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Asymmetric Catalytic *N*-Phosphonyl Imine Chemistry: The Use of Primary Free Amino Acids and Et_2AlCN for Asymmetric Catalytic Strecker Reaction

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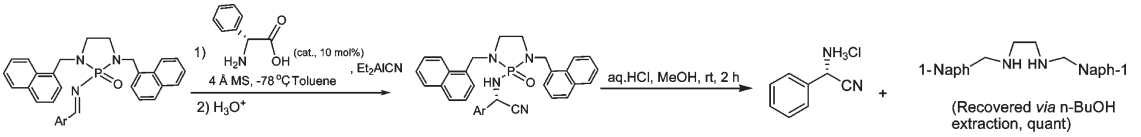

The new asymmetric catalytic Strecker reaction of achiral *N*-phosphonyl imines has been established. Excellent enantioselectivity (95.2−99.7% ee) and yields (89−97%) have been achieved by using primary free natural amino acids as catalysts and Et_2AlCN as nucleophile. This work also presents the novel use of nonvolatile and inexpensive Et_2AlCN in asymmetric catalysis. The *N*-phosphonyl protecting group enabled simple product purification to be achieved simply by washing the crude products with hexane, which is defined as the GAP chemistry (GAP: Group-Assistant-Purification).[15] It can also be readily cleaved and recycled under mild condition to give a quantitative recovery of *N*,*N*′-bis(naphthalen-1-ylmethyl)ethane-1,2-diamine. A new mechanism was proposed for this reaction and was supported by experimental observations.

Introduction

Imine chemistry has been one of the most important and active topics in asymmetric catalysis and synthesis due to its importance in drug discovery and development, which heavily depend on the amine functionality.[1−3] *N*-protected imines serve as both electrophiles and dienophiles for many asymmetric reactions;[2,3] they are represented by Ar_2CH-/Bn-,[4] alkoxycarbonyl,[5] Ar_2PO-,[6] aryl-,[7] and $ArSO_2$[8] imines in which the protecting groups are often crucial for controlling regio-, enantio-, and chemoselectivity for asymmetric reactions.[9] The search for novel imines of general use for both racemic and asymmetric reactions, particularly for asymmetric catalysis, has been challenging.[1−3] In the past several years, we have established chiral *N*-phosphonyl imine chemistry and successfully utilized it for a variety of asymmetric reactions to produce chiral amino products in good

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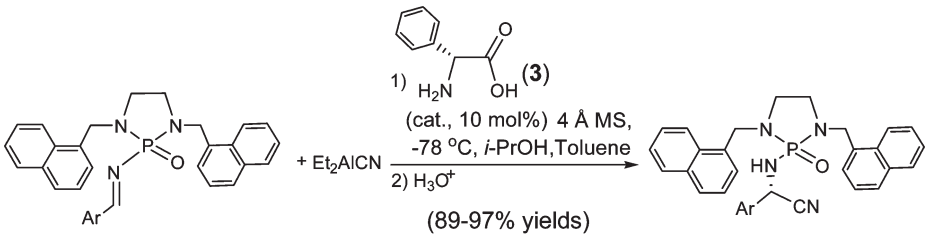
SCHEME 1



1a-k **2** **4a-k**

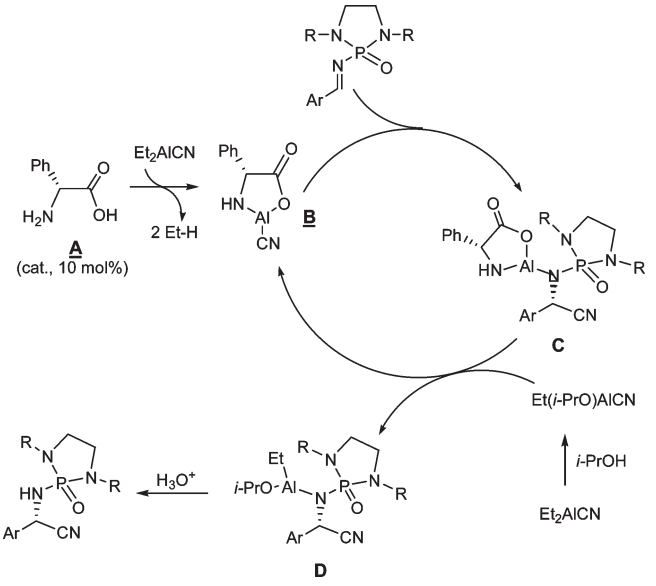
yields and excellent diastereoselectivities.[10] During our continuous study of this project, we envisioned that if achiral *N*-phosphonyl imines are designed and synthesized, they would serve as a new family of C=N electrophiles and dienophiles for general use in advanced synthesis and asymmetric catalysis.

Results and Discussion

N-Phosphonyl imines and *N*-phosphoramides have stronger Lewis basicity as compared with their counterparts.[11] During the reaction process, the resulting *N*-phosphoramide species can strongly bind to catalytic centers and thus retard catalytic cycles, which consequently makes it extremely difficult to achieve asymmetric catalysis with *N*-phosphonyl imines as electrophiles. In this report, we would like to describe the new asymmetric catalytic Strecker reaction of *N*-phosphonyl imines under a concise catalytic system (Scheme 1); in fact, this reaction has recently become an active topic due to its practical use for the synthesis of unnatural α-amino acids and their derivatives and its versatility as a superior model reaction for organocatalysis.[2−4,6] The present *N*-phosphonyl imine-based Strecker reaction was conducted by using free primary amino acids as catalysts and Et_2AlCN[12] as nucleophile. Excellent chemical yields (89−97%) and enantioselectivities (95.2−99.7% ee) have been achieved by performing the reaction at −78 °C in dry toluene in the presence of 4 Å mol sieves (Scheme 1).

Our new work described here shows several attractive characteristics as compared with previous known systems: (1) the first asymmetric catalytic reaction of achiral *N*-phosphonyl imines; (2) the first use of nonvolatile and inexpensive Et_2AlCN as the cyanide source for catalytic Strecker reaction; (3) *N*-phosphonyl group can be readily cleaved under mild conditions without racemization; (4) the new *N*-phosphonyl protection group enabled the pure Strecker products to be obtained simply by washing the crude products with hexane without further purification; (5) the cleavaged *N*,*N*-dialkyl diamine auxiliary can be recovered quantitatively for reuse; (6) free primary natural amino acid catalysts are common commercial chemicals; and (7) the modifiable flexibility of C_2-symmetric structure by changing its ring sizes and *N*,*N*-protection groups can result in various C=N electrophiles with changed reactivity for different catalytic reactions.

