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# Aziridine-derived iminophosphine ligands in palladium-catalyzed allylic substitution

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**Abstract**

New iminophosphines have been synthesized from (*R*,*R*)-1-amino-2-diphenylphosphino cyclohexane (*R*.*R*)-**1** in good to excellent yields. The catalysts obtained from iminophosphines **3a**–**g** and $[Pd(C_3H_5)Cl]_2$ promote the enantioselective allylic substitution of 1,3-diphenyl-2-propenyl acetate (**6**) with diethyl malonate with good enantioselectivity. The air-stable complex $PdCl_2[\kappa^2$-*P*,*N*-(*R*,*R*)-2-$Ph_2PC_6H_{10}N{=}CHPh]$ (**4**) has been prepared and structurally characterized by X-ray crystallography.
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*Keywords:* Iminophosphines; Allylic substitution; P,N ligands; Palladium catalysis; Bidentate ligands; Square-planar complexes

## 1. Introduction

Many industrial processes require access to chiral catalysts, which are used in enantioselective transformations of broad classes of substrates [1]. As the catalyst is typically composed of a metal ion surrounded by a chiral ligand, development of new and improved ligands is prerequisite to fast progress in the field of asymmetric synthesis. Bidentate ligands are ubiquitous components of many transition-metal-based catalysts [2]. Among them, chiral P,N ligands have found applications in a variety of asymmetric processes ranging from allylic substitution to hydrogenation of ketones [3]. From the standpoint of reactivity, a P,N-ligand is a combination of hard (nitrogen) and soft (phosphorus) centers. Within this environment, metal ions can be stabilized in their low oxidation states by the π-accepting character of the softer phosphorus site. On the other hand, the harder nitrogen site better stabilizes higher oxidation states [4,5]. These properties have been explored in many reactions, such as cross-coupling involving organostannanes [6], oligomerization of olefins [7], copolymerization of CO with olefins [8], Heck reaction [9], transfer hydrogenation [10], and Suzuki coupling [11]. In several cases, the iminophosphines exhibit different reactivity from the conventional chelating diphosphines. For instance, Shirakawa reported that N-(2-diphenylphosphinobenzylidene)-2-phenylethylamine possesses higher activity than DPPP in the cross-coupling reaction between organostannanes and aryl iodides. This phenomenon was attributed to an alternative catalytic cycle, where the P,N-coordinated palladium undergoes oxidative addition to the tin reagent rather than to the aryl halide [6].

The literature reports on iminophosphines with an alkyl backbone are quite scarce. One of the notable examples is the P,N-ligand based on the chiral 1-diphenylphosphino-2-amino-3-methylbutane scaffold, which has been used in several examples of allylic substitution reactions with enantioselectivities reaching 95% [12]. We recently reported [13] the synthesis of a new class of P,N-ligands based on *trans*-1-amino-2-diphenylphosphino cyclohexane backbone. The resolution of *trans*-1-amino-2-diphenylphosphino cyclohexane (**1**) was

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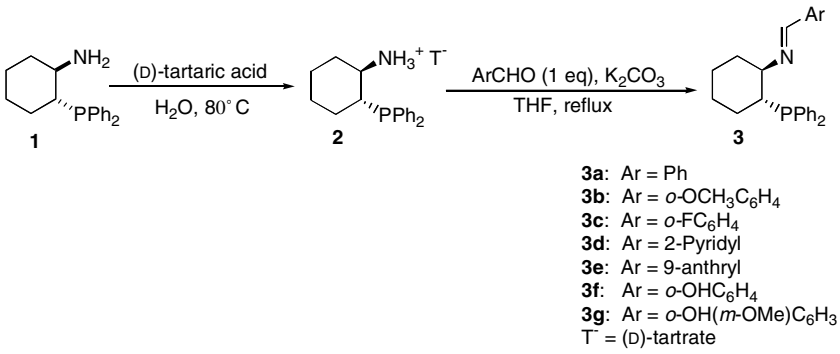



Scheme 1.

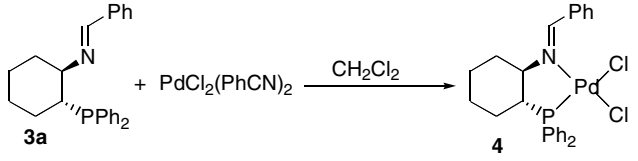
accomplished via the (D)-tartrate salts (**2**). The possibility of further derivatizing the primary amino group in (**1**) using a series of aldehydes in order to prepare new iminophosphines led us to synthesize (*R*,*R*)-1-(*N*-benzylideneamino)-2-(diphenylphosphino)-cyclohexane (**3a**). The coordination ability of **3a** was explored by preparing the $RuCl_2[\kappa^2\text{-}P,N\text{-}(R,R)\text{-}2\text{-}Ph_2PC_6H_{10}N{=}CHPh)](\kappa\text{-}P\text{-}PPh_3)$, a stable Ru(II) complex [14].

In this paper, we report the synthesis of several (*R*,*R*)-1-(*N*-arylideneamino)-2-(diphenylphosphino)-cyclohexanes (**3a**–**g**) obtained by condensation of (*R*.*R*)-**1** with aldehydes (Scheme 1). The structural features of the complex between iminophosphine (**3a**) and Pd (II) are presented and catalytic activity of the *in situ* formed complexes is described.

