Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 942–951

Preparation of *N*-phenyl-(*S*)-prolinol-derived P,N-ligands and their application in Pd-catalyzed asymmetric allylic alkylation

Biao Jiang,* Zuo-Gang Huang and Ke-Jun Cheng

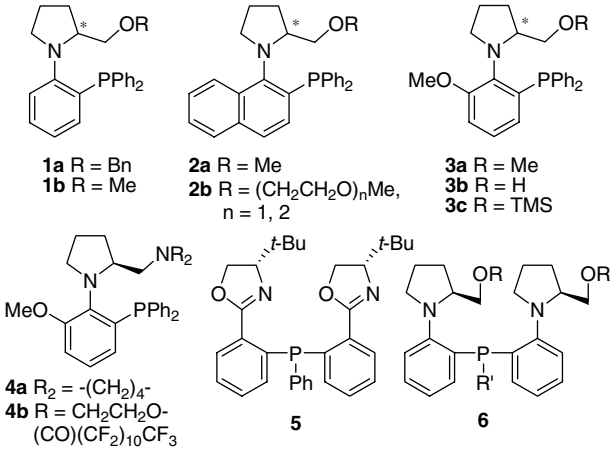
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

Received 26 January 2006; revised 13 March 2006; accepted 14 March 2006
Available online 12 April 2006

Abstract—Several NPN-type ligands bearing two chiral pyrrolidinyl groups derived from *N*-phenyl-(*S*)-prolinol were prepared by two synthetic methods. Their palladium-complex-catalyzed asymmetric allylic alkylation of malonates with 1,3-diphenyl 2-propenyl acetate delivered the products with good to high enantioselectivities (84–97% ee), including an optically active fluorine-containing compound.

1. Introduction

Palladium-catalyzed asymmetric allylic alkylation is a powerful method for carbon–carbon bond construction in organic synthesis.[1,2] Chiral P,N-ligands were found to be effective asymmetric inductors for this reaction owing to their sterically and electronically unsymmetrical nature.[3] Hiroi et al. reported several (*S*)-proline-derived chiral ligands bearing phosphorous, sulfuric, or selenic functionality as a chelating site for the Pd-catalyzed asymmetric 1,3-diphenylallylic alkylation of dimethyl malonate in the presence of bis(trimethylsilyl)acetamide (BSA).[4] The *N*-phenyl-type ligand **1a** gave a moderate yield and a relatively poor enantiomeric excess. Mino et al. developed a series of similar P,N-ligands containing *N*-aryl pyrrolidinyl moieties derived from chiral prolinol for the same reaction.[5] Employment of the *N*-naphthyl type ligand **2a** improved the enantiomeric excess. The ee was further increased by using ligand **3a** with a 6′-substituted methoxy group; restricted C–N bond rotation contributed to a better result. The in situ trimethylsilylation of **3b** with BSA to **3c** as a sterically more hindered ligand also had a beneficial effect. The applications of diamino-phosphine ligand **4a**, or the recyclable fluorous ligand **4b**, which were prepared through amination of *N*-aryl prolinol via a ring expansion and contraction technique, were also reported. Kondo et al. also prepared similar pyrrolidinyl or piperidinyl diaminophosphine ligands with an emphasis on an *N*-aryl axially chiral mimic designed for asymmetric catalysis.[6] Recently, Yamagishi et al. reported that a P-stereogenic center could be created by selective ligation of NPN-type ligand **5** in Pd-catalyzed asymmetric catalysis.[7] Inspired by this concept and in continuation of our work on chiral amino alcohol-derived ligands for asymmetric catalysis,[8] we herein report the preparation of NPN-type ligand **6** bearing two chiral pyrrolidinyl groups and their application in Pd-catalyzed asymmetric allylic alkylation.



1a R = Bn
1b R = Me

2a R = Me
2b R = $(CH_2CH_2O)_nMe$, n = 1, 2

3a R = Me
3b R = H
3c R = TMS

4a R_2 = -$(CH_2)_4$-
4b R = CH_2CH_2O-$(CO)(CF_2)_{10}CF_3$

5

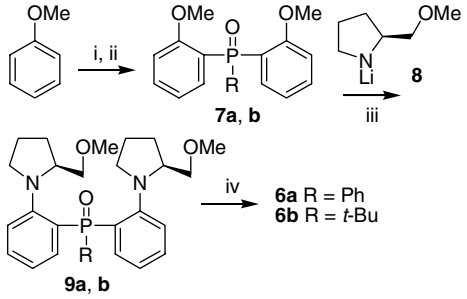
6

2. Results and discussion

The synthesis of ligand **6** is illustrated in Scheme 1. *ortho*-Lithiation of anisole with *n*-BuLi/TMEDA in dry ether

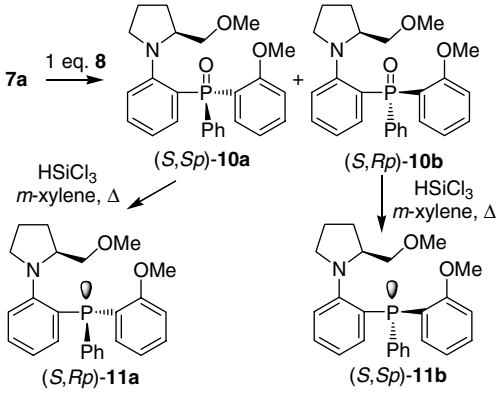
* Corresponding author. Fax: +86 21 64166128; e-mail: jiangb@mail.sioc.ac.cn

0957-4166/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2006.03.010



Scheme 1. Reagents and conditions: (i) *n*-BuLi/TMEDA, Et_2O, rt, 2 h, then 0.5 equiv $PhPCl_2$ or *t*-$BuPCl_2$, 1 h; (ii) H_2O_2, acetone, rt, 2 h; (iii) (*S*)-2-methoxymethylpyrrolidine, *n*-BuLi, THF, −78 °C to rt, 2 h, then 0.5 equiv **7a** or **7b**, 20 h; (iv) $HSiCl_3/Et_3N$, *m*-xylene, 140 °C, 8 h.

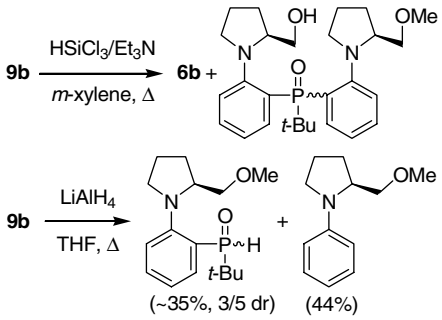
at room temperature, followed by the addition of 0.5 equiv of dichlorophenylphosphine or *tert*-butyldichlorophosphine, afforded tertiary phosphines, which were converted into phosphine oxides **7** by hydrogen peroxide in moderate to high yields. Nucleophilic aromatic substitution (S_NAr) on **7** with 2 equiv of chiral lithium amide **8** in THF at −78 °C afforded bis-substituted phosphine oxides **9**, along with isomers of mono-substituted products. The isolated yields for **9a** and **9b** were 62% and 73%, respectively. Raising the amount of **8** slightly increased the yield of bis-substituted **9a**. Using of only 1 equiv of **8** provided ca. 50% yield of isomeric mono-substituted products **10a** and **10b**, along with ca. 10% yield of **9a** based on ^{31}P NMR analysis (Scheme 2). The isolated yields for (*S*,*Sp*)-**10a** and (*S*,*Rp*)-**10b** were 28% and 21%, respectively. The absolute configuration of **10a** was determined by X-ray analysis of its single crystal (CCDC 291785).[9] However, the isomeric mono-substituted products for **7b** could not be fully separated.



Scheme 2.

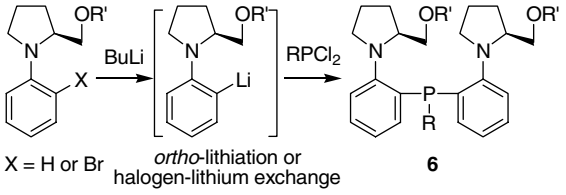
Trichlorosilane is a reducing agent for converting phosphine oxides into phosphines.[10] Generally, the P-chirogenic relative configuration is retained when a phosphine oxide is reduced by trichlorosilane alone, while the relative configuration is inverted when trichlorosilane was used in combination with an organic base, such as triethylamine. Reduction of **9a** with trichlorosilane/triethylamine afforded NPN-type ligand **6a** in 74% yield. Reduction of (*S*,*Sp*)-**10a** or (*S*,*Rp*)-**10b** with trichlorosilane alone gave (*S*,*Rp*)-**11a** or (*S*,*Sp*)-**11b**, respectively, in moderate yields and with high diastereoisomeric purity, as determined by ^1H NMR and ^{31}P NMR spectra (Scheme 2).

However, the reduction of **9b** was troubled by problems related to steric bulk. Refluxing **9b** with trichlorosilane/triethyl-amine in *m*-xylene at 140 °C for 15 h resulted in an unexpected demethoxy product (34%) with 42% recovery of the starting phosphine oxide (Scheme 3). Only a trace amount of reduced **6b** could be detected by ^{31}P NMR analysis and was easily reoxidized to **9b** by air. Using trichlorosilane in the absence of triethylamine, there was no formation of **6b**, and 86% of **9b** was recovered. Employing $LiAlH_4$ led to the C–P bond fission compounds: an air-oxidized secondary phosphine oxide (35%) and the *O*-methyl-*N*-phenyl (*S*)-prolinol (44%).[11]

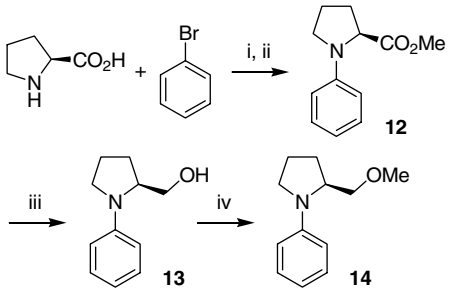


Scheme 3.

