DOI: 10.1002/ejoc.201100259

Helicene-Based Phosphite Ligands in Asymmetric Transition-Metal Catalysis: Exploring Rh-Catalyzed Hydroformylation and Ir-Catalyzed Allylic Amination

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Keywords: Asymmetric catalysis / Helical structures / P ligands / Hydroformylation / Amination

Starting from the optically pure [6]helicene-like alcohol (*P*,3*S*)-3-methyl-4-(4-methylphenyl)-1,3,6,7-tetrahydrobenzo-[*c*]benzo[5,6]phenanthro[4,3-*e*]oxepin-14-ol, four helical phosphites were prepared from the corresponding chlorophosphites. These ligands containing parent or substituted 1,3,2-dioxaphospholan-2-yl or dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl moieties were applied to the asymmetric hydroformylation of terminal alkenes catalyzed by $Rh(acac)(CO)_2$ and the asymmetric allylic amination of cinnamyl-type carbonates catalyzed by $[Ir(cod)Cl]_2$. The helical phosphite containing the dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl group was most successful in the asymmetric hydroformylation of styrene, leading to moderate enantiomeric excess values (up to 32 % *ee*), high regioselectivity in favor of the branched product, and mostly high conversion, whereas the helical ligand containing the 4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-yl fragment was most effective in asymmetric allylic aminations, exhibiting high enantioselectivity (up to 94 % *ee*), excellent regioselectivity in favor of the branched products, and good reactivity. This study represents the first use of helicene-like ligands in asymmetric reactions, including hydroformylation and allylic amination, and the promising results indicate the potential of the helicene moieties as chiral inductors.

Introduction

Myriads of chiral ligands have successfully been explored in asymmetric transition-metal catalysis.[1] In the quest to reach the highest enantioselectivity, turnover frequency, catalyst lifetime, and effective recycling, the chiral ligands screened in homogeneous catalysis have been of virtually unlimited diversity. When classifying ligands by the type of the element(s) of chirality comprised, practically all of them are molecules exhibiting central, axial, or planar chirality. Among them, a gradually increasing group of "privileged ligands"[2,3] plays a pivotal role. Ligand "blockbusters", for example, DuPhos,[4] BINAP,[5] Solvias ferrocenes,[6] salen ligands,[7] and phosphoramidite ligands[8] (vide infra), have gained remarkable fame and glory,[9,10] thus documenting the exceptionality of "priviledged ligands" as well as the usefulness of the chirality elements mentioned above.

Keeping the focus on ligand scaffolds, the remaining type of chirality, that is, helicity, has rarely been used in asymmetric catalysis. Indeed, the efficiency of chirality induction by using helical ligands has virtually been unexplored. This fact can be illustrated by the limited number of examples for which ligands derived from helicenes[11] are explored.[12] After it was originally prepared by Brunner et al. in racemic form,[13] Reetz et al. pioneered the utilization of optically active PHelix[14] (**1**, Figure 1) in a Rh-catalyzed asymmetric hydrogenation of the ester of itaconic acid (reaching up to 39 % *ee*).[14] Helical diphosphane **1** was used by Reetz et al. in the Pd-catalyzed kinetic resolution of a racemic allylic substrate (obtaining up to >99 % *ee* for the starting material and up to 86 % *ee* for the substitution product).[15] Soai et al.[16] and later Soai, Maiorana et al.[17] reported remarkable asymmetric induction by unfunctionalized helicenes, for example, **2**, or thiahelicenes, for example, **3**, in the enantioselective addition of diisopropylzinc to pyrimidine-5-carbaldehyde (in conjunction with asymmetric autocatalysis, achieving up to 95 % *ee* with **2** or 99 % *ee* with **3**). Katz et al. successfully used [5]HELOL (**4**) in the addition of diethylzinc to aromatic aldehydes (receiving up to 81 % *ee*).[18] In this case, however, the helicene ligand exhibits mixed chirality, as **4** contains two helical aromatic units linked by a single bond, which introduces a chirality axis typical for 1,1′-biaryls. Furthermore, Yamaguchi et al. studied helicene phosphites, for example, **5**, being a medley of three types of chirality: helical, axial, and central.[19] They observed a significant effect of matched/mismatched helical and axial chirality on the stereochemical outcome of the Rh-catalyzed enantioselective hydrogenation of di-

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201100259.

methyl itaconate (monitoring up to 96%*ee*). Recently, Takenaka et al. used helical pyridine *N*-oxides **6**–**8** as organocatalysts in a desymmetrization of *meso*-epoxides (reaching up to 94%*ee*)[20a,20b] and the enantioselective propargylation of aldehydes with allenyltrichlorosilane (receiving up to 96%*ee*).[20c] Moreover, they applied helical 2-aminopyridinium ions **9** and **10** as hydrogen-bond donors to an acid-catalyzed asymmetric Friedel–Crafts reaction, reporting high enantioselectivities up to 96%*ee*.[21] We have demonstrated the organocatalytic activity of parent 2-aza[6]helicene **11** in asymmetric acyl transfer reactions to describe a moderate selectivity factor (of up to 10).[22] Recently, Carbery et al. developed helicene DMAP Lewis base catalyst **12**, which exhibited excellent reactivity as well as selectivity in the kinetic resolution of chiral secondary alcohols (reaching a selectivity factor of up to 116).[23] Thus, to the best of our knowledge, there are no other examples of true helicene-based ligands that are used in asymmetric transition-metal catalysis or organocatalysis.

In addition to the helical ligands discussed so far, newly emerging family of monodentate phosphites **13**, phosphinites **14**, and phosphoramidites **15** (Figure 2) derived from BINOL can definitely not be neglected. Soon after the independent discovery by Reetz et al. (cf. **13**),[24] Pringle et al. (cf. **14**),[25] and Feringa et al. (cf. **15**)[26] in 2000 that such compounds are excellent chiral ligands in Rh-catalyzed olefin hydrogenations, they started to attract considerable attention (owing to their chirality induction efficiency, versatility, facile availability, and possibility to apply new combinatorial approaches to asymmetric catalysis).[8] Despite the fact that the axially chiral 2,2′-dihydroxy-1,1′-binaphthyl moiety is embodied in their scaffolds, they can also be viewed as hetero[5]helicene counterparts,[27] having a 1,3,2-dioxaphosphepine unit incorporated into the helical backbone.

