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Journal of Organometallic Chemistry 643–644 (2002) 98–104

Journal of Organometallic Chemistry

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New P,N ligands with chiral nitrogen center: applications in homogeneous catalysis

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Received 12 June 2001; accepted 30 July 2001

Abstract

In order to perform homogeneous asymmetric hydroformylation, hydrosilylation and Grignard cross-coupling reaction, we have developed a new family of P,N ligands derived from quincorine and quincoridine.

Keywords: Asymmetric catalysis; Aminophosphine; Aminophosphite; Hydroformylation; Hydrosilylation; Cross-coupling reaction

1. Introduction

For the last three decades, chiral diphosphines have played a crucial role in asymmetric catalytic reactions as an alternative to the synthesis of optically pure compounds either from the chiral pool or by resolution of their racemic form.

Kagan [1] and Knowles [2] have first developed rhodium complexes of chiral chelating diphosphines, DIOP and DIPAMP, respectively, for asymmetric hydrogenation. Other optically pure diphosphines have been synthesized later on. Among them, BPPFA [3], BPPM [4] or BINAP [5] have been involved in various applications. For all these phosphines, the asymmetric induction stands on the molecular skeleton [1,3–5] or on the phosphorus atom itself [2]. Unfortunately, the latter suffers from the relatively easy epimerization of the phosphorus atom. More recently, Mathey [6] and Imamoto [7] have reported the synthesis of a new chiral ligand with an asymmetric non-epimerizable phosphorus atom.

In the 1990s, the concept which involves the asymmetric induction by electronic differentiation has been extensively studied [8]. This differentiation was observed with hybrid ligands having a soft electron-donating atom such as phosphorus and a hard electron-donating atom such as nitrogen [8b]. In this context amino-phosphine, -phosphite, -phosphonite and -phosphinite ligands were developed leading to complexes used for asymmetric catalytic reactions, such as allylic alkylation [9], hydrogenation [10], hydrosilylation [11], cross-coupling reaction [12], hydrogen transfer reduction [13], and hydroformylation [14].

Cinchona alkaloids and their derivatives, relatively cheap and readily available in both pseudo-enantiomeric forms, have been extensively used. Partly due to the bicyclic structure, they present at least four stereogenic centers, including the N-chiral bridgehead. This nitrogen atom is stabilized in the same way as the phosphorus one in the BIPNOR [7], avoiding the rapid inversion of usual amines. The use of transition metal complexes of cinchona alcaloids and their derivatives in catalysis is based on their bidentate nature which allows optimal binding to transition metals [15]. They were employed in catalytic asymmetric dihydroxylation [16] and in various enantioselective phase transfer catalytic reactions [17]. Nevertheless, their aminophosphorated derivatives were less studied [18].

Hoffmann has described the transformation of quinidine and quinine, two cinchona alkaloids, into

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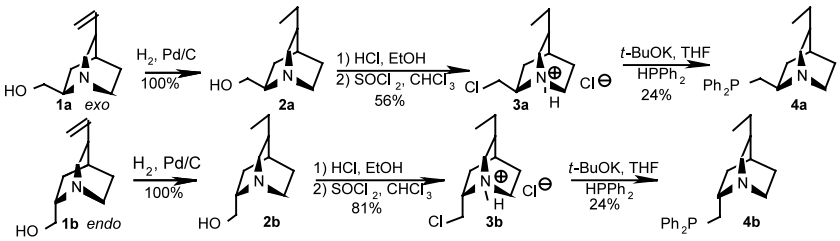
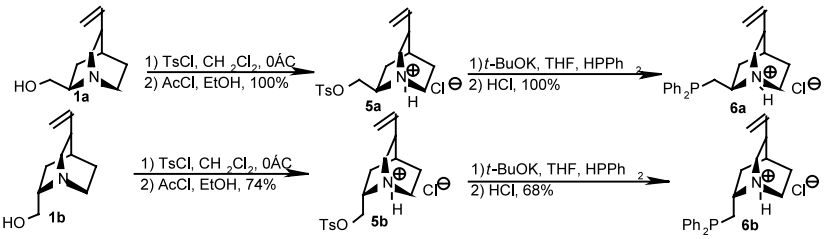
0022-328X/02/$ - see front matter
PII: S0022-328X(01)01148-2



Scheme 1.



