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# Diastereoselective Addition of 2*H*-2-Oxo-1,4,2-oxazaphosphinanes to Aldehydes and Imines

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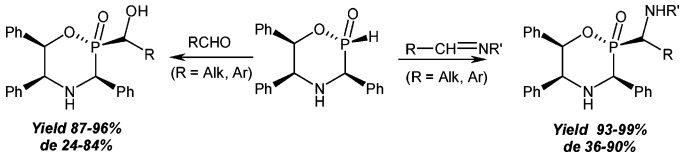


Diastereoselective additions of 2-hydrogeno-2-oxo-1,4,2-oxazaphosphinanes to aldehydes and imines are described. α,α′-Diaminophosphinic and α-amino-α′-hydroxyphosphinic derivatives were obtained with de's ranging from 24 to 90%.

## Introduction

During the past decade, preparation of α-hydroxy- and α-aminophosphoryl derivatives[1] (especially phosphonic and phosphinic acids, esters, or salts) has attracted significant attention due to the potential biological activities of such compounds which show broad applications as enzyme inhibitors. In addition, α-substituted phosphonates (or phosphinates) are useful intermediates in the synthesis of various functionalized organophosphorus compounds.[2]

Furthermore, it can be pointed out that the conjunction of two functionalities in the same molecule (α-amino-α′-hydroxyphosphinates **A** or α,α′-diaminophosphinates **B** and **C**)[2b,3] affords powerful inhibitors of human immunodeficiency virus type 1 (HIV-1) protease (Figure 1).

Although stereoselective syntheses of α-amino or α-hydroxy phosphonic derivatives are well described, there are only few examples dealing with the stereoselective syntheses of phosphinic derivatives (using heterobimetallic complexes, chiral imines or sulfinimines).[4]

We report herein the diastereoselective addition of a cyclic 2-hydrogeno-2-oxo-1,4,2-oxazaphosphinane to aldehydes and imines.

## Results and Discussion

We recently published[5] the first synthesis of 2*H*-2-oxo-1,4,2-oxazaphosphinanes **3a** and **3b** via addition of meth-

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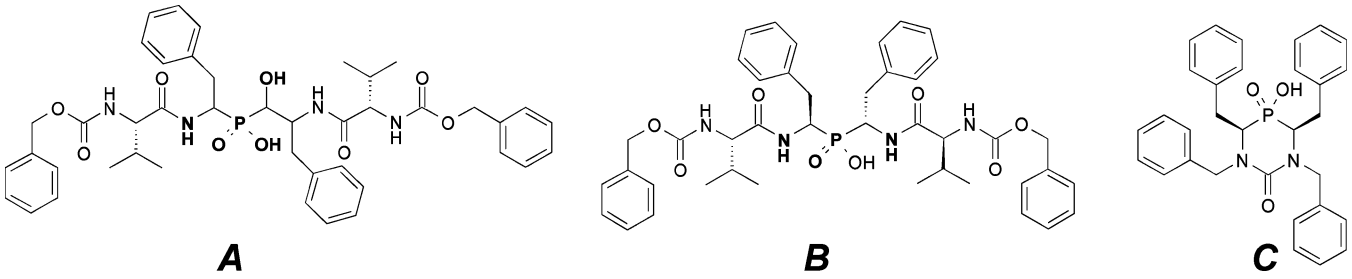
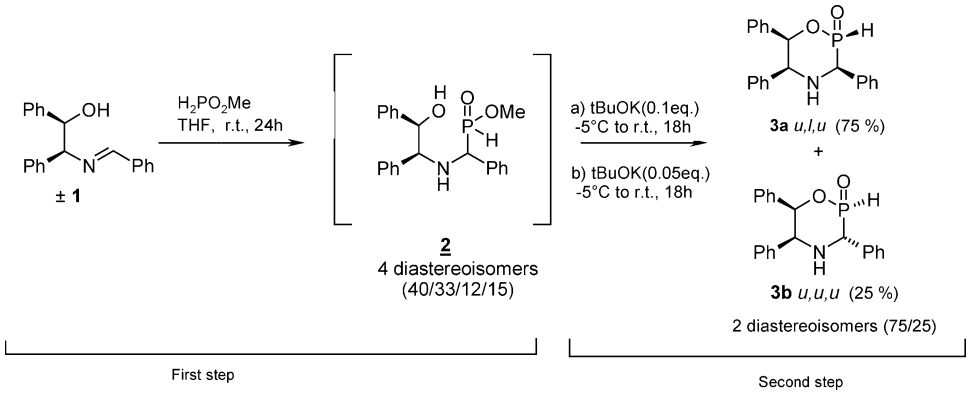



**FIGURE 1.** Published structures of HIV-1 protease inhibitors.

**SCHEME 1**




yl hypophosphite to a chiral imine followed by an intramolecular transesterification (Scheme 1). Owing to their cyclic structure, enhancing their rigidity, and the relative position of the substituents, these heterocyclic compounds could be used as chiral inductors for diastereoselective nucleophilic addition of the reactive P−H bond to electrophiles.

From the stereochemical point of view, four diastereoisomers could be formed in the first addition step, because there are two new stereogenic centers created (compounds **2**), and indeed four diastereoisomers are detected by $^{31}$P NMR in the ratio (40/33/12/15) in THF.

But after the second step, only two diastereoisomers (**3a** and **3b**) are obtained, probably as a result of a rapid epimerization at phosphorus during the cyclization process, in the basic conditions used. It seems probable that the epimerization at phosphorus does not take place through simple deprotonation−reprotonation of the P−H bond, which is well-known to occur with retention of configuration,[6] but more likely through fast pseudorotation of a pentacoordinated phosphorus species detected at −32 ppm in the $^{31}$P NMR spectrum of the reaction mixture.

The *u*,*l*,*u*[7] structure of diastereoisomer **3a** (*u*,*l*,*u*) was determined by a monocrystal X-ray analysis.[5] All NMR data could be assigned and they were in good agreement with the twisted boat cycle characteristic of the crystal. We could not obtain suitable crystals for the second diastereoisomer **3b** for X-ray analysis but we could ascertain indirectly the *u*,*u*,*u* structure.[8]

For the stereochemical outcome of the reaction, we could state, following the simultaneous changes in $^{31}$P NMR signals for intermediates **2** and for cyclic compounds **3** during the cyclization step, that the diastereoisomeric ratio for the cycles (75/25) is directly related to the ratio of the open intermediates (73/27) showing that the carbon chirality α to phosphorus is determined in the first step (Scheme 2 and Figure 3).

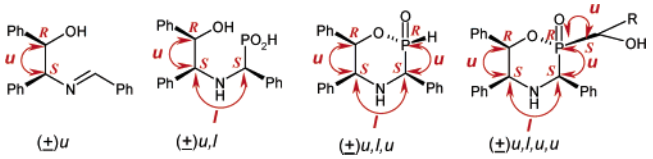
Concerning the diastereoselectivity observed in the creation of the α-carbon chirality, we could show that the P−C bond formation is irreversible and that no C−H epimerization takes place in the reaction conditions: The results of the study dealing with the transformation of **3a** (*u*,*l*,*u*) into **3b** (*u*,*u*,*u*), and of **3b** into **3a**, using increasing quantities of potassium *tert*-butoxide is described in Table 1. Scheme 2 shows all the possible cyclic diastereoisomers **3**.

The transformation of compound **3a** (*u*,*l*,*u*) into **3b** (*u*,*u*,*u*) is possible with 0.1 equiv of *t*-BuOK (entry 2) but

(5) **5.** Cristau, H.-J.; Monbrun, J.; Tillard, M.; Pirat, J.-L. *Tetrahedron Lett.* **2003**, *44*, 3183−3186.