## 2. Results and discussion

Iminophosphines **3** were prepared by refluxing the (D)-tartrate of (*R*,*R*)-1-amino-2-diphenylphosphino cyclohexane (**2**) with the corresponding aldehyde in THF in the presence of $K_2CO_3$ (Scheme 1). The final products were recovered sufficiently pure for the subsequent catalytic studies or purified by crystallization. The iminophosphines proved to be stable to oxidation for several days even if no particular precaution was taken for their storage.

The addition of a dichloromethane solution of iminophosphine **3a** to a dichloromethane solution of $PdCl_2(PhCN)_2$ led to quantitative formation of $PdCl_2[\kappa^2\text{-}P,N\text{-}(R,R)\text{-}2\text{-}Ph_2PC_6H_{10}N{=}CHPh]$ (**4**) (Scheme 2). A quick color change from deep orange (palladium precursor in dichloromethane) to light yellow was observed in the course of the process.




Scheme 2.

The $^{31}P\{^1H\}$ NMR spectrum in $CD_2Cl_2$ shows a singlet at 46.6 ppm, which accounts for the coordination of the phosphorous atom to palladium. The $^1H$ NMR ($CD_2Cl_2$) shows a singlet at 8.58 ppm, due to the C–H imine proton and a downfield quartet at 4.48 ppm due to the methine cyclohexane proton at the α position to the imine moiety. The complex was obtained as an air-stable yellow solid in 65% yield. The X-ray structure determination was carried out on crystals grown from $CH_3NO_2$/ether mixture and a perspective view of the molecular structure along with the atomic numbering scheme is shown in Fig. 1. A selection of bond lengths and angles for the molecule is listed in Table 1.

The key geometric parameters of complex **4** are similar to $PdCl_2[\kappa^2\text{-}P,N\text{-}2\text{-}Ph_2PC_6H_4N{=}CHPh)]$ (**5**), which contains a phenyl ring in place of the cyclohexane moiety [11]. The coordination around palladium is close to square-planar [N(1)–Pd(1)–Cl(1) = 170.14(7)° and P(1)–Pd(1)–Cl(2) = 177.68(3)°] while the bite angle N(1)–Pd(1)–P(1) is 81.06(7)° which is similar to the analogous angle in **5** [82.10(6)°]. The stronger *trans* influence of the phosphorous atom with respect to the nitrogen is

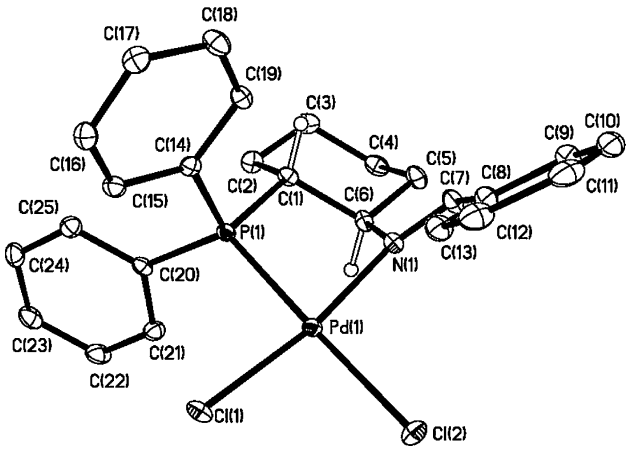



Fig. 1. X-ray crystallographic structure of $PdCl_2[\kappa^2\text{-}P,N\text{-}(R,R)\text{-}2\text{-}Ph_2PC_6H_{10}N{=}CHPh]$.

Table 1
Selected bond distances (Å) and angles (°) for compound **4**

| Bond lengths | | Bond angles | |
|---|---|---|---|
| Pd(1)–N(1) | 2.057(2) | N(1)–Pd(1)–P(1) | 81.06(7) |
| Pd(1)–P(1) | 2.2165(8) | N(1)–Pd(1)–Cl(1) | 170.14(7) |
| Pd(1)–Cl(1) | 2.2966(11) | P(1)–Pd(1)–Cl(1) | 89.15(3) |
| Pd(1)–Cl(2) | 2.3825(8) | N(1)–Pd(1)–Cl(2) | 96.78(7) |
| P(1)–C(20) | 1.800(3) | P(1)–Pd(1)–Cl(2) | 177.68(3) |
| P(1)–C(14) | 1.806(3) | Cl(1)–Pd(1)–Cl(2) | 92.99(3) |
| P(1)–C(1) | 1.857(3) | C(20)–P(1)–C(14) | 109.56(15) |
| N(1)–C(7) | 1.279(4) | C(1)–P(1)–Pd(1) | 102.90(10) |
| N(1)–C(6) | 1.487(4) | C(7)–N(1)–Pd(1) | 131.9(2) |

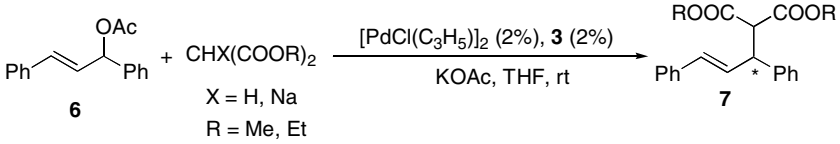
reflected in the longer Pd(1)–Cl(2) bond [2.3825(8) Å] with respect to Pd(1)–Cl(1) bond [2.2966(11) Å]. This is a typical feature of P,N-coordinated systems [15] which can be found in the complex **5** and in *trans*-1-[2-diphenylphosphinocyclohexyl]-3,5-dimethyl-1H-pyrazole] palladium(II) dichloride, previously reported by us [13]. The Pd(1)–Cl(2) bond length is in the range expected for the palladium complexes of iminophosphines [7,11]. To the best of our knowledge, this is the first reported X-ray structure of a Pd(II) complex containing a γ-iminophosphine ligand with an alkyl backbone. Crystallographic data for compound **4** is included in Table 2.