SCHEME 2



The reaction is believed to proceed through the mechanism as shown in Scheme 2. The first step is the reaction of amino acid **A** with Et_2AlCN to form the catalytic species **B**. The evolution of ethane gas and the solubility change of amino acid (which is insoluble in toluene but was dissolved after species **B** was formed) are evidence of this step occurring. The Lewis acidic center can activate the oxygen of the *N*-phosphonyl group of the substrate before species **B** delivers cyanide onto the C=N bond from its *Si*-face to afford intermediate **C**. During the reaction process, Et_2AlCN reacts with additive *i*-PrOH to give species Et(*i*-PrO)AlCN, and its activation of imine nitrogen is also anticipated prior to C=N addition. At the third step, the catalyst **B** is regenerated via the homotransmetalation between species **C** and Et(*i*-PrO)-AlCN, which is derived from the reaction of Et_2AlCN and *i*-PrOH; simultaneously, the actual catalytic complex **D** was generated, which was followed by deprotonation and quenching to afford the final product.

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i-PrOH has been proven to be a crucial additive for this reaction, which is similar to other asymmetric Strecker processes.[6a,12d] A tiny amount of product was formed without the addition of *i*-PrOH in the reaction mixture. Usually, in aromatic solvents, Et_2AlCN exists as tetramers or pentamers[6a] that show lower reactivity. However, its coordination with phosphonyl imine followed by conversion to intermediate **B** and Et(*i*-PrO)AlCN, which was evidenced by the release of ethane bubbles during the reaction process, led to the present success.

Starting materials, achiral *N*-phosphonyl imines (**1a**−**k**), were readily prepared by following the procedure which is similar to that developed by our group for asymmetric chiral *N*-phosphonyl imine chemistry.[10] The four-step preparation of *N*-phosphoramides showed quantitative yields for all steps. Products were obtained as white solids without the need of special purification. The final step of imine formation showed higher yields (76−87%) than the formation of *N*-phosphonyl imine counterparts. It is somewhat surprising that the design and synthesis of achiral *N*-phosphonyl imines have not been well documented in the literature so far.

Our initial effort on this reaction was made with the use *N*,*N*-dibenzyl *N*-phosphonyl imine as the substrate and free primary amino acid,[13] L-valine, as the catalyst in dry toluene in the presence of 4 Å MS. The reaction was conducted by using Et_2AlCN (1.5 equiv, 1.0 M in toluene) together with *i*-PrOH (1.0 equiv) as an additive at −78 °C for 5 h, followed by quenching with dilute aq HCl to produce product in 75% yield and poor enantioselectivity (22.6% ee). Next, we attempted to improve the reaction by replacing benzyl with isopropyl in *N*-phosphonyl imine substrates, which has been proven to be successful for several chiral *N*-phosphonyl imine-based reactions. However, the resulting *N*-diisopropyl phosphonyl imine was found to be insoluble in toluene at −78 °C and even at rt. We then utilized *N*,*N*-naphthalen-1-ylmethyl to replace benzyl, i.e., to use *N*,*N*-naphthalen-1-ylmethyl *N*-phosphonyl imine (**1a**) as the electrophile. We were pleased to find that not only the solubility problem was solved, but also enantioselectivity and chemical yield were substantially increased to 70% ee and 98%, respectively.

Several catalysts were then screened under the above conditions. As revealed in Scheme 3, *N*-tosyl L-valine resulted in a much lower enantioselectivity of 38% ee, albeit the yield remained high. This was somewhat surprising because nearly all successful asymmetric catalytic reactions utilize amino acids that are based on the use of *N*-protected ones.[14] *N*-Tosyl phenylalanine and *N*-tosyl phenylglycine also showed poor enantioselectivities of 28% ee and 36% ee, respectively. We then turned our attention back to free amino acids and found that free L-phenylalanine afforded 63% ee and 65% yield. Amazingly, the use of free L-phenylglycine (10 mol %) as the catalyst resulted in 99% ee and 95% yield under this new catalytic system.

It should be noted that well-activated 4 Å MS are also very important for this reaction. Much lower yields were observed in the absence of 4 Å MS. Other solvents, such as DCM, THF, and $CHCl_3$, proved to be unsuitable for this reaction as they afforded poor yields and percent ee values. During the preparation of catalytic species, it is important to allow chiral amino acids to react with Et_2AlCN for at least 15 min at rt before the reaction mixture is cooled to −78 °C. Keeping the reaction at −78 °C was necessary for achieving high enantioselectivity, albeit yield was not affected by temperature. TMSCN was also employed as the nucleophile, but poor yields (< 10%) were obtained.

Having identified the optimal catalyst and catalytic condition, we turned our attention to the substrate scope. As shown in Table 1, the reaction proceeded very well for all eleven substrates that were examined with excellent enantioselectivities (95.2−99.7% ee) and chemical yields (89−97%) (Scheme 4). Electron-rich substrates (entries 5 and 6) showed nearly the same reaction rates as other substrates and led to similar results. Strong electron-deficient substrates (entries 2 and 7) that sometimes showed less efficiency in chiral *N*-phosphonyl imine-based asymmetric reactions[10] resulted in excellent yields (96% and 94%, respectively) and enantioselectivity (94% and 96.1% ee, respectively) under the present system. Interestingly, the present *N*-phosphonyl protection group enabled the pure products to be obtained simply by washing with hexane