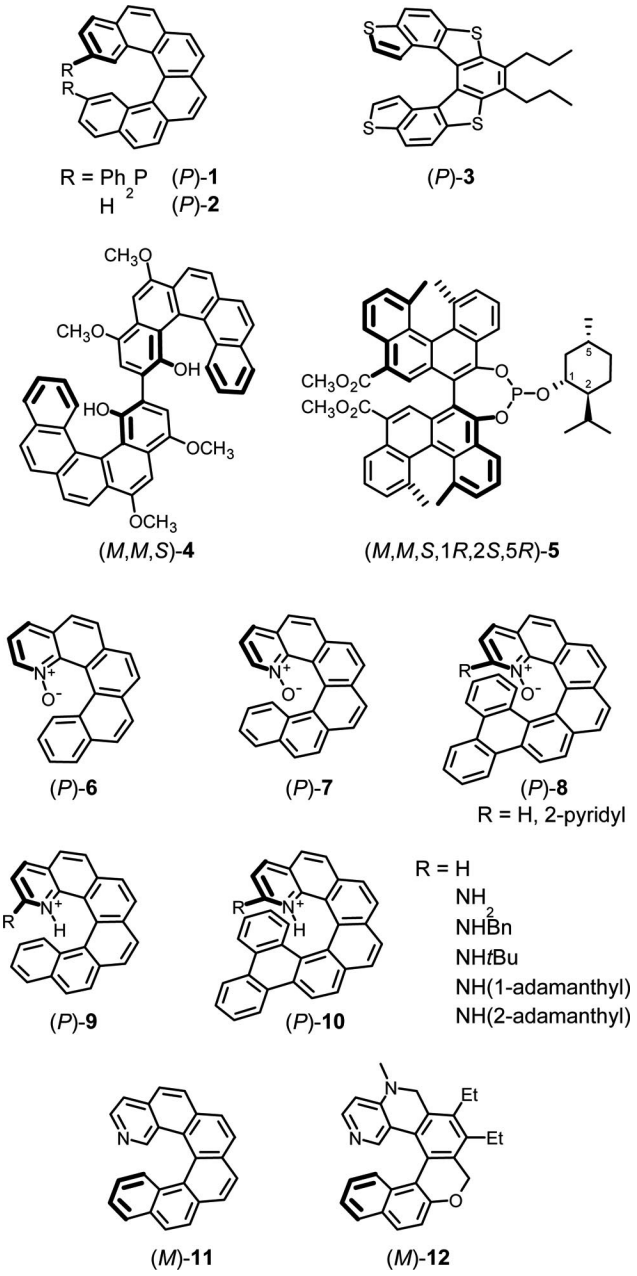


Figure 1. Helical ligands used in asymmetric catalysis.

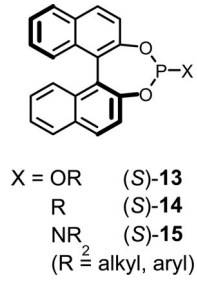


Figure 2. Helicene congeners used in asymmetric catalysis.

Apparently, helically chiral ligands can serve as effective chiral inducers in asymmetric catalysis, competing successfully against "traditional" ligands possessing central, axial, or planar chirality. As the former have not been systematically studied and, accordingly, their potential has not been fully explored, further effort in this direction is required.

Results and Discussion

In conjunction with the progress in the synthesis of helicenes and their congeners based on general triyne [2+2+2] cyclotrimerization methodology, we already attempted the preparation of possible ligands such as racemic 3-diphenylphosphanyl[6]helicene **16**[28] and optically pure 1-aza[6]helicene **17** and 2-aza[6]helicene **11**.[29] Even though they have not yet been used in asymmetric transition-metal catalysis, we have demonstrated the ability of these compounds to form intriguing complexes with silver. Recently, we established the basis of the diastereoselective synthesis of helicene-like molecules.[27a–27d] Having developed reliable access to optically pure alcohol **18** (Figure 3) on a preparative scale,[27b] we could attempt the exploitation of this unique helical scaffold in asymmetric catalysis. We have proposed that placement of a coordinating group on the most sterically congested position of the helical backbone

(i.e., C-1 of the terminal benzene ring) would lead, after metal coordination, to the well-defined chiral environment of the reaction center and, accordingly, to a considerably large enantiomeric excess value for the reaction studied. In this paper, we report on the preparation of a series of new helical phosphites **23**–**26** (Scheme 1) derived from alcohol **18**, which we subsequently explored in Rh-catalyzed hydroformylation and Ir-catalyzed allylic amination reactions.

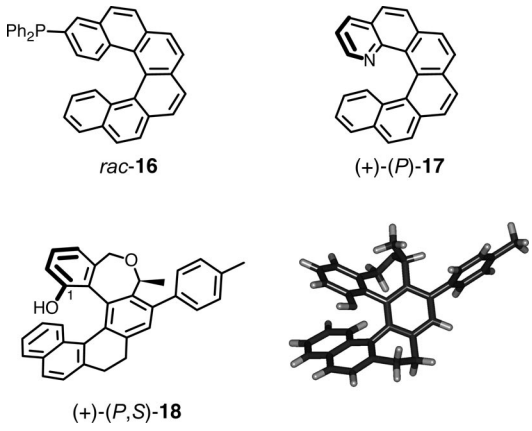


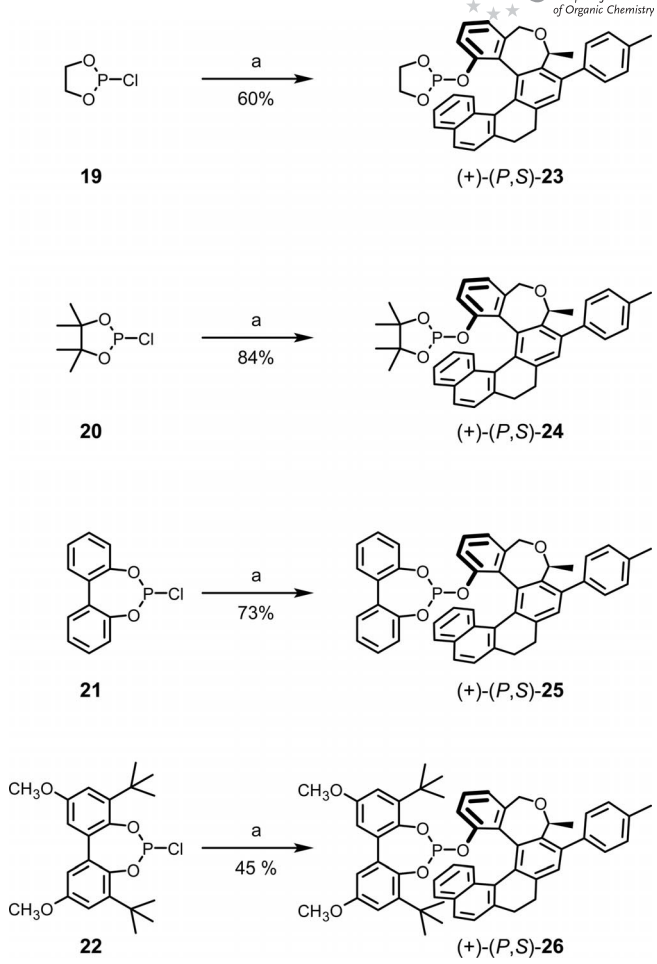
Figure 3. Helical phosphane *rac*-**16**, azahelicene (+)-(*P*)-**17** and helical alcohol (+)-(*P*,*S*)-**18** with its X-ray structure.[27b]

Synthesis of Helical Phosphites

The asymmetric synthesis of alcohol (+)-(*P*,*S*)-**18** was recently published.[27b] It employs optically pure (*S*)-but-3-yn-2-ol as a chiral building block, which is commercially available in both enantiomeric forms. Although the methyl ether of (+)-(*P*,*S*)-**18** can undergo thermal epimerization to reach the equilibrium (*P*,*S*)/(*M*,*S*) = 87:13; the barrier of 27.7 kcal/mol to the (*P*,*S*)→(*M*,*S*) process (26.4 kcal/mol for the backward one)[27b] is high enough to prevent any configurational scrambling at room temperature or at elevated temperatures for a limited period of time.