These drawbacks prompted us to try an alternative synthetic route (Scheme 4), which made unnecessary the troublesome reduction step of a bulky phosphine oxide. As shown in Scheme 5, the CuI-catalyzed coupling of (*S*)-proline and bromobenzene in the presence of 3 equiv of



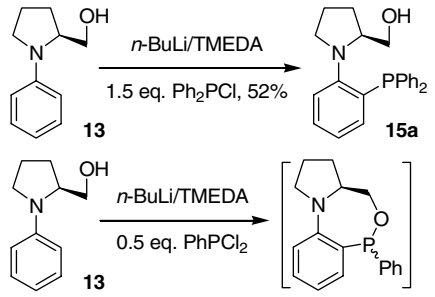
Scheme 4.



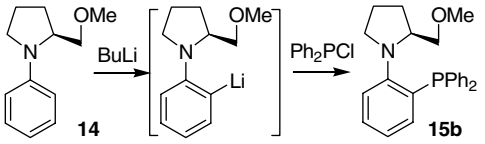
Scheme 5. Reagents and conditions: (i) 10 mol % CuI, 3 equiv K_2CO_3, DMF, 100 °C, 24 h; (ii) 0 °C, 1.5 equiv Me_2SO_4, 12 h, 66%; (iii) 1.5 equiv $LiAlH_4$, THF, rt to reflux, 4 h, 88%; (iv) 2.5 equiv NaH, THF, 2 equiv Me_2SO_4, 12 h, 92%.

K_2CO_3 with heating in DMF or DMA for 24 h,[12] followed by addition of Me_2SO_4 at 0 °C, afforded methyl *N*-phenyl (*S*)-prolinate **12** in 66% yield over two steps (>99.5% ee, chiral HPLC, the racemate was obtained by treating **12** with LDA). Reduction of **12** with $LiAlH_4$ gave (*S*)-*N*-phenyl prolinol **13** in 88% yield (>99.8% ee, chiral HPLC), which was converted to methyl ether **14** in 92% yield.

The double lithiation[13] of **13** with *n*-BuLi, followed by the addition of 1–2 equiv of Ph_2PCl and acidic workup, afforded a pendant-hydroxyl-group-containing P,N-ligand **15a** in 52% yield (Scheme 6). However, treatment with 0.5 equiv of $PhPCl_2$ did not give the NPN-type ligand, probably due to the formation of a cyclic phosphite intermediate, which was prone to polymerization as indicated by ^{31}P NMR analysis.[14] The deprotonation of **14** was also problematic. Attempts with different sets and combinations of BuLi, additives, solvents, and conditions were unsuccessful. Essentially, there was no formation of P,N-ligand **15b** upon addition of Ph_2PCl (Scheme 7).



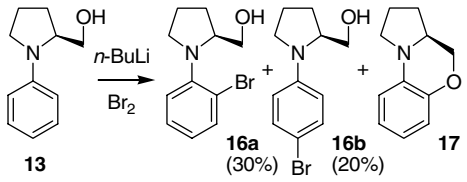
Scheme 6.



1-2 eq *n*-BuLi, hexane/ether or THF;
1-2 eq *n*-BuLi/TMEDA, hexane/ether;
1 eq *n*-BuLi/2 eq TMEDA, hexane/ether;
1 eq (*n*-BuLi-TMEDA), hexane;
1-2 eq *s*-BuLi/TMEDA, *c*-hexane/ether;
1-2 eq *t*-BuLi/TMEDA, pentane/ether.

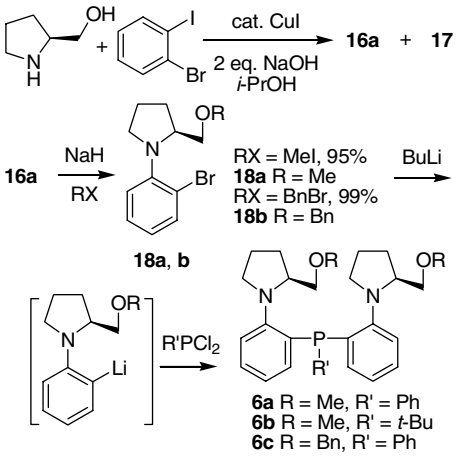
Scheme 7.

The halogen–lithium exchange route was next sought. Although the direct bromination of **13** or **14** with CBr_4/PPh_3 or CBS resulted in a mess, the mixture from treatment of double lithiated **13** with bromine could be separated by column chromatography to give *ortho*- and *para*-bromination products, and a cyclic *N*,*O*-(1, 2-phenylene) prolinol **17**, with 20% recovery of **13** (Scheme 8). Buchwald's 2002 report of CuI-catalyzed selective C–N or C–O bond formation for amino alcohol with iodoarene drew our attention.[15] In the presence of 2.5 mol % CuI and 2 equiv of NaOH, mixing of (*S*)-prolinol and 1-bromo-2-iodobenzene in 2-propanol with heating for 8 h afforded **16a** and **17** in 58% and 9% yields, respectively. Compound **16a** was converted into methyl ether **18a** or benzyl ether



Scheme 8.

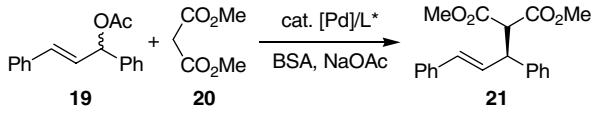
18b in quantitative yields. The bromine–lithium exchange between **18a** or **18b** and *n*-BuLi (1 equiv) or *t*-BuLi (2 equiv) in THF at −78 °C, followed by the addition of 0.5 equiv of $PhPCl_2$, afforded NPN-type ligands **6a** or **6c** in 21–72% yields, along with 60–20% recovery of the debromination products. The yield for **6b** from lithiated **18a** with *t*-$BuPCl_2$ was 39% (Scheme 9).



Scheme 9.

With these chiral P,N-ligands in hand, we set out to investigate their application in Pd-catalyzed allylic substitution of 1,3-diphenyl-2-propenyl acetate **19** with dimethyl malonate **20** in the presence of BSA/NaOAc. The details are shown in Table 1. Dimeric allyl palladium chloride and NPN-type ligand **6a** were mixed in situ to form the catalyst. Comparable results (92–97% yield and 82–84% ee) were obtained in THF and toluene at room temperature (entries 1 and 2). The reaction gave a slightly higher enantiomeric excess with toluene than that with THF, albeit the reaction took a shorter time to reach completion in THF. The reaction carried out in MeCN was much rapid, but the enantiomeric excess was somewhat lower (entry 3). Methylene dichloride was found to be an inferior solvent with low conversion of **19** and poor ee for **21** (entry 4). Increasing the ratio of the chiral ligand to the palladium source accelerated the reactions, but essentially there were no improvements in enantioselectivities (entries 5 and 6). Switching to the bulkier *P*-*tert*-butyl-substituted ligand **6b** gave only 24% ee, while the use of *O*-benzyl-substituted ligand **6c** afforded a moderate yield and enantiomeric excess (entries 7 and 8). It is interesting to note that using P-chirogenic ligand **11a** gave 84% ee, while the asymmetric induction of its diastereoisomer **11b** was very low (entries 9 and 10). Focussing on ligand **6a**, the enantioselectivities were increased when the reactions were carried out at 0 °C with

Table 1. Pd-catalyzed asymmetric allylic alkylation[a]



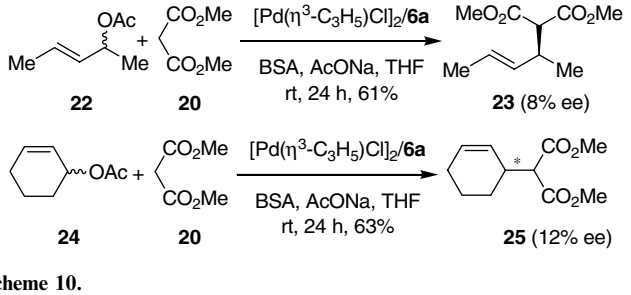
19 **20** **21**

Entry	Solvent	Temp.	Time (h)	Yield (%)[b]	ee (%)[c]
1	THF	rt	10	97	82
2	PhMe	rt	24	92	84
3	MeCN	rt	2	>99	74
4[d]	CH_2Cl_2	rt	48	47	67
5[e]	PhMe	rt	12	91	84
6[f]	PhMe	rt	8	>99	84
7[g]	THF	rt	24	83	24
8[h]	THF	rt	24	66	63
9[i]	THF	rt	48	40	84
10[j]	THF	rt	48	46	<3
11	THF	0 °C	48	88	88
12	PhMe	0 °C	48	81	91
13	MeCN	0 °C	48	29	80
14	PhMe	−20 °C	7 d	67	94
15	PhMe	−40 °C	7 d	10	97

[a] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**6a**/NaOAc/**19**/**20**/BSA = 2:4:4:100:300:300.
[b] Isolated yield.
[c] Determined by chiral HPLC, and all the products are of an (*S*)-configuration.
[d] LiOAc as additive.
[e] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**6a** = 2:6.
[f] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**6a** = 2:8.
[g] **6b** as ligand.
[h] **6c** as ligand.
[i] **11a** as ligand.
[j] **11b** as ligand.

88% and 91% ees in THF and toluene, respectively (entries 11 and 12). However, the reaction in MeCN became sluggish at this temperature with only 29% conversion of **19** for 48 h (entry 13). At −20 °C, it took 7 days to achieve 67% yield and 94% ee in toluene, and the enantioselectivity was further increased to 97% ee at −40 °C, but the conversion was only 10% (entries 14 and 15).

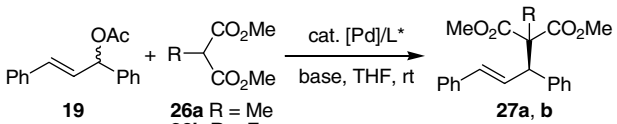
As an extension, the reactions of simpler substrate 1, 3-dimethyl allylic acetate **22** and cyclic **24** with dimethyl malonate were carried out. However, the ees were around 10% (Scheme 10).



Scheme 10.