SCHEME 3. Results of Screening Catalysts

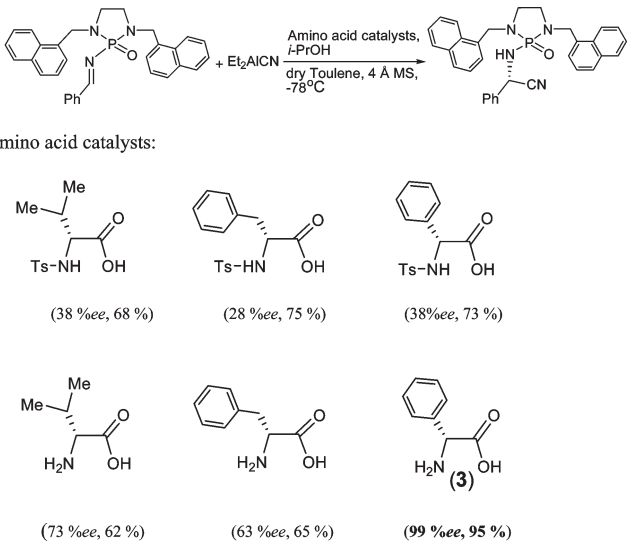

TABLE 1. Results of the Synthesis of *N*-Phosphonyl-Substituted Chiral α-Aminonitriles 4a−k[a]

entry	substrate	R_1	product	yield (%)[b]	ee[c]
1	**1a**	H	**4a**	95	99.7
2	**1b**	*p*-fluoro	**4b**	96	94
3	**1c**	*p*-bromo	**4c**	97	96
4	**1d**	*p*-chloro	**4d**	95	95.2
5	**1e**	*p*-methyl	**4e**	94	98.8
6	**1f**	*p*-methoxy	**4f**	93	97.6
7	**1g**	o-fluoro	**4g**	94	96.1
8	**1h**	*o*-bromo	**4h**	92	97
9	**1i**	*o*-chloro	**4i**	90	95.2
10	**1j**	*o*-methyl	**4j**	92	98.9
11	**1k**	*o*-furyl	**4k**	89	99

[a]All reactions were carried out at −78 °C in 0.06 M solution of imine in toluene. [b]Combined yields of both isomers. [c]Enantiomeric ratio has been determined by using chiral HPLC OD-H column (3:7 IPA:hexane), flow rate = 0.60 mL/min.

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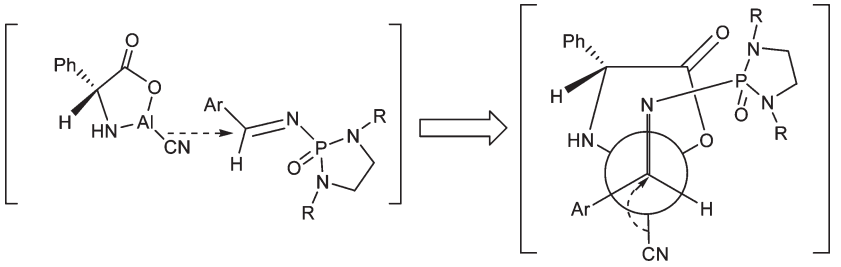
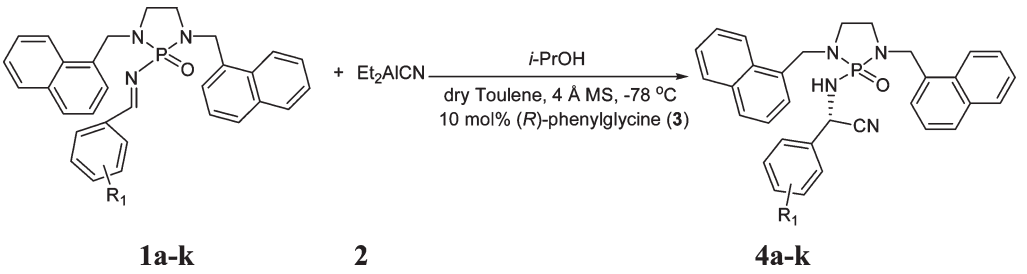
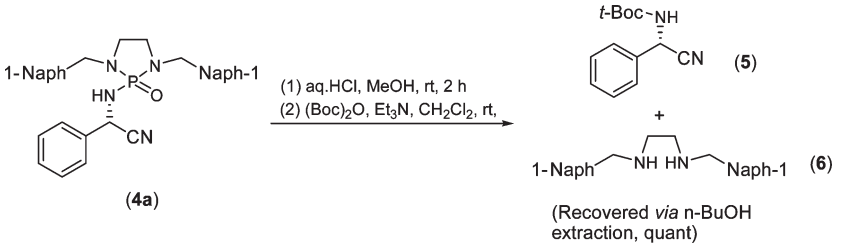


FIGURE 1. Working model of asymmetric induction in which the nucleophilic species of $^{-}$CN attacks *N*-phosphonyl imine from its *Si* face.

SCHEME 4



SCHEME 5



without further purification; we tentatively define this phenomenon as the GAP Chemistry (GAP: Goup-Assistant-Purification).[15] It is noteworthy that the resulting halogenated Strecker adducts (entries 3, 4, 8, and 9) can be readily converted to a variety of useful synthetic building blocks via metal-catalyzed coupling reactions.[16] 2-Furyl substrate led to complete enantioselectivity (99% ee) and 89% yield, which is important because the furyl functionality can be subjected to other transformations, such as Diels–Alder and oxidative ring-opening.[3] Our preliminary results also confirmed that this asymmetric catalytic system showed promising results for aliphatic *N*-dialkoxyphosphoryl imines.[17] More substrates will be under investigation with this system.

The absolute configuration for this asymmetric induction was determined by converting product (**4a**) to an authentic sample.[18] In this conversion, **4a** was subjected to deprotection with 2.0 M aq HCl at rt in methanol followed by in situ *t*-Boc protection by treating with $(t\text{-Boc})_2O$ in the presence of triethylamine (Scheme 5) to yield product **5**. Optical rotation of this product was confirmed to be consistent with that of the known sample with *S* configuration. During this transformation, the cleaved N^1,N^2-bis(naphthalen-1-ylmethyl)-ethane-1,2-diamine was subjected to a one-time extraction with *n*-butanol from the acidic mixture, prior to *t*-Boc protection, to give a quantitative recovery yield.

(15) So far, the GAP chemistry has been realized by eight asymmetric reactions that were developed in our labs. These reactions were associated with achiral/chiral *N*-phosphonyl groups and chiral *N*-phosphinyl group, and have resulted in similar simple purification and recovery of auxiliary quantitatively for re-use. It is anticipated more reactions will be converted into GAP chemistry when C_2-groups of auxiliaries are re-designed in the near future.

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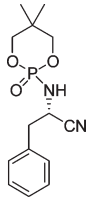
(17) An aliphatic *N*-phosphonyl-substituted imine was prepared in situ and subject to asymmetric strecker reaction with the optimized conditions.