The preparation of each helical phosphite **23**–**26** was a single-step operation (Scheme 1). After optimizing the reaction conditions, we found that sodium alcoholate generated from optically pure (+)-(*P*,*S*)-**18** reacted smoothly with commercially available chlorophosphites **19** and **20** or chlorophosphites **21**[30] and **22**,[31] whose syntheses have been described in the literature. The formation of phosphites could be easily monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy, as the conversion of chlorophosphites into phosphites was indicated by a significant shift in the signal of the phosphorus atom (for the chemical shifts of phosphorus atoms in chlorophosphites **19**–**22** and phosphites **23**–**26**, see the Supporting Information).[30–33] Phosphites **23**–**26** were obtained in moderate to good yields, reflecting in this way their stability during the workup and subsequent fast filtration through a pad of silica.

The conformational behavior of phosphites **23**–**26** requires more detailed analysis. The (*P*,*S*) helicene platform is well defined, because it is rather rigid. However, the P–O–C junction between the helicene platform and a phosphite moiety is flexible to some extent. While the rotation around the O–C bond (Figure 4, a) is limited because of steric reasons, the rotation of the phosphite moiety around the P–O bond (Figure 4, b) is less restricted. In **23**, there are two resolved methylene signals of the 1,3,2-dioxaphospholane unit in the ^{13}C NMR spectrum (63.70 and 63.72 ppm), indicating a partially restricted rotation around the P–O bond (Figure 4, b). Similarly, the 4,4,5,5-tetramethyl-1,3,2-dioxaphospholane unit in **24** displays non-equivalency of the four methyl groups in the ^{1}H and ^{13}C NMR spectra (1.00, 1.12, 1.14, 1.24 ppm and 24.08, 24.95, 25.34, 25.85 ppm, respectively). The presence of an axially chiral dibenzo[*d*,*f*][1,3,2]dioxaphosphepine unit in **25** raises the question of its configuration. As there is only one set of signals in the ^{1}H and ^{13}C NMR spectra, either rapid interconversion between the (R_a) and (S_a) atropoisomers or preferential formation of only one of them (cf. Waldvogel et al.[31]) should occur along with free rotation of the phosphite moiety around the P–O bond (Figure 4, b). Similarly, **26** displays one set of signals except for the resolved signals of the two methoxy groups in the ^{1}H and ^{13}C NMR spectra (3.81, 4.00 ppm and 55.58, 55.77 ppm, respectively) and two



Scheme 1. Synthesis of helical phosphites **23**–**26**. Reagents and conditions: (a) (+)-(*P*,*S*)-**18** (1.0 equiv.), NaH (2.5–4.0 equiv.), chlorophosphite **19**–**22** (1.6 equiv.), THF, 0 °C to room temp., 2 h.

quaternary carbon atoms of the *tert*-butyl groups in the ^{13}C NMR spectrum (34.98, 35.17 ppm). Such features might be attributed to a partially hindered revolution of the phosphite moiety around the P–O bond (Figure 4, b).

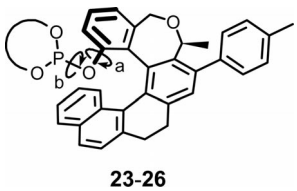


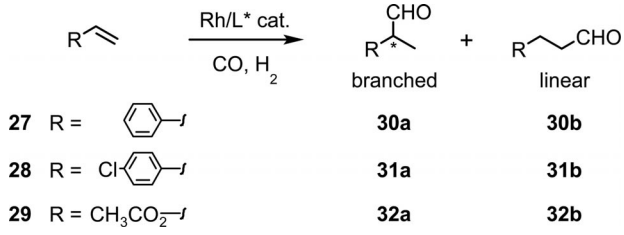
Figure 4. Conformational freedom of phosphites **23**–**26**.

Rh-Catalyzed Hydroformylation

The hydroformylation of alkenes under transition-metal catalysis represents an ideal chemical process from the point of view of atom economy as well as the exploitation of inexpensive feedstock.[34] Terminal olefins are uniformly used as substrates for asymmetric hydroformylation reactions along with rhodium catalysts and chiral (bis)phosphane/(bis)-phosphite ligands.[34,35] Despite the significant effort recently devoted to the further development of asymmetric hydroformylations,[36] the question of the chirality induction efficiency by helical ligands has so far remained unanswered.

Accordingly, we decided to screen the regioselectivity and enantioselectivity of the Rh^I-catalyzed hydroformylation of terminal alkenes **27**–**29** in the presence of helical phosphites **23**–**26** (Table 1). We started with the hydroformylation of the model substrate styrene (**27**) to find the conditions where the widely used catalyst $Rh(acac)(CO)_2$ in combination with phosphites **23**–**26** is sufficiently active but where the reaction proceeds under mild enough conditions to prevent any undesired side reaction of the starting material or products (i.e., hydrogenation, isomerization, polymerization, aldol condensation). The test experiments showed that the reaction catalyzed by the Rh^I–**25** (1:2.5) system went to completion at 50 °C within 20 h (with a yield of 97%), whereas at room temperature the reaction slowed significantly (with a yield of 50%). For the initial hydroformylation experiments in toluene, we choose the partial pressure of CO and H_2 to be 10:10 bar (in the case of **27**, regioselectivity can be affected by changing the CO/H_2 partial pressure only at high temperature). Employing helical ligands **23**–**26**, the hydroformylation of **27** proceeded with high regioselectivity (up to 95:5) in favor of branched product **30a**[36a] with enantiomeric excess values ranging from 0 to 29% (Table 1, Entries 1–3, 8). Although ligand **25** exhibited a moderate level of chirality induction, ligands **23**, **24**, and **26** were ineffective in this regard. By changing the solvent from toluene to dichloromethane, the moderate enantioselectivity was found to drop slightly (Table 1, Entry 4). To examine the effect of the Rh^I-to-ligand ratio, we changed this proportion from 1:2.5 to 1:5 and 1:10 (Table 1, Entries 4–6). However, we observed that a higher loading of the ligand led to a lower enantiomeric excess value of **30a**. After other optimizations, we monitored the best stereochemical outcome of an asymmetric hydroformylation of styrene **27** (32%*ee*) when the reaction was performed in the presence of $Rh(acac)(CO)_2$ (0.5 mol-%) and **25** (1.25 mol-%) in toluene under partial pressure of CO (40 bar) and H_2 (40 bar) at 40 °C (Table 1, Entry 7). The hydroformylation of 4-chlorostyrene (**28**) under Rh^I catalysis with ligands **23**–**26** was found to proceed with excellent regioselectivity and a low or moderate enantioselectivity to afford **31a**[37,38] (Table 1, Entries 9–12). Similar to the hydroformylation of **27**, helical phosphite **25** was most effective in chirality induction (20%*ee*). The hydroformylation of vinyl acetate **29** to afford **32a**[37b] differed from the abovementioned examples in several aspects (Table 1, Entries 13–16). Electronically rich terminal alkene **29** was reactive like **27** and **28** (with ligands **23** and **25**; Table 1, Entries 13 and 15) or slightly less reactive (with ligands **24** and **26**; Table 1, Entries 14 and 16), which resulted in conversions around 70% within the 20-hour reaction period. As for **29**, the acetone medium and the higher-ligand loading (5 mol-%) were found to be superior to toluene and a lower loading of the ligand, respectively, in terms of reaching higher regioselec-