(6) (a) Farnham, W. B.; Murray, R. K.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 5809−5810. (b) Farnham, W. B.; Murray, R. K.; Mislow, K. *J. Chem. Soc., Chem. Commun.* **1971**, 605−606. (c) Reiff, L. P.; Aaron, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 5275−5276. (d) Van den Berg, G. R.; Platenburg, D. H. J. M.; Benschop, H. P. *J. Chem. Soc., Chem. Commun.* **1971**, 606−607. (e) Haynes, R. K.; Au−Yeung, T. L.; Chan, W. K.; Lam, W. L.; Li, Z. Y.; Yeung, L. L.; Chan, A. S. C.; Li, P.; Koen, M.; Mitchell, C. R.; Vonwiller, S. C. *Eur. J. Org. Chem.* **2000**, 3205−3216. (f) Kers, A.; Stawinski, J. *Tetrahedron Lett.* **1999**, *40*, 4263−4266. (g) Johansson, T.; Kers, A.; Stawinski, J. *Tetrahedron Lett.* **2001**, *42*, 2217−2220.

(7) The descriptors "unlike *u* or like *l*" of the diastereoisomers are used according to Prelog and Seebach (Prelog, V.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654−660) and complied with the iteration's rule starting from the inductor structure (±) *u*, as exemplified hereafter.




(8) Pirat, J.-L.; Monbrun, J.; Virieux, D.; Cristau, H.-J. *Tetrahedron* **2005**, *61*, 7029−7036.

**SCHEME 2**

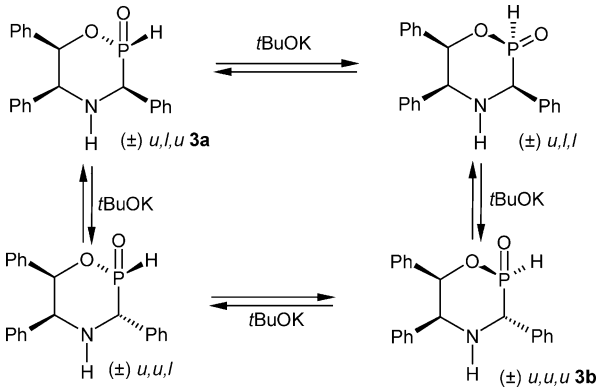



**TABLE 1. Transformation of 3a (*u,l,u*) into 3b (*u,u,u*), and of 3b into 3a, under Basic Activation Using Increasing Quantities of *t*-BuOK**

| compd | entry | *t*-BuOK (nb equiv) | ratio *u,l,u*/*u,u,u* | dec (%) |
|---|---|---|---|---|
| **3a** *u,l,u* | 1 | 0 | 100:0 | / |
| | 2 | 0.1 | 98:2 | 0 |
| | 3 | 0.2 | 55:45 | 9 |
| | 4 | 0.5 | 4:96 | 5 |
| **3b** *u,u,u* | 5 | 0 | 0:100 | 0 |
| | 6 | 0.1 | 0:100 | 0 |
| | 7 | 0.5 | 4:96 | 2 |
| **3a** *u,l,u* and **3b** *u,u,u* | 8 | 0 | 57:43 | / |
| | 9 | 0.5 | 4:96 | 10 |

is minimal, seeing that only traces of **3b** (*u*,*u*,*u*) are obtained. Increasing quantities of *t*-BuOK (20% mol, entry *3*) allowed the transformation of **3a** (*u*,*l*,*u*) into **3b** (*u*,*u*,*u*) in the ratio 55/45.

Moreover, the use of *t*-BuOK (50% mol, entry 4) allowed the transformation of **3a** (*u*,*l*,*u*) into **3b** (*u*,*u*,*u*) in the ratio 4/96 as observed entry 7 starting from **3b**. Finally, a mixture of **3a** (*u*,*l*,*u*) and **3b** (*u*,*u*,*u*) in the ratio 50/50 again gives, with 0.5 equiv of *t*-BuOK, compounds **3a** (*u*,*l*,*u*) and **3b** (*u*,*u*,*u*) in the ratio 4/96 (entry *9*).

These studies show that no significant thermodynamic equilibrium occurs in the presence of 0.1 equiv of *t*-BuOK during the reaction and also that **3b** is the thermodynamically more stable compound (The $\Delta\Delta G°$ for the two diastereoisomers **3a** and **3b**, corresponding to the ratio 4/96 obtained during the experiment is equal to 1.85 kcal $mol^{-1}$). It can be noticed that the concentration of the diastereomeric *u,u,l* and *u,l,l* adducts is not high enough to be observed during the transformation of **3a** into **3b**. The absence of these diastereomers both in the final mixture and during the isomerization process tends to show that their energies are higher than **3a** and **3b** (see Figure 2).

The same manipulation using triethylamine as a base does not afford any change of the reaction mixture even after 4 days. This experiment ascertains that triethylamine is not basic enough to give interconversion.

Therefore, the diastereoselectivity of the first step is clearly under kinetic control and the *S*-chirality at the α-carbon is the result of the preferential formation of the transition state corresponding to the addition on the *Si* face of the imine which is certainly in the *anti* configuration as shown in Figure 3. The diastereoselectivity

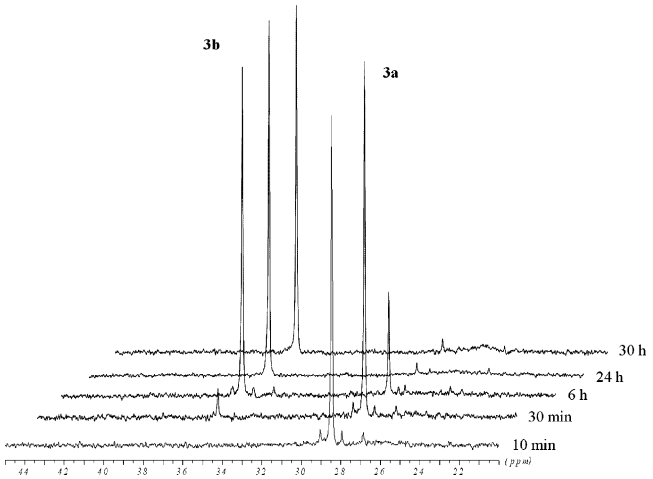



**FIGURE 2.** Interconversion of **3a** into **3b** using 0.5 equiv of *t*-BuOK.

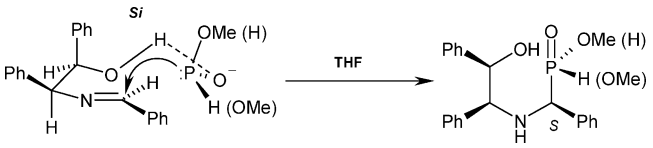



**FIGURE 3.** Potential explanation for the preferential *S*-chirality at the α-carbon.

**SCHEME 3**

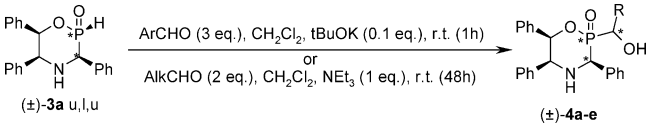



**TABLE 2. Diastereoselective Addition of 2-Hydrogeno-1,4,2-oxazaphosphinane 3a to Aldehydes**

| compd | R | yield[a] (%) (isolated yield[b] (%)) | de[a] (%) |
|---|---|---|---|
| **4a** | Et | 87 (62) | 24 |
| **4b** | *i*-Pr | 93 (60) | 40 |
| **4c** | Ph | 95 (58) | 84 |
| **4d** | *p*-$CF_3$Ph | 85 (64) | 80 |
| **4e** | 2-furyl | 96 (71) | 82 |

[a] Determined by NMR $^{31}P$ spectroscopy. [b] Yield after purification by column chromatography.

observed results more likely from the hydrogen bonding between the free hydroxy group and the polar phosphorus reagent.