Yellow oil, yield (0.090 g, 92%); $[\alpha]^{24}_{D}$ +12.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.16–4.08 (m, 4H), 3.96–3.84 (m, 3H), 3.35 (br s, 1H), 1.32 (t, J = 5.5 Hz, 1H), 1.25 (s, 3H), 1.07 (s, 3H), 0.93 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.7, 76.3 (2C), 68.0, 45.5, 38.5, 21.5, 21.49, 21.43, 20.8, 19.9; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.1. Ee 92% (retention time = 5.43 (major) and 5.86 (minor); flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system). HPLC conditions need to be further optimized (overlapping of peaks still exists).

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On the basis of the assignment of absolute configuration of the resulting products, a working model has been proposed and shown in Figure 1 to explain the possible source of asymmetric induction. In this model, *N*-phosphonyl imine approaches the catalytic nucleophilic source of $^{-}$CN from its less hindered side of hydrogen instead of the bulkier phenyl group of the chiral center of the catalyst. Although several conformational arrangements are possible, it is more likely for the C=N bond to be arranged on the *anti* position of the Al−CN bond as shown in Figure 1.

Conclusion

The new asymmetric catalytic Strecker reaction of achiral *N*-phosphonyl imines has been established. Excellent enantioselectivities and yields have been achieved by using primary free natural primary amino acids as catalysts and Et_2AlCN as the nucleophile. This work presents a new use of nonvolatile Et_2AlCN in asymmetric catalysis. *N*,*N*′-Protection groups on achiral *N*-phosphonyl imine were found to play an important role for the present success. This new protection group enabled simple product purification to be achieved simply by washing the crude products with hexane; it can also be readily cleaved and recycled under mild condition to give a quantitative recovery of *N*,*N*′-bis(naphthalen-1-ylmethyl)ethane-1,2-diamine. A new mechanism has been proposed that is consistent with experimental observations.

Experimental Section

Typical Procedure for the Synthesis of Achiral *N*-Phosphonyl Imine (1a−k). In a dry vial, under inert gas protection, *N*,*N*-naphthalen-1-ylmethyl phosphoramide (1.0 equiv) was taken and dissolved in dry dichloromethane. To the solution was added corresponding aldehyde (1.5 equiv) followed by the addition of triethylamine (3.0 equiv). The reaction was cooled to 0 °C and titanium(IV) chloride (1.0 M solution in DCM, 0.5 equiv) was added to the reaction (Scheme 1). The reaction was allowed to stir at room temperature for 36 h and after that the mixture was loaded directly to silica gel. The reaction mixture was purified through column chromatography (ethyl acetate:hexane:1% Et_3N). Pure product was obtained by eluting the reaction mixture with ethyl acetate:hexane:triethylamine (60:40:1 mL) as a white or pale yellow solid in all of the cases reported.

Compound 1a: white solid; yield 0.172 g (76%); mp 84−86 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (d, J = 33.5 Hz, 1H), 8.28 (d, J = 9.0 Hz, 2H), 7.86−7.82 (m, 4H), 7.78 (d, J = 8.0 Hz, 2H), 7.53−7.46 (m, 9H), 7.42−7.39 (m, 2H), 4.67−4.64 (m, 2H), 4.55−4.52 (m, 2H), 3.13 (d, J = 9.5 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5 (d, J = 7.0 Hz), 139.6, 135.8, 135.6 (2C), 133.7, 133.1, 132.7(2C), 132.6, 131.7 (2C), 129.9 (2C), 128.7 (2C), 128.4, 128.3, 126.7 (2C), 126.2, 125.7, 125.4, 125.0 (2C), 123.8, 120.5, 47.43, 47.40 (d, J = 7.3 Hz), 44.9, 42.3; ^{31}P NMR (202 MHz, $CDCl_3$) δ 24.2.

Compound 1b: white foamy solid; yield 0.214 g (82%); mp 68−70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, J = 32.9 Hz, 1H), 8.24 (dd, J = 8.9, 1.8 Hz, 2H), 7.83−7.76 (m, 6H), 7.52−7.46 (m, 6H), 7.41−7.38 (m, 2H), 7.15 (t, J = 8.5 Hz, 2H), 4.66−4.49 (m, 4H), 3.15−3.11 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3 (d, J = 6.45 Hz), 166.8, 164.8, 133.8 (2C), 132.65 (d, J = 6.94 Hz, 2C), 132.18 (d, J = 8.9 Hz, 2C), 131.7 (2C), 128.5 (2C), 128.4 (2C), 126.8 (2C), 126.3 (2C), 125.8 (2C), 125.1 (2C), 123.9 (2C), 116.1, 115.9, 47.5 (d, J = 4.9 Hz, 2C), 45.0 (d, J = 10.4 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.1.

Compound 1c: pale yellow solid; yield 0.355 g (82%); mp 60−62 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 33.0 Hz, 1H), 8.24 (d, J = 8 Hz, 2H), 7.83 (dd, J = 2.5, 7.5 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 11 Hz, 2H), 7.51−7.47 (m, 8H), 7.41−7.38 (m, 2H), 4.64 (dd, J = 7.5, 15.0 Hz, 2H), 4.52 (dd, J = 5.5, 15.0 Hz, 2H), 3.13 (d, J = 9.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3 (d, J = 6.9 Hz), 134.6, 134.4, 133.7 (2C), 132.5 (d, J = 6.9 Hz, 2C), 132.0 (2C), 131.7 (2C), 131.5, 131.1 (2C), 128.4 (d, J = 7.5 Hz, 2C), 127.9, 126.8 (2C), 126.3 (2C), 125.7 (2C), 125.1 (2C), 123.8 (2C), 47.4 (d, J = 4.5 Hz, 2C), 45.0 (d, J = 10.9 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.0.

Compound 1e: white solid; yield 0.208 g (87%); mp 64−66 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.33 (d, J = 33.3 Hz, 1H), 8.27 (d, J = 8.5 Hz, 2H), 8.02 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.5 Hz, 2H), 7.53−7.39 (m, 9H), 7.31 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 8.0 Hz, 1H), 4.66 (d, J = 7.0 Hz, 2H), 4.55 (d, J = 5.0 Hz, 2H), 3.13 (d, J = 10.0 Hz, 4H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (d, J = 12.5 Hz), 140.6 (2C), 133.7 (2C), 132.8 (d, J = 7.4 Hz), 132.6 (2C), 131.7, 131.2 (2C), 129.3 (2C), 128.4 (2C), 128.3 (2C), 126.5 (2C), 126.3 (2C), 126.1, 125.7 (2C), 125.1 (2C), 123.8 (2C), 47.5 (d, J = 4.7 Hz, 2C), 45.0 (d, J = 10.6 Hz, 2C), 19.4; ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.4.