Table 1. The asymmetric hydroformylation of alkenes **27**–**29**.[a]



Entry	Alkene	Ligand	Product (% conv.)[b]	Branched/linear [c]	*ee* [%][d]
1	**27**	**23**	**30** (96)	91:9	5 (*S*)
2	**27**	**24**	**30** (93)	92:8	7 (*S*)
3	**27**	**25**	**30** (96)	93:7	29 (*S*)
4[e]	**27**	**25**	**30** (98)	94:6	24 (*S*)
5[e]	**27**	**25**[f]	**30** (99)	98:2	18 (*S*)
6[e]	**27**	**25**[g]	**30** (97)	94:6	16 (*S*)
7[h]	**27**	**25**	**30** (99)	n.d.	32 (*S*)
8	**27**	**26**	**30** (96)	95:5	0
9	**28**	**23**[f]	**31** (98)	99:1[i]	6 (*S*)
10	**28**	**24**[f]	**31** (96)	97:3[i]	6 (*S*)
11	**28**	**25**[f]	**31** (98)	98:2	20 (*S*)
12	**28**	**26**[f]	**31** (97)	98:2	11 (*S*)
13[j]	**29**	**23**[f]	**32** (98)	67:33	4 (*S*)
14[j]	**29**	**24**[f]	**32** (70)	91:9	25 (*S*)
15[j]	**29**	**25**[f]	**32** (99)	92:8	15 (*S*)
16[j]	**29**	**26**[f]	**32** (69)	86:14	0

[a] $Rh(acac)(CO)_2$ (1 mol-%), (*P*,*S*)-ligand (2.5 mol-%), toluene, CO (10 bar), H_2 (10 bar), 50 °C, 20 h. [b] Determined by GC (Chrompack DB-1701 column) by using dodecane as internal standard. [c] Determined by GC. [d] The enantiomeric excess value of the branched isomer was determined by GC (Beta Dex 225 column by Supelco), the absolute configuration of the prevailing enantiomer is given in parentheses; for the assignment of the absolute configuration, see ref.[37,38]. [e] In dichloromethane. [f] 5 mol-% of the ligand. [g] 10 mol-% of the ligand. [h] $Rh(acac)(CO)_2$ (0.5 mol-%), ligand (1.25 mol-%), toluene, CO (40 bar), H_2 (40 bar), 40 °C, 20 h. [i] Determined by ^1H NMR spectroscopy. [j] In acetone.

tivity and enantioselectivity. In the case of the hydroformylation of **29**, ligand **24** was the most effective in chirality induction to provide branched product **32a** with a moderate enantiomeric excess value (25%*ee*) and with high regioselectivity (Table 1, Entry 14).

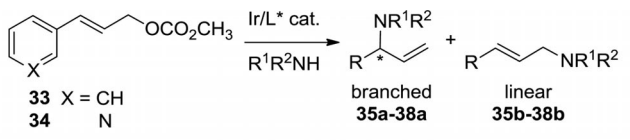
Ir-Catalyzed Allylic Amination

The fact that secondary allylamines can advantageously be utilized in the synthesis of natural products raises the question of how to prepare these valuable building blocks in a nonracemic form. Recently, significant progress has been achieved in transition-metal catalyzed asymmetric allylic aminations, where chiral Ir^{I} complexes have played a prominent role.[39] Axially chiral BINOL-derived phosphoramidites[40] have been identified as privileged ligands to generate a catalytically active species after the coordination of Ir^{I} followed by base-induced C–H activation.[41] The high regioselectivity (in favor of the branched isomer) and enantioselectivity that are usually observed, the detailed mechanistic insight, along with the simplicity of the reaction protocol make asymmetric allylic aminations an attractive synthetic tool. Although various chiral ligands have been examined, the helical ones are still awaiting application in this reaction.

To examine the regioselectivity and enantioselectivity of asymmetric allylic aminations in the presence of $[Ir(cod)Cl]_2$ and helical phosphites **23**–**26**, we treated cinnamyl carbonate **33**[42] and (pyridinyl)allyl carbonate **34**[43] with a primary (benzylamine) or secondary amine (pyrrolidine, piperidine, or morpholine; Table 2). Initial experiments with **33** and benzylamine carried out in THF at 50 °C showed that the use of ligand **24** resulted in a high enantiomeric excess value of **35a**[40b] (93%*ee*), whereas **25** provided moderate enantioselectivity and **23** was ineffective in this regard (Table 2, Entries 1, 2 and 4). We observed excellent regioselectivity in favor of branched product **35a**, but the yields were typically low. Ligand **26** completely impeded the reaction and, therefore, was not further tested (Table 2, Entry 5).

We found that the problem with the low reactivity could be resolved simply by replacing THF with dichloromethane. Indeed, performing the reaction with **24** in this solvent at 35 °C led to a comparable enantioselectivity (90%*ee*), but the preparative yield was significantly increased (95%; Table 2, Entry 3). The reaction of **33** with pyrrolidine as nucleophile in dichloromethane followed the trends mentioned above. Here, we observed the exclusive formation of branched product **36a**[40b,43a] in the presence of phosphites **23**–**25**, but only **24** gave rise to a high enantioselectivity (up to 92%*ee*), whereas **23** and **25** provided moderate and no enantiomeric excess, respectively (Table 2, Entries 6, 8, and 9). Similarly, dichloromethane was found to be superior to THF in terms of the reactivity of **33** (Table 2, Entry 7 vs. 8). Like pyrrolidine, morpholine reacted with **33** in dichloromethane to afford predominantly branched product **37a**[40b,44] (accompanied by a small amount of linear isomer **37b**), whose enantiomeric excess was high when using phosphite **24** (91%*ee*) or **23** (79%*ee*) but low with phosphite **25** (Table 2, Entries 10, 12, and 13). As described above, the use of THF led to a diminished yield of **37a**; whereas the enantioselectivity remained unaffected (Table 2, Entry 11 vs. 12). The reaction of the pyridine analogue **34** of cinnamyl carbonate **33** with piperidine in dichloromethane provided the best results, as the use of phosphite **24** led to excellent regioselectivity (only branched product **38a**[43a] was detected), high enantioselectivity (94%*ee*), and a good yield (Table 2, Entry 15). Similarly to the examples mentioned above, phosphites **23** and **25** were less successful, as they yielded only a moderate enantiomeric excess value of **38a** (Table 2, Entries 14 and 16). The efficiency of phosphite **24** within the series **23**–**26** leading to the best enantioselectivities along with predominantly the highest reactivities regardless of the substrate and N nucleophile used might be related to its proposed C–H activation to generate a catalytically active P–C-chelated iridium species[41] (owing to the presence of the CH_3 groups in the dioxaphospholanyl moiety).