In order to examine the catalytic efficiency of the newly synthesized iminophosphines **3**, the allylic substitution reaction was chosen as a test reaction, using 1,3-diphenyl-2-propenyl acetate (**6**) as a substrate and dialkyl malonates as pro-nucleophiles under the standard experimental conditions (Scheme 3) [16]. The results are summarized in Table 3.

The first nucleophile used for this investigation was the sodium salt of diethyl malonate and the reactions were carried out in the presence of several catalyst precursors. The best palladium catalyst precursor in terms of yield and enantioselectivity turned out to be $[PdCl(C_3H_5)]_2$ (entry 2), and only $Pd_2(dba)_3$ provided comparable results (entry 3). $Pd(OAc)_2$ showed poor activity (entry 4), while the catalyst derived from $Pd(PhCN)_2Cl_2$ did not catalyze the process at all (entry 5). By switching the nucleophile to diethyl malonate along with *N*,*O*-bistrimethyl silyl acetamide (BSA) and increasing the substrate/nucleophile ratio to 1:3, the enantioselectivity increased to 87% (entry 6). In addition, the reaction time was decreased to 4–5 h compared to 12 h for reactions using the sodium salt of diethyl malonate. Raising the temperature to 60 °C or decreasing it to −10 °C did not dramatically affect the outcome (entries 8 and 10). Changing the palladium precursor to $Pd_2(dba)_3$ had a detrimental effect as can be seen in entry 11. Dimethyl malonate provided a slightly lower enantioselectivity (81%) but similar yield (85%) compared to diethyl malonate (entry 9). The free amine ligand (*R*,*R*)-1-amino-2-diphenylphosphino cyclohexane (*R*.*R*)-**1** was also active in this reaction albeit in low yield and enantioselectivity (entry 1). The pre-formed complex **4** was also tested under these experimental conditions, but it only led to traces of **7** after 48 h with large amounts of unidentified byproducts. A 2:1 ratio of

Table 2
Crystallographic data for compound **4**

| Empirical formula | $C_{25}H_{26}Cl_2NPPd$ |
|---|---|
| Formula weight | 548.74 |
| Temperature (K) | 150 (1) |
| Wavelength (Å) | 0.71073 |
| Crystal system | Monoclinic |
| Space group | *P*2(1) |
| Unit cell dimensions | |
| *a* (Å) | 7.7247(15) |
| *b* (Å) | 15.761(3) |
| *c* (Å) | 10.035(2) |
| α (°) | 90 |
| β (°) | 106.98(3) |
| γ (°) | 90 |
| *V* (Å$^3$) | 1168.6(4) |
| *Z* | 2 |
| $D_{calc}$ (mg/m$^3$) | 1.56 |
| μ (mm$^{-1}$) | 1.104 |
| *F*(000) | 556 |
| Crystal size (mm$^3$) | 0.24 × 0.20 × 0.10 |
| $\theta_{max}$ | 27.49° |
| Index ranges | $-10 \leqslant h \leqslant 9$, $-20 \leqslant k \leqslant 20$, $-12 \leqslant l \leqslant 13$ |
| Reflections measured | 9383 |
| Independent reflections | 4816 |
| Completeness to theta = 27.49° | 99.5% |
| Absorption correction | Semi-empirical from equivalents |
| Transmission | 0.853–0.896 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Number of parameters | 272 |
| Goodness-of-fit on $F^2$ | 1.040 |
| Final *R* indices [$I > 2\sigma(I)$] | $R_1 = 0.0279$, $wR_2 = 0.0603$ |
| *R* indices (all data) | $R_1 = 0.0314$, $wR_2 = 0.0620$ |
| Absolute structure parameter | −0.04(2) |
| Extinction coefficient | 0.0057(8) |
| Largest difference peak and hole (e Å$^{-3}$) | 0.777 and −0.717 |




Scheme 3.

Table 3
Palladium-catalyzed allylic substitution in the presence of iminophosphine **3a**: the influence of experimental parameters[a]

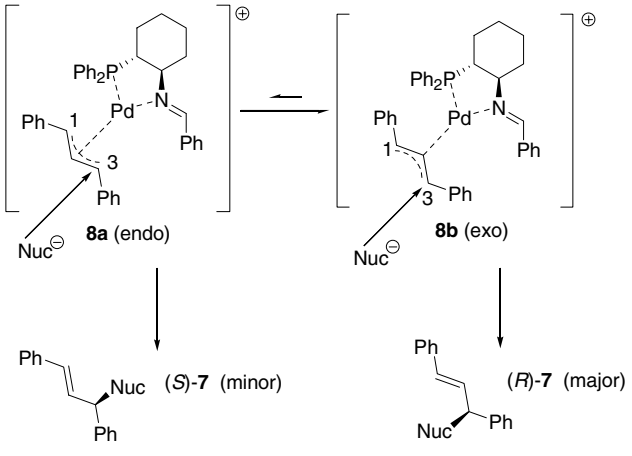
| Entry | Nucleophile | Pd precursor | Ligand | $T$ (°C) | Substrate/nucleophile | Yield[b] (%) | ee[c] (%) |
|---|---|---|---|---|---|---|---|
| **1** | $NaCH(COOEt)_2$ | $[PdCl(C_3H_5)]_2$ | (*R.R*)-**1** | rt | 1:1.2 | 45 | 30 (S) |
| **2** | $NaCH(COOEt)_2$ | $[PdCl(C_3H_5)]_2$ | **3a** | rt | 1:1.2 | 76 | 66 (R) |
| **3** | $NaCH(COOEt)_2$ | $Pd_2(dba)_3$ | **3a** | rt | 1:1.2 | 70 | 61 (R) |
| **4** | $NaCH(COOEt)_2$ | $Pd(OAc)_2$ | **3a** | rt | 1:1.2 | 43 | 19 (S) |
| **5** | $NaCH(COOEt)_2$ | $PdCl_2(PhCN)_2$ | **3a** | rt | 1:1.2 | – | – |
| **6** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3a** | rt | 1:3 | 89 | 87 (R) |
| **7**[d] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3a** | rt | 1:3 | 80 | 50 (R) |
| **8** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3a** | 60 | 1:3 | 83 | 76 (R) |
| **9** | $CH_2(COOMe)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3a** | 60 | 1:3 | 85 | 81 (R) |
| **10** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3a** | −10 | 1:3 | 90 | 75 (R) |
| **11** | $CH_2(COOEt)_2$/BSA | $Pd_2(dba)_3$ | **3a** | rt | 1:3 | 57 | 51 (R) |