Compound 1f: white solid; yield 0.198 g (87%); mp 64−66 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, J = 33.3 Hz, 1H), 8.31 (d, J = 8.4 Hz, 2H), 7.88−7.79 (m, 6H), 7.57−7.41 (m, 8H), 7.02 (d, J = 8.7 Hz, 2H), 4.71−4.53 (m, 4H), 3.92 (s, 3H), 3.13 (d, J = 9.6 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4 (d, J = 6.52 Hz), 164.1 (2C), 134.1 (2C), 133.16 (d, J = 7.4 Hz, 2C), 132.4 (2C), 132.1 (2C), 128.7 (2C), 128.6 (2C), 127.0 (2C), 126.6 (2C), 126.0 (2C), 125.4 (2C), 124.2 (2C), 114.4 (2C), 55.8, 47.8 (d, J = 4.7 Hz, 2C), 45.3 (d, J = 10.6 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.8.

Compound 1g: white solid; yield 0.214 g (81%); mp 64−66 °C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (d, J = 33.0 Hz, 1H), 8.32−8.25 (m, 2H), 8.12−8.07 (m, 1H), 7.88−7.56 (m, 5H), 7.59−7.38 (m, 10H), 4.72−4.49 (m, 4H), 3.13−2.92 (m, 4H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.3;. HRMS (ESI) m/z calcd for $C_{31}H_{28}FN_3OP$ 508.1954, found 508.1983.

Compound 1h: pale yellow solid; yield 0.362 g (79%); mp 54−56 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (d, J = 32.5 Hz, 1H), 8.27 (d, J = 8.5 Hz, 2H), 8.15−8.13 (m, 1H), 7.83 (d, J = 8.25 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.62−7.60 (m,1H), 7.54−7.44 (m, 6H), 7.42−7.36 (m, 4H), 4.71 (dd, J = 7.0, 15.0 Hz, 2H), 4.56 (dd, J = 5.0, 14.5 Hz, 2H), 3.12 (d, J = 10.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (d, J = 5.4 Hz), 134.23, 133.9, 133.8, 133.4, 132.6 (d, J = 7.0 Hz, 2C), 131.7 (2C), 129.6 (2C), 128.4 (d, 11.2 Hz, 2C), 127.6 (2C), 127.5 (2C), 126.6 (2C), 126.4 (2C), 125.8 (2C), 125.1 (2C), 123.8 (2C), 47.5 (d, J = 4.5 Hz, 2C), 44.9 (d, J = 10.7 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.0

Compound 1i: white foamy solid; yield 0.225 g (85%); mp 66−68 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.39 (d, J = 32.7 Hz, 1H), 8.43−8.14 (m, 2H), 7.88−7.75 (m, 5H), 7.58−7.29 (m, 11H), 4.74−4.52 (m, 4H), 3.14−2.85 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0 (d, J = 5.7 Hz), 135.1 (d, J = 8.9 Hz), 134.0 (2C), 132.8 (d, J = 6.8 Hz), 131.9 (2C), 128.8, 128.7 (2C), 128.6 (2C), 128.5 (2C), 126.9 (2C), 126.5 (2C), 126.5, 126.0 (2C), 125.4, 125.3 (2C), 124.6, 124.0 (2C), 123.9, 116.4, 47.6 (d, J = 4.8 Hz, 2C), 45.1 (d, J = 10.9 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.2; HRMS (ESI) m/z calcd for $C_{31}H_{28}ClN_3OP$ 524.1659, found 524.0652.

Compound 1j: pale yellow solid; yield 0.284 g (82%); mp 62−64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (d, J = 33.5 Hz, 1H), 8.29 (d, J = 8.0 Hz, 2H), 7.82−7.76 (m, 6H), 7.53−7.38 (m, 10H), 4.69 (dd, J = 7.0, 15.0 Hz, 2H), 4.54 (dd, J = 5.0, 14.5 Hz, 2H), 3.08 (d, J = 10.0 Hz, 4H), 2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8 (d, J = 5.4 Hz), 134.7 (2C), 133.6 (2C), 132.8 (d, J = 7.3 Hz, 2C), 131.6 (2C), 128.3 (2C), 128.2 (2C),

128.0 (2C), 126.4, (2C), 126.2 (2C), 125.8 (2C), 125.1 (2C), 123.8 (2C), 120.4, 111.1, 47.3 (d, J = 4.5 Hz, 2C), 44.8 (d, J = 10.7, 2C), 14.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 25.8.

Compound 1k: yellow color solid; yield 0.216 g (90%); mp 68−70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, J = 34.2 Hz, 1H), 8.29 (d, J = 7.8 Hz, 2H), 7.86−7.78 (m, 4H), 7.71 (s, 1H), 7.57−7.41 (m, 8H), 7.07(d, J = 3.6 Hz, 1H), 6.62−6.61 (m, 1H), 4.71−4.64 (m, 2H), 4.56−4.49 (m, 2H), 3.22−3.09 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2 (d, J = 5.9 Hz), 152.1, 151.8, 147.4, 133.7 (2C), 132.6 (d, J = 7.3 Hz), 131.7 (2C), 128.4 (d, J = 13.7 Hz, 2C), 126.7 (2C), 126.3 (2C), 125.7 (2C), 125.1 (2C), 123.8 (2C), 121.2 (2C), 112.7 (2C), 47.2 (d, J = 5.0 Hz, 2C), 44.8 (d, J = 10.3 Hz, 2C); ^{31}P NMR (202 MHz; $CDCl_3$) δ 26.4; HRMS (ESI) m/z calcd for $C_{29}H_{27}N_3O_2P$ 480.1841, found 480.1839.

Typical Procedure for the Synthesis of *N*,*N*-Naphthalen-1-ylmethyl *N*-Phosphonyl Imine-Substituted α-Aminonitriles. In a dry vial, under inert gas protection, 4 Å MS and the chiral amino acid (**3**) were added followed by loading dry toluene. A turbid solution was obtained in which diethylaluminium cyanide (**2**, 1.0 M solution in toluene, 1.50 mmol) was added followed by the addition of *i*-PrOH (1.0 mmol). The reaction was stirred for 15 min at room temperature, and then cooled to −78 °C. The resulting mixture was stirred at −78 °C for 30 min followed by the addition of achiral *N*-phosphonyl imine, which was dissolved in 3 mL of toluene. The reaction mixture was stirred for 5 h at this temperature before it was quenched by aq 0.05 M HCl, followed by addition of ethyl acetate (10 mL) and water (10 mL). The reaction mixture was filter off through Celite. The organic layer was separated (3 × 10 mL of ethyl acetate) and dried over anhydrous sodium sulfate. Sodium sulfate was filtered off, and organic phase was evaporated to obtain crude product, which upon washing with hexane afforded the pure product as a white solid without further purification.