The reactions of **19** with 2-substituted malonates **26a** and **26b** were also examined. The results are summarized in Table 2. Dimethyl 2-methylmalonate afforded **27a** in moderate yield and enantioselectivity (entry 1). When dimethyl

Table 2. Pd-catalyzed asymmetric allylic alkylation[a]



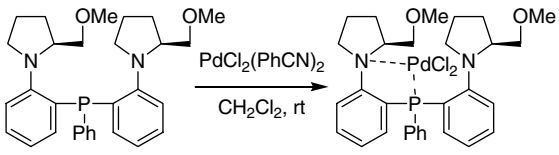
19 **26a** R = Me, **26b** R = F **27a**, **b**

Entry	Base	Time (h)	Yield (%)[b]	ee (%)[c]
1	BSA/NaOAc	24	**27a** (50)	75
2	BSA/NaOAc	6	**27b** (>99)	84
3	NaH	6	**27b** (>99)	9
4	Cs_2CO_3	24	**27b** (50)	35
5[d]	BSA/NaOAc	<0.5	**27b** (99)	95
6[d]	NaH	<0.5	**27b** (>99)	61

[a] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/**6a**/**19**/**26**/base = 2:4:100:300:300.
[b] Isolated yield.
[c] Determined by chiral HPLC, and all the products are (*R*)-configuration.
[d] (*S*)-*i*-Pr-PHOX as ligand.

2-fluoromalonate **26b** was used as a nucleophile, the allylic alkylation was completed in 6 h in the presence of BSA/NaOAc, delivering **27b** with 84% ee (entry 2). However, the enantioselectivity was only 9% when NaH was used as base (entry 3). Using Cs_2CO_3 resulted in a low conversion of **19** and poor ee for **27b** (entry 4). Resorting to the privileged ligand (*S*)-*i*-Pr-PHOX,[16] the reactions proceeded much more rapidly and quantitative yields were obtained in less than 30 min (entries 5 and 6). The enantioselectivities for BSA/NaOAc and NaH were 95% and 61%, respectively. The optically active product **27b** might serve as a valuable intermediate for asymmetric transformation to fluorine-containing compounds.[17]

In a mechanistic consideration, the coordination mode of NPN-type ligand **6a** with palladium was probed. Due to the complications of the chiral quaternary phosphorous and nitrogen centers resulting from the selective ligations to the metal ion and the *endo* or *exo* orientations of the ally group, the coordination of **6a** with bis(benzonitrile)palladium dichloride was chosen as a simplified mode (Scheme 11). The ^{31}P NMR spectroscopic study of the 1:1 complexation showed only one singlet peak at +36.6 ppm **28a**, indicating a highly selective ligation pattern. Another peak at +33.4 ppm **28b** appeared at higher concentrations, typically in 1:9 ratio to that at +36.6 ppm. Isolation of the Pd(II)-complex gave an orange solid, the recrystallization of which did not provide suitable crystals for X-ray diffraction analysis. Thus, the coordination mode and the absolute configuration could not be fully assigned. However,



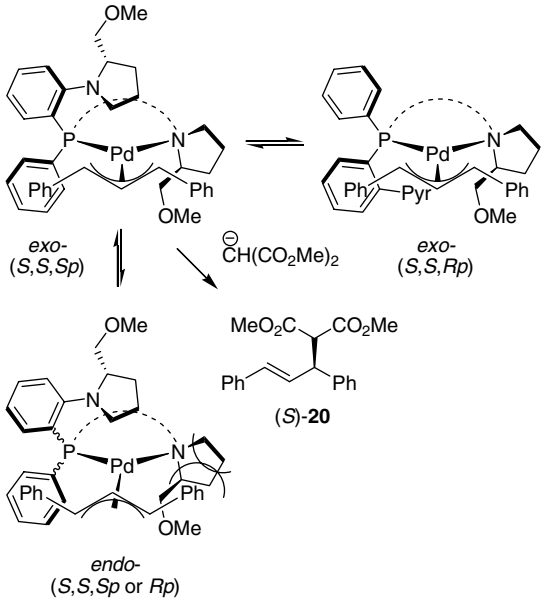
6a
^{31}P NMR: -19.1
^{13}C NMR: 153.8 (C), 153.5 (C), 60.7 (NCH), 59.9 (NCH), 55.6 (NCH_2), 55.5 (NCH_2)

28a, **b**
^{31}P NMR: +36.6/+33.4 (9:1)
^{13}C NMR: **164.1** (**C**), 154.0 (C), **81.9** (**NCH**), **71.3** (**NCH_2**), 62.3 (NCH), 57.5 (NCH_2)

Scheme 11.

the ^{13}C NMR spectrum of **28a** showed one set of sharply down-field-shifted signals of the carbons adjacent to the coordinating nitrogen atom, revealing a highly selective P,N-bidentate mode.

The mechanism for asymmetric induction with these NPN-type ligands is rationalized on the basis of the above NMR data and the stereochemical results. The installation of an additional chiral pyrrolidinyl moiety might facilitate internal ligation over disassociation of the weak N-donor to the transition metal and enable the selective construction of a P-stereogenic center (Scheme 12). Preferential attack of deprotonated malonate *trans* to the phosphorous atom at the *exo*-(*S*,*S*,*Sp*)-complex among all the species possibly formed in the equilibrium would lead to an (*S*)-product.



Scheme 12. Proposed asymmetric induction (the dashed arch represents the 1,2-phenylene backbone).

3. Conclusion

In conclusion, several *N*-phenyl-(*S*)-prolinol-derived P,N-ligands were prepared through two complementary synthetic routes: one comprising stepwise nucleophilic aromatic substitution (S_NAr) and trichlorosilane reduction of the phosphine oxides to tertiary phosphines, the other involving sequential C–N bond formation, bromine–lithium exchange and C–P bond formation. These NPN-type ligands bearing two chiral pyrrolidinyl groups were applied in the Pd-catalyzed asymmetric allylic alkylation of malonates with 1,3-diphenyl-2-propenyl acetate, affording the products with high yields and good enantioselectivities, including one fluorine-containing compound of synthetic potential.

4. Experimental

Air-sensitive compounds and reactions were manipulated under an inert atmosphere of argon in vacuum lines using Schlenk techniques. Ether, THF, and TMEDA were distilled from sodium/ketyl. PhMe, *m*-xylene, Et_3N, CH_2Cl_2, and MeCN were distilled from CaH_2. Melting points were uncorrected. Specific rotations were recorded on a PERKIN–ELMER 341 polarimeter. ^1H NMR (300 MHz), ^{13}C NMR (75 MHz), ^{31}P NMR (121 MHz) (from external standard 85% H_3PO_4) and ^{19}F NMR (282 MHz) (from external standard $PhCF_3$) spectra were obtained on a VARIAN MERCURY 300 spectrometer using $CDCl_3$ as solvent. IR spectra (film from $CDCl_3$) were recorded on a BIO-RAD FTS-185 spectrometer. EI-MS and HRMS were obtained on an AGILENT 5973N MSD and an IONSPEC 4.7 TESLA FTMS spectrometer. ESI MS were obtained on an APEXIII 7.0 TESLA FTMS spectrometer.

4.1. Bis(2-methoxylphenyl)phenyl phosphine oxide 7a[18]

Into a solution of anisole (5.5 mL, 50 mmol) and TMEDA (7.6 mL, 50 mmol) in dry ether (50 mL) was added dropwise *n*-BuLi (2.5 M in hexane, 20 mL, 50 mmol) for 15 min at rt. After stirring for 2 h, $PhPCl_2$ (3.4 mL, 24 mmol) was added dropwise into the resulting yellow slurry for 30 min. The mixture was diluted with ether (100 mL) after 1 h and washed with 2 M HCl (100 mL), 20% Na_2CO_3 (100 mL), and brine (3 × 100 mL). The ether layer was dried over $MgSO_4$. Filtration and evaporation in vacuo afforded bis(2-methoxylphenyl)phenyl phosphine as a white solid (7.6 g, 94% yield). The phosphine (6.6 g, 20 mmol) was dissolved in acetone (200 mL) and treated with H_2O_2 (30%, 5 mL, 45 mmol) with stirring for 1 h. After being concentrated to dryness with caution,[19] the residue was taken in CH_2Cl_2 (200 mL) and dried over $MgSO_4$. After filtration and evaporation in vacuo, the product was recrystallized from EtOAc–CH_2Cl_2 to give a white solid (6.1 g, 90% yield). Mp: 208 °C. IR: 3011, 1591, 1479, 1279, 1182, 1017, 803, 757, 703 cm^{-1}. ^1H NMR: δ 7.82–7.74 (m, 2H), 7.62–7.54 (m, 2H), 7.53–7.36 (m, 5H), 7.05–6.99 (m, 2H), 6.93–6.89 (m, 2H), 3.55 (s, 6H). ^{13}C NMR: δ 161.1–161.0 (d, $J = 2.9$ Hz), 134.6–133.1 (d, $J = 110$ Hz), 134.4–134.2 (d, $J = 8.8$ Hz), 133.58–133.55 (d, $J = 2.0$ Hz), 131.6–131.5 (d, $J = 10.3$ Hz), 130.81 (d, $J = 2.9$ Hz), 127.7–127.5 (d, $J = 12.7$ Hz), 121.6–120.2 (d, $J = 108$ Hz), 120.7, 120.5, 111.2, 111.1, 55.3. ^{31}P NMR: +26.9. EIMS: 338 (M^+, 54%). Anal. Calcd for $C_{20}H_{19}O_3P$: C, 71.00; H, 5.66. Found: C, 70.77; H, 5.59.

4.2. *tert*-Butyl bis(2-methoxylphenyl)phosphine oxide 7b

Following the procedure described for **7a** and using *t*-$BuPCl_2$, 52% yield. Mp: 93–95 °C. IR: 2968, 1589, 1576, 1480, 1464, 1432, 1277, 1247, 1163, 1016, 756 cm^{-1}. ^1H NMR: δ 7.68 (dd, 2H, $J = 7.8$, 12.6 Hz), 7.47 (t, 2H, $J = 7.8$ Hz), 7.01 (t, 2H, $J = 7.5$ Hz), 6.93 (dd, 2H, $J = 4.8$, 8.1 Hz), 3.75 (s, 6H), 1.29 (d, 9H, $J = 9.6$ Hz). ^{13}C NMR: δ 160.1 (d, $J = 3.0$ Hz), 134.7 (d, $J = 6.6$ Hz), 132.9 (d, $J = 2.4$ Hz), 121.7–120.5 (d, $J = 92$ Hz), 120.6 (d, $J = 10$ Hz), 110.5 (d, $J = 6.3$ Hz), 54.8, 34.8–33.9 (d, $J = 73$ Hz), 26.8 (d, $J = 2.3$ Hz). ^{31}P NMR: δ +52.6. EIMS: 318 (M^+, 3%), 261 (64%), 262 (56%), 121 (100%); HRMS: $[M+H]^+$ calcd for $C_{18}H_{24}O_3P^+$ 319.1458, found 319.1459.