We investigated the reactivity of the 2-hydrogeno-1,4,2-oxazaphosphinane on the major isomer (±) **3a** *u*,*l*,*u* obtained by addition in THF, which can be easily isolated by preferential crystallization. Moreover, this stereoisomer **3a** presents the bulky groups on the same side of the reactive P−H bond. As a consequence, we can expect that the diastereoselectivities will be better with **3a**.

**Additions to Aldehydes.** When diastereoisomer (±)-**3a** *u*,*l*,*u* is engaged in nucleophilic additions on aldehydes in an Abramov[9] (or Pudovik[10]) addition reaction affording

(9) (a) Abramov, V. S. *Dokl. Akad. Nauk SSSR* **1954**, *95*, 991−992. (b) Abramov, V. S. *Zh. Obshch. Khim.* **1952**, *22*, 647−652.

(10) (a) Pudovik, A. N.; Arbuzov, B. A. *Dokl. Akad. Nauk SSSR* **1950**, *73*, 327−330. (b) Pudovik, A. N.; Arbuzov, B. A. *Zh. Obshch. Khim.* **1951**, *21*, 382−388.

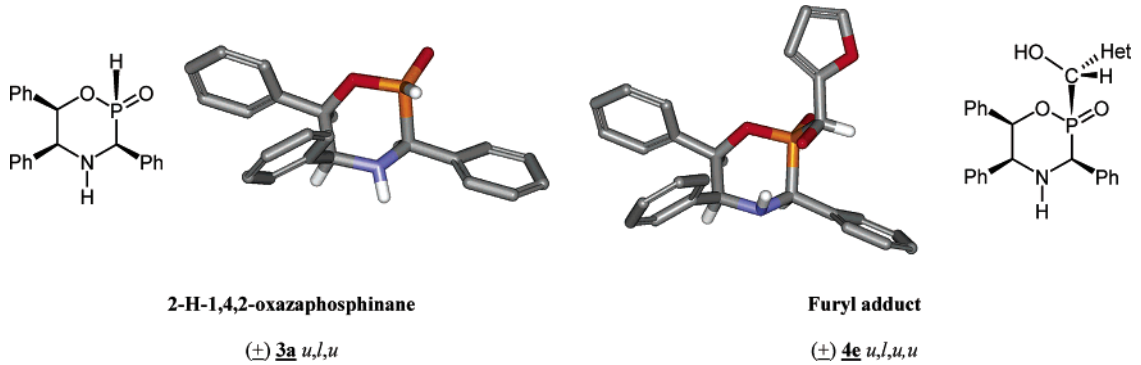
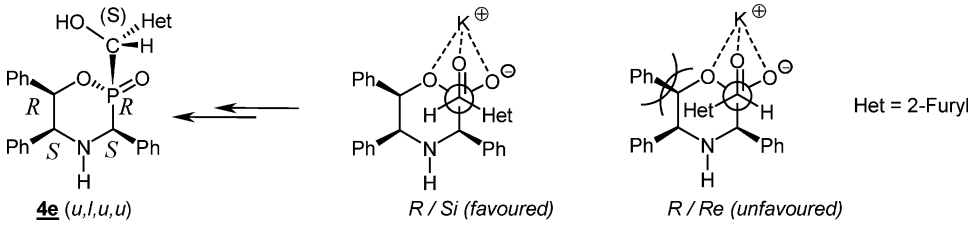



**FIGURE 4.** Compared X-ray structures of starting compounds **3a** and furyl adduct **4e**.

**SCHEME 4**




the corresponding α-hydroxyalkyl adducts, the presence of the three phenyl groups on the same side of the ring should enhance diastereoselection.

After several optimizations, it appeared that according to the aldehyde nature (aromatic or aliphatic), two different nucleophilic activations can be used: potassium *tert*-butoxide for aromatic and triethylamine for aliphatic derivatives (Scheme 3, Table 2).

The α-hydroxyalkyl adducts **4** were obtained in good yields (Table 2). Aliphatic aldehydes give relatively low diastereoisomeric excesses (24−40% de). However, as expected, isobutyraldehyde (compound **4b**) gives higher de than propanal **4a**, with respect to the greater steric hindrance of the isopropyl substituent. Aromatic aldehydes afforded better results, with diastereoisomeric excesses over 80%, demonstrating effective induction of the chiral 2*H*-1,4,2-oxazaphosphinane ring.

Concerning the diastereoselectivity of the phosphoaldol reaction, we obtained suitable crystals for X-ray analysis of the major isomer of the adduct **4e** from furfural. The corresponding structure is outlined in Figure 4. The boatlike conformation of starting hydrogenophosphinic heterocycle **3a** *u,l,u* is maintained after addition but slightly more twisted. Further, the structure shows retention of configuration on phosphorus **4e** *u,l,u,u*, as previously described in the literature for similar reactions.[11]

Interestingly, an intramolecular H-bonding occurs between the hydrogen of intracyclic secondary amine and the oxygen of hydroxyl function, indeed, pseudoequatorial N−H bond of 2-H-1,4,2-oxazaphosphinane **3a** *u,l,u* would move up during addition to pseudoaxial position **4e** *u,l,u,u* in order to allow intramolecular H-bonding.

**SCHEME 5**

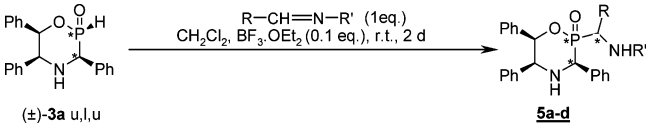



**TABLE 3. Addition of 2-Hydrogeno-1,4,2-oxazaphosphinane to Various Imines**

| compd | R | R′ | yield[a] (%) (isolated yield (%)) | de[a] (%) |
|---|---|---|---|---|
| **5a** | Ph | Bn | 93 (84[b]) | 42 |
| **5b** | Ph | *t*-Bu | 93 (43[c]) | 38 |
| **5c** | 2-furyl | Bn | 96 (46[c]) | 36 |
| **5d** | *i*-Pr | Bn | 99 (52[c]) | 50 |
| **5e** | Ph | $CH_2CO_2Et$ | 94[d] (73[b]) | 6 |

[a] Determined by $^{31}P$ NMR. [b] After purification by column chromatography. [c] After crystallization. [d] 24 h. [e] 96 h.

In agreement with Spilling et al. in a similar case,[12] we have shown that the phosphoaldol reaction is under kinetic control in our reaction conditions: Epimerisation attempts, using the same reaction conditions (0.1 equiv. of *t*BuOK) on a diastereoisomeric mixture of compounds **4c** (composed of a ratio 72/28) did not modify the ratio. Moreover, reversibility attempts, using compounds **4c**, in the same reaction conditions (0.1 equiv of *t*-BuOK) in the presence of 2-furylaldehyde (2 equiv.) did not show any evolution of the reaction.

According to these observations, we can propose the following models (Scheme 4) as an explanation to the diastereoselectivity of the addition. Examinating the molecular models of the two transitions states, resulting of the attack of the *R*-phosphorus either on the *Si* side or the *Re* side of the aldehyde with a coordination of the carbonyl oxygen to the potassium ion associated to the

(11) (a) Reiff, L. P.; Aaron, H. S. *J. Am. Chem. Soc.* **1970**, *92*, 5275. (b) Farnham, W. B.; Murray, R. K.; Mislow, K. *Chem. Commun.* **1971**, 605−606. (c) Farnham, W. B.; Murray, R. K.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 5809−5810. (d) Van den Berg, G. R.; Platenburg, D. H. J. M.; Benschop, H. P. *Chem. Commun.* **1971**, 606−607.