Scheme 2.

quincoridine **1a** and quincorine **1b**, respectively [19], but, to the best of our knowledge, only phosphinite derivatives of **1a** and **1b** were involved in asymmetric hydrosilylation [18].

This paper deals with our efforts to synthesize and evaluate new ligands containing P and N donor atoms derived from quincoridine **1a** ((2*R*,4*S*,5*R*)-2-hydroxymethyl-5-vinyl-2-quinuclidine) and quincorine **1b** ((2*R*,4*S*,5*R*)-2-hydroxymethyl-5-vinyl-2-quinuclidine), having a stable chiral nitrogen center. Aminophosphite and aminophosphine derivatives were tested in catalytic asymmetric hydroformylation and aminophosphines also in asymmetric reduction of C=O bonds (hydrosilylation) and in the asymmetric cross-coupling reaction [20].

2. Synthesis of P,N ligands

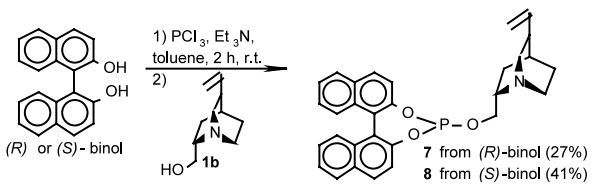
2.1. Aminophosphines synthesis

Commercially available quincoridine **1a** and quincorine **1b**, two aminoalcohols which differ only in the position of the hydroxymethyl group (*exo* for **1a** and *endo* for **1b** referred to the unsubstituted piperidine ring (Scheme 1)) were transformed into their corresponding saturated derivatives **2a** and **2b** by means of catalytic hydrogenation in the presence of Pd/C. These compounds were treated with hydrogen chloride in ethanol to afford the corresponding ammonium chlorides. The further transformation of the hydroxy group into a chloromethyl moiety was performed with thionyl chloride in chloroform leading to products **3a** and **3b**. These compounds were transformed into phosphines **4a** and **4b** with diphenylphosphine in the presence of potassium *tert*-butoxide in tetrahydrofuran according to the procedure of Kumada [21].

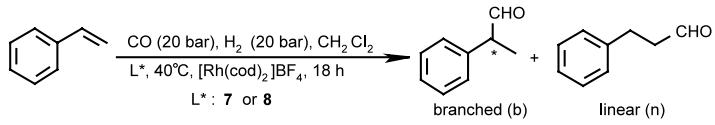
The second type of ligands keeps the unsaturation of quincorine and quincoridine unchanged. It has been prepared in two steps by treatment of quincoridine **1a** and quincorine **1b** with *p*-toluenesulfonyl chloride in dichloromethane, followed by phosphination. This latter reaction was carried out with diphenylphosphine in tetrahydrofuran in the presence of potassium *tert*-butoxide according to the Whitesides procedure [22]. Under these conditions, ligands **6a** and **6b** were obtained, respectively, with 100 and 50% overall yield (Scheme 2). The non-hydrochlorinated ligands **6** were obtained in a similar way from the mesylate derivative [23].

2.2. Aminophosphites synthesis

Monophosphites **7** and **8** (Scheme 3) were prepared from quincorine **1b**, according to Takaya [24]. (*R*)- or (*S*)-binol was transformed into its phosphochloridite by means of phosphorous trichloride in the presence of triethylamine, at −40 °C, then quincorine **1b** was added. Phosphites **7** and **8** were obtained in 27 and 41% yield, respectively.



Scheme 3.



Scheme 4.