4.3. Bis[2-(*S*)-(2-methoxylmethylpyrrolidinyl)phenyl]phenyl phosphine oxide (9a)

Into the solution of (*S*)-2-methoxyl-methyl-pyrrolidine (0.5 mL, 4.0 mmol) in THF (4 mL) was added dropwise 2.5 M *n*-BuLi (1.6 mL, 4.0 mmol) at −78 °C. After warming to rt in 3 h, **7a** (0.676 g, 2.0 mmol) was added into the resulting lithium amide **8** solution in one portion under an argon flow. The mixture was diluted with ether (100 mL) after stirring for 20 h and washed with saturated NH_4Cl (2 × 50 mL) and brine (2 × 50 mL). The ether layer was dried over $MgSO_4$. After filtration and concentration to dryness, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc/acetone = 10:1:4) to give a foaming solid. Recrystallization from hexane gave a light brown solid (0.63 g, 62% yield). Mp: 160.5–160.7 °C. $[\alpha]_D^{20} = +43$ (*c* 1.00, $CHCl_3$). IR: 2981, 2873, 2808, 1584, 1568, 1470, 1440, 1280, 1195, 1107, 950, 771, 709 cm^{-1}. ^1H NMR: 7.60–6.92 (m, 13H), 3.95–3.86 (m, 2H), 3.70–3.65 (m, 2H), 3.13 (s, 3H), 3.07 (dd, 1H, $J = 3.4$, 9.4 Hz), 3.00 (s, 3H), 2.85–2.61 (m, 4H), 2.28 (t, 1H, $J = 8.7$ Hz), 2.03–1.49 (m, 8H). ^{13}C NMR: 154.4–154.3 (d, C, $J = 3.8$ Hz), 153.7 (d, C, $J = 3.9$ Hz), 135.5–134.1 (d, C, $J = 107$ Hz), 134.7, 134.6, 134.5, 134.3, 132.6, 132.4, 132.37, 132.34, 132.27, 132.24, 130.6–129.1 (d, C, $J = 106$ Hz), 130.51, 130.47, 130.1–128.7 (d, C, $J = 105$ Hz), 127.5, 127.4, 122.6, 122.51, 122.49, 122.32, 122.29, 122.2, 121.8, 121.6, 74.80 (CH_2), 74.75 (CH_2), 60.8 (CH), 60.2 (CH), 58.6 (CH_3), 57.1 (CH_2), 55.9 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 23.8 (CH_2), 23.6 (CH_2). ^{31}P NMR: +30.2. EIMS: 503 ($[M-H]^+$), 473 ($[M-OMe]^+$, 13%); HRMS: M^+ calcd for $C_{30}H_{37}N_2O_3P^+$, found 504.2501. Anal. Calcd for $C_{30}H_{37}N_2O_3P$: C, 71.41; H, 7.39; N, 5.55. Found: C, 71.21; H, 7.47; N, 5.52.

4.4. *tert*-Butyl bis[2-(*S*)-(2-methoxylmethylpyrrolidinyl)-phenyl]phosphine oxide 9b

Following the procedure described for **9a**, 73% yield. Mp: 147–149 °C. $[\alpha]_D^{20} = +143$ (*c* 1.02, $CHCl_3$). IR: 2966, 1715, 1586, 1472, 1438, 1113, 949, 768, 749 cm^{-1}. ^1H NMR: δ 7.97 (t, 1H, $J = 8.4$ Hz), 7.55–7.47 (m, 2H), 7.33–7.18 (m, 3H), 6.75–6.69 (m, 2H), 4.43–4.36 (m, 1H), 4.12–4.05 (m, 1H), 3.96–3.90 (m, 1H), 3.53–3.44 (m, 2H), 3.30 (s, 3H), 3.18 (t, 1H, $J = 8.5$ Hz), 3.07–2.99 (m, 1H), 2.95 (s, 3H), 2.59–2.50 (m, 2H), 2.27–2.18 (m, 1H), 2.09–1.88 (m, 3H), 1.80–1.64 (m, 4H), 1.50–1.40 (m, 2H), 1.31–1.26 (d, 9H, $J = 14.1$ Hz). ^{13}C NMR: δ 155.71 (d, $J = 2.2$ Hz), 154.84 (d, $J = 2.5$ Hz), 134.43, 134.27, 133.63, 132.39, 132.37, 132.34, 132.11, 131.99, 131.24, 131.21, 126.82, 125.62, 125.21, 125.12, 123.59, 123.43, 119.76, 119.58, 119.48, 119.38, 75.59, 75.28, 61.90, 59.09, 58.96, 58.61, 58.15, 36.44, 35.47, 29.78, 29.49, 26.56, 23.56, 22.97. ^{31}P NMR: δ +43.6. EIMS: 484 (M^+, 1%); HRMS: $[M+H]^+$ calcd for $C_{28}H_{42}N_2O_3P^+$ 485.2928, found 485.2937.

4.5. (*Sp*)-[2-(*S*)-(2-Methoxylmethylpyrrolidinyl)phenyl](2-methoxyl-phenyl)phenyl phosphine oxide 10a

Following the procedure described for **9a** and using 1 equiv of **8**, 28% yield. Mp: 119–120 °C. $[\alpha]_D^{20} = +146$ (*c* 1.05, $CHCl_3$). IR: 2985, 1587, 1475, 1437, 1276, 1242, 1173, 1105, 1020, 770 cm^{-1}. ^1H NMR: δ 8.16–8.08 (m, 1H), 7.99–7.91 (m, 2H), 7.50–7.38 (m, 5H), 7.28–7.19 (m, 2H), 7.12–7.07 (m, 1H), 6.99–6.94 (m, 1H), 6.83–6.78 (m, 1H), 3.78–3.68 (m, 2H), 3.48 (s, 3H), 3.12 (s, 3H), 3.00–2.95 (dd, 1H, $J = 3.6$, 9.3 Hz), 2.65–2.58 (m, 1H), 2.46–2.40 (t, 1H, $J = 8.4$ Hz), 1.85–1.78 (m, 1H), 1.62–1.53 (m, 1H), 1.43–1.29 (m, 2H). ^{13}C NMR: δ 159.4 (d, C, $J = 4.0$ Hz), 153.4 (d, C, $J = 4.6$ Hz), 134.6–133.2 (d, C, $J = 107$ Hz), 134.2–134.1 (d, CH, $J = 5.7$ Hz), 133.9 (CH), 132.79–132.77 (d, CH, $J = 1.7$ Hz), 132.23–132.20 (d, CH, $J = 2.3$ Hz), 132.1 (CH), 131.9 (CH), 131.00–130.96 (d, CH, $J = 2.7$ Hz), 130.5–129.1 (d, C, $J = 110$ Hz), 127.9 (CH), 127.7 (CH), 123.4–121.9 (d, C, $J = 105$ Hz), 122.4–122.2 (d, CH, $J = 13.7$ Hz), 121.6–121.5 (d, CH, $J = 9.1$ Hz), 120.9–120.8 (d, CH, $J = 11.6$ Hz), 110.35–110.26 (d, CH, $J = 6.8$ Hz), 74.5 (CH_2), 60.6 (CH), 58.6 (CH_3), 55.9 (CH_2), 54.6 (CH_3), 28.9 (CH_2), 23.3 (CH_2). ^{31}P NMR: δ +25.3. EIMS: 390 ($[M-MeO]^+$, 20%); HRMS: 390.1661 ($[M-MeO]^+$, 13%), calcd for $C_{24}H_{25}NO_2P^+$.

4.6. (*Rp*)-[2-(*S*)-(2-Methoxylmethylpyrrolidinyl)phenyl](2-methoxyl-phenyl)phenyl phosphine oxide 10b

Following the procedure described for **9a** and using 1 equiv of **8**, 21% yield. Yellow oil. $[\alpha]_D^{20} = -5$ (*c* 1.00, $CHCl_3$). IR: 2938, 1712, 1590, 1478, 1437, 1277, 1167, 1135, 1109, 802, 760, 710 cm^{-1}. ^1H NMR: δ 8.12–8.05 (m, 1H), 7.81–7.74 (m, 2H), 7.52–7.23 (m, 7H), 7.15–7.09 (m, 1H), 6.99–6.93 (m, 1H), 6.87–6.83 (dd, H, $J = 5.4$, 7.8 Hz), 3.88–3.85 (m, 1H), 3.57 (s, 3H), 3.53–3.45 (m, 1H), 3.16 (s, 3H), 3.13–3.09 (dd, 1H, $J = 3.6$, 9.3 Hz), 2.78–2.68 (m, 2H), 1.83–1.77 (m, 1H), 1.55–1.23 (m, 3H). ^{13}C NMR: δ 159.90–159.86 (d, C, $J = 3.5$ Hz), 153.53–153.47 (d, C, $J = 4.7$ Hz), 134.8–133.4 (d, C, $J = 109$ Hz), 127.4–126.0 (d, C, $J = 108$ Hz), 122.5–121.1 (d, C, $J = 105$ Hz), 134.75–134.66 (d, CH, $J = 6.4$ Hz), 134.52 (CH), 133.48–133.45 (d, CH, $J = 2.3$ Hz), 132.60–132.57 (d, CH, $J = 2.1$ Hz), 131.9 (CH), 131.7 (CH), 130.6–130.5 (d, CH, $J = 2.9$ Hz), 127.3 (CH), 127.2 (CH), 122.0–121.9 (d, CH, $J = 3.8$ Hz), 121.8–121.7 (d, CH, $J = 7.5$ Hz), 121.1–120.9 (d, CH, $J = 10.5$ Hz), 110.9–110.8 (d, CH, $J = 6.2$ Hz), 74.6 (CH_2), 60.8 (CH), 58.7 (CH_3), 55.4 (CH_2), 54.8 (CH_3), 28.9 (CH_2), 23.6 (CH_2). ^{31}P NMR: δ +27.3. ESIMS: 444 ($[M+Na]^+$, 25%), 422 ($[M+H]^+$, 100%); HRMS: $[M+Na]^+$ calcd for $C_{25}H_{28}O_3NPNa^+$ 444.1699, found 444.1684.