(12) (a) Blazis, V. J.; Koeller, K. J.; Spilling, C. D. *J. Org. Chem.* **1995**, *60*, 931−940. (b) Blazis, V. J.; De La Cruz, A.; Koeller, K. J.; Spilling, C. D. *Phosphorus, Sulfur Silicon* **1993**, *75*, 159−162.

**SCHEME 6**

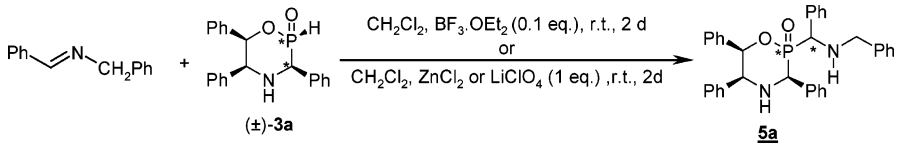



**TABLE 4. Effect of Electrophilic Activation on Diastereoselectivity for 5a**

| Lewis acid | Yield[a] % (isolated yield %) | *de*[a] % |
|---|---|---|
| $LiClO_4$ | 84 | 4[d] |
| $BF_3{\cdot}OEt_2$ | 93 − (84[b]) | 42[d] |
| $ZnCl_2$ | 86 − (42[c]) | 90[d] (100[c]) |

[a] Determined by NMR $^{31}P$. [b] After purification by column chromatography. [c] After crystallization. [d] Same stereodirecting effects.

**TABLE 5. Addition of 2-Hydrogeno-1,4,2-oxazaphosphinane to Various Imines Using $ZnCl_2$**

| compd | R | R′ | yield[a] (%) | de[a] (%) |
|---|---|---|---|---|
| **5a** | Ph | Bn | 86[b] | 90 |
| **5b** | Ph | *t*-Bu | 90[b] | 84 |
| **5c** | 2-Furyl | Bn | 49[b] | 59 |
| **5e** | Ph | $CH_2CO_2Et$ | 93[c] | 33 |

[a] Determined by $^{31}P$ NMR. [b] 48h [1 equiv of imine, using $ZnCl_2$ (1 equiv)] [c] 96h [2 equiv of imine, using $ZnCl_2$ (0.2 equiv)].

P−O group, it appears that the steric overcrowding between the phenyl ring α to oxygen and the incoming furyl group, well accounts for the diastereoselectivity observed.

**Additions to Imines.** Following the previous results obtained for aldehydes, we decided to investigate the diastereoselective additions to aldimines. Using the same nucleophilic activation as described for aromatic aldehydes, only very low yields of adducts (<5%) were obtained, even after several days. Therefore, electrophilic activation was preferred for the reaction of oxazaphosphinane **3a** with aldimines (Scheme 5, Table 3).

Using boron trifluoride etherate, very good yields were obtained, unfortunately with low diastereoselectivities (de 6−50%). Contrasting with aldehydes, additions to imines show no significant de differences between aliphatic and aromatic derivatives, the highest value (de = 50%) certainly be due to higher steric hindrance of *i*Pr group compared with aromatic ones. Besides, steric hindrance on nitrogen substituent (compound **5b**, R′ = *t*-Bu) gave no improved diastereoselection.

Several other Lewis acids were used for the activation of imines, as lithium perchlorate and zinc chloride (Scheme 6, Table 4), the latter was especially chosen for the bidentate complexing properties and the well-known affinity between phosphoryl group and zinc cation.[13]

Contrary to lithium perchlorate which afforded no significant diastereoselection, zinc chloride gave high de (90%) in good yield (86%). Direct crystallization of the crude extracted reaction mixture afforded pure diastereoisomer. This excellent diastereoselectivity is probably the result of a more rigid transition state formed by a double coordination of the zinc cation with the nitrogen of the imine and the phosphoryl group.

To verify the general behavior of the reaction with zinc chloride, we submitted the previously used imines to these conditions. All the results are listed in Table 5. As expected, the diastereoselectivity is always enhanced from a factor 1.6 (compound **5c**) to 5.5 (compound **5e**).

## Conclusion

2-Hydrogeno-1,4,2-oxazaphosphinane **3a** was investigated as chiral substrate for diastereoselective additions. It reacts easily with aldehydes or aldimines, under nucleophilic or electrophilic activations, with good diastereoisomeric excesses affording an effective way for stereoselective syntheses of α-hydroxyalkyl- or α−aminoalkyl- P-substituted phosphorus heterocycles **4** or **5**. Diastereoselectivity using electrophilic activation for the reaction of imines presents a strong dependence of the Lewis acid effect. Zinc chloride, as a bidentate ligand, afforded the highest de in comparison to the other ones such as lithium perchlorate or boron trifluoride etherate corroborating our diastereoselection model.

## Experimental Section

**General Procedure for Addition to Aliphatic Aldehydes (4a,b).** In a 10 mL flask containing 500 mg of **3a** (1.43 mmol, 1 equiv) under $N_2$, dry dichloromethane (2.5 mL) followed by 953 μL of a 3 N solution of the aldehyde in dichloromethane (2.86 mmol, 2 equiv) at ambient temperature. A 477 μL portion of a 3 N solution of triethylamine in dichloromethane (1.43 mmol, 1 equiv) was added under stirring. After 48 h of stirring, a white precipitate appeared and starting compound **3a** was completely consumed. After addition of saturated aqueous NaCl solution and extraction with chloroform, organic layers were dried on sodium sulfate and evaporated. The white solid was purified by column chromatography (gradient hexane/ethyl acetate 50/50 to 10/90) to afford two diastereoisomers.

**(2*R**,3*R**,5*R**,6*S**)-(±)-2-Methyl-1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)propan-1-ol (4a):** white solid (361 mg, two diastereoisomers); yield 62%, de = 24%; $^{31}P$ NMR (81.015 MHz, $CDCl_3$) major $\delta$ = 45.99; minor $\delta$ = 44.60; $^1H$ NMR (400.13 MHz, $CDCl_3$) major $\delta$ = 1.01 (t, 3H, $J$ = 7.3 Hz), 1.85 (m, 2H), 3.70 (m, 1H), 4.72 (d, 1H, $J$ = 5.6 Hz), 4.95 (d, 1H, $J_{HP}$ = 15.9 Hz), 5.98 (dd, 1H, $J_{HP}$ = 6.9 Hz, $J$ = 5.6 Hz), 7.06−7.71 (m, 15H); minor $\delta$ = 0.94 (t, 3H, $J$ = 7.3 Hz), 1.41 (m, 1H), 1.73 (m, 1H), 4.01 (dd, 1H, $J$ = 3.2 Hz, $J_{HP}$ = 10.1 Hz), 4.81 (d, 1H, $J$ = 5.3 Hz), 4.96 (d, 1H, $J_{HP}$ = 14.7 Hz), 5.88 (dd, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 5.3 Hz), 7.06−7.69 (m, 15H); $^{13}C$ NMR (100.61 MHz, $CDCl_3$): major $\delta$ = 10.6 (d, $J_{PC}$ = 11.4 Hz), 23.9 (s), 60.5 (d, $J_{PC}$ = 79.8 Hz), 64.7 (s), 69.7 (d, $J_{PC}$ = 107.0 Hz), 126.7−129.5 (m), 134.6 (s), 136.8 (d, $J_{PC}$ = 5.9 Hz), 138.9 (s); minor $\delta$ = 10.9 (d, $J_{PC}$ = 11.8 Hz), 24.4 (s), 62.2 (d, $J_{PC}$ = 84.1 Hz), 64.2 (s), 69.5 (d, $J_{PC}$ = 106.2 Hz), 126.7−129.5 (multiple s), 134.9 (d, $J_{PC}$ = 4.2 Hz), 136.5 (d, $J_{PC}$ = 5.9 Hz), 138.8 (s); IR (NaCl cell, $CHCl_3$) $\nu$ = 3664, 3288, 3027, 3064, 2873, 2970, 1453, 1469, 1497, 1601, 1167, 1203, 1238, 1125,

(13) (a) Kafarski, P.; Gumienna-Kontecka, E.; Galesowska, J.; Drag, M.; Latajka, R.; Kozlowski, H. *Inorg. Chim. Acta* **2004**, *357*, 1632−1636. (b) Matthews, B. W.; Lowther, W. T.; Zhang, Y.; Sampson, P. B.; Honek, J. F. *Biochemistry* **1999**, *38*, 14810−14819. (c) Maskos, K.; Jozic, D.; Kaiser, J. T.; Huber, R.; Bode, W. *J. Mol. Biol.* **2003**, *332*, 243−256.