3. Evaluation of P,N ligands in asymmetric catalysis

3.1. Hydroformylation

Hydroformylation is a very powerful synthetic tool for the preparation of fine chemicals [25]. This reaction is interesting if the chemoselectivity (hydroformylation vs. hydrogenation), the regioselectivity (branched vs. linear aldehyde) and the enantioselectivity are controlled. For instance, with styrenic substrates, this reaction provides a straightforward method for the preparation of branched aldehyde precursors of arylpropionic acids largely used in pharmaceutical applications (ibuprofen, naproxen) [26]. For this type of reaction, chiral phosphites have received particular attention for the last 20 years. Their rhodium complexes showed high regioselectivities and enantioselectivities for hydroformylation of arylsubstituted olefins [27]. We carried out the asymmetric hydroformylation of styrene leading to 2-phenylpropanal and 3-phenylpropanal, with aminophosphite ligands **7** and **8,** previously synthesized from quincoridine (Scheme 4). Their corresponding rhodium complexes were prepared in situ from $[Rh(cod)_2]BF_4$ and the hydroformylation reaction was performed in mild conditions [28] (Table 1).

After 18 h, the regioselectivities and enantioselectivities are identical for both complexes. The only difference observed concerns the activity. Rhodium complex of ligand **8** (90% of conversion) was found to be more efficient than that of ligand **7** (only 62% of conversion). In both cases, b/n ratio is about 90/10. These results show that this catalytic system is at least as regioselective as most of the catalytic systems described in the literature but it is less enantioselective. The stereochemistry of the phosphite part of the ligand has a major influence upon the absolute configuration. With (*R*)-phosphite **7** (*R*)-aldehyde was formed, whereas the (*S*)-phosphite **8** gave the (*S*)-aldehyde. For ligands **4a** and **4b** (runs 3 and 4), after one week, lower conversions but no enantiomeric excess (ee) are observed, although b/n ratios are similar.

3.2. Asymmetric hydrosilylation

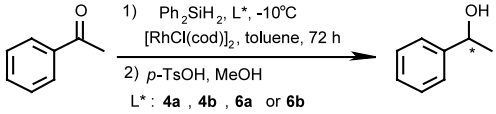
Asymmetric hydrosilylation is a useful synthetic tool for the production of chiral amines and alcohols [29]. This reaction provides an alternative route to hydrogenation, avoiding pressurized hydrogen. Moreover, hydrosilylation is known to be tolerant towards a variety of functional groups in the substrate. In a pioneering work on asymmetric hydrosilylation, chiral diphosphine ligands such as DIOP gave moderate enantioselectivities for the asymmetric hydrosilylation of ketone (DIOP–Rh:58–85% ee) [30]. Chiral nitrogen ligands were tested later on. Most of them present an oxazoline skeleton such as pyridinyloxazoline, bisoxazoline. These nitrogen-containing ligands have given rise to high levels of enantioselectivity [31]. More recently, new ligands which present a combination of oxazolinyl and phosphine structures were synthesized. Their rhodium complexes could efficiently catalyze hydrosilylation of aromatic as well as aliphatic ketones with excellent conversions and ees up to 90% [32].

Ligands **4** and **6** were used in asymmetric hydrosilylation of acetophenone using $[RhCl(cod)]_2$ as precursor. The reaction was carried out with diphenylsilane, at -10 °C, in toluene for 72 h (Scheme 5, Table 2).

Table 1
Hydroformylation of styrene

Run	Ligand L*	Conversion [a] (%)	b/n [a]	ee [a] (%) (configuration)
1	**7**	62	88/12	16 (*R*)
2	**8**	90	89/11	13 (*S*)
3	**4a**	42 [b]	93/7	0
4	**4b**	35 [b]	90/10	0

[a] Determined by GC analysis on a Supelco β-DEX™ 225, (60 m × 0.25 mm) chiral column.
[b] After one week.

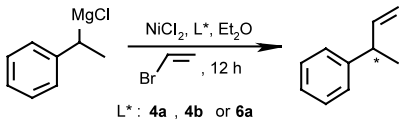


Scheme 5.

Table 2
Hydrosilylation of acetophenone

Run	Ligand	Conversion [a] (%)	ee [a] (%) (configuration)
1	**4a**	96	54 (*R*)
2	**4b**	89	1 (*S*)
3	**6a**	73	54 (*R*)
4	**6b**	42	4 (*S*)

[a] Determined by GC analysis on a Supelco β-DEX™ 225, (60 m × 0.25 mm) chiral column.