[a] Reactions were carried under glove box atmosphere (argon) and monitored via TLC analysis. Solvent: THF. Pd/L = 1:1.
[b] Isolated yields based on 1,3-diphenylprop-2-enyl acetate (**6**).
[c] Determined on HPLC (chiralcel OJ column); hexane/AcOEt:95/5. Configuration assigned through comparison with HPLC data reported in the literature [17].
[d] The Pd/L ratio is 1:2.

ligand **3a** to $[PdCl(C_3H_5)]_2$ also catalyzed the reaction, although the final product **7** was obtained in lower enantioselectivity compared to a 1:1 ratio of ligand:Pd (entry 7).

The selectivity observed in the presence of ligand **3a** can be explained on the basis of the relative rates of reaction at C1 and C3 positions of the diasteromeric π-allyl intermediates **8a** (*endo*) and **8b** (*exo*) arising from the reaction between the catalyst and allyl acetate **6** (Scheme 4) [3f,18,19].

Previous mechanistic studies on allylic substitution reactions provide evidence that the attack *trans* to the Pd–P bond is more facile than the attack *trans* to the Pd–N bond, as was shown by Pfaltz and coworkers with Pd complexes of $C_2$-symmetric bis(oxazoline) ligands. In this case, the reaction at the allylic carbon connected to the weaker (longer) Pd–P bond was demonstrated [20]. The major enantiomer of the final product (*R* configuration) can only arise from the attack of malonate on




Scheme 4.

intermediate **8b**. The differentiation between **8a** and **8b** accounts for the observed enantioselectivity in our system. Presumably, the favorable stacking interaction between the phenyl ring in C3 position of the allyl moiety in **8b** and the imine aryl substituent positioned over the plane of the complex shifts the equilibrium towards **8b** leading to the major enantiomer observed.

Other iminophosphines **3b–g** were tested in the same reaction using the diethyl malonate/BSA method, in order to investigate the effect of different aryl rings in the imine moiety on enantioselectivity. The results are summarized in Table 4.

The selectivity obtained in the presence of ligand **3b** is similar to the selectivity observed using **3a** (entry 1). This means that the presence of an electron-donating methoxy group at the ortho position to the imine moiety neither enhances nor decreases the yield and enantioselectivity of the reaction, thereby not affecting equilibrium between the two π-allyl intermediates **8a** and **8b**. In the case of electron-withdrawing substituents in the ortho position to the imine moiety such as in compound **3c**, the enantioselectivity is significantly decreased (entry 2). In addition, the final product is formed with opposite selectivity (*S*) as opposed to the predominantly formed (*R*) configuration in all other instances. The same outcome is obtained in the case of **3d**, where the pyridine nitrogen may engage in side coordination (entry 3). In the case of ligand **3e**, the reactivity of the catalyst is significantly enhanced with the reaction reaching completion after only five minutes, although enantioselectivities are diminished (entry 4). This is most likely due to unfavorable destabilizing interactions in the π-allyl intermediates between the bulky anthracenyl substituent and the phenyl groups of the acetate. The ligands with *ortho*-OH groups (compounds **3f** and **3g**) catalyzed the reaction with good yield but low enantioselectivity and longer reaction times (entries 7 and 8).

Table 4
Palladium-catalyzed allylic substitution in the presence of iminophosphines **3b**–**g**[a]

| Entry | Nucleophile | Pd precursor | Ligand | Substrate/nucleophile | Yield[b] (%) | ee[c] (%) |
|---|---|---|---|---|---|---|
| **1** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3b** | 1:3 | 84 | 76 (R) |
| **2** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3c** | 1:3 | 83 | 18 (S) |
| **3** | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3d** | 1:3 | 60 | 51 (S) |
| **4**[d] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3e** | 1:3 | 70 | 21 (R) |
| **5**[e] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3e** | 1:3 | 69 | 30 (R) |
| **6**[f] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3e** | 1:3 | 70 | 36 (R) |
| **7**[g] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3f** | 1:3 | 75 | 20 (R) |
| **8**[g] | $CH_2(COOEt)_2$/BSA | $[PdCl(C_3H_5)]_2$ | **3g** | 1:3 | 80 | 25 (R) |

[a] Reactions were carried out under glove box atmosphere (argon) and monitored via TLC analysis. Solvent: THF. Pd/L = 1:1. Unless otherwise mentioned, all reactions went to completion in 4–5 h.
[b] Isolated yields based on 1,3-diphenylprop-2-enyl acetate (**6**).
[c] Determined on HPLC (chiralcel OJ column); hexane/AcOEt:95/5. Configuration assigned through comparison with HPLC data reported in the literature [17].
[d] Reaction went to completion after only 5 min.
[e] Reaction was carried out at −10 °C.
[f] Reaction was carried out at −30 °C.
[g] Reactions went to completion after 48 h.