4.7. Bis[2-(*S*)-(2-methoxylmethylpyrrolidinyl)phenyl]phenyl phosphine 6a

Into the solution of **9a** (0.40 g, 0.8 mmol) and Et_3N (0.9 mL, 3.2 mmol) in dry *m*-xylene (6 mL) with ice-water cooling, $HSiCl_3$ (0.65 mL, 3.2 mmol) was added with caution. The mixture was heated to 140 °C for 8 h. After cooling to 0 °C and diluting with ether (50 mL), the mixture was treated with 2 M NaOH with caution to dissolve all the solid and extracted with ether. The ether layer was dried over $MgSO_4$. After filtration and concentration to dryness, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 20:1) to give a light yellow solid (0.29 g, 74% yield). Mp 114.0–114.5 °C.

$[\alpha]_D^{20} = -165$ (*c* 1.05, $CHCl_3$). IR: 2973, 2872, 2808, 1579, 1566, 1462, 1438, 1282, 1112, 952, 767, 699 cm^{-1}. ^1H NMR: 7.30–7.18 (m, 9H), 6.95–6.87 (m, 2H), 6.81–6.80 (m, 1H), 6.72–6.68 (m, 1H), 3.85–3.57 (m, 4H), 3.12 (s, 3H), 3.06 (s, 3H), 3.11–3.07 (m, 1H), 2.95–2.90 (m, 1H), 2.78–2.69 (m, 3H), 2.63–2.57 (t, 1H, $J = 9.0$ Hz), 2.13–2.03 (m, 2H), 1.87–1.57 (m, 6H). ^{13}C NMR: 153.8–153.7 (d, C, $J = 8.4$ Hz), 153.5–153.4 (d, C, $J = 7.5$ Hz), 139.0–138.8 (d, C, $J = 15.1$ Hz), 136.2–136.1 (d, C, $J = 11.8$ Hz), 135.5–135.3 (d, C, $J = 15.1$ Hz), 135.0, 134.7, 134.4, 134.1, 134.0, 129.5, 129.3, 128.03, 128.00, 127.9, 123.4, 123.3, 121.20, 121.17, 120.6, 120.5, 75.8 (CH_2), 75.5 (CH_2), 60.69–60.66 (d, CH, $J = 2.3$ Hz), 59.88–59.84 (d, CH, $J = 3.1$ Hz), 58.77 (CH_3), 58.72 (CH_3), 55.65–55.56 (d, CH_2, $J = 6.8$ Hz), 55.5–55.4 (d, CH_2, $J = 5.7$ Hz), 29.90 (CH_2), 29.87 (CH_2), 24.1 (CH_2), 23.9 (CH_2). ^{31}P NMR: −19.1. EIMS: 488 (M^+, 9%); HRMS: M^+ 488.26263, calcd for $C_{30}H_{37}N_2O_2P^+$. Anal. Calcd for $C_{30}H_{37}N_2O_2P$: C, 73.75; H, 7.63; N, 5.73. Found: C, 73.60; H, 7.76; N, 5.74.

4.8. (*Rp*)-[2-(*S*)-(2-Methoxylmethylpyrrolidinyl)phenyl](2-methoxyl-phenyl)phenyl phosphine oxide 11a

Following the procedure described for **6a** in the absence of Et_3N, 52% yield. Slightly yellow oil. $[\alpha]_D^{20} = -43$ (*c* 0.84, $CHCl_3$). IR: 2872, 1572, 1433, 1273, 1095, 1042, 952, 731, 699 cm^{-1}. ^1H NMR: δ 7.37–7.20 (m, 8H), 6.96–6.91 (m, 1H), 6.87–6.78 (m, 3H), 6.65–6.60 (m, 1H), 3.73–3.65 (m, 1H), 3.70 (s, 3H), 3.31–3.24 (m, 2H), 3.20 (s, 3H), 2.99–2.93 (t, 1H, $J = 9.0$ Hz), 2.75–2.67 (m, 1H), 2.12–2.03 (m, 1H), 1.78–1.61 m, 3H). ^{13}C NMR: δ 161.3–161.1 (d, C, $J = 16.1$ Hz), 154.0–153.7 (d, C, $J = 20.7$ Hz), 137.5–137.3 (d, C, $J = 12.1$ Hz), 134.9–134.8 (d, C, $J = 9.8$ Hz), 134.6 (CH), 134.3–134.1 (d, CH, $J = 14.3$ Hz), 133.7 (CH), 129.8–129.6 (d, CH, $J = 15.5$ Hz), 128.3–128.2 (d, CH, $J = 5.13$ Hz), 128.1 (CH), 123.6 (CH), 121.43–121.39 (d, CH, $J = 2.9$ Hz), 120.8 (CH), 110.2 (CH), 75.7 (CH_2), 61.31–61.28 (d, CH, $J = 2.0$ Hz), 58.9 (CH_3), 55.8–55.7 (d, CH_2, $J = 8.0$ Hz), 55.6 (CH_3), 29.9 (CH_2), 24.0 (CH_2). ^{31}P NMR: δ −24.2. EIMS: 405 (M^+, 6.8), HRMS: 405.1865, calcd for $C_{25}H_{28}NO_2P^+$ 405.1858.

4.9. (*Sp*)-[2-(*S*)-(2-Methoxylmethylpyrrolidinyl)phenyl](2-methoxyl-phenyl)phenyl phosphine oxide 11b

Following the procedure described for **6a** in the absence of Et_3N, 60% yield. Slightly yellow oil. $[\alpha]_D^{20} = -105$ (*c* 0.94, $CHCl_3$). IR: 2808, 1582, 1467, 1246, 1124, 1026, 952, 744, 699 cm^{-1}. ^1H NMR: δ 7.31–7.18 (m, 8H), 6.91–6.82 (m, 4H), 6.73–6.71 (m, 1H), 3.85–3.70 (m, 2H), 3.76 (s, 3H), 3.07 (s, 3H), 2.94–2.89 (m, 1H), 2.83–2.76 (m, 1H), 2.49–2.43 (t, 1H, $J = 9.0$ Hz), 2.13–2.02 (m, 1H), 1.88–1.54 (m, 3H). ^{13}C NMR: δ 161.3–161.1 (d, C, $J = 15.8$ Hz), 153.4–153.1 (d, C, $J = 20.3$ Hz), 137.7–137.6 (d, C, $J = 11.3$ Hz), 134.8, 134.5, 134.2, 134.1, 133.9, 133.8, 133.6, 129.84–129.79 (d, CH, $J = 4.3$ Hz), 129.5, 128.3, 128.1–128.0 (d, CH, $J = 7.5$ Hz), 126.5, 125.8, 123.0, 121.0, 120.34–120.30 (d, CH, $J = 3.2$ Hz), 109.8, 75.2 (CH_2), 59.54–59.50 (d, CH, $J = 2.6$ Hz), 58.7 (CH_3), 55.7–55.6 (d, CH_2, $J = 10.3$ Hz), 55.63–55.62 (d, CH_3, $J = 1.1$ Hz), 29.8 (CH_2), 24.0 (CH_2). ^{31}P NMR: δ −21.4. EIMS: 405 (M^+, 7%); HRMS: 405.1865, calcd for $C_{25}H_{28}NO_2P^+$ 405.1858.

4.10. Methyl (*S*)-*N*-phenyl-prolinate 12[20]

Under an argon flow, CuI (10 g, 0.05 mol) and K_2CO_3 (200 g, 1.4 mol) were added into a solution of (*S*)-proline (57 g, 0.50 mol) and bromo-benzene (60 mL, 0.57 mol) in DMF (500 mL) with mechanical stirring. The mixture was heated at 100 °C for 24 h. After cooling to 0 °C and diluting with DMF (200 mL), 75 mL (0.75 mol) of Me_2SO_4 was added. The mixture was stirred at 0 °C for 12 h and then poured into ice-water (2 kg, 1/1). The organic phase was separated, and the aqueous phase extracted with EtOAc (2 × 200 mL). The combined organic phase was washed with 2 M HCl (2 × 200 mL) and brine, and dried over Na_2SO_4. After filtration and evaporation in vacuo, the residual solvents were removed by oil pump (40 Pa, 100 °C) to give a light brown oil (68 g, 66% yield). $[\alpha]_D^{20} = -149$ (>99.5% ee, *c* 1.05, $CHCl_3$). ^1H NMR: δ 7.25–7.19 (dd, 2H, $J = 7.2$, 8.4 Hz), 6.71 (t, 1H, $J = 7.4$ Hz), 6.54 (d, 2H, $J = 7.5$ Hz), 4.25 (dd, 1H, $J = 2.1$, 8.4 Hz), 3.71 (s, 3H), 3.61–3.55 (m, 1H), 3.40–3.32 (m, 1H), 2.31–2.03 (m, 4H). ^{13}C NMR: δ 174.3, 146.2, 128.7, 116.1, 111.4, 60.2, 51.5, 47.7, 30.3, 23.4. Chiral HPLC: Chiracel OD-H, hexane/*i*-PrOH = 90:0.5, flow rate 1.0 mL/min, $t_S = 9.6$ min, $t_R = 12.6$ min.