1082, 1016, 755, 773, 698, 714; HRMS (FAB+) calcd for $C_{24}H_{26}NO_3P$ 407.1729, found 407.1727; MS (FAB+) *m/z* = 408 $[M + H]^+$, 284, 180, 106.

**(2*R**,3*R**,5*R**,6*S**)-(±)-1-(3,5,6-Triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)propan-1-ol (4b):** white solid (361 mg, two diastereoisomers); yield 60%, de = 40%; $^{31}P$ NMR (121.49 MHz, $CDCl_3$) major $\delta$ = 47.87; minor $\delta$ = 45.37; $^1H$ NMR (400.13 MHz, $CDCl_3$) major $\delta$ = 1.03 (d, 3H, $J$ = 6.8 Hz), 1.14 (d, 3H, $J$ = 6.8 Hz), 2.29 (m, 1H), 3.59 (d, 1H, $J_{HP}$ = 4.5 Hz), 4.66 (d, 1H, $J_{HP}$ = 5.7 Hz), 4.90 (d, 1H, $J_{HP}$ = 15.3 Hz), 6.02 (dd, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 5.9 Hz), 7.06−7.69 (m, 15H); minor $\delta$ = 0.98 (d, 3H, $J$ = 6.8 Hz), 0.99 (d, 3H, $J$ = 6.8 Hz), 2.08 (m, 1H), 4.00 (d, 1H, $J_{HP}$ = 3.2 Hz), 4.78 (d, 1H, $J_{HP}$ = 5.2 Hz), 4.93 (d, 1H, $J_{HP}$ = 11.6 Hz), 5.91 (dd, 1H, $J_{HP}$ = 7.6 Hz, $J$ = 5.4 Hz), 7.06−7.69 (m, 15H); $^{13}C$ NMR (100.62 MHz, $CDCl_3$) major $\delta$ = 18.1 (d, $J_{PC}$ = 4.2 Hz), 20.8 (d, $J_{PC}$ = 9.9 Hz), 30.0 (s), 60.0 (d, $J_{PC}$ = 80.2 Hz), 64.8 (s), 73.2 (d, $J_{PC}$ = 104.7 Hz), 77.1 (d, $J_{PC}$ = 7.2 Hz), 126.2−129.5 (m), 134.7 (s), 136.5 (d, $J_{PC}$ = 6.4 Hz), 139.0 (s); minor $\delta$ = 17.2 (d, $J_{PC}$ = 3.6 Hz), 20.5 (d, $J_{PC}$ = 11.4 Hz), 29. 8 (s), 62.1 (d, $J_{PC}$ = 85.7 Hz), 64.1 (s), 70.9 (d, $J_{PC}$ = 103.8 Hz), 79.7 (d, $J_{PC}$ = 7.8 Hz), 126.2−129.5 (m), 135.1 (d, $J_{PC}$ = 4.8 Hz), 136.5 (d, $J_{PC}$ = 5.8 Hz), 138.8 (s); IR (NaCl cell, $CHCl_3$) $\nu$ = 3658, 3257, 3036, 3064, 2873, 2961, 1453, 1467, 1497, 1603, 1169, 1199, 1244, 1126, 1080; HRMS (FAB+) calcd for $C_{25}H_{28}NO_3P$ 421.1885, found 421.1873; MS (FAB+) *m/z* = 422 $[M + H]^+$, 284, 180, 106.

**General Procedure for Addition to Aromatic Aldehydes (4c−e).** In a 10 mL flask containing 500 mg of **3a** (1,43 mmol, 1 equiv) under $N_2$ was added dry dichloromethane (2.5 mL) followed by 953 $\mu$L of a 3 N solution of the aldehyde in dichloromethane (2.86 mmol, 2 equiv) at ambient temperature. A 477 $\mu$L portion of a 0.3 N solution of potassium *tert*-butylate in tetrahydrofuran (0.14 mmol, 0.1 equiv) was added under stirring. After 1 h, a white precipitate appeared and starting compound **3a** was completely consumed. After addition of saturated aqueous NaCl solution (pH ∼7) and extraction with chloroform, the organic layers were dried on sodium sulfate and evaporated. The white solid was purified by column chromatography (gradient hexane/ethyl acetate: 50/50 to 10/90) to afford two diastereoisomers.

**(2*R**,3*R**,5*R**,6*S**)-(±)-Phenyl(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)methanol (4c):** white solid (378 mg, two diastereoisomers); yield 58%, de = 86%; $^{31}P$ NMR (121.49 MHz, $CDCl_3$) $\delta$ = 41.32; $^1H$ NMR (400.13 MHz, $CDCl_3$) major $\delta$ = 2.9 (s, 1H), 4.25 (s, 1H), 4.55 (d, 1H, $J$ = 5.7 Hz), 4.74 (d, 1H, $J_{HP}$ = 3.5 Hz), 4.84 (d, 1H, $J_{HP}$ = 15.5 Hz), 5.84 (dd, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 6.0 Hz), 7.0−7.7 (m, 15H), minor $\delta$ = 2.9 (s, 1H), 4.25 (s, 1H), 4.62 (d, 1H, $J$ = 5.2 Hz), 4.91 (d, 1H, $J_{HP}$ = 13.6 Hz), 5.09 (d, 1H, $J_{HP}$ = 3.7 Hz), 5.74 (dd, 1H, $J$ = 5.7 Hz, $J_{HP}$ = 7.0 Hz), 7.06−7.69 (m, 15H); $^{13}C$ NMR (100.62 MHz, $CDCl_3$) major $\delta$ = 59.7 (d, $J_{PC}$ = 79.1 Hz), 64.9 (s), 71.7 (d, $J_{PC}$ = 104.7 Hz), 77.2 (d, $J_{PC}$ = 7.0 Hz), 126.7−129.5 (m), 134.2 (s), 135.2 (d, $J_{PC}$ = 5.7 Hz), 136.7 (d, $J_{PC}$ = 6.1 Hz), 138.9 (s); IR (NaCl cell, $CHCl_3$) $\nu$ = 3607, 3380, 3317, 3032, 3064, 2816, 2893, 1465, 1494, 1601, 1167, 1235, 1121, 1083, HRMS (FAB+) calcd for $C_{28}H_{26}NO_3P$ 455.1729, found 455.1736; MS (FAB+) *m/z* = 456 $[M + H]^+$, 284, 180, 106.