Compound 4a: yield 0.246 g (92%); mp 112−114 °C; $[\alpha]^{24}_D$ +2.52 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 9.5 Hz, 2H), 8.15 (d, J = 7.5 Hz, 2H), 7.86 (t, J = 7.0 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.51−7.45 (m, 5H), 7.44−7.39 (m, 4H), 7.35−7.34 (m, 2H), 5.42 (t, J = 9.0 Hz, 1H), 4.65−4.55 (m, 4H), 3.44 (t, J = 9.5 Hz, 1H), 3.05−3.01 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.36, 135.31, 133.8, 133.7, 132.37, 132.31, 131.6 (d, J = 8.0 Hz, 2C), 128.6 (d, J = 7.3 Hz, 2C), 128.5, 128.4, 128.3, 126.7, 126.6, 126.5, 126.4, 126.3, 125.9, 125.8, 125.24, 125.20, 123.4, 123.3 (2C), 119.98, 119.92, 47.5, 46.8 (d, J = 7.3 Hz), 44.6 (d, J = 7.8 Hz), 44.0, 43.9; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.9; HRMS (ESI) m/z calcd for $C_{32}H_{30}N_4OP$ 517.2152, found 517.2156; 99.7% ee, retention time = 6.77 (major), flow rate = 0.60 mL/min, OD-H chiral column (hexane:*i*-PrOH (v/v) = 3:7).

Compound 4b: off-white solid; yield 0.172 g (96%); mp 126−128 °C; $[\alpha]^{24}_D$ +7.0 (c 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, J = 9.2, 27.2 Hz, 2H), 7.82 (dd, J = 8.0, 36.0 Hz, 4H), 7.51−7.44 (m, 6H), 7.40 (q, J = 8.2 Hz, 2H), 7.33 (q, J = 5.1 Hz, 2H), 6.95 (t, J = 8.5 Hz, 2H), 5.36 (t, J = 9.0 Hz, 1H), 4.67−4.52 (m, 4H), 3.82 (q, J = 9.8 Hz, 1H, NH), 3.12−3.02 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 161.9, 133.8 (d, J = 8.9 Hz, 2C), 132.3 (d, J = 2.5 Hz), 132.2, 131.5 (d, J = 9.9 Hz), 131.2, 128.7 (d, J = 6.9 Hz, 2C), 128.6 (2C), 128.5, 128.4, 126.7, 126.4 (d, J = 12.4 Hz, 2C), 126.3, 125.9 (d, J = 9.9 Hz, 2C), 125.2 (d, J = 3.9 Hz, 2C), 123.3 (d, J = 12.9 Hz, 2C), 119.7 (d, J = 3.5 Hz), 116.14 (d, J = 21.8 Hz, 2C), 46.84 (d, J = 3.9 Hz), 46.82, 46.1 (d, J = 4.9 Hz), 44.8 (d, J = 12.4 Hz), 44.0 (d, J = 13.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.1; HRMS (ESI) m/z calcd for $C_{32}H_{28}FN_4OPNa$ 557.1877, found 557.1884; 94% ee, retention time = 6.49 (minor) and 7.17 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4c: white solid; yield 0.13 5 g (97%); mp 138−140 °C; $[\alpha]^{25}_D$ +8.0 (c 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, J = 7.5, 16.5 Hz, 2H), 7.86 (d, J = 7.5 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.51−7.45 (m, 6H), 7.43−7.36 (m, 4H), 7.20 (d, J = 8.0 Hz, 2H), 5.32 (t, J = 9.0 Hz, 1H), 4.66−4.49 (m, 4H), 3.90 (q, J = 6.5 Hz, 1H), 3.11−3.05 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.4 (d, J = 5.9 Hz), 133.8 (d, J = 7.9 Hz), 132.3 (2C), 132.2, 131.6 (d, J = 8.4 Hz), 128.7 (d, J = 3.5 Hz, 2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 126.6 (2C), 126.4 (d, J = 7.9 Hz, 2C), 126.2 (2C), 125.9 (d, J = 7.5 Hz, 2C), 125.2 (d, J = 2.9 Hz, 2C), 123.4, 123.3 (d, J = 12.8 Hz), 119.5 (d, J = 3.5 Hz), 46.9, 46.8 (d, J = 4.4 Hz), 46.1 (d, J = 4.9 Hz), 44.8 (d, J = 12.2 Hz), 44.1 (d, J = 13.