4.11. (*S*)-*N*-phenyl-prolinol 13

Into 500-mL THF was added $LiAlH_4$ (18 g, 0.47 mol) in small portions with caution. A solution of **12** (60 g, 0.29 mol) in THF (100 mL) was added dropwise over 1 h into the above suspension with mechanical stirring. The reaction was heated at reflux for 3 h. After cooling to 0 °C, 2 M NaOH (150 mL) was added into the mixture dropwise over 1 h, and then refluxed for 1 h. After being cooled to rt, the organic phase was separated, and the aqueous phase extracted with ether (3 × 100 mL). The combined organic phase was dried over Na_2SO_4. After filtration and evaporation in vacuo, the residual solvents were removed by oil pump (20 Pa, 100 °C) to give a light yellow oil (46 g, 88% yield). $[\alpha]_D^{20} = -119$ (>99.8% ee, *c* 1.15, $CHCl_3$). IR: 3347, 2966, 1919, 1598, 1506, 1363, 1159, 1035, 993, 747, 693 cm^{-1}. ^1H NMR: δ 7.26–7.21 (m, 2H), 6.73–6.69 (m, 3H), 3.88–3.84 (m, 1H), 3.68–3.65 (m, 2H), 3.54–3.49 (m, 1H), 3.17–3.13 (m, 1H), 2.07–1.96 (m, 4H). ^{13}C NMR: δ 147.9, 129.1, 116.2, 112.2, 63.5, 60.0, 49.3, 28.6, 23.6. EIMS: 177 (M^+, 14%); 146 (100%); HRMS: M^+ calcd for $C_{11}H_{15}NO^+$ 177.1154, found 177.1148. Chiral HPLC: Chiracel OD-H, hexane/*i*-PrOH = 90:1, flow rate 1.0 mL/min, $t_R = 5.3$ min, $t_S = 8.0$ min.

4.12. (*S*)-2-(Methoxymethyl)-1-phenylpyrrolidine 14

Into a solution of **13** (3.30 g, 19 mmol) in THF (100 mL) was added NaH (60% in mineral oil, 2 g, 50 mmol). A solution of Me_2SO_4 (4 mL, 40 mmol) in THF (50 mL) was added dropwise. After stirring for 12 h, the mixture was treated with 2 M NaOH (50 mL), and extracted with ether (2 × 100 mL). The ether layer was dried over Na_2SO_4. Filtration and evaporation in vacuo afforded a colorless

oil (3.29 g, 92% yield). $[\alpha]_D^{20} = -155$ (*c* 1.04, $CHCl_3$). IR: 2877, 1598, 1506, 1364, 1162, 1112, 747, 693 cm^{-1}. ^1H NMR: δ 7.26–7.20 (m, 2H), 6.71–6.64 (m, 3H), 3.91–3.84 (m, 1H), 3.53 (dd, 1H, $J = 3.6$, 9.1 Hz), 3.47–3.38 (m, 1H), 3.39 (s, 3H), 3.19 (t, 1H, $J = 9.1$ Hz), 3.16–3.09 (m, 1H), 2.08–1.92 (m, 4H). ^{13}C NMR: δ 147.5, 129.2, 115.8, 111.8, 73.1, 59.1, 58.1, 48.4, 28.9, 23.3. EIMS: 191 (M^+, 16%), 146 (100%); HRMS: $[M+H]^+$ calcd for $C_{12}H_{18}NO^+$ 192.1383, found 192.1378.

4.13. (*S*)-[1-(2-Diphenylphosphanylphenyl)pyrrolidin-2-yl]-methanol 15a

Into the solution of **13** (200 mg, 1.1 mmol) and TMEDA (0.4 mL, 2.3 mmol) in dry ether (5 mL) was added 2.5 M *n*-BuLi (1.0 mL, 2.3 mmol) at 0 °C. After stirring for 6 h at rt, the mixture was heated at reflux for 2 h. After cooling to 0 °C, Ph_2PCl (0.25 mL, 1.4 mmol) was added into a solution. After being stirred for 8 h, the reaction was diluted with ether (30 mL) and quenched with saturated NH_4Cl (5 mL). The ether layer was washed with 2 M HCl, 20% Na_2CO_3 and brine, and dried over $MgSO_4$. After filtration and concentration to dryness, the residue was purified by flash chromatography on silica gel to give an oil (218 mg, 52% yield). $[\alpha]_D^{20} = +3.4$ (*c* 1.05, $CHCl_3$). ^1H NMR: 7.28–7.14 (m, 12H), 7.01–6.95 (m, 1H), 6.79–6.75 (ddd, 1H, $J = 1.5$, 4.5, 7.5 Hz), 3.52–3.42 (m, 2H), 3.29 (m, 2H), 2.56–2.48 (m, 1H), 2.40–2.34 (m, 1H), 1.94–1.86 (m, 2H), 1.60–1.44 (m, 2H). ^{13}C NMR: 153.8 (d, $J = 20.0$ Hz), 138.18, 137.01, 136.89, 136.27, 136.21, 134.50, 134.22, 133.82, 133.56, 133.12, 130.27, 128.92, 128.52, 128.44, 128.41, 128.35, 128.31, 125.70, 124.15, 124.12, 65.99, 61.59, 56.72, 56.70, 26.72, 24.49. ^{31}P NMR: −16.9. EIMS: 360 ($[M-H]^+$, 2%); HRMS; $[M-OH]^+$ 344.1571, calcd for $C_{23}H_{23}NP^+$ 344.1563.

4.14. (*S*)-(1-(2-Bromophenyl)pyrrolidin-2-yl)methanol 16a

Method in Scheme 8: Into a solution of **13** (1.8 g, 10 mmol) and TMEDA (3.8 mL, 20 mmol) in dry ether (100 mL) was added 2.5 M *n*-BuLi (9 mL, 22 mmol) at 0 °C. After stirring for 6 h at rt, the mixture was heated to reflux for 2 h. After cooling to −78 °C, Br_2 (0.9 mL, 16 mmol) was added into the solution. After being stirred for 12 h, the reaction was quenched with water (40 mL). The organic phase was separated and dried over Na_2SO_4. After filtration and evaporation in vacuo, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 8:1) to give two major products **16a** (30%) and **16b** (20%). Method in Scheme 9: Under an argon flow, into the solution of CuI (5 mg, 0.026 mmol) and NaOH (80 mg, 2.0 mmol) in *i*-propanol (1 mL) were added 1-bromo-2-iodobenzene (0.14 mL, 1.1 mmol) and (*S*)-prolinol (0.10 mL, 1.0 mmol). The reaction was heated at 80 °C for 8 h. The mixture was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 10:1) to give two products **17** (9%) and **16a** (58%). Slightly yellow oil. $[\alpha]_D^{20} = +51$ (*c* 1.16, $CHCl_3$). IR: 3400, 2964, 2875, 1671, 1586, 1474, 1317, 1026, 752 cm^{-1}. ^1H NMR: δ 7.55 (dd, $J = 1.8$, 7.8 Hz), 7.28–7.22 (m, 1H), 7.18–7.15 (m, 1H), 6.92 (m, 1H), 3.89–3.75 (m, 2H), 3.52–3.38 (m, 2H), 2.88–2.80 (m, 1H), 2.29 (br s, 1H), 2.16–1.82 (m, 4H). ^{13}C NMR: δ 147.7, 133.8, 128.1, 124.7, 122.3, 121.0, 61.8, 61.3, 55.0, 27.8, 24.6. EIMS: 255 (M^+, 3.4%), 257 ($[M+2]^+$, 3.4%), 224 (100%), 226 (94%); HRMS: $[M+H]^+$ calcd for $C_{11}H_{15}NOBr^+$ 256.0331, found 256.0316.

4.15. (*S*)-(1-(4-Bromophenyl)pyrrolidin-2-yl)methanol 16b

20% yield. Slightly yellow oil. $[\alpha]_D^{20} = -79$ (*c* 0.98, $CHCl_3$). IR: 3366, 2877, 1861, 1593, 1495, 1362, 1187, 1037, 805, 757 cm^{-1}. ^1H NMR: δ 7.27 (d, 2H, $J = 9.0$ Hz), 6.54 (d, 2H, $J = 9.0$ Hz), 3.82–3.76 (m, 1H), 3.62–3.56 (m, 2H), 3.48–3.42 (m, 1H), 3.13–3.08 (m, 1H), 2.10–1.95 (m, 4H), 1.73 (s, 1H). ^{13}C NMR: δ 146.9, 131.8, 113.9, 108.2, 63.6, 60.2, 49.5, 28.7, 23.7. EIMS: 255 (M^+, 11.4%), 257 ($[M+2]^+$, 10.9%), 224 (100%), 226 (92%); HRMS: $[M+H]^+$ calcd for $C_{11}H_{15}NOBr^+$ 256.0331, found 256.0316.

4.16. (3a*S*)-2,3,3a,4-Tetrahydro-1*H*-5-oxa-9b-aza-cyclopenta [*a*]naphthalene 17

9% yield. Yellow oil. $[\alpha]_D^{20} = +46$ (*c* 1.19, $CHCl_3$). IR: 2970, 2868, 1608, 1506, 1363, 1324, 1209, 1044, 740 cm^{-1}. ^1H NMR: δ 6.91–6.86 (m, 2H), 6.64–6.56 (m, 2H), 4.42 (dd, 1H, $J = 2.8$, 9.7 Hz), 3.57–3.40 (m, 3H), 3.22 (dd, 1H, $J = 8.1$, 16.8 Hz), 2.14–1.98 (m, 3H), 1.50–1.37 (m, 1H). ^{13}C NMR: δ 142.8, 135.0, 121.8, 116.3, 115.7, 112.3, 68.5, 55.3, 47.7, 28.3, 23.6. EIMS: 175 (M^+, 100%); HRMS: $[M+H]^+$ calcd for $C_{11}H_{14}NO^+$ 176.1070, found 176.1076.

4.17. (*S*)-1-(2-Bromophenyl)-2-(methoxymethyl)pyrrolidine 18a

Following the procedure described for **14**, 95% yield. Slightly yellow oil. $[\alpha]_D^{20} = +23$ (*c* 1.30, $CHCl_3$). IR: 2972, 2875, 1586, 1476, 1320, 1110, 1024, 953, 751 cm^{-1}. ^1H NMR: δ 7.49 (d, 1H, $J = 8.1$ Hz), 7.24–7.17 (m, 1H), 7.07 (d, 1H, $J = 8.1$ Hz), 6.79 (t, 1H, $J = 7.5$ Hz), 4.08–4.02 (m, 1H), 3.77 (dd, 1H, $J = 4.8$, 15.6 Hz), 3.34 (dd, 1H, $J = 3.6$, 9.6 Hz), 3.22 (s, 3H), 3.10 (dd, 1H, $J = 7.8$, 9.3 Hz), 2.93–2.87 (m, 1H), 2.23–2.16 (m, 1H), 1.96–1.76 (m, 3H). ^{13}C NMR: δ 147.9, 134.1, 127.7, 122.7, 120.7, 117.6, 74.8, 59.1, 58.6, 53.4, 29.6, 24.2. EIMS: 269 (M^+, 1.16%), 271 ($[M+H]^+$, 0.97%), 224 ($[M-45]^+$, 100%), 226 (88%). Anal. Calcd for $C_{12}H_{16}NBrO$: C, 53.35; H, 5.97; N, 5.18. Found: C, 53.19; H, 5.52; N, 4.74.