**(2*R**,3*R**,5*R**,6*S**)-(±)-(4-(Trifluoromethyl)phenyl)(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)methanol (4d):** white solid (479 mg, two diastereoisomers); yield 64%, de = 80%; $^{31}P$ NMR (81.02 MHz, DMSO-$d_6$) major $\delta$ = 44.51; minor $\delta$ = 44.99; $^{19}F$ NMR (235.36 MHz, DMSO-$d_6$) major $\delta$ = 61.32; minor $\delta$ = 61.37; $^1H$ NMR (250.13 MHz, DMSO-$d_6$) major $\delta$ = 3.23 (m, 1H), 6.90 (dd, 1H, $J$ = 4.0 Hz, $J_{HP}$ = 23.5 Hz), 4.63 (dd, 1H, $J$ = 6.0 Hz, $J$ = 8.1 Hz), 4.87 (dd, 1H, $J_{HP}$ = 6.0 Hz, $J$ = 3.8 Hz), 5.19 (dd, 1H, $J_{HP}$ = 16.7 Hz, $J$ = 12.1 Hz), 6.16 (dd, 1H, $J_{HP}$ = 6.4 Hz, $J$ = 6.4 Hz), 7.00−7.80 (m, 19H); $^{13}C$ NMR (50.32 MHz, DMSO-$d_6$) major $\delta$ = 56.3 (d, $J_{PC}$ = 73.3 Hz), 63.6 (s), 69.9 (d, $J_{PC}$ = 105.7 Hz), 74.7 (d, $J_{PC}$ = 6.0 Hz), 124.2 (s), 125−130 (s), 141.8 (d, $J_{PC}$ = 4.5 Hz), 134.8 (d, $J_{PC}$ = 2.6 Hz), 137.3 (d, $J_{PC}$ = 5.2 Hz), 139.6 (s); IR (KBr) $\nu$ = 3370, 3310, 3020, 3080, 2690, 2890, 1450, 1490, 1600, 1320, 1170, 1230, 1120, 1080, 700, 710; HRMS (FAB+) calcd for $C_{29}H_{25}F_3NO_3P$ 523.1602, found 523.1589; MS (FAB+) *m/z* = 524 $[M + H]^+$, 284, 180, 106.

**(2*R**,3*R**,5*R**,6*S**)-(±)-2-Furyl(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)methanol (4e):** white solid (446 mg, two diastereoisomers); yield 70%, de = 82%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 41.63; minor $\delta$ = 41.75; $^1H$ NMR (250.13 MHz, DMSO-$d_6$) major $\delta$ = 3.19 (m, 1H), 6.75 (s, 1H), 4.63 (bs, 1H), 4.70 (d, 1H, $J_{HP}$ = 5.2 Hz), 5.13 (dd, 1H, $J_{HP}$ = 15.5 Hz), 6.22 (dd, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 7.3 Hz), 6.48−6.52 (m, 2H), 7.1−8.3 (m, 16H); $^{13}C$ NMR (50.32 MHz, DMSO-$d_6$) major $\delta$ = 56.2 (d, $J_{PC}$ = 75.2 Hz), 63.5 (s), 63.9 (d, $J_{PC}$ = 112.8 Hz), 74.8 (d, $J_{PC}$ = 6.0 Hz), 109.7 (d, $J_{PC}$ = 4.5 Hz), 110.8 (s), 125.3−128.4 (m), 150.2 (d, $J_{PC}$ = 3.0 Hz), 134.7 (s), 137.4 (d, $J_{PC}$ = 5.6 Hz), 139.6 (s); IR (KBr) $\nu$ = 3400, 3260, 3030, 3100, 2780, 2960, 1460, 1465, 1500, 1600, 1175, 1225, 1250, 1135, 1070, 700, 720; HRMS (FAB+) calcd for $C_{26}H_{24}NO_4P$ 445.1521, found 445.1539.

**General Procedure for Addition to Imine Catalyzed by $BF_3{\cdot}OEt_2$ (5a−d).** In a 10 mL flask containing 600 mg of **3a** (1.71 mmol, 1 equiv) under $N_2$ was added dry dichloromethane (8 mL) followed by imine (1.71 mmol, 1 equiv) at ambient temperature. A 567 $\mu$L portion of a 0.3 N solution of $BF_3{\cdot}OEt_2$ in dichloromethane (0.17 mmol, 0.1 equiv) was added under stirring. After 48 h of stirring, saturated aqueous NaCl solution was added and followed by extraction with chloroform. Organic layers were dried on sodium sulfate and evaporated. The crude oil was purified by column chromatography (compound **3a**: gradient of dichloromethane/ethyl acetate 100/0 to 80/20) or by crystallization on ethyl acetate to afford two diastereoisomers. (compounds **5b−d**).

**(2*S**,3*R**,5*R**,6*S**)-(±)-*N*-Benzyl-1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)-1-phenylmethanamine (5a):** white solid (782 mg, 2 diastereoisomers); yield 84%, de = 42%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 45.19; minor $\delta$ = 43.76; $^1H$ NMR (250.13 MHz, $CDCl_3$) major $\delta$ = 2.16 (s, 1H), 2.95 (m, 1H), 3.11 (d, 1H, $J$ = 11.7 Hz), 3.46 (d, 1H, $J$ = 11.5 Hz), 3.74 (d, 1H, $J_{HP}$ = 13.7 Hz), 4.72 (dd, 1H, $J$ = 6.3 Hz, $J$ = 5.7 Hz), 5.04 (d, 1H, $J_{HP}$ = 9.2 Hz), 5.98 (dd, 1H, $J_{HP}$ = 6.9 Hz, $J$ = 6.1 Hz), 6.82−7.77 (m, 20H); minor $\delta$ = 2.29 (s, 1H), 2.95 (m, 1H), 3.06 (d, 1H, $J$ = 11.9 Hz), 3.41 (d, 1H, $J$ = 9.8 Hz), 4.23 (d, 1H, $J_{HP}$ = 12.3 Hz), 4.72 (dd, 1H, $J$ = 6.3 Hz, $J$ = 5.7 Hz), 4.96 (d, 1H, $J_{HP}$ = 9.6 Hz), 5.83 (dd, 1H, $J_{HP}$ = 6.3 Hz, $J$ = 6.1 Hz), 6.82−7.77 (m, 20H); $^{13}C$ NMR (62.89 MHz, $CDCl_3$) major $\delta$ = 51.7 (d, $J_{PC}$ = 17.3 Hz), 58.7 (d, $J_{PC}$ = 104.1 Hz), 61.7 (d, $J_{PC}$ = 86.9 Hz), 63.6 (d, $J_{PC}$ = 1.0 Hz), 78.2 (d, $J_{PC}$ = 6.7 Hz), 126.8−129.5 (s), 135.9 (s), 135.9 (s), 136.8 (d, $J_{PC}$ = 6.7 Hz), 139.0 (s), 139.3 (s); minor $\delta$ = 52.5 (d, $J_{PC}$ = 15.8 Hz), 60.7 (d, $J_{PC}$ = 97.4 Hz), 60.9 (d, $J_{PC}$ = 84.4 Hz), 64.7 (s), 77.3 (d, $J_{PC}$ = 6.7 Hz), 126.6−129.6 (s), 134.6 (d, $J_{PC}$ = 3.8 Hz), 135.2 (s), 136.0 (s), 137.2 (d, $J_{PC}$ = 5.8 Hz), 139.5 (d, $J_{PC}$ = 4.3 Hz); IR (KBr) $\nu$ = 3440, 3280, 3340, 3020, 3080, 2910, 2940, 1450, 1490, 1600, 1580, 1390, 1180, 1230, 1110, 1070, 1000, 1030, 700; HRMS (FAB+) calcd for $C_{35}H_{33}N_2O_2P$ 544.2358, found 544.2372; MS (FAB+) *m/z* = 545 $[M + H]^+$, 348, 284, 196, 180, 106, 91.