Table 2. Asymmetric allylic amination of allyl carbonates **33** and **34**.[a]



Entry	Allyl carbonate	R^1R^2NH	Ligand	Product (% yield)[b]	Branched/linear[c]	*ee* [%][d]
1	**33**		**23**	**35** (11)	>97:3	0
2	**33**		**24**	**35** (25)	>97:3	93 (*S*)
3[e]	**33**	$PhCH_2NH_2$	**24**	**35** (95)	>97:3	90 (*S*)
4	**33**		**25**	**35** (4)	>97:3	39 (*S*)
5	**33**		**26**	n.r.		
6[e]	**33**		**23**	**36** (13)	>99:1	56 (+)
7	**33**	NH	**24**	**36** (39)	>99:1	89 (+)
8[e]	**33**		**24**	**36** (60)	>99:1	92 (+)
9[e]	**33**		**25**	**36** (44)	>99:1	0
10[e]	**33**		**23**	**37** (70)	>95:5	79 (+)[f]
11	**33**	O NH	**24**	**37** (52)	>95:5	91 (+)[f]
12[e]	**33**		**24**	**37** (69)	>95:5	91 (+)[f]
13[e]	**33**		**25**	**37** (89)	>95:5	19 (+)[f]
14[e]	**34**		**23**	**38** (44)	>99:1	46 (+)[g]
15[e]	**34**	NH	**24**	**38** (70)	>99:1	94 (+)[g]
16[e]	**34**		**25**	**38** (65)	>99:1	40 (+)[g]

[a] $[Ir(cod)Cl]_2$ (1.0 mol-%), (*P*,*S*)-ligand (2.0 mol-%), amine (1.3–1.6 equiv.), THF, 50 °C, 2 h to 3 d. [b] Isolated. [c] Determined by ^1H NMR spectroscopy. [d] Determined by HPLC (Chiracel OD-H column by Daicel), the absolute configuration or the sense of optical rotation of the prevailing enantiomer is given in parentheses; for the assignment of the absolute configuration, see ref.[37] [e] In dichloromethane at 35 °C. [f] Determined by HPLC (Chiracel OJ-H column by Daicel). [g] Determined by ^1H NMR spectroscopy with a TFAE shift reagent.

Conclusions

Here we have described the synthesis of four new [6]helicene-related phosphites (+)-(*P*,*S*)-**23**–**26** starting from optically pure helical alcohol (+)-(*P*,*S*)-**18** and corresponding chlorophosphites **19**–**22**. We have applied these helically chiral phosphites to the asymmetric Rh^I-catalyzed hydroformylation of terminal alkenes and to asymmetric Ir^I-catalyzed allylic aminations. Ligand (+)-(*P*,*S*)-**25** containing the biphenyl-2,2′-diol fragment in the phosphite moiety was the most successful ligand in asymmetric hydroformylation reactions, leading to moderate enantiomeric excess values (up to 32%*ee* in the hydroformylation of **27**), high regioselectivity in favor of the branched products, and mostly high conversions. In contrast, ligand (+)-(*P*,*S*)-**24** containing the pinacol fragment in the phosphite moiety was most effective in an asymmetric allylic amination, exhibiting high enantioselectivity (up to 94%*ee* in the amination of the cinnamyl-type substrates), excellent regioselectivity in favor of the branched products, and good reactivity. This study represents the first use of helicene-like ligands in asymmetric reactions such as hydroformylation and allylic amination. The promising results indicate the potential of the helicene moieties as chiral inductors, whose use in asymmetric catalysis has remained rather unexplored.

Experimental Section

General: ^1H and ^{13}C NMR spectra were measured at 499.88 and 125.71 MHz, respectively, in $CDCl_3$ with TMS as an internal standard. ^{31}P NMR spectra were measured at 121.50 or 161.98 MHz in $CDCl_3$ with H_3PO_4 as an external standard. HMBC experiments were set up for $J_{C,H}$ = 5 Hz. For the correct assignment of both the ^1H and ^{13}C NMR spectra of the key compounds, COSY, HMQC, and HMBC experiments were performed. The IR spectra were measured in CCl_4. The APCI mass spectra were recorded by using a ZQ micromass mass spectrometer (Waters) equipped with an ESCi multimode ion source and controlled by MassLynx software. Methanol was used as the solvent. Accurate mass measurements were obtained by APCI MS. Optical rotations were measured in CH_2Cl_2 by using an Autopol IV (Rudolph Research Analytical) instrument. For gas chromatographic analyses, a Carlo Erba HRGC Mega2 Series MFC 800 chromatograph with a Carlo Erba EL 580 flame-ionization detector (FID) was used with dodecane as an internal standard. Separations were performed on a Chrompack DB-1701 column (25 m × 0.32 mm × 1.0 mm). Enantiomeric excess values were determined with a GC Beta Dex 225 column from Supelco or by HPLC with a Chiracel OD-H (250 × 4.6 mm) or a Chiracel OJ-H (250 × 4.6 mm) column by Daicel using heptane/2-propanol as the mobile phase or by ^1H NMR spectroscopy by using TFAE as a shift reagent. Commercially available, reagent-grade materials were used as received. Dichloromethane was distilled from calcium hydride under an atmosphere of argon, and THF was freshly distilled from sodium/benzophenone under an atmosphere of nitrogen. TLC was performed on Silica gel 60 F_{254} coated aluminum sheets (Merck); spots were detected by using a solution of $Ce(SO_4)_2{\cdot}4H_2O$ (1%) and $H_3P(Mo_3O_{10})_4$ (2%) in sulfuric acid (10%) or a solution (2.5%) of $NH_4SCN/CoCl_2$ (3:1) in water. Flash chromatography was performed on Silica gel 60 (0.040–0.063 mm, Fluka). $Rh(acac)(CO)_2$, $[Ir(cod)Cl]_2$, **19**, **20**, and **27**–**29** were purchased; (+)-(*P*,*S*)-**18**,[27b] **21**,[30] **22**,[31] **33**,[42] and **34**[43] were synthesized according to procedures in the literature.