Scheme 6.

Table 3
Asymmetric nickel-catalyzed cross-coupling of 1-phenylethylmagnesium chloride with vinyl bromide

Run	Ligand	Temperature (°C)	Yield [a] (%)	ee [a] (%)
1	**4a**	25	80	65 (−)
2	**4b**	25	65	75 (+)
3	**4b**	0	50	86 (+)
4	**6a**	25	45	52 (−)

[a] Determined by GC analysis on a Supelco β-DEX™ 225, (60 m × 0.25 mm) chiral column.

The reaction was carried out with free nitrogen ligands **4** and **6**. Similar enantiomeric excesses were observed with **4a** and **6a** and with **4b** and **6b**. The presence or the absence of the vinyl group in the structure of the ligand has no influence upon the enantioselectivity (runs 1, 3 and 2, 4, respectively). But the position of the phosphine group plays a crucial role upon the enantioselectivity. Ligands **4a** and **6a**, having their phosphine group in the *exo* position, showed better enantioselectivities (54%, runs 1 and 3) than those presenting this group in the *endo* position (**4b** and **6b**), which gave rise to an almost racemic product (runs 2 and 4).

This difference should be attributed to the cumulative effect of the chiralities of **4a** and **6a** while those of **4b** and **6b** lead to the opposite effect [33]. Another possible explanation for the difference in enantioselectivity is the steric hindrance of the *exo* compounds, because the vinyl (or ethyl), and the phosphine moieties are in *syn* position to each other. Concerning the conversions, they are better with *exo* ligands **4a** or **6a** than with the *endo* ones **4b** or **6b**.

3.3. Asymmetric Grignard cross-coupling reaction

One of the first uses of nitrogen-containing ligands is in the Grignard cross-coupling of organometallic reagents with alkenyl or aryl halide. The metal precursors used are nickel or palladium complexes. With P,N ligands derived from aminoacids, good results were obtained [34].

We performed the Grignard cross-coupling reaction of 1-phenylethylmagnesium chloride with vinylbromide in the presence of nickel chloride and aminophosphines **4** and **6a** (Scheme 6). Aminophosphine **6a** was neutralized prior to use. Results are presented in Table 3.

According to the literature, we supposed that, for the cross-coupling reaction, aminophosphine ligands **4** and **6** acted as bidentate ligands [4,35]. In this case, the presence of a vinyl group has an effect upon both the enantioselectivity and the activity. With unsaturated ligand **6a**, a decrease of both the ee and the yield was observed (runs 1 and 4). With the more hindered *exo* ligand **4a** (run 1), selectivity is lower than that observed with the *endo* **4b** (run 2). Compared to hydrosilylation, the steric hindrance between the phosphine and the ethyl groups, in *syn* position to each other, has the opposite effect on the selectivity. The enantioselectivity was improved at low temperature: 86% ee at 0 °C (run 3) and 75% ee at 25 °C (run 2).

In terms of enantioselectivity, nickel systems could be considered as one of the most efficient. The highest enantioselectivity (88% ee) has been obtained by means of the homomethphos ligand [36].

4. Conclusions

Aminophosphines **4** and **6** and aminophosphites **7** and **8** are readily prepared from quincorine and quincoridine. This paper shows that rhodium complexes of aminophosphines **4** and **6** can be used in various asymmetric catalytic reactions.

In the case of hydroformylation, the regioselectivity obtained with ligands **7** and **8** is about the same as the one reported in the literature, but the enantioselectivity remains low.

Best results were achieved for hydrosilylation and Grignard cross-coupling reactions. For the latter, the best enantioselectivities were obtained with the *endo* aminophosphine **4b** nickel complex. This system was shown to be among the best ever described in the literature, using the same conditions.

Other substrates and catalytic reactions have to be tested in order to reveal the scope and the limitations of these new catalytic systems. The commercial availability of the two aminoalcohols allows their use as building blocks in order to obtain a large variety of ligands, whose nitrogen chirality could be controlled. The work presented in this paper could thus be considered only as a starting point.