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 23.0; HRMS (ESI) m/z calcd for $C_{32}H_{29}BrN_4OP$ 595.1257, found 595.1262; 96% ee, retention time = 6.41 (minor) and 6.84 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4d: pale yellow color solid; yield 0.128 g (95%); mp 134−136 °C, $[\alpha]^{24}_D$ +8.60 (c 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, J = 8.3, 23.4 Hz, 2H), 7.86 (d, J = 7.8 Hz, 2H), 7.78 (d, J = 8.1 Hz, 2H), 7.51−7.45 (m, 6H), 7.40 (q, J = 7.8 Hz, 2H), 7.28−7.22 (m, 4H), 5.35 (t, J = 9.0 Hz, 1H), 4.66−4.51 (m, 4H), 3.77 (br s, 1H, NH), 3.12−3.03 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 133.85, 133.81, 133.7, 132.27, 132.25, 132.21, 131.5 (d, J = 9.9 Hz), 129.3 (2C), 128.7 (d, J = 4.9 Hz, 2C), 128.5 (d, J = 17.9 Hz, 2C), 127.9 (2C), 126.7, 126.4 (d, J = 9.9 Hz, 2C), 126.3, 125.9 (d, J = 8.4 Hz, 2C), 125.3 (d, J = 2.9 Hz, 2C), 123.2 (d, J = 14.4 Hz, 2C), 119.5 (d, J = 3.5 Hz), 46.9, 46.8 (d, J = 4.5 Hz), 46.1 (d, J = 5.4 Hz), 44.8 (d, J = 11.9 Hz), 44.1 (d, J = 13.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.6; HRMS (ESI) m/z calcd for $C_{32}H_{29}ClN_4OP$ 551.1761, found 551.1768; 95.2% ee, retention time = 6.27 (minor) and 6.72 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4e: white solid; yield 0.110 g (94%); mp 176−178 °C; $[\alpha]^{24}_D$ +7.45 (c 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 7.0 Hz, 1H), 8.15 (d, J = 7.5 Hz, 1H), 7.87−7.85 (m, 2H), 7.79 (d, J = 5.0 Hz, 1H), 7.31 (d, J = 7.0 Hz, 7H), 7.12 (d, J = 7.0 Hz, 6H), 5.37 (t, J = 8.5 Hz, 1H), 4.66−4.48 (m, 4H), 3.67 (t, J = 10.0 Hz, 1H, NH), 3.07−2.99 (m, 4H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 133.7 (d, J = 8.4 Hz), 132.5 (d, J = 6.5 Hz), 132.4 (d, J = 5.5 Hz), 132.3 (d, J = 6.0 Hz), 131.6 (d, J = 8.4 Hz), 129.8 (2C), 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.3, 126.5 (2C), 126.4 (d, J = 6.4 Hz), 126.3, 125.8 (2C), 125.7 (2C), 125.2 (d, J = 4.0 Hz), 123.3 (d, J = 7.5 Hz), 120.0 (d, J = 4.0 Hz), 47.2, 46.6 (d, J = 4.5 Hz), 46.1 (d, J = 5.4 Hz), 44.6 (d, J = 11.9 Hz), 44.0 (d, J = 12.9 Hz), 21.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.5. HRMS (ESI) m/z calcd for $C_{33}H_{31}N_4O_2PNa$ 569.2077, found 569.2070; 98.8% ee, retention time = 6.82 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4f: white solid; yield 0.132 g (93%); mp 182−184 °C; $[\alpha]^{24}_D$ +1.45 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23−8.19 (m, 1H), 8.16−8.14 (m, 1H), 7.89−7.84 (m, 2H), 7.80−7.78 (m, 2H), 7.52−7.47 (m, 6H), 7.43−7.39 (m, 2H), 7.32−7.28 (m, 2H), 6.83−6.79 (m, 2H), 5.34 (t, J = 8.7 Hz, 1H), 4.66−4.52 (m, 4H), 3.75 (s, 3H), 3.50 (t, J = 9.6 Hz, 1H, NH), 3.09−3.00 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 133.8 (d, J = 8.4 Hz), 132.4 (d, J = 6.5 Hz), 131.6 (d, J = 8.4 Hz, 2C), 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.3 (2C), 128.0 (2C), 127.5 (d, J = 6.4 Hz), 126.6, 126.4, 126.3, 125.9 (2C), 125.8 (2C), 125.2 (d, J = 4.0 Hz), 123.4 (d, J = 7.5 Hz), 120.1 (d, J = 4.0 Hz), 114.5 (2C), 55.3, 46.9, 46.7 (d, J = 4.5 Hz), 46.1 (d, J = 5.4 Hz), 44.7 (d, J = 11.9 Hz), 44.0 (d, J = 12.9 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.5; HRMS (ESI) m/z calcd for $C_{33}H_{31}N_4O_2P$-Na 569.2077, found 569.2070; 97.6% ee, retention time = 6.06 (minor) and 6.88 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4g: off-white solid; yield 0.101 g (94%); mp 180−182 °C; $[\alpha]^{24}_D$ +3.30 (c 1.1, $CHCl_3$); ^{1}H NMR (500