(+)-(*P*,3*S*)-14-(1,3,2-Dioxaphospholan-2-yloxy)-3-methyl-4-(4-methylphenyl)-1,3,6,7-tetrahydrobenzo[*c*]benzo[5,6]phenanthro[4,3-*e*]oxepine (23): A Schlenk flask was charged with NaH (80% suspension in mineral oil, 24 mg, 1.014 mmol, 3.8 equiv.) and put under an atmosphere of argon. THF (1 mL) was added, and the stirred suspension was cooled to 0 °C. A solution of (+)-(*P*,3*S*)-**18** (100 mg, 0.213 mmol) in THF (1.5 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 15 min, then warmed slowly to room temperature and stirred for 45 min. Subsequently, the mixture was cooled again to 0 °C and phosphorochloridite **19** (30 μL, 0.342 mmol, 1.6 equiv.) was added dropwise. The reaction mixture was warmed slowly to room temperature over 3 h, after which triethylamine (300 μL) was added. The solvent was removed in vacuo, and the crude product was purified by chromatography on silica gel (cyclohexane/diethyl ether/acetone, 80:10:10 + 3% Et_3N) to afford (+)-(*P*,3*S*)-**23** (90 mg, 76%) as an amorphous solid. $[a]_{589}^{22}$ = +369 (*c* = 0.09, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.62 (d, *J* = 7.1 Hz, 3 H), 2.43 (s, 3 H), 2.73–2.81 (m, 1 H), 2.87–2.94 (m, 1 H), 3.08–3.15 (m, 2 H), 3.76–3.86 (m, 4 H), 4.74 (d, *J* = 11.4 Hz, 1 H), 5.01 (d, *J* = 11.4 Hz, 1 H), 5.31 (q, *J* = 7.1 Hz, 1 H), 6.36 (dd, *J* = 8.1, 1.3 Hz, 1 H), 6.73 (ddd, *J* = 8.6, 6.7, 1.4 Hz, 1 H), 6.90 (dd, *J* = 8.1, 7.5 Hz, 1 H), 7.03 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 1 H), 7.11 (dd, *J* = 7.5, 1.3 Hz, 1 H), 7.18 (dq, *J* = 8.6, 1.0, 1.0, 1.0 Hz, 1 H), 7.28 (m, 2 H), 7.40 (d, *J* = 1.1 Hz, 1 H), 7.40 (m, 2 H), 7.42 (d, *J* = 8.0 Hz, 1 H), 7.56 (dd, *J* = 8.1, 1.4 Hz, 1 H), 7.63 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.21 (q), 22.53 (q), 30.55 (t), 30.70 (t), 63.70 (t), 63.72 (t), 67.87 (t), 72.40 (d), 119.75 (d), 123.59 (d), 123.79 (d), 124.53 (d), 125.56 (d), 125.93 (d), 127.02 (d), 127.39 (d), 128.92 (s), 128.92 (d), 128.99 (2 d), 129.28 (d), 132.40 (s), 132.60 (s), 132.84 (s), 133.61 (s), 134.05 (s), 135.56 (s), 136.67 (s), 138.70 (s), 138.73 (s), 138.94 (s), 140.58 (s), 141.32 (s), 147.70 (s) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 127.25 (s) ppm. IR (CCl_4): $\tilde{\nu}$ = 3053 (m), 1622 (vw, sh.), 1612 (w), 1596 (w, sh.), 1587 (w), 1578 (w), 1514 (m), 1465 (s), 1438 (m), 1380 (m, sh.), 1368 (s), 1303 (w, sh.), 1293 (m), 1277 (m), 1249 (s), 1238 (m), 1213 (m), 1181 (m), 1159 (m, sh.), 1138 (w), 1110 (w), 1090 (vs), 1073 (s), 1037 (m, sh.), 1022 (m), 1012 (s), 888 (m), 863 (w), 847 (m), 837 (m), 822 (vs), 729 (m), 701 (w), 565 (w), 545 (w), 529 (w), 492 (w) cm^{-1}. MS (APCI): *m*/*z* = 559 $[M + H]^+$, 526, 451, 391, 317, 301, 282, 254. HRMS (APCI): calcd. for $C_{36}H_{32}O_4P$ $[M + H]^+$ 559.2038; found 559.2031.

(+)-(*P*,3*S*)-3-Methyl-4-(4-methylphenyl)-14-[(4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-yl)oxy]-1,3,6,7-tetrahydrobenzo[*c*]benzo-[5,6]phenanthro[4,3-*e*]oxepine (24): A Schlenk flask was charged with NaH (80% suspension in mineral oil, 24 mg, 1.014 mmol, 3.8 equiv.) and put under an atmosphere of argon. THF (1 mL) was added, and the stirred suspension was cooled to 0 °C. A solution of (+)-(*P*,3*S*)-**18** (100 mg, 0.213 mmol) in THF (1.5 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 15 min, then warmed slowly to room temperature and stirred for 45 min. Subsequently, the mixture was cooled again to 0 °C and phosphorochloridite **20** (54 μL, 0.342 mmol, 1.6 equiv.) was added dropwise. The reaction mixture was warmed slowly to room temperature over 2 h, after which triethylamine (300 μL) was added. The solvent was removed in vacuo, and the crude product was purified by chromatography on silica gel (cyclohexane/diethyl ether/acetone, 80:10:10 + 3% Et_3N) to afford (+)-(*P*,3*S*)-**24** (110 mg, 84%) as an amorphous solid. $[a]_{589}^{22}$ = +543 (*c* = 0.16, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.60 (d, *J* = 7.1 Hz, 3 H), 1.00 (s, 3 H), 1.12 (s, *J* = 1.6 Hz, 3 H), 1.14 (s, *J* = 4.2 Hz, 3 H), 1.24 (s, 3 H), 2.43 (s, 3 H), 2.75 (dddd, *J* = 15.2, 13.9, 3.8, 1.0 Hz, 1 H), 2.82–2.91 (m, 1 H),