4.18. (*S*)-2-(Benzyloxymethyl)-1-(2-bromophenyl)pyrrolidine 18b

Following the procedure described for **14** and using benzyl bromide, 99% yield. Slightly yellow oil. $[\alpha]_D^{20} = +3.8$ (*c* 1.01, $CHCl_3$). IR: 2966, 2869, 1586, 1475, 1320, 1104, 1025, 750, 698 cm^{-1}. ^1H NMR: 7.46 (dd, 1H, $J = 1.5$, 7.5 Hz), 7.28–7.12 (m, 6H), 7.02 (dd, 1H, $J = 1.5$, 8.1 Hz), 6.76 (mt, $J = 7.8$ Hz), 4.34 (s, 2H), 4.16–4.08 (m, 1H), 3.80–3.73 (m, 1H), 3.41 (dd, 1H, $J = 3.6$, 9.3 Hz), 3.23 (dd, 1H, $J = 6.7$, 9.4 Hz), 2.92–2.86 (m, 1H), 2.23–2.17 (m, 1H), 1.95–1.74 (m, 3H). ^{13}C NMR: 147.92, 138.47, 134.05, 128.22, 127.66, 127.38, 127.37, 122.50, 120.70, 117.38, 73.1, 72.2, 58.6, 53.4, 29.5, 24.3. EIMS: 345 (M^+, 1.2%), 347 (1.0%), 224 (100%), 226 (78%). Anal. Calcd for

$C_{18}H_{20}NBrO$: C, 62.44; H, 5.82; N, 4.05. Found: C, 62.90; H, 5.85; N, 3.87.

4.19. *tert*-Butyl bis[2-(*S*)-(2-methoxylmethylpyrrolidinyl)-phenyl] phosphine 6b

Into a solution of **18a** (135 mg, 0.50 mmol) in THF (5 mL) was added 2.5 M *n*-BuLi (0.22 mL, 0.55 mmol) at −78 °C, and the temperature was kept stable for 2 h with stirring. Into a solution was added *t*-$BuCl_2$ (50 mg, 0.30 mmol), and the low temperature maintained for 5 h before warming to rt. After stirring for 12 h at rt, the reaction was quenched with MeOH (20 mL). After concentration to dryness, the residue was taken in CH_2Cl_2 (50 mL) and washed with brine. The organic layer was separated and dried over Na_2SO_4. After filtration and concentration to dryness, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 20:1) to give a yellow oil (39%). $[\alpha]_D^{20} = -125$ (*c* 1.10, $CHCl_3$). IR: 2965, 2973, 1716, 1585, 1471, 1113, 950, 763 cm^{-1}. ^1H NMR: δ 7.80 (d, 1H, $J = 7.2$ Hz), 7.34–7.23 (m, 2H), 7.20–7.12 (m, 2H), 7.05–7.01 (m, 1H), 6.79–6.76 (m, 1H), 6.67 (t, 1H, $J = 7.3$ Hz), 4.40–4.33 (m, 1H), 3.97–3.87 (m, 2H), 3.55–3.45 (m, 2H), 3.31 (s, 3H), 3.24–3.17 (m, 1H), 3.12 (t, 1H, $J = 8.7$ Hz), 2.90 (s, 3H), 2.57 (dd, 1H, $J = 8.7$, 16.8 Hz), 2.49 (dd, 1H, $J = 3.7$, 8.8 Hz), 2.30–2.26 (m, 1H), 2.09–1.90 (m, 4H), 1.83–1.68 (m, 4H), 1.51–1.42 (m, 1H), 1.16 (d, 9H, $J = 12.3$ Hz). ^{13}C NMR: δ 154.4 (d, $J = 77.4$ Hz), 153.6 (d, $J = 90.6$ Hz), 138.7 (d, $J = 98.7$ Hz), 136.8 (d, $J = 14.4$ Hz), 133.5, 131.8 (d, $J = 96$ Hz), 128.8 (d, $J = 21.3$ Hz), 124.2 (d, $J = 3.9$ Hz), 122.4 (d, $J = 6.6$ Hz), 120.1, 116.9 (d, $J = 21.6$ Hz), 111.8, 75.36, 75.27, 60.9, 59.04, 58.60, 58.2 (d, $J = 5.4$ Hz), 56.3 (d, $J = 25.5$ Hz), 55.2 (d, $J = 80.1$ Hz), 31.0 (d, $J = 73.5$ Hz), 30.5, 29.7, 29.0 (d, $J = 63.9$ Hz), 24.1 (d, $J = 10.5$ Hz), 23.1. ^{31}P NMR: δ +0.88. ESIMS: 469.35 ($[M+H]^+$, 100%), 485.40 ($[M+H+O]^+$, 15%); HRMS: $[M+H]^+$ calcd for $C_{28}H_{42}N_2O_2P^+$ 469.2978, found 469.2980.

4.20. Bis-[2-(*S*)-(2-benzoxymethylpyrrolidinyl)phenyl]phenyl phosphine 6c

Following the procedure described for **6b** and using $PhPCl_2$, 21% yield. Colorless oil. $[\alpha]_D^{20} = -78$ (*c* 0.90, $CHCl_3$). IR: 2960, 2858, 1581, 1465, 1436, 1276, 1097, 740, 697 cm^{-1}. ^1H NMR: δ 7.36–7.15 (m, 19H), 6.93 (t, 1H, $J = 7.4$ Hz), 6.88–6.80 (m, 2H), 6.71–6.68 (m, 1H), 4.34–4.15 (m, 4H), 3.93–3.92 (m, 1H), 3.80–3.78 (m, 2H), 3.64–3.58 (m, 1H), 3.20 (dd, 1H, $J = 3.6$, 9.0 Hz), 3.04 (dd, 1H, $J = 3.6$, 9.0 Hz), 2.90–2.69 (m, 4H), 2.18–2.06 (m, 2H), 1.80–1.61 (m, 6H). ^{13}C NMR: δ 153.83 (d, $J = 5.1$ Hz), 153.55 (d, $J = 4.6$ Hz), 138.95, 138.75, 138.63, 138.53, 135.79, 135.64, 135.16, 134.97, 134.77, 134.54, 134.26, 134.09, 129.43, 129.28, 128.18, 128.13, 128.00, 127.95, 127.91, 127.37, 127.34, 127.31, 127.23, 123.20, 123.12, 121.10, 121.05, 120.41, 120.38, 73.34, 72.92, 72.90, 60.71, 60.67, 59.84, 59.80, 55.71, 55.58, 55.52, 55.41, 29.94, 29.88, 24.06, 23.96. ^{31}P NMR: δ −18.9. ESIMS: 641.45 ($[M+H]^+$, 100%), 663.45 ($[M+Na]^+$, 50%), 679.45 ($[M+K]^+$, 20%); HRMS: $[M+H]^+$ calcd for $C_{42}H_{46}N_2O_2P^+$ 641.3291, found 641.3289.

4.21. Typical procedure for the asymmetric allylic alkylation

Allyl palladium chloride dimer (2.9 mg, 0.008 mmol) **6a** (8–12 mg, 0.016–0.024 mmol) and NaOAc (1 mg) were dissolved in THF (1 mL), and the solution was stirred at rt for 15 min before 1,3-diphenyl 2-propenyl acetate (100 mg, 0.40 mmol) was introduced. The mixture was stirred at rt for another 15 min and cooled to the desired temperature before malonate (1.2 mmol) and BSA (0.3 mL, 1.2 mmol) were added. The reaction was monitored by TLC. The mixture was quenched by cold saturated NH_4Cl (2 mL) and extracted with EtOAc. The organic phase was dried over $MgSO_4$. After filtration and concentration, the residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc = 10:1) to give the product. The ees were determined by chiral HPLC or GC: Chiral HPLC, Chiracel OD-H, hexane/*i*-PrOH=99:1, flow rate 0.7 mL/min, $t_R = 17.4$ min, $t_S = 18.7$ min for **21**;[21] Chiral GC, CP-Chirasil-DEX-CB, 38.10 min, 38.53 min for **23**;[22] Chiral HPLC, Chiracel OD, hexane/*i*-PrOH = 25:1, flow rate 1.0 mL/min, $t_1 = 9.0$ min, $t_2 = 10.5$ min for **25**;[23] Chiral HPLC, Chiracel OF, hexane/*i*-PrOH = 100:2.5, flow rate 1.0 mL/min, $t_S = 15.1$ min, $t_R = 17.5$ min for **27a**;[24] and chiral HPLC, Chiracel AD, hexane/*i*-PrOH = 7:3, flow rate 0.7 mL/min, $t_R = 7.3$ min, $t_S = 8.3$ min for **27b**.

4.22. (*R*,*E*)-Dimethyl 2-(1,3-diphenylallyl)-2-fluoro-malonate 27b

Mp: 129–131 °C. $[\alpha]_D^{20} = +35$ (84% ee, *c* 0.22, $CHCl_3$). IR (KBr): 2855, 1764, 1743, 1496, 1458, 1429, 1295, 1266, 1242, 1134, 746, 704, 536 cm^{-1}. ^1H NMR: 7.41–7.22 (m, 10H), 6.58 (d, 1H, $J = 15.6$ Hz), 6.46 (dd, 1H, 8.7, 15.9 Hz), 4.53 (dd, 1H, $J = 8.8$, 31 Hz), 3.82 (s, 3H), 3.61 (s, 3H). ^{13}C NMR: 165.6 (d, $J = 25.2$ Hz), 165.2 (d, $J = 26.3$ Hz), 136.5 (d, $J = 16$ Hz), 134.2, 129.05, 129.02, 128.6, 128.5, 127.9, 127.8, 126.5, 124.6 (d, $J = 4.6$ Hz), 97.5 (d, $J = 208$ Hz), 53.8 (d, $J = 18.3$ Hz), 53.6, 53.2. ^{19}F NMR: −181 (d, $J = 32$ Hz). EIMS: 342 (M^+, 1%); HRMS: M^+ calcd for $C_{20}H_{19}O_4F^+$ 342.1262, found 342.1258.