## 3. Conclusions

Novel iminophosphines **3** have been synthesized from (*R*,*R*)-1-amino-2-diphenylphosphino cyclohexane (*R*.*R*)-**1** in good yields. The complexation chemistry of Pd(II) with **3a** was investigated by preparing the air stable complex $PdCl_2[\kappa^2$-*P*,*N*-(*R*,*R*)-2-$Ph_2PC_6H_{10}N$=CHPh)] (**4**). In the allylic substitution reaction of 1,3-diphenyl-2-propenyl acetate, the ligands **3a** and **3b** provided the best results. The main advantage of these systems is their modular nature, which allows for a potentially wide screening of different aldehydes and consequently the possibility of fine tuning the electronic and steric properties of the ligands. Further studies and improvement on the catalytic activity of these ligands are currently under investigation.

## 4. Experimental

### 4.1. General

Chemicals were purchased from Aldrich Chemical Co., Strem Chemical Co., Fischer Scientific Ltd. and Lancaster and used without further purification. In experiments requiring dry solvents, ether, toluene, hexanes, acetonitrile, dichloromethane were purchased in anhydrous form from Aldrich Chemical Co. Tetrahydrofuran (THF) was distilled over sodium-benzophenone ketyl under argon. Unless otherwise stated, all reactions were performed under nitrogen or argon atmosphere using flame-dried glassware and standard syringe-pump techniques. Analytical thin layer chromatography (TLC) was performed on Macherey Nagel precoated glass-backed TLC plates (SIL G/$UV_{254}$, 0.25 mm) purchased from Rose Scientific Limited and visualized by UV lamp (254 nm), iodine, ninhydrin, potassium permanganate, and cerium. Column chromatography was carried out using Silicycle 230–400 mesh silica gel or aluminum oxide, neutral, Brockman type 1. High-performance liquid chromatography (HPLC) was performed on HP-1100 series instrument using 4.6 mm × 25 cm Daicel CHIRALPAK OJ column. Gas–liquid-phase chromatography (GC) was done with HP-6890 series GC system using high performance capillary column HP-5. $^1$H NMR spectra were referenced to residual $CHCl_3$ ($\delta$ 7.27 ppm), $^{13}$C NMR spectra were referenced to $CDCl_3$ ($\delta$ 77.23 ppm), $^{19}$F NMR were referenced to $CFCl_3$ ($\delta$ 0 ppm) and $^{31}$P NMR spectra were referenced to 85% $H_3PO_4$ as internal standard ($\delta$ 0 ppm).

### 4.2. General synthesis of iminophosphine ligands

To a solution of $K_2CO_3$ (105 mg, 0.762 mmol) and (*R*,*R*)-1-amino-2-diphenylphosphino tartrate salt (**2**) [13] (300 mg, 0.693 mmol) in degassed $H_2O$ (5 mL) was added degassed THF (2.1 mL), and the solution was heated to reflux. A solution of aldehyde (0.762 mmol) in degassed THF (1 mL) was added dropwise. The addition funnel was washed with 1 mL degassed THF and the reaction was stirred at reflux for 2 h. After cooling the reaction mixture to room temperature, the solution was poured into degassed $Et_2O$ (10 mL) and the organic layer was separated. The aqueous layer was extracted with degassed $Et_2O$ (3 × 2 mL), and the combined organic layers were washed with degassed $H_2O$ (3 mL), dried over $Na_2SO_4$, filtered, and concentrated in vacuo.

#### 4.2.1. Trans-N-benzylidene-1-amino-2-diphenlyphosphino cyclohexane (*3a*)

Crystallized using degassed EtOH and obtained as a white solid (177 mg, 89% yield). $^1$H NMR ($CDCl_3$,

400 MHz): $\delta$ 8.13 ppm (s, 1H), 7.42–7.51 ppm (m, 5H), 7.13–7.36 ppm (m, 10H), 3.2–3.3 ppm (m, 1H), 2.68–2.78 ppm (m, 1H), 1.7–1.9 ppm (m, 4H), 1.58–1.66 ppm (m, 1H), 1.1–1.46 ppm (m, 3H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 159.8 (s), 135.0 (d, $J$ = 20.5 Hz), 133.4 (d, $J$ = 19 Hz), 130.4 (s), 128.9 (s), 128.3 (d, $J$ = 3 Hz), 128.2 (s), 128.1 (d, $J$ = 6.9 Hz), 127.9 (s), 74.4 (s), 74.2 (s), 40.5 (d, $J$ = 12.9 Hz), 35.5 (s), 35.4 (s), 27.9 (s), 27.8 (s), 26.3 (d, $J$ = 6.8 Hz), 24.9 (s); $^{31}$P NMR ($CDCl_3$, 300 MHz): $\delta$ −4.372 ppm; $[\alpha]_D^{25} = -31.7$ (c 1.0, EtOH); m.p. 94–96 °C; HR-MS (FAB) *m/z*: Calc. for $C_{25}H_{26}NP$, 371.1803. Found: 371.1808.