2.82–2.91 (m, 1 H), 3.21 (br. dt, J = 15.0, 15.0, 4.5 Hz, 1 H), 4.74 (d, J = 11.5 Hz, 1 H), 5.03 (d, J = 11.5 Hz, 1 H), 5.30 (q, J = 7.1 Hz, 1 H), 6.36 (ddt, J = 8.0, 1.9, 0.7, 0.7 Hz, 1 H), 6.73 (ddd, J = 8.4, 6.7, 1.4 Hz, 1 H), 6.90 (dd, J = 8.0, 7.4 Hz, 1 H), 7.01 (ddd, J = 8.1, 6.7, 1.2 Hz, 1 H), 7.10 (ddt, J = 7.4, 1.9, 0.7, 0.7 Hz, 1 H), 7.19 (dq, J = 8.4, 1.0, 1.0, 1.0 Hz, 1 H), 7.27 (m, 2 H), 7.39 (m, 1 H), 7.38 (d, J = 1.0 Hz, 1 H), 7.39 (d, J = 8.0 Hz, 1 H), 7.53 (ddt, J = 8.1, 1.4, 0.6, 0.6 Hz, 1 H), 7.59 (br. d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.21 (q), 22.65 (q), 30.56 (t), 30.82 (t), 67.92 (t), 72.46 (d), 121.02 (d), 123.46 (d), 123.58 (d), 124.49 (d), 125.57 (d), 126.32 (d), 126.99 (d), 127.15 (d), 128.84 (d), 128.96 (s), 128.96 (2 d), 129.20 (d), 132.33 (s), 132.89 (2 s), 134.11 (s), 134.16 (s), 135.48 (s), 136.57 (s), 138.62 (s), 138.81 (s), 139.16 (s), 140.62 (s), 141.10 (s), 147.52 (s) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 134.98 (s) ppm. IR (CCl_4): $\tilde{\nu}$ = 1612 (vw), 1595 (w, sh.), 1589 (w), 1576 (w, sh.), 1514 (w), 1465 (m), 1438 (w), 1383 (w, sh.), 1375 (m), 1368 (w, sh.), 1237 (w), 1213 (w), 1181 (m), 1112 (w), 1090 (m), 1073 (w), 1023 (w), 1009 (m), 881 (m), 865 (w, sh.), 846 (w), 821 (m), 729 (w), 701 (w), 565 (w), 545 (w), 529 (w), 497 (w) cm^{-1}. MS (APCI): m/z = 615 [M + H]$^+$, 469, 451, 366, 301, 252. HRMS (APCI): calcd. for $C_{40}H_{40}O_4P$ [M + H]$^+$ 615.2664; found 615.2642.

(+)-(*P*,3*S*)-14-(Dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yloxy)-3-methyl-4-(4-methylphenyl)-1,3,6,7-tetrahydrobenzo[*c*]benzo[5,6]phenanthro[4,3-*e*]oxepine (25): A solution of 2,2′-biphenol (10 g, 0.054 mol) in phosphorus trichloride (30 mL) was heated at reflux for 2 h. The excess amount of phosphorus trichloride was distilled off. The residue was purified by vacuum distillation (b.p. 183–186 °C at 0.7 Torr) to give phosphorochloridite **21** (10.10 g, 75%) as an oil. ^{31}P NMR (162 MHz, [D$_8$]toluene): δ = 180.64 (s) ppm. A Schlenk flask was charged with NaH (60% suspension in mineral oil, 43 mg, 1.79 mmol, 4.0 equiv.) and put under an atmosphere of argon. THF (1 mL) was added, and the stirred suspension was cooled to 0 °C. A solution of (+)-(*P*,3*S*)-**18** (125 mg, 0.267 mmol) in THF (2 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 15 min then warmed slowly to room temperature and stirred for 3 h. Subsequently, the mixture was cooled again to 0 °C and phosphorochloridite **21** (107 mg, 0.427 mmol, 1.6 equiv.) in THF (1 mL) was added dropwise. The reaction mixture was warmed slowly to room temperature over 2 h, after which triethylamine (300 μL) was added. The solvent was removed in vacuo, and the crude product was purified by chromatography on silica gel (cyclohexane/diethyl ether, 90:10 + 3% Et_3N) to afford (+)-(*P*,3*S*)-**25** (133 mg, 73%) as an amorphous solid. $[\alpha]_{589}^{22}$ = +264 (c = 0.16, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27 (d, J = 7.1 Hz, 3 H), 3.06 (s, 3 H), 3.30–3.41 (m, 2 H), 5.40 (d, J = 11.5 Hz, 1 H), 5.68 (d, J = 11.5 Hz, 1 H), 5.94 (q, J = 7.1 Hz, 1 H), 7.27 (m, 1 H), 7.27 (dd, J = 8.2, 1.7 Hz, 1 H), 7.38 (ddd, J = 8.5, 6.8, 1.4 Hz, 1 H), 7.61 (dd, J = 8.2, 7.5 Hz, 1 H), 7.67 (ddd, J = 8.1, 6.8, 1.2 Hz, 1 H), 7.73 (m, 1 H), 7.78 (m, 2 H), 7.78 (d, J = 8.6 Hz, 1 H), 7.79 (dd, J = 7.5, 1.7 Hz, 1 H), 7.81 (ddt, J = 8.5, 1.2, 0.5, 0.5 Hz, 1 H), 7.89 (s, 1 H), 7.92 (m, 1 H), 7.96 (m, 2 H), 8.05 (dd, J = 7.6, 1.7 Hz, 1 H), 8.19 (ddt, J = 8.1, 1.4, 0.6, 0.6 Hz, 1 H), 8.25 (dt, J = 8.6, 0.6, 0.6 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.20 (q), 22.50 (q), 30.36 (t), 30.42 (t), 67.82 (t), 72.40 (d), 119.40 (d), 121.48 (d), 122.05 (d), 123.63 (d), 123.71 (d), 124.67 (d), 124.89 (d), 125.39 (d), 125.44 (d), 127.11 (d), 127.73 (d), 128.85 (d), 128.91 (s), 129.00 (d), 129.09 (d), 129.47 (d), 129.83 (d), 131.83 (s), 132.34 (s), 132.70 (s), 133.30 (s), 134.25 (s), 135.43 (s), 136.69 (s), 138.66 (s), 138.98 (s), 139.46 (s), 140.80 (s), 141.24 (s), 148.00 (s), 148.62 (s), 149.14 (s) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 142.33 (s) ppm. IR (CCl_4): $\tilde{\nu}$ = 3070 (m, sh.), 3053 (m), 1620 (w), 1601 (m), 1586 (m), 1576 (m), 1568 (m), 1513 (s), 1500 (s), 1476 (vs), 1468 (s), 1437 (vs), 1379 (m, sh.), 1368 (s), 1205 (vs), 1184 (vs), 1138 (m), 1116 (m), 1097 (s), 1089 (vs), 1074 (s), 1036 (s), 1024 (m), 1011 (m), 890 (s, sh.), 864 (vs), 815 (vs), 708 (s), 570 (w), 559 (w), 545 (m), 528 (m), 493 (w) cm^{-1}. MS (APCI): m/z = 683 [M + H]$^+$, 665, 369, 316, 288. HRMS (APCI): calcd. for $C_{46}H_{36}O_4P$ [M + H]$^+$ 683.2351; found 683.2330.