5. Experimental

5.1. General

Quincoridine and quincorine were purchased from Buchler GmbH and all other reagents from Aldrich.

Polarimetric measurements were performed on a Perkin–Elmer 241 instrument, at ambient temperature, at 589 nm, and at a concentration of grams per 100 ml.

Elemental analyses and mass spectra (electrospray: HP 5989/MS Engine) were carried out by the CNRS (Service Central d'Analyse—Département d'Analyse Elémentaire) Solaize, France. Infrared spectra were recorded on a Mattson 5000 FT apparatus (ν in cm^{-1}). ^1H-, ^{13}C-, and ^{31}P-NMR spectra were recorded with a Bruker AM200 (^1H, 200 MHz; ^{13}C, 50 MHz; and ^{31}P, 81 MHz) using TMS as internal standard (^1H-, ^{13}C-NMR) or phosphoric acid 85% in D_2O as external standard (^{31}P-NMR) and $CDCl_3$ as solvent. Conversions and enantiomeric excesses were determined by GC analysis on a Supelco β-DEX™ 225, (60 m × 0.25 mm) chiral column, using a Shimadzu GC 14A apparatus equipped with FID connected to a Schimadzu CR6A integrator.

5.2. Synthesis of P,N ligands

5.2.1. Aminophosphines **4**

*5.2.1.1. Synthesis of saturated compounds **2a** and **2b**.* A suspension of 10% Pd/C (0.9 mmol) and quincoridine **1a** or quincorine **1b** (6 mmol) in THF (60 ml) was stirred under hydrogen (1 bar) during 8 h. The resulting solution was filtered over celite 545 and the solvent was removed. Pure compounds **2a** and **2b** were obtained in 100% yields. They present the same spectral data as those obtained by Hoffman [37].

*5.2.1.2. Synthesis of chloride **3a** or **3b**.* A solution of alcohol **2a** (0.9 g, 5.3 mmol) in EtOH (10 ml) was carefully added to an excess of HCl (37%) (4 ml). The reaction mixture was stirred for 30 min at room temperature (r.t.), and then the solvent and the excess of acid were removed under reduced pressure. To the chlorhydrate dissolved in $CHCl_3$ (10 ml), thionyl chloride (1 ml, 2.5 equivalents) was added at 0 °C. After the reaction mixture was refluxed for 2 h, the solvent was removed, at r.t. under vacuum. The residue was dissolved in EtOH (2 ml) and the dropwise addition of ether gave crystallization. The crystals were filtered and dried under vacuum at 50 °C over P_2O_5 (yield: 56%). The same procedure was used for **3b** (Yield 81%).

3a: ES-MS (ES^+): 188.0 ($[M+H])^+$), 411.2 ($[2M+HCl+H]^+$), (ES^-): 258.0 ($[M+Cl]^-$), 296.0 ($[M+HCl+Cl]^-$), 483.0 $(2M+Cl]^-$). ^1H-NMR: δ 0.92 (t, 3H, $^3J = 7.1$ Hz), 1.3–2.2 (m, 8H); 2.7–4.4 (m, 7H), 12.28 (br s, 1H). $^{13}C\{^1H\}$-NMR: δ 11.4, 23.9, 24.5, 24.8, 24.9, 35.2, 42.7, 48.5, 48.6, 57.5. **3b**: ES-MS (ES^+): 188.0 ($[M+H])^+$), 411.2 ($[2M+HCl+H]^+$), (ES^-): 258.0 ($[M+Cl]^-$), 296.0 ($[M+HCl+Cl]^-$), 483.0 ($[2M+Cl]^-$). ^1H-NMR: δ 0.82 (t, 3H, $^3J = 7.1$ Hz), 1.4–2.2 (m, 8H), 2.8–4.0 (m, 7H), 11.89 (br s, 1H). $^{13}C\{^1H\}$-NMR: δ 11.5, 24.3, 24.6, 26.6, 34.9, 41.6, 43.5, 55.6, 57.4.