**(2*R**,3*R**,5*R**,6*S**)-(±)-*N*-*tert*-Butyl-1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)-1-phenylmethanamine (5b):** white solid (375 mg, two diastereoisomers); yield 43%, de = 38%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 47.61; minor $\delta$ = 45.20; $^1H$ NMR (250.13 MHz, $CDCl_3$) major $\delta$ = 0.67 (s, 9H), 1.94 (s, 1H), 2.95 (m, 1H), 4.21 (d, 1H, $J_{HP}$ = 17.1 Hz), 4.77 (dd, 1H, $J_{HP}$ = 8.5 Hz, $J$ = 5.8 Hz), 5.03 (dd, 1H, $J_{HP}$ = 16.1 Hz, $J$ = 11.1 Hz), 6.05 (dd, 1H, $J_{HP}$ = 7.8 Hz, $J$ = 5.9 Hz), 7.13−7.87 (m, 20H); minor $\delta$ = 0.69 (s, 9H), 1.88 (s, 1H), 2.25 (m, 1H), 4.37 (d, 1H, $J_{HP}$ = 17.4 Hz), 4.72 (dd, 1H, $J_{HP}$ = 5.4 Hz, $J$ = 5.4 Hz), 5.04 (dd, 1H, $J_{HP}$ = 14.9 Hz, $J$ = 6.3 Hz), 5.85 (dd, 1H, $J_{HP}$ = 6.5 Hz, $J$ = 6.5 Hz), 6.86−7.74 (m, 20H); $^{13}C$ NMR (100.62 MHz, $CDCl_3$) major $\delta$ = 29.7 (s), 51.5 (d, $J_{PC}$ = 17.3 Hz), 54.8 (d, $J_{PC}$ = 127.0 Hz), 61.2 (d, $J_{PC}$ = 104.7 Hz), 63.4 (d, $J_{PC}$ = 1.9 Hz), 77.2 (d, $J_{PC}$ = 8.4 Hz), 125.9−128.9 (s), 135.6 (d, $J_{PC}$ = 2.8 Hz), 136.5 (d, $J_{PC}$ = 7.9 Hz), 138.8 (s), 139.3

(s); minor $\delta$ = 29.9 (s), 52.4 (d, $J_{PC}$ = 19.1), 56.2 (d, $J_{PC}$ = 127.0 Hz), 59.2 (d, $J_{PC}$ = 97.2 Hz), 64.3 (d, $J_{PC}$ = 1.9 Hz), 76.0 (d, $J_{PC}$ = 8.4 Hz), 125.9−128.9 (s), 135.1 (d, $J_{PC}$ = 2.3 Hz), 137.1 (d, $J_{PC}$ = 6.5 Hz), 137.5 (d, $J_{PC}$ = 4.2 Hz), 139.0 (s), 139.4 (s); IR (KBr) $\nu$ 3430m, 3260, 3020, 3060, 2860, 2890, 2960, 1450, 1490, 1600, 1360, 1390, 1180, 1230, 1110, 1070, 1000, 1010, 1040, 700; HRMS (FAB+) calcd for $C_{32}H_{35}N_2O_2P$ 510.2514, found 510.2509; MS (FAB+) 511 $[M + H]^+$, 348, 284, 162, 180, 106, 91, 57.

**(2*R**,3*R**,5*R**,6*S**)-(±)-1-(2-Furyl)-*N*-methyl-1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)-1-phenylmethanamine (5c):** white solid (420 mg, two diastereoisomers); yield 46%, de = 36%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 45.0; minor $\delta$ = 42.5; $^1H$ NMR (250.13 MHz, $CDCl_3$) major $\delta$ = 2.02 (bs, 1H), 3.11 (m, 1H), 3.17 (d, 1H, $J$ = 10.4 Hz), 3.54 (d, 1H, $J$ = 11.8 Hz), 3.86 (d, 1H, $J_{HP}$ = 15.5 Hz), 4.77 (dd, 1H, $J$ = 6.8 Hz, $J$ = 6.8 Hz), 5.00 (dd, 1H, $J_{HP}$ = 15.8 Hz, $J$ = 10.6 Hz), 6.03 (dd, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 6.0 Hz), 6.40 (m, 2H), 6.90−7.75 (m, 21H); minor $\delta$ = 1.75 (bs, 1H), 2.31 (m, 1H), 3.15 (d, 1H, $J$ = 12.5 Hz), 3.51 (d, 1H, $J$ = 12.6 Hz), 4.40 (d, 1H, $J_{HP}$ = 15.0 Hz), 4.79 (dd, 1H, $J$ = 3.2 Hz, $J$ = 3.2 Hz), 5.07 (d, 1H, $J_{HP}$ = 11.2 Hz), 5.90 (dd, 1H, $J_{HP}$ = 6.1 Hz, $J$ = 6.1 Hz), 6.33 (m, 2H), 6.89−7.74 (m, 21H); $^{13}C$ NMR (62.90 MHz, $CDCl_3$) major $\delta$ = 52.8 (d, $J_{PC}$ = 15.3 Hz), 54.3 (d, $J_{PC}$ = 107.5 Hz), 60.6 (d, $J_{PC}$ = 79.2 Hz), 64.8 (d, $J_{PC}$ = 2.4 Hz), 77.4 (d, $J_{PC}$ = 6.7 Hz), 110.6 (d, $J_{PC}$ = 6.7 Hz), 111.2 (d, $J_{PC}$ = 1.9 Hz), 126.6−129.2 (s), 134.9 (s), 137.1 (d), 138.8 (s), 139.2 (d, $J_{PC}$ = 1.0 Hz), 143.6 (d, $J_{PC}$ = 1.6 Hz), 148.6 (d, $J_{PC}$ = 3.9 Hz); minor $\delta$ = 51.97 (d, $J_{PC}$ = 15.1 Hz), 51.99 (d, $J_{PC}$ = 110.4 Hz), 61.6 (d, $J_{PC}$ = 87.8 Hz), 63.7 (d, $J_{PC}$ = 1.4 Hz), 77.4 (d, $J_{PC}$ = 7.4 Hz), 109.8 (d, $J_{PC}$ = 6.3 Hz), 111.0 (d, $J_{PC}$ = 1.9 Hz), 126.9−129.3 (s), 135.6 (d, $J_{PC}$ = 3.8 Hz), 136.6 (d, $J_{PC}$ = 7.3 Hz), 139.2 (d, $J_{PC}$ = 9.1 Hz), 143.0 (d, $J_{PC}$ = 2.9 Hz), 149.8 (d, $J_{PC}$ = 4.8 Hz); IR (KBr) $\nu$ = 3420, 3280, 3000, 3100, 2800, 2890, 1450, 1495, 1600, 1390, 1180, 1230, 1250, 1110, 1070, 1000, 1020, 1030, 700; HRMS (FAB+) calcd for $C_{33}H_{31}N_2O_3P$: 534.2151, found 534.2168; MS (FAB+) $m/z$ = 535 $[M + H]^+$, 348, 284, 186, 180, 154, 136, 106, 91.