MHz, $CDCl_3$) δ 8.21 (d, J = 8.2 Hz, 1H), 8.11 (d, J = 8.1 Hz, 1H), 7.86−7.83 (m, 2H), 7.79−7.76 (m, 2H), 7.54−7.29 (m, 10H), 7.13−7.05 (m, 2H), 5.64 (t, J = 9.8 Hz, 1H), 4.66−4.39 (m, 4H), 3.95 (t, J = 10.0 Hz, 1H, NH), 2.99 (d, J = 10.7 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 158.9, 133.72 (d, J = 4.9 Hz, 2C), 132.29 (d, J = 6.9 Hz), 132.23 (d, J = 8.4 Hz), 131.6 (d, J = 8.9 Hz), 131.3 (d, J = 8.4 Hz), 128.7 (d, J = 2.5 Hz), 128.6 (d, J = 3.5 Hz, 2C), 128.4 (d, J = 12.4 Hz, 2C), 126.6, 126.4 (2C), 126.3, 126.2 (2C), 125.8 (d, J = 6.9 Hz, 2C), 125.1 (d, J = 4.9 Hz, 2C), 125.0 (d, J = 3.5 Hz), 123.3 (d, J = 10.9 Hz, 2C), 116.2 (d, J = 20.3 Hz), 46.3 (d, J = 4.9 Hz), 46.1 (d, J = 4.9 Hz), 44.1 (dd, J = 20.3, 12.9 Hz, 2C), 42.6; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.0; HRMS (ESI) m/z calcd for $C_{32}H_{28}FN_4OPNa$ 557.1877, found 557.1886; 96.1% ee, retention time = 6.52 (minor) and 7.04 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4h: white solid; yield 0.135 g (94%); mp 128−130 °C; $[\alpha]^{25}_D$ +7.7 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 7.5 Hz, 2 H), 7.77 (d, J = 8.0 Hz, 2H), 7.60−7.57 (m, 2H), 7.54−7.37 (m, 8 H), 7.33−7.30 (m, 1H), 7.21−7.18 (m, 1H), 5.77 (t, J = 9.5 Hz, 1H), 4.64 (dd, J = 6.5, 14.5 Hz, 1H), 4.57 (t, J = 6 Hz, 2H), 4.36 (dd, J = 6.5, 15 Hz, 1H), 3.88 (t, J = 10 Hz, 1H), 3.03−2.94 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.0 (d, J = 5.0 Hz), 133.8 (d, J = 8.9 Hz, 2C), 132.4, 132.3 (d, J = 3.4 Hz), 132.2, 131.6 (d, J = 6.4 Hz), 130.9 (s, 2C), 129.3 (s, 2C), 128.6 (d, J = 1.4 Hz, 2C), 128.4 (t, J = 3.0 Hz, 2C), 126.5 (d, J = 4.9 Hz, 2C), 126.3 (s, 2C), 125.8 (d, J = 5.4 Hz, 2C), 125.2 (d, J = 9.9 Hz, 2C), 123.4 (d, J = 5.5 Hz, 2C), 122.6, 118.8 (d, J = 5.4 Hz), 47.8 (d, J = 2 Hz), 46.4 (t, J = 5.9 Hz, 2C), 44.2 (dd, J = 6.0, 12.9 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.1; HRMS (ESI) m/z calcd for $C_{32}H_{29}BrN_4OP$ 595.1257, found 595.1253; 97% ee, retention time = 6.49 (minor) and 6.95 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4i: white solid; yield 0.146 g (90%); mp 220−222 °C; $[\alpha]^{24}_D$ +4.50 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 7.8 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H), 7.60 (dd, J = 2.0, 7.2 Hz, 1H), 7.53−7.37 (m, 9H), 7.28−7.22 (m, 2H), 5.76 (t, J = 9.8 Hz, 1H), 4.63 (dd, J = 6.5, 14.8 Hz, 1H), 4.55 (d, J = 6.3 Hz, 2H), 4.36 (dd, J = 6.2, 14.8 Hz, 1H), 4.13 (t, J = 10.0 Hz, 1H, NH), 3.04−2.96 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.72 (d, J = 1.5 Hz), 133.44 (d, J = 4.9 Hz), 132.7, 132.3 (d, J = 6.9 Hz), 132.2 (d, J = 7.4 Hz), 131.6 (d, J = 6.9 Hz), 130.6 (d, J = 32.3 Hz, 2C), 129.1 (2C), 128.6 (2C), 128.4 (d, J = 5.4 Hz, 2C), 127.8 (2C), 126.4 (2C), 126.3 (d, J = 20.8 Hz, 2C), 125.8 (d, J = 4.9 Hz, 2C), 125.2 (d, J = 9.4 Hz, 2C), 123.3 (d, J = 7.9 Hz, 2C), 118.8 (d, J = 5.5 Hz), 46.4 (d, J = 4.9 Hz), 46.2 (d, J = 4.9 Hz), 45.6 (d, J = 2.5 Hz), 44.2 (d, J = 2.9 Hz), 44.1 (d, J = 2.9 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.3; HRMS (ESI) m/z calcd for $C_{32}H_{29}ClN_4OP$ 551.1761, found 551.1757; 95.2% ee, retention time = 6.28 (minor) and 6.82 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4j: white solid; yield 0.152 g (92%); mp 204−206 °C; $[\alpha]^{24}_D$ +3.50 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 7.2 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.88−7.78 (d, J = 7.8 Hz, 7H), 7.50−7.26 (m, 10H), 5.56 (t, J = 9.8 Hz, 1H), 4.46−4.14 (m, 4H), 3.52 (t, J = 10.0 Hz, 1H, NH), 3.04−2.96 (m, 4H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 133.7 (d, J = 4.9 Hz), 132.3, 131.7 (d, J = 6.9 Hz), 131.4 (2C), 129.4 (2C), 128.6 (2C), 128.4 (d, J = 5.4 Hz, 2C), 128.2, 126.9 (d, J = 7.5 Hz, 2C), 126.6 (2C), 126.4 (d, J = 20.8 Hz, 2C), 126.3 (d, J = 4.9 Hz, 2C), 125.8, 125.1 (d, J = 9.0 Hz, 2C), 123.6, 123.4, 123.3, 46.9 (d, J = 4.9 Hz), 46.6 (d, J = 4.9 Hz), 46.3 (d, J = 2.5 Hz), 44.3 (t, J = 2.9 Hz), 43.9 (d, J = 3.0 Hz), 19.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.3; 98.9% ee, retention time = 6.13 (minor) and 6.68 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 4k: white solid; yield 0.156 g (89%); mp 148−150 °C; $[\alpha]^{25}_D$ +1.74 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25(d, J = 8.5 Hz, 1H), 8.19−8.17 (m, 1H), 7.88−7.84 (m, 2H), 7.79 (t, J = 7.0 Hz, 2H), 7.55−7.47 (m, 6H), 7.43−7.39 (m, 2H), 7.37−7.36 (m, 1H), 6.46−6.45 (m, 1H), 6.35−6.34 (m, 1H), 5.60 (t, J = 9.5 Hz, 1H), 4.65−4.53 (m, 4H), 3.62 (t, J = 10.0 Hz, 1H), 3.03−2.93 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5 (d, J = 6.4 Hz), 143.8, 133.8 (d, J = 7.8 Hz), 132.3, 131.7 (d, J = 7.3 Hz), 128.7, 128.4, 126.9, 126.5 (d, J = 13.4 Hz), 125.9 (d, J = 7.8 Hz), 125.2 (d, J = 5.9 Hz), 123.4 (d, J = 9.3 Hz), 117.9 (d, J = 4.4 Hz), 46.6 (d, J = 5.0 Hz), 46.1 (d, J = 5.3 Hz), 44.4 (d, J = 12.8 Hz), 43.9 (d, J = 13.3 Hz), 41.9 (d, J = 1.0 Hz); ^{31}P NMR (202 MHz; $CDCl_3$) δ 21.6; HRMS (ESI) m/z calcd for $C_{30}H_{27}N_4O_2PNa$ 529.1764, found 529.1761; 99% ee, retention time = 6.55 (minor) and 6.83 (major), flow rate = 0.60 mL/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Absolute Configuration Determination. The absolute configuration for this asymmetric induction was determined by converting a product (**4a**) to an authentic sample.[18] In this conversion, **4a** was subjected to deprotection with 2.0 M aq HCl at rt in methanol followed by in situ *t*-Boc protection by treating with $(t\text{-Boc})_2O$ in the presence of Et_3N to give product **5**. The optical rotation of this product was confirmed to be consistent with that of the known sample with *S* configuration. During this transformation, the cleaved N^1,N^2-bis(naphthalen-1-ylmethyl)ethane-1,2-diamine (**6**) was extracted with *n*-butanol from the acidic mixture prior to *t*-Boc protection to give a quantitative yield. $[\alpha]^{24}_D$ −1.71 (c 1.2, $CHCl_3$) {lit. $[\alpha]^{24}_D$ −1.82 (c 1.1, $CHCl_3$)}.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all pure products **1a**−**k** and **4a**−**k**. This material is available free of charge via the Internet at http://pubs.acs.org.