*5.2.1.3. Synthesis of phosphine **4a** or **4b**.* Under argon, diphenylphosphine (0.4 ml, 2.2 mmol) was added to a suspension of potassium *tert*-butoxide (11.5 mmol) in anhydrous THF (20 ml). After 30 min of stirring at r.t., the chlorhydrate **3a** (0.5 g, 2.2 mmol) was added to the red solution. The reaction mixture was refluxed until the red color disappeared. After removal of the solvent, HCl 10% (10 ml) was added to the residue. The aqueous layer was extracted with toluene (30 ml), neutralized with NaOH 10% (20 ml), and then washed with toluene. The combined organic layers were rinsed with brine and dried with Na_2SO_4. The solvent was evaporated and a yellow oil was obtained. Purification by filtration through neutral alumina led to the phosphite **4a** (yield: 24%) as a colorless oil. The same procedure was used for **4b** (yield: 24%).

4a: $[\alpha]_D^{25} = -16.2$ ($c = 1.0$, THF). ES-MS: 338.2 ($[M+H]^+$). $^{31}P\{^1H\}$-NMR: δ −22.0. ^1H-NMR: δ 0.87 (t, 3H), 1.0–1.8 (m, 9H), 2.0–3.0 (m, 6H), 7.2–7.6 (m, 10H), $^{13}C\{^1H\}$-NMR: δ 12.1; 25.8; 26.5 (d, $J_{CP} = 5$ Hz), 27.3, 29.6 (d, $J_{CP} = 7$ Hz), 35.1 (d, $J_{CP} = 12$ Hz), 37.9, 49.1 (d, $J_{CP} = 11$ Hz), 53.4 (d, $J_{CP} = 17$ Hz), 128.3, 128.4, 128.5, 133.0, 133.1. **4b**: $[\alpha]_D^{25} = +15.9$ ($c = 1.0$, THF). ES-MS: 338.2 ($[M+H]^+$). $^{31}P\{^1H\}$-NMR: δ −22.0. ^1H-NMR: δ 0.75 (t, 3H), 1.0–3.2 (m, 15H), 7.2–7.7 (m, 10H). $^{13}C\{^1H\}$-NMR: δ 11.9, 25.7, 26.9 (d, $J_{CP} = 5$ Hz), 29.2, 29.7 (d, $J_{CP} = 7$ Hz), 37.4 (d, $J_{CP} = 12$ Hz), 37.9, 48.7 (d, $J_{CP} = 11$ Hz), 48.9 (d, $J_{CP} = 17$), 128.4, 128.5, 128.6, 132.7, 132.9.

5.2.2. Aminophosphines **6**

*5.2.2.1. Synthesis of tosylates **5a** and **5b**.* At 0 °C, tosyl chloride (1.53 g, 8.02 mmol) was added to a solution of quincorine **1a** or quincoridine **1b** (1 g, 6 mmol) in CH_2Cl_2 (20 ml). The reaction was allowed to stir for 6 h at 0 °C. The reaction mixture was washed with a saturated aqueous solution of $NaHCO_3$, and then with water. The organic phase was dried over $MgSO_4$. After removal of the solvent, an oily residue was isolated. This latter compound was dissolved in a solution of acetyl chloride (0.85 ml) in EtOH–ether (0.84/20 ml). After 1 h of stirring, the white solid formed was filtered over celite, and then washed with ether (yield: 74%). The same procedure was used for **5b** (yield: 100%).

5a: $[\alpha]_D = +86.58$ ($c = 1.57$, CH_2Cl_2). ^1H-NMR: δ 1.6–1.8 (m, 2H), 1.8–1.9 (m, 2H), 1.9–2.0 (m, 1H), 2.30 (s, 3H), 2.5–2.6 (m, 1H), 2.8–3.5 (m, 4H), 3.6–3.8 (m, 1H), 4.26 (d, 1H, $^3J = 10.3$ Hz), 4.52 (d, 1H, $^3J = 10.3$ Hz), 4.96 (d, 1H, $^3J = 16.6$ Hz), 5.04 (d, 1H, $^3J = 9.9$ Hz), 5.75 (ddd, 1H, $^3J = 16.6$, 9.9, 5.9 Hz), 7.24 (d, 2H, $^3J = 7.7$ Hz), 7.71 (d, 2H, $^3J = 7.7$ Hz), 11.80 (br s, 1H). $^{13}C\{^1H\}$-NMR: δ 21.9, 22.1, 23.7, 27.2, 37.0, 47.6, 49.1, 56.0, 67.8, 118.2, 128.5, 130.6, 132.2, 136.8, 145.6. IR (KBr, cm^{-1}): ν 3420, 2900, 2500, 1680, 1590, 1450, 1400, 1360, 1290, 1170, 1120, 1120, 1090, 1070,