#### 4.2.2. Trans N-(2′-methoxybenzylidene)-1-amino-2-diphenylphosphino cyclohexane (**3b**)

Obtained as clear oil (177 mg, 80% yield) after chromatography on basic alumina column with hexanes:ethyl acetate (7:3). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 8.63 ppm (s, 1H), 7.55–7.43 ppm (m, 5H), 7.17–7.29 ppm (m, 7H), 6.81 ppm (d, $J$ = 8 Hz, 1H), 6.73 (t, $J$ = 7.6 Hz, 1H), 3.83 ppm (s, 3H), 3.21–3.29 ppm (m, 1H), 2.69–2.76 ppm (m, 1H), 1.60–1.81 ppm (m, 6H), 1.31–1.40 ppm (m, 2H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 155.9 (s), 135.1 (d, $J$ = 20.5 Hz), 133.4 (d, $J$ = 18.2 Hz), 131.5 (s), 128.9 (s), 128.25 (s), 128.17 (s), 128.1 (s), 128.06 (s), 127.8 (d, $J$ = 9.1 Hz), 120.6 (s), 110.7 (s), 74.5 (s), 74.4 (s), 55.6 (s), 40.5 (d, $J$ = 13 Hz), 35.7 (s), 35.6 (s), 27.8 (s), 27.7 (s), 26.3 (d, $J$ = 6.1 Hz), 24.9 (s); $^{31}$P NMR ($CDCl_3$, 300 MHz): $\delta$ −4.617 ppm; $[\alpha]_D^{25} = -34.8$ (c 1.0, EtOH); HR-MS (FAB) *m/z*: Calc. for $C_{26}H_{28}NPO$, 401.1908. Found: 401.1898.

#### 4.2.3. Trans N-(2′-fluorobenzylidene)-1-amino-2-diphenylphosphino cyclohexane (**3c**)

Obtained as yellow oil (yield 70%). $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 8.48 ppm (s, 1H), 7.52–7.41 ppm (m, 4H), 7.21–7.13 ppm (m, 7H), 6.97–6.90 ppm (m, 3H), 3.25–3.31 ppm (m, 1H), 2.70–2.76 ppm (m, 1H), 1.85–1.62 ppm (m, 6H), 1.15–1.43 ppm (m, 2H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 153.1 (d, $J$ = 5.4 Hz), 134.9 (d, $J$ = 20.7 Hz), 133.4 (d, $J$ = 19 Hz), 128.9 (s), 128.3 (s), 128.2 (s), 128.1 (s), 128.0 (s), 127.8 (s), 124.0 (d, $J$ = 4 Hz), 115.5 (s), 115.2 (s), 74.7 (s), 74.5 (s), 40.2 (d, $J$ = 13 Hz), 35.5 (s), 35.3 (s), 27.8 (s), 27.7 (s), 26.2 (d, $J$ = 6.8 Hz), 24.8 (s); $^{31}$P NMR ($CDCl_3$, 300 MHz): $\delta$ −4.521 ppm; $^{19}$F NMR ($CDCl_3$, 300 MHz): $\delta$ −122.77 ppm (dd, $J_1$ = 11.7 Hz, $J_2$ = 5.7 Hz); $[\alpha]_D^{25} = -28.5$ (c 1.0, EtOH); HR-MS (FAB) *m/z*: Calc. for $C_{25}H_{25}NPF$, 389.4524. Found: 389.6638.

#### 4.2.4. Trans N-(2′-pyridinyl)-1-amino-2-diphenylphosphino cyclohexane (**3d**)

Obtained as a yellow solid after column chromatography on alumina, hexanes: ethyl acetate (8:2) in 80% yield. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 8.28 (s, 1H), 7.15–7.53 (m, 14H), 3.33–3.41 (m, 1H), 2.70–2.78 (m, 1H), 1.64–1.82 (m, 4H), 1.32–1.43 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 160.7 (s), 149.2 (s), 136.3 (s), 134.9 (d, $J$ = 20.8 Hz), 133.4 (d, $J$ = 18.8 Hz), 128.9 (s), 128.3 (d, $J$ = 15 Hz), 128.2 (d, $J$ = 14.2 Hz), 127.9 (s), 124.6 (s), 121.5 (s), 73.6 (s), 73.4 (s), 40.3 (d, $J$ = 13.0 Hz), 35.2 (s), 35.1 (s), 27.6 (s), 27.5 (s), 26.2 (d, $J$ = 6.6 Hz), 24.7 (s); $^{31}$P NMR ($CDCl_3$, 300 MHz): $\delta$ −4.957 ppm; $[\alpha]_D^{25} = -40.6$ (c 1.0, EtOH); m.p. 65–67 °C; HR-MS (FAB) *m/z*: Calc. for $C_{24}H_{25}N_2P$, 372.4498. Found: 372.4486.

