,5-dihydro-oxazole] (**6a**).* From **3a** (785 mg, 2.78 mmol) and chlorodiisopropylphosphine following the previous procedure. Yield: 1.01 g (91%) as a pale yellow oil. IR (ν cm^{-1}): 1648 (C=N). Elemental analysis ($C_{21}H_{39}N_2O_3P$): theoretical C 63.29, H 9.86, N 7.03; experimental C 63.25; H 9.92; N 6.99. *m/z* (ESI): $[M+H]^+$=399.2. ^{1}H NMR: 4.19–4.13 (m, 2H; CH_2 oxazole), 4.06–4.04 (m, 2H; C(CH_3)CH_2OP^{i}Pr$_2$), 3.98–3.91 (m, 4H; CH_2 and CH oxazole), 1.81–1.73 (m, 2H; C$H$$CH_3$), 1.72–1.63 (m, 2H; PC$H$$CH_3$), 1.58 (s, 3H; C(C$H_3$)$CH_2$OP^{i}Pr$_2$), 1.05 (dd, $J_{(H-P)}$=10.8, $J_{(H-H)}$=6.8, 3H; PCHCH_3), 1.04 (dd, $J_{(H-P)}$=10.8, $J_{(H-H)}$=6.0, 3H; PCHCH_3), 1.00 (dd, $J_{(H-P)}$=13.0, $J_{(H-H)}$=7.1, 3H; PCHCH_3), 0.97 (dd, $J_{(H-P)}$=13.0, $J_{(H-H)}$=7.4, 3H; PCHCH_3), 0.90 (d, J=6.8, 3H; CHCH_3), 0.89 (d, J=6.8, 3H; CHCH_3), 0.83 (d, J=6.8, 6H; CHCH_3). ^{13}C NMR: 165.84 (s, C=N), 74.40 (d, $J_{(C-P)}$=20.8, C(CH_3)CH_2OP^{i}Pr$_2$), 71.82, 71.59 (2×s, CH oxazole), 69.67, 69.48 (2×s, CH_2 oxazole), 44.42 (d, $J_{(C-P)}$=9.6, C(CH_3)CH_2OP^{i}Pr$_2$), 32.28, 32.14 (2×s, C$H$$CH_3$), 28.10 (d, $J_{(C-P)}$=18.8, PC$H$$CH_3$), 27.94 (d, $J_{(C-P)}$=17.3, PC$H$$CH_3$), 18.63, 18.56 (2×s, CH$CH_3$) 19.84 (s; C(C$H_3$)$CH_2$OP^{i}Pr$_2$), 17.86 (d, $J_{(C-P)}$=5.9, PCHCH_3), 17.64 (s, CHCH_3), 17.29, 17.11, 17.02 (3×s, PCHCH_3). ^{31}P NMR: 152.45 (s).

*5.2.11. 2,2′-[1-(Diphenylphosphinomethyl)ethylidene]-bis [(4S)-4-isopropyl-4,5-dihydro-oxazole] (**8a**).* To a solution of **7a** (1 g, 3.9 mmol) in THF (20 ml) at 0 °C $KPPh_2$ (2.5 ml, 4 mmol) was added and the mixture was stirred for 1 h. The solvent was evaporated under reduced pressure, toluene (20 ml) was added to the crude and the solid was filtered off. The resulting solution was evaporated under reduced pressure, and the solid obtained was repeatedly washed with hexane. Yield: 587 mg (45%) as white solid. IR (ν cm^{-1}): 1655 (C=N). Elemental analysis ($C_{27}H_{35}N_2O_2P$): theoretical C 71.97, H 7.83, N 6.21; experimental C 72.78; H 8.14; N 5.86. *m/z* (ESI): $[M+H]^+$=451.2. ^{1}H NMR: 7.50–7.44 (m, 4H; CH_{o-Ph}), 7.32–7.27 (m, 6H; $CH_{m\text{-}p\text{-}Ph}$), 4.10 (m, 1H; CH_2 oxazole), 3.89–3.77 (m, 2H; CH_2 oxazole, 1H; CH oxazole, 1H; CH_2 oxazole, 1H; CH oxazole), 3.83 (ABX: δ_A=2.87, δ_B=2.79, J_{AB}=14.2, J_{AX}=4.0, J_{BX}=3.1, 2H, $CCH_3CH_2PPh_2$), 1.77 (m, 1H; C$H$$CH_3$), 1.69 (m, 1H; C$H$$CH_3$), 1.60 (s, 3H, $CCH_3CH_2PPh_2$), 0.92 (d, J=6.8, 3H; CHCH_3), 0.88 (d, J=6.8, 3H; CHCH_3), 0.82 (d, J=6.8, 6H; CHCH_3), 0.81 (d, J=6.8, 6H; CHCH_3). ^{13}C NMR: 167.89 (d, J_{CP}=5.5, C=N), 167.53 (d, J_{CP}=4.5, C=N), 139.44 (d, J_{CP}=4.1, $C_{ipso-Ph}$), 139.26 (d, J_{CP}=5.0, $C_{ipso-Ph}$), 133.40 (d, J_{CP}=20.1,