**(2*S**,3*R**,5*R**,6*S**)-(±)-*N*-Benzyl-2-methyl-1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl)propan-1-amine (5d):** white solid (454 mg, 2 diastereoisomers); yield 52%, de = 50%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 54.5; minor $\delta$ = 52.3; $^1H$ NMR (250.13 MHz, $CDCl_3$) major $\delta$ = 1.21 (d, 3H, $J$ = 6.8 Hz), 1.24 (d, 3H, $J$ = 6.8 Hz), 1.72 (s, 1H), 2.41 (m, 1H), 2.78 (dd, 1H, $J_{HP}$ = 12.6 Hz, $J$ = 2.7 Hz), 3.15 (m, 1H), 3.75 (d, 1H, $J$ = 11.5 Hz), 3.07 (d, 1H, $J$ = 11.2 Hz), 4.69 (dd, 1H, $J$ = 5.7 Hz, $J$ = 8.9 Hz), 4.84 (dd, 1H, $J_{HP}$ = 16.0 Hz, $J$ = 11.2 Hz), 6.02 (dd, 1H, $J_{HP}$ = 8.2 Hz, $J$ = 6.2 Hz), 6.88−7.71 (m, 20H); minor $\delta$ = 1.06 (dd, 3H, $J$ = 7.0 Hz, $J_{HP}$ = 1.3 Hz), 1.07 (d, 3H, $J$ = 6.8 Hz), 1.72 (s, 1H), 2.40 (m, 1H), 2.30 (m, 1H), 3.07 (m, 1H), 3.15 (m, 1H), 3.75 (m, 1H, $J$ = 11.2 Hz), 4.86 (m, 1H), 5.01 (d, 1H, $J_{HP}$ = 12.6 Hz), 5.99 (dd, 1H, $J_{HP}$ = 6.0 Hz, $J$ = 6.0 Hz), 6.88−7.71 (m, 20H); $^{13}C$ NMR (62.90 MHz, $CDCl_3$) major $\delta$ = 19.4 (d, $J_{PC}$ = 1.4 Hz), 21.7 (d, $J_{PC}$ = 10.6 Hz), 29.0 (d, $J_{PC}$ = 1.0 Hz), 53.9 (d, $J_{PC}$ = 14.9 Hz), 60.1 (d, $J_{PC}$ = 76.3 Hz), 60.4 (d, $J_{PC}$ = 101.7 Hz), 64.9 (d, $J_{PC}$ = 1.0 Hz), 75.9 (d, $J_{PC}$ = 6.2 Hz), 126.2−129.4 (s), 135.7 (d, $J_{PC}$ = 1.0 Hz), 137.6 (d, $J_{PC}$ = 5.3 Hz), 139.2 (s), 139.8 (s); minor $\delta$ = 18.6 (d, $J_{PC}$ = 1.9 Hz), 21.8 (d, $J_{PC}$ = 12.0 Hz), 30.4 (d, $J_{PC}$ = 2.4 Hz), 53.5 (d, $J_{PC}$ = 7.2 Hz), 58.5 (d, $J_{PC}$ = 90.7 Hz), 62.2 (d, $J_{PC}$ = 84.0 Hz), 63.5 (s), 78.1 (d, $J_{PC}$ = 7.2 Hz), 126.2−129.4 (s), 136.4 (d, $J_{PC}$ = 3.8 Hz), 137.2 (d, $J_{PC}$ = 6.7 Hz), 139.6 (s), 140.9 (d, $J_{PC}$ = 1.9 Hz); IR (KBr) $\nu$ = 3400, 3280, 3300, 3030, 3080, 2880, 2960, 1450, 1500, 1600, 1580, 1370, 1390, 1180, 1230, 1250, 1110, 1080, 1000, 1010, 1030, 700; HRMS (FAB+) calcd for $C_{32}H_{35}N_2O_2P$ 510.2514, found 510.2523; MS (FAB+) 511 $[M + H]^+$, 350, 348, 284, 162, 180, 106, 91.

**(2*S**,3*R**,5*R**,6*S**)-(±)-Ethyl (1-(3,5,6-triphenyl-2-oxo-1,4,2-oxazaphosphinan-2-yl))benzyl)carbamate (5e):** white solid (703 mg, two diastereoisomers); yield 76%, de = 6%; $^{31}P$ NMR (81.02 MHz, $CDCl_3$) major $\delta$ = 45.0; minor $\delta$ = 42.5; $^1H$ NMR (400.13 MHz, $CDCl_3$) major $\delta$ = 1.25 (t, 3H, $J$ = 7.1 Hz), 2.81 (d, 1H, $J$ = 16.6 Hz), 3.09 (d, 1H, $J$ = 16.6 Hz), 3.62 (d, 1H, $J_{HP}$ = 14.1 Hz), 4.17 (q, 2H, $J$ = 7.1 Hz), 4.81 (d, 1H, $J$ = 5.7 Hz), 5.01 (d, 1H, $J_{HP}$ = 15.2 Hz),6.02 (dd, 1H, $J_{HP}$ = 6.1 Hz, $J$ = 6.0 Hz), 6.9−7.4 (m, 18 H), 7.71 (d, 2H, $J$ = 7.2 Hz); minor $\delta$ = 1.20 (t, 3H, $J$ = 7.1 Hz), 2.76 (d, 1H, $J$ = 16.9 Hz), 2.99 (d, 1H, $J$ = 16.9 Hz), 4.03 (q, 2H, $J$ = 7.1 Hz), 4.22 (d, 1H, $J_{HP}$ = 11.4 Hz), 4.78 (bs, 1H), 5.08 (d, 1H, $J_{HP}$ = 13.4 Hz), 5.84 (t, 1H, $J_{HP}$ = 6.0 Hz, $J$ = 6.0 Hz), 6.8−7.0 (m, 4H), 7.0−7.2 (m, 6H), 7.28 (bs, 5H), 7.40 (td, 1H, $J_{HP}$ = 7.3 Hz, $J$ = 2.0 Hz), 7.47 (t, 2H, $J$ = 7.3 Hz), 7.78 (d, 2H, $J$ = 7.3 Hz); $^{13}C$ NMR (100.62 MHz, $CDCl_3$) major $\delta$ = 14.2 (s), 48.8 (d, $J_{PC}$ = 17.6 Hz), 59.4 (d, $J_{PC}$ = 103.9 Hz), 60.7 (d, $J_{PC}$ = 79.8 Hz), 61.0 (s), 64.5 (s), 78.2 (d, $J_{PC}$ = 6.6 Hz), 126.3−128.8 (s), 133.3 (d, $J_{PC}$ = 2.9 Hz.), 134.5 (s.), 136.7 (d, $J_{PC}$ = 5.9 Hz.), 138.4 (s.), 171.1 (s); minor $\delta$ = 14.1 (s), 48.6 (d, $J_{PC}$ = 17.6 Hz), 58.5 (d, $J_{PC}$ = 104.5 Hz), 60.5 (s), 61.8 (d, $J_{PC}$ = 86.4 Hz), 63.2 (s), 78.2 (d, $J_{PC}$ = 6.6 Hz), 126.6−129.1 (s), 134.5 (d, $J_{PC}$ = 4.4 Hz), 135.3 (s), 136.2 (d, $J_{PC}$ = 6.6 Hz.), 138.6 (s), 171.0 (s); IR (KBr) $\nu$ = 3400, 3330, 3130, 3090, 2870, 3000, 1770, 1450, 1550, 1200, 1220, 1260, 700; HRMS (FAB+) calcd for $C_{32}H_{34}N_2O_4P$ 541.2256, found 541.2239; MS (FAB+) 541 $[M + H]^+$, 348, 284, 192.

**Addition to *N*-Benzylidenebenzylamine Catalyzed by $ZnCl_2$.** In a 10 mL flask containing 301 mg of **3a** (0.86 mmol, 1 equiv) under $N_2$ was added dry dichloromethane (4 mL) followed by 161 $\mu$L of imine (0.86 mmol, 1 equiv) at ambient temperature. A 118 mg portion of anhydrous $ZnCl_2$ (0.86 mmol, 1 equiv) was added under stirring. After 48 h of stirring, addition of saturated aqueous NaCl solution (pH ∼7) and extraction with chloroform were done. Organic layers were dried on sodium sulfate and evaporated. The crude oil (de = 90%) was crystallized in ethyl acetate to afford one diastereoisomer as colorless crystals (197 mg, yield 42% after crystallization).

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**Supporting Information Available:** Detailed description of experimental procedures, NMR spectra, MS spectra not reported previously, designated by their entries in Tables 2 and 3, and for compounds **3a** and **3b**. X-ray crystal structure of **4e** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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