#### 4.2.5. Trans N-anthracenyl-1-amino-2-diphenlyphosphino cyclohexane (**3e**)

Obtained as a yellowish-white solid in 89% yield. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 9.44 (s, 1H), 8.65–8.68 (m, 2H), 8.47 (s, 1H), 7.98–8.01 (m, 2H), 7.43–7.56 (m,8H), 7.34–7.36(m, 3H), 7.13–7.22 (m, 3H), 3.44–3.54 (m, 1H), 2.77–2.85 (m, 1H), 1.82–2.05 (m, 1H), 1.25–1.46 (m, 8H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 159.7 (s), 135.5 (d, $J$ = 20.9 Hz), 132.7 (d, $J$ = 16.5 Hz), 131.5 (s), 130.2 (s), 129.2 (s), 128.9 (s), 128.4 (s), 128.3 (s), 128.26 (s), 128.2 (s), 127.6 (s), 126.7 (s), 125.6 (d, $J$ = 4.2 Hz), 125.4 (s), 73.9 (s), 73.8 (s), 40.9 (d, $J$ = 14.8 Hz), 36.3 (s), 36.2 (s), 27.0 (s), 26.2 (d, $J$ = 3.4 Hz), 24.8 (s); $^{31}$P NMR ($CDCl_3$, 100 MHz): $\delta$ −5.149 ppm; $[\alpha]_D^{25} = -41.5$ (c 1.0, EtOH); HR-MS (FAB) *m/z*: Calc. for $C_{33}H_{30}NP$, 471.5817. Found: 471.5825.

#### 4.2.6. Trans N-(2′-hydroxobenzylidene)-1-amino-2-diphenylphosphino cyclohexane (**3f**)

Obtained as a yellow oil in 88% yield. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 8.19 (s, 1H), 7.41–7.49 (m, 4H), 7.11–7.32 (m, 8H), 6.80–6.83 (m, 2H), 3.22–3.28 (m, 1H), 2.60–2.65 (m, 1H), 1.93–1.96 (m, 1H), 1.66–1.81 (m, 3H), 1.21–1.44 (m, 5H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 163.5 (s), 134.8 (d, $J$ = 21.2 Hz), 133.3 (d, $J$ = 19.8 Hz), 132.1 (s), 131.5 (s), 129.2 (s), 128.6 (s), 128.5 (d, $J$ = 3 Hz), 128.4 (s), 128.3 (s), 118.4 (s), 117.0 (s), 71.1 (s), 70.9 (s), 40.5 (d, $J$ = 13.6 Hz), 34.7 (s), 34.6 (s), 27.0 (s), 26.9 (s), 25.4 (d, $J$ = 6 Hz), 24.2 (s); $^{31}$P NMR ($CDCl_3$, 100 MHz): $\delta$ −6.895 ppm; $[\alpha]_D^{25} = -95.2$ (c 1.0, EtOH); HR-MS (FAB) *m/z*: Calc. for $C_{25}H_{26}NPO$, 387.4614. Found: 387.4612.

#### 4.2.7. Trans N-(2′-hydroxo-3′-methoxybenzylidene)-1-amino-2- diphenylphosphino cyclohexane (**3g**)

Obtained as a yellowish-white solid in 89% yield. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 8.16 (s, 1H), 7.42–7.48 (m, 4H), 7.30–7.32 (m, 2H), 7.14–7.22 (m, 2H), 6.87 (dd, $J_1$ = 7.2 Hz, $J_2$ = 2.4 Hz, 1H), 6.73–6.77 (m, 1H), 3.88 (s, 3H), 3.24–3.30 (m, 1H), 2.60–2.64 (m, 1H), 1.99–2.04 (m, 1H), 1.81–1.83 (m, 3H), 1.39–1.46 (m, 8H); $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ 163.4 (s), 134.6 (d, $J$ = 20.5 Hz), 133.3 (d, $J$ = 19.7 Hz), 129.2 (s), 128.6 (s), 128.56 (s), 128.52 (s), 128.49 (s), 128.46 (s), 123.2 (s), 117.7 (s), 114.2 (s), 95.7 (s), 69.7 (s), 69.6 (s), 56.4

(s), 40.5 (d, $J = 13.7$ Hz), 33.9 (s), 29.9 (s), 26.5 (s), 24.9 (s), 23.7 (s); $^{31}$P NMR ($CDCl_3$, 100 MHz): $\delta$ −8.30 ppm; $[\alpha]_D^{25} = -71.7$ (c 1.0, EtOH); HR-MS (FAB) *m/z*: Calc. for $C_{26}H_{28}NPO_2$, 417.4877. Found: 417.4870.

### 4.3. Synthesis of $PdCl_2[\kappa_2$-P-N-(R,R)-2-$Ph_2PC_6H_{10}N{=}CHPh]$ (4)

$PdCl_2(PhCN)_2$ (16.5 mg, 43 μmol) was dissolved in 1 mL of $CH_2Cl_2$, and a solution ligand **3a** (18 mg, 48 μmol) in $CH_2Cl_2$ was added dropwise, providing a yellow solution after 1 min. After 2 h, the solvent was evacuated and the residual orange solid was washed with ether three times. The complex was crystallized by slow diffusion of ether into a nitromethane solution of the complex. Crystals suitable for X-ray crystallography were obtained in 65% yield. $^1$H NMR ($CD_2Cl_2$, 400 MHz): $\delta$ 8.49 (s, 1H), 8.40 (d, $J = 7.6$ Hz, 1H), 8.10–8.14 (m, 2H), 7.81–7.86 (m, 2H), 7.47–7.68 (m, 10H), 4.40–4.43 (m, 1H), 2.53–2.56 (m, 1H), 2.22–2.28 (m, 2H), 1.63–1.83 (m, 2H), 1.23–1.37 (m, 2H), 0.88–0.98 (m, 2H)); $^{13}$C NMR ($CD_2Cl_2$, 125 MHz): $\delta$ 167.8 (s), 135.0 (d, $J = 19$ Hz), 133.9 (s), 133.6 (s), 133.5 (d, $J = 15.75$ Hz), 132.7 (s), 131.6 (s), 130.1 (s), 129.9 (s), 129.6 (s), 129.1 (d, $J = 20.4$ Hz), 128.7 (s), 76.4 (s), 47.9 (s), 47.5 (s), 32.8 (s), 32.6 (s), 30.5 (s), 30.2 (s), 26.8 (d, $J = 13.75$ Hz), 24.1; $^{31}$P NMR ($CD_2Cl_2$, 100 MHz): $\delta$ 46.6 ppm; m.p. 278–279 °C