990, 930, 910, 880, 820, 790, 760, 710, 660. Mass $[M+H]^+$: 322.14760. Elemental analysis: Calc.: C, 56.85; H, 6.79; Cl, 9.99; N, 4.01; O, 13.37; S, 8.87. Found: C, 56.76; H, 6.95; Cl, 9.72, N, 3.91; O, 13.66; S, 8.96%. **5b**: ^{1}H-NMR: δ 1.7–1.8 (m, 1H), 1.8–2.2 (m, 4H), 2.39 (s, 3H), 2.6–2.7 (m, 1H), 3.0–3.7 (m, 5H), 4.32 (dd, 1H, $^2J=11.7$, $^3J=4.4$ Hz), 4.59 (dd, 1H, $^2J=11.7$, $^3J=3.1$ Hz), 5.13 (d, 1H, $^3J=17.6$ Hz), 5.22 (d, 1H, $^3J=10.7$ Hz), 5.85 (ddd, 1H, $^3J=17.6$, 10.7, 6.6 Hz), 7.32 (d, 2H, $^3J=8.3$ Hz); 7.78 (d, 2H, $^3J=8.3$ Hz), 12.21 (br s, 1H). ^{13}C{^{1}H}-NMR: δ 21.9, 22.1, 24.3, 26.9, 36.8, 43.0, 53.7, 55.9, 68.2, 117.8, 128.4, 130.6, 132.2, 137.3, 146.1. IR (cm^{-1}): ν 3410, 2900, 2500, 1680, 1590, 1450, 1360, 1290, 1170, 1120, 1120, 1090, 1070, 990, 930, 910, 880, 820, 790, 760, 710. Mass $[M+H]^+$: 322.147.

*5.2.2.2. Synthesis of phosphines **6a** and **6b***. Under argon, to a stirred suspension of potassium *tert*-butoxide (0.74 g, 6.6 mmol) in anhydrous THF (19 ml) was added diphenylphosphine (0.542 ml, 3.1 mmol). After 5 min at r.t., the tosylate **5a** (0.81 g, 2.5 mmol) was added to the reaction mixture, which was refluxed during 16 h. Hexane (36 ml) was then added, at r.t. and the organic layer was washed with an aqueous solution of NaOH 10% (twice with 8.5 ml), and then with brine (10 ml). Compound **6a** was isolated in its chlorhydrate form (yield: 100%). The same procedure was used for **6b** (yield: 68%).

6a: $[\alpha]_D = +93.0$ ($c=1.65$, $CHCl_3$). Mass $[M+H]^+$: 336.188. ^{31}P-NMR (D_2O): δ −24.8. ^{1}H-NMR (D_2O): δ 1.6–2.9 (m, 7H), 3.1–3.5 (m, 6H), 5.1–5.3 (m, 2H), 5.7–6.0 (m, 1H), 7.2–7.8 (m, 10H), 12.15 (br s, 1H). Elemental analysis: Calc.: C, 71.09; H, 7.27; Cl, 9.54; N, 3.72; P, 8.31. Found: C, 58.65; H, 6.47; Cl, 14.03;N, 3.18; P, 7.03%. **6b**: $[\alpha]_D = -48.96$ ($c=1.26$, $CHCl_3$). Mass $[M+H]^+$: 336.188. ^{31}P-NMR (D_2O): δ −24.7. ^{1}H-NMR (D_2O): δ 1.9–3.9 (m, 13H), 5.0–5.2 (m, 2H), 5.7–5.9 (m, 1H), 7.4–7.8 (m, 10H), 12.10 (br s, 1H). Elemental analysis: Calc: C, 64.71; H, 6.91; Cl, 17.36; N, 3.43; P, 7.59. Found: C, 64.64; H, 6.67; Cl, 17.03; N, 3.30; P, 7.30%.