4.23. Pd(II)-complex 28a

The mixture of ligand **6a** (49 mg, 0.10 mmol) and $PdCl_2(PhCN)_2$ (38 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) was stirred under Ar at rt for 1 h. Degassed hexane (8.0 mL) was then added slowly. The resulting yellow precipitate was collected and washed with hexane. The residual of benzonitrile was removed off under oil pump (15 Pa, rt) to give an orange powder (54 mg, 82% yield). Mp: 176–178 °C. $[\alpha]_D^{20} = +487$ (*c* 0.10, $CHCl_3$). IR (KBr): 3055, 2923, 1579, 1470, 1436, 1265, 1094, 925 cm^{-1}. ^1H NMR: 7.70–7.32 (m, 8H), 7.27–7.15 (m, 2H), 7.10–7.03 (m, 2H), 6.95–6.88 (m, 1H), 5.66–5.57 (m, 1H), 4.59–4.56 (m, 1H), 4.09–4.04 (m, 2H), 3.97–3.92 (m, 1H), 3.78–3.71 (m, 1H), 3.64–3.55 (m, 1H), 2.98 (s, 3H), 2.70–2.63 (m, 1H), 2.54 (s, 3H), 2.54–2.50 (m, 1H), 2.32–1.97 (m, 6H), 1.66–1.59 (m, 3H). ^{13}C NMR: 164.07 (d, C, $J = 17.2$ Hz), 154.03 (d, C, $J = 7.4$ Hz), 135.7–124.7 (Ar), 81.88 (NCH), 75.37 (OCH_2), 74.29 (OCH_2), 71.34 (NCH_2), 62.33 (NCH), 58.58 (OCH_3), 57.94 (OCH_3), 57.48 (NCH_2), 30.52 (CH_2), 29.00 (CH_2), 27.11 (CH_2), 23.40 (CH_2). ^{31}P

NMR: +36.6. MALDI-HRMS: $[M-Cl]^+$ calcd for $C_{30}H_{37}N_2O_2PClPd^+$ 629.1310, found 629.1307.

Acknowledgements

We thank the National Natural Science Foundation of China and Shanghai Municipal Committee of Science and Technology for financial support.

References

1. (a) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: Chichester, 2004, Chapter 4; (b) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; 2nd ed.; Ojima, I., Ed.; Wiley: New York, 2000; (c) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., Ed.; Wiley: New York, 2002; (d) Tsuji, J. *Pure Appl. Chem.* **1999**, *71*, 1539–1547.
2. (a) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385–393; (b) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361–4401; (c) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257–276; (d) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089–1122; (e) Reiser, O. *Angew. Chem., Int. Ed.* **1993**, *32*, 547–549; (f) Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355–364; (g) Trost, B. M.; van Vraken, D. L. *Chem. Rev.* **1996**, *96*, 395–422; (h) Williams, J. M. J. *Synlett* **1996**, 705–710; (i) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689–1708; (j) Helmchen, G. *J. Organomet. Chem.* **1999**, *576*, 203–214; (k) Pfaltz, A. *Chimia* **2001**, *55*, 708–714; (l) Hayashi, T. *J. Organomet. Chem.* **1999**, *576*, 195–202; (m) Dai, L.-X.; Tu, T.; You, S.-L.; Deng, W.-P.; Hou, X.-L. *Acc. Chem. Res.* **2003**, *36*, 659–667; (n) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944; (o) Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813–5837.
3. (a) Pfaltz, A.; Drury, W. J., III *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5723–5726; (b) Guiry, P. J.; Saunders, C. P. *Adv. Synth. Catal.* **2004**, *346*, 497–537; (c) Vyskocil, S.; Smrcina, M.; Hanus, V.; Polasek, M.; Kocovsky, P. *J. Org. Chem.* **1998**, *63*, 7738–7748.
4. (a) Suzuki, Y.; Abe, I.; Hiroi, K. *Heterocycles* **1999**, *50*, 89–94; (b) Hiroi, K.; Suzuki, Y.; Abe, I. *Tetrahedron: Asymmetry* **1999**, *10*, 1173–1188.
5. (a) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Heterocycles* **2000**, *53*, 1485–1488; (b) Mino, T.; Tanaka, Y.; Akita, K.; Anada, K.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 1677–1682; (c) Mino, T.; Tanaka, Y.; Sakamoto, M.; Fujita, T. *Tetrahedron: Asymmetry* **2001**, *12*, 2435–2440; (d) Mino, T.; Tanaka, Y.; Akita, K.; Sakamoto, M.; Fujita, T. *Heterocycles* **2003**, *60*, 9–13; (e) Tanaka, Y.; Mino, T.; Akita, K.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2004**, *69*, 6679–6687; (f) Mino, T.; Tanaka, Y.; Akita, K.; Saito, A.; Sakamoto, M.; Fujita, T. *Tetrahedron Lett.* **2003**, *44*, 4677–4679; *Tetrahedron Lett*. **2003**, *44*, 5759; (g) Mino, T.; Saito, A.; Tanaka, Y.; Hasegawa, S.; Sato, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 1937–1940; (h) Mino, T.; Sato, Y.; Saito, A.; Tanaka, Y.; Saotome, H.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2005**, *70*, 7979–7984.
6. (a) Kondo, K.; Kazuta, K.; Fujita, H.; Sakamoto, Y.; Murakami, Y. *Tetrahedron* **2002**, *58*, 5209–5214; (b) Horibe, H.; Kazuta, K.; Kotoku, M.; Kondo, K.; Okuno, H.; Murakami, Y.; Aoyama, T. *Synlett* **2003**, 2047–2051.
7. Yamagishi, T.; Ohnuki, M.; Kiyooka, T.; Masui, D.; Sato, K.; Yamaguchi, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3275–3279.
8. (a) Zhang, A.; Feng, Y.; Jiang, B. *Tetrahedron: Asymmetry* **2000**, *11*, 3123–3130; (b) Zhang, A.; Jiang, B. *Tetrahedron Lett.* **2001**, *42*, 1761–1763.
9. CCDC-291785 contains the supplementary crystallographic data for compound **10a**. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
10. (a) Quin, L. D. *A Guide to Organophosphorous Chemistry*; Wiley: New York, 2000; (b) Horner, L.; Balzer, W. D. *Tetrahedron Lett.* **1965**, *6*, 1157–1162; (c) Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7012–7023.
11. Similar observations of demethoxylation by trichlorosilane and cleavage of C–P bond with $LiAlH_4$ reduction during synthesis of MOP-type ligands: Higham, L. J.; Clarke, E. F.; Muller-Bunz, H.; Gilheany, D. G. *J. Organomet. Chem.* **2005**, *690*, 211–219.
12. (a) Ma, D.; Yao, J. *Tetrahedron: Asymmetry* **1996**, *7*, 3075–3078; (b) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* **1998**, *120*, 12459–12467; (c) Ma, D.; Xia, C. *Org. Lett.* **2001**, *3*, 2583–2586.
13. (a) Kostas, I. D.; Screttas, C. G. *J. Organomet. Chem.* **1999**, *585*, 1–6; (b) Kostas, I. D. *J. Organomet. Chem.* **2001**, *643*, 90–98; (c) Kostas, I. D. *J. Organomet. Chem.* **2001**, *626*, 221–226; (d) Kostas, I. D. *Inorg. Chim. Acta* **2003**, *355*, 424–427.
14. Kostas, I. D.; Screttas, C. G.; Raptopoulou, C. P.; Terzis, A. *Tetrahedron Lett.* **1997**, *38*, 8761–8764.
15. Job, G. E.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3703–3706.
16. Zhou, Q.-L.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467–4478.
17. (a) Zhang, F.; Song, Z. J.; Tschaen, D.; Volante, R. P. *Org. Lett.* **2004**, *6*, 3775–3777; (b) Kawasaki, T.; Kitazume, T. *Israel J. Chem.* **1999**, *39*, 129–131; (c) Yamazaki, T.; Umettani, H.; Kitazume, T. *Israel J. Chem.* **1999**, *39*, 193–205; (d) Komatsu, Y.; Sakamoto, T.; Kitazume, T. *J. Org. Chem.* **1999**, *64*, 8369–8374.
18. (a) Horner, L.; Simons, G. *Phosphorus Sulfur* **1983**, 189–210; (b) Levy, J. B.; Sutton, S. B.; Olsen, R. E. *Phosphorus, Sulfur Silicon Relat. Elem.* **1999**, *144*, 601–604.
19. Excess of large volume of H_2O_2 should be disposed with Na_2SO_3 or $Na_2S_2O_3$ before concentration.
20. (a) Ishikawa, T.; Uedo, E.; Tani, R.; Saito, S. *J. Org. Chem.* **2001**, *66*, 186–191; (b) Clement, J.-B.; Hayes, J. F.; Sheldrake, H. M.; Sheldrake, P. W.; Wells, A. S. *Synlett* **2001**, 1423–1427; (c) Hosokami, T.; Kuretani, M.; Higashi, K.; Asano, M.; Ohya, K.; Takasugi, N.; Mafune, E.; Miki, T. *Chem. Pharm. Bull.* **1992**, *40*, 2712–2719.
21. Trabesinger, G.; Albinati, A.; Feiken, N.; Kunz, R. W.; Pregosin, P. S.; Tschoerner, M. *J. Am. Chem. Soc.* **1997**, *119*, 6315–6323.
22. Allen, J. V.; Coote, S. J.; Dawson, G. J.; Frost, C. G.; Martin, C. J.; Williams, J. M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2065–2072.
23. You, S.-L.; Luo, Y.-M.; Deng, W.-P.; Hou, X.-L.; Dai, L.-X. *J. Organomet. Chem.* **2001**, *637*, 845–849.
24. Farrell, A.; Goddard, R.; Guiry, P. J. *J. Org. Chem.* **2002**, *65*, 4209–4217.