(+)-(*P*,3*S*)-14-[(4,8-Di-*tert*-butyl-2,10-dimethoxydibenzo[*d*,*f*][1,3,2]-dioxaphosphepin-6-yl)oxy]-3-methyl-4-(4-methylphenyl)-1,3,6,7-tetrahydrobenzo[*c*]benzo[5,6]phenanthro[4,3-*e*]oxepine (26): A solution of 3,3′-di-*tert*-butyl-5,5′-dimethoxybiphenyl-2,2′-diol (200 mg, 0.558 mmol) in toluene (2 mL), triethylamine (310 μL, 2.232 mmol, 4.0 equiv.), and phosphorus trichloride (290 μL, 3.348 mmol, 6.0 equiv.) was heated at reflux for 2 h. The excess amount of phosphorus trichloride was distilled off to give phosphorochloridite **22** (137 g, 58%) as an amorphous solid. ^{31}P NMR (162 MHz, [D$_8$]-toluene): δ = 204.21 (s) ppm. A Schlenk flask was charged with NaH (60% suspension in mineral oil, 13 mg, 0.534 mmol, 2.5 equiv.) and put under an atmosphere of argon. THF (2 mL) was added, and the stirred suspension was cooled to 0 °C. A solution of (+)-(*P*,3*S*)-**18** (100 mg, 0.213 mmol) in THF (2 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 10 min then warmed slowly to room temperature and stirred for 3 h. Subsequently, the mixture was cooled again to 0 °C and phosphorochloridite **22** (135 mg, 0.320 mmol, 1.5 equiv.) in THF (1.5 mL) was added dropwise. The reaction mixture was warmed slowly to room temperature over 2 h, after which triethylamine (300 μL) was added. The solvent was removed in vacuo and the crude product was purified by chromatography on silica gel (cyclohexane/diethyl ether, 90:10 with 3% Et_3N) to afford (+)-(*P*,3*S*)-**26** (82 mg, 45%) as an amorphous solid. $[\alpha]_{589}^{22}$ = +98 (c = 0.05, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.62 (d, J = 7.1 Hz, 3 H), 1.06 (s, 18 H), 2.44 (s, 3 H), 2.58 (m, 2 H), 2.64 (m, 2 H), 3.81 (s, 3 H), 4.00 (s, 3 H), 4.82 (d, J = 11.3 Hz, 1 H), 5.09 (d, J = 11.3 Hz, 1 H), 5.38 (q, J = 7.1 Hz, 1 H), 6.69 (d, J = 3.1 Hz, 1 H), 6.75 (ddd, J = 8.4, 6.8, 1.4 Hz, 1 H), 6.82 (d, J = 3.1 Hz, 1 H), 7.02 (ddd, J = 8.0, 6.8, 1.2 Hz, 1 H), 7.03 (br. t, J = 7.4 Hz, 1 H), 7.09 (br. d, J = 7.3 Hz, 1 H), 7.21 (dd, J = 7.5, 1.0 Hz, 1 H), 7.25 (s, 1 H), 7.28 (m, 1 H), 7.28 (br. dq, J = 8.4, 1.0, 1.0, 1.0 Hz, 1 H), 7.29 (br. d, J = 8.0 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 1 H), 7.38 (m, 1 H), 7.49 (br. d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.20 (q), 22.75 (q), 30.80 (t), 30.83 (t), 30.90 (q), 34.98 (s), 35.17 (s), 55.58 (q), 55.77 (q), 67.93 (t), 72.26 (d), 112.17 (d), 112.93 (d), 114.08 (q), 114.53 (d), 123.19 (d), 123.61 (d), 125.36 (d), 125.36 (d), 125.99 (d), 127.08 (d), 127.36 (d), 128.33 (d), 128.39 (s), 128.93 (2 d), 129.32 (d), 131.96 (s), 132.38 (s), 132.39 (s), 134.39 (s), 134.66 (s), 135.12 (s), 136.60 (s), 138.17 (s), 138.77 (s), 138.86 (s), 139.18 (s), 141.02 (s), 142.37 (s), 142.81 (s), 155.34 (s), 155.81 (s) ppm. ^{31}P NMR (162 MHz, $CDCl_3$): δ = 142.85 (s) ppm. IR (CCl_4): $\tilde{\nu}$ = 3052 (w), 2835 (w), 1590 (m), 1513 (w), 1481 (w), 1463 (m), 1447 (m), 1436 (m), 1411 (s), 1394 (w), 1380 (w, sh.), 1364 (m), 1203 (vs), 1187 (m), 1088 (m), 1032 (m), 1024 (w), 883 (s), 860 (m) cm^{-1}. MS (APCI): m/z = 855 [M + H]$^+$, 745, 583, 451, 421, 405, 391, 279. HRMS (APCI): calcd. for $C_{56}H_{56}O_6P$ [M + H]$^+$ 855.3815; found 855.3803.

Typical Procedure for Hydroformylation: To a solution of Rh(acac)(CO)$_2$ (1 mg, 0.004 mmol, 1 mol-%) in dichloromethane (2 mL) in a vial was added ligand (+)-(*P*,3*S*)-**25** (0.019 mmol, 5 mol-%). The solution was stirred for 5 min and then charged with styrene **27** (40 mg, 0.384 mmol) and dodecane (20 mg, 0.117 mmol, 30 mol-%). The vial was transferred to an autoclave, pressurized with CO (10 bar) and H_2 (10 bar), and heated to 50 °C for 20 h. Then the autoclave was cooled down to room temperature, de-

pressurized, flushed with argon, and opened to obtain a sample of product **30** for GC analysis.

Typical Procedure for Asymmetric Allylic Amination: A Schlenk flask was charged with $[Ir(cod)Cl]_2$ (6.4 mg, 0.010 mmol, 1 mol-%), ligand (+)-(*P*,3*S*)-**24** (0.020 mmol, 2 mol-%), and flushed with argon. The materials were dissolved in THF (0.3 mL), and the reaction mixture was stirred at 50 °C for 30 min. Benzylamine (135 μL, 1.230 mmol, 1.26 equiv.) was added by syringe. The reaction mixture was stirred at room temperature for 5 min, and then a solution of cinnamyl methyl carbonate (**33**; 188 mg, 0.978 mmol) in THF (0.3 mL) was added dropwise. The reaction mixture was warmed to 50 °C and stirred for 2 d. Subsequently, the solvent was removed in vacuo. ^{1}H NMR spectroscopic analysis of the residual crude mixture indicated the ratio of *branched* **35a** to *linear* **35b** to be >97:3. The crude product was then purified by chromatography on silica gel (cyclohexane/ethyl acetate, 90:10 + 0.5% Et_3N) to afford *branched* **35a** (64 mg, 25%) as an oil.

Supporting Information (see footnote on the first page of this article): The chemical shifts of the phosphorus atoms in chlorophosphites **19**–**22** and phosphites **23**–**26**; ^{1}H, ^{13}C, and ^{31}P NMR spectra of (+)-(*P*,3*S*)-**23**–**26**; GC or HPLC analyses of racemic and enantioenriched **30a**–**32a**, **35a**–**38a** on chiral columns.

Acknowledgments

This research was supported by the Czech Science Foundation under Grant No. 203/09/1766, by the Ministry of Education, Youth and Sports of the Czech Republic under Project No. LC512 (the Centre for Biomolecules and Complex Molecular Systems), and by the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic (this work is part of the Research Project Z4 055 0506).

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Received: February 24, 2011
Published Online: May 12, 2011