$C_{o\text{-Ph}}$), 132.81 (d, J_{CP}=19.3, $C_{o\text{-Ph}}$), 128.46 (s, $C_{p\text{-Ph}}$), 128.27 (d, J_{CP}=6.4, $C_{m\text{-Ph}}$), 128.23 (s, $C_{p\text{-Ph}}$), 128.22 (d, J_{CP}=6.8, $C_{m\text{-Ph}}$), 71.95, 71.51 (2×s, CH oxazole), 70.15, 69.67 (2×s, CH_2 oxazole), 41.99 (d, J_{CP}=20.6, $CCH_3CH_2PPh_2$), 37.35 (d, J_{CP}=16.8, $CCH_3CH_2PPh_2$), 32.43, 32.13 (2×s, $CHCH_3$), 23.06 (d, J_{CP}=12.6, $CCH_3CH_2PPh_2$), 18.85, 18.65, 17.83, 17.39 (4×s, $CHCH_3$). ^{31}P NMR: −23.06 (s).

5.3. Catalytic reactions

5.3.1. Allylic substitution in dichloromethane. To a solution of the chiral ligand (0.029 mmol) in anhydrous dichloromethane (2 ml), was added [{PdCl(η-C_3H_5)}$_2$] (3.5 mg, 0.0096 mmol). The resulting mixture was deoxygenated and stirred for 2 h at rt. To this solution were sequentially added *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate (126.05 mg, 0.5 mmol), diethyl malonate (164.1 μl, 1.07 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 352.1 μl, 1.44 mmol) and sodium acetate (small amount), and the mixture was again deoxygenated. The reaction was monitored by gas chromatography (HP 5890 Series II, FID, HP-1 column 30m×0.25 mm×0.25 μm; 20 psi helium, oven temperature program: 50 °C (1 min), 20 °C/min, 270 °C (5 min); retention times: substrate 11.2 min, product 13.2 min). At the end of the reaction, the solution was diluted with diethyl ether, washed with saturated aqueous solution of NH_4Cl, dried over $MgSO_4$, and evaporated at reduced pressure. The crude was purified by flash chromatography. The enantiomeric excess was determined by HPLC (Waters Alliance 2695, PDA 2996, ChiralPak AD-H 0.46 cm×25 cm, hexane/^{i}PrOH (90/10) 1 ml/min, retention times: substrate 5.9 and 6.2 min, (*R*)-product 10.1 min (*S*)-product 13.7 min).

5.3.2. Allylic substitution in [bmim][PF_6]. To a solution of the chiral ligand (0.029 mmol) in [bmim][PF_6] (0.5 ml pre-dried under vacuum in the presence of P_2O_5) was added [{PdCl(η-C_3H_5)}$_2$] (3.5 mg, 0.0096 mmol). The resulting mixture is deoxygenated and stirred for 2 h at rt. To this solution were sequentially added *rac*-(*E*)-1,3-diphenylprop-2-enyl acetate (126.05 mg, 0.5 mmol), diethyl malonate (164.1 μl, 1.07 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 352.1 μl, 1.44 mmol) and sodium acetate (small amount), and the mixture was again deoxygenated. At the end of the reaction, the products were extracted with hexane, and treated and analyzed as described before.

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Supplementary data

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