*5.2.3. Synthesis of phosphites **7** and **8***

Under argon, at −40 °C, a solution of PCl_3 (210 μl, 2.4 mmol) and Et_3N (0.5 ml, 4.8 mmol) in anhydrous toluene (5 ml) was added dropwise to a solution of (*R*)-BINOL (690 mg, 2.4 mmol) first dissolved at 60 °C in anhydrous toluene (40 ml). The reaction mixture was allowed to stir for 2 h at r.t. The triethylamine hydrochloride formed was removed by filtration through alumina. After evaporation of the solvent, the chlorophosphite was dissolved in anhydrous ether, and cooled at 0 °C. To this mixture, quincoridine **1b** (0.4 g, 2.4 mmol) in solution with Et_3N (0.5 mL, 4.8 mmol) was added dropwise. After one night of stirring at r.t., the chlorhydrate formed was removed by decantation, and the ethereal solution was concentrated under vacuum. The pure compound was obtained by precipitation with pentane. After filtration, the phosphite **7** was obtained in 27% yield. Phosphite **8** was obtained in the same way, using (*S*)-BINOL in 41% yield.

7: $[\alpha]_D = -22.9$ ($c=1.0$, THF). ^{31}P{^{1}H}-NMR: δ 145. ^{1}H-NMR: δ 1.0–4.0 (m, 13H), 4.3–4.6 (m, 1H), 5.6–5.9 (m, 2H), 7.0–8.0 (m, 12H). Elemental analysis: Calc.: C, 74.83; H, 5.86; N, 2.91; O 9.97; P, 6.43. Found: C, 74.71; H, 5.77; N, 3.30; O, 9.70; P, 6.32%. **8**: $[\alpha]_D = +23.4$ ($c=1.0$, THF). ^{31}P{^{1}H}-NMR: δ 145. ^{1}H-NMR: δ 1.0–4.0 (m, 13H), 4.3–4.6 (m, 1H), 5.6–5.9 (m, 2H), 7.0–8.0 (m, 12H). IR (KBr, cm^{-1}): 3056, 2995, 1620, 1589, 1463, 1431, 1359, 1326, 1259, 1218, 1154, 1070, 978, 949, 866, 771, 750, 694, 646, 598, 556, 527.

5.3. Asymmetric catalysis

5.3.1. Hydroformylation of styrene

Under argon, styrene (18 mmol) was added to a solution of $[Rh(cod)_2]BF_4$ (18 μl) and ligand **7** or **8** (36 μl) in anhydrous CH_2Cl_2 (4 ml). After 18 h under H_2 (P_{H_2}: 20 bar) and CO (P_{CO}: 20 bar), the autoclave was vented.

5.3.2. Hydrosilylation

Under argon, to a solution of $[RhCl(cod)]_2$ (0.02 mmol) and ligand **4a**, **4b**, **6a** or **6b** (0.08 mmol) in toluene (5 ml), acetophenone (4 mmol) was added. After cooling the solution at −10 °C, diphenylsilane (4.4 mmol) was introduced. The resulting mixture was maintained and stirred at −10 °C for 72 h, and then 0.5 ml of this solution was poured into a solution of *p*-toluene sulfonic acid (some crystals) in anhydrous methanol (2 ml).

5.3.3. Grignard cross-coupling reaction

Under argon, at −40 °C, vinyl bromide (0.75 ml, 10 mmol) was added to a solution of phosphine **4a**, **4b** or **6a** (0.08 mmol) with $NiCl_2$ (0.08 mmol) in anhydrous Et_2O (2 ml). Freshly prepared 1-phenyl magnesium chloride 1 M (5 mmol) was then added. The mixture was kept at r.t. for 12 h. After hydrolysis by means of a saturated aqueous solution of NH_4Cl and extraction with Et_2O, the organic layer was rinsed with brine and then dried over $MgSO_4$.

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