### 4.4. Crystallographic data measurements

Data were collected on a Nonius Kappa-CCD diffractometer using monochromated Mo Kα radiation. Each data set was measured using a combination of ϕ scans and ω scans with κ offsets, to fill the Ewald sphere. The data were proceesed using the Denzo-SMN package [21]. Absorption corrections were carried out using SORTAV [22]. The structure was solved and refined using SHELXTL V6.1 [23] for full-matrix least-squares refinement that was based on $F^2$. Crystallographic data for the compound is given in Tables 1 and 2.

### 4.5. General procedure for allylic alkylation reactions

*Method A*: Pd(π-allyl)Cl]$_2$ (2 mol%) from a stock solution in dry THF (0.033 M) and the iminophosphine ligand (2 mol%) also from a stock solution in dry THF (0.022 M) were mixed together in a 25 mL vial equipped with a stir bar inside the glove box. After stirring at room temperature for approximately 10 min, 1,3-diphenyl-2-propenyl acetate (0.496 mmol, 125 mg) was added to the Pd/ligand mixture from a stock solution in dry THF (0.5M). After stirring the mixture again at room temperature for approximately 10 min, sodium salt of diethyl malonate (0.99 mmol, 2 equiv.) was added to the vial and the reaction was stirred at room temperature inside the glovebox. The reactions were followed by TLC (9:1 hexanes/ethyl acetate) and GC until completion. The reaction mixture was quenched with $H_2O$ (5 mL), and extracted with ether ($3 \times 5$ mL). The combined organic layers were dried with $MgSO_4$, filtered, and evacuated under vacuum.

*Method B*: [Pd(π-allyl)Cl]$_2$ (2 mol%, 1.81 mg) from a stock solution in dry THF (0.033 M) and the iminophosphine ligand (2 mol%) also from a stock solution in dry THF (0.022 M) were mixed together in a 25 mL vial equipped with a stir bar inside the glove box. After stirring at room temperature for approximately 10 min, 1,3-diphenyl-2-propenyl acetate (0.496 mmol, 125 mg) was added to the Pd/ligand mixture from a stock solution in dry THF (0.5 M). After stirring the mixture again at room temperature for approximately 10 min, diethyl malonate (1.488 mmol, 238 mg), N,O-bis trimethylsilyl acetamide (1.488 mmol, 332.5 mg) and potassium acetate (10 mg) were added to the vial and the reaction was stirred at room temperature inside the glovebox. The reactions were followed by TLC (9:1 hexanes/ethyl acetate) and GC until completion. The reaction mixture was quenched with $H_2O$ (5 mL), and extracted with ether ($3 \times 5$ mL). The combined organic layers were dried with $MgSO_4$, filtered, and evacuated under vacuum. The final product was purifed by flash column chromatography (silica gel, hexanes: ethyl acetate 9:1). The enantioselectivity was determined by chiracel HPLC OJ column, 95:5 hexanes:isopropanol, flow rate 0.5 ml/min.

Diethyl 1-(1,3-diphenylprop-2-enyl)malonate: $^1$H NMR ($CDCl_3$): $\delta$ 1.02 (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 3.98 (d, $J = 10.9$ Hz, 1H), 3.99 (q, $J = 7.1$ Hz, 2H), 4.19 (q, $J = 7.1$ Hz, 2H), 4.28 (dd, $J = 8.2$, 10.9 Hz, 1H), 6.38 (dd, $J = 8.2$, 15.7 Hz, 1H), 6.49 (d, $J = 15.7$ Hz, 1H), 7.20–7.32 (m, 10H).

## 5. Supplementary material

Crytallographic data for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 232269 for compound (**4**). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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## References


[1] (a) R. Noyori (Ed.), Adv. Synth. Cat., 345, 2003, p. 15;
(b) I. Ojima (Ed.), Catalytic Asymmetric Synthesis, Wiley-VCH, New York, 2000;
(c) E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, Springer, New York, 1999.

[2] (a) For recent developments in bidentate ligands chemistry, see: A. Pfaltz, Chimia 55 (2001) 708;
(b) M. McCarthy, P.J. Guiry, Tetrahedron 57 (2001) 3809;
(c) P.W.N.M. Van Leeuwen, P.C.J. Kamer, J.N.H. Reek, P. Dierkes, Chem. Rev. 100 (2000) 2741, See also:;
(d) R. Noyori (Ed.), Asymmetric Catalysis in Organic Synthesis, Wiley, New York, 1994.

[3] (a) For general reviews on P,N-ligands, see: P. Braunstein, F. Naud, Angew. Chem., Int. Ed. 40 (2001) 680;
(b) K.N. Gavrilov, A.I. Polosukhin, Russ. Chem. Rev. 69 (2000) 661;
(c) C.S. Slone, D.A. Weinberger, C.A. Mirkin, Prog. Inorg. Chem. 48 (1999) 233;
(d) P. Espinet, K. Soulantica, Coord. Chem. Rev. 193–195 (1999) 499, For allylic substitution, see:;
(e) Reference 2a;
(f) G. Helmchen, A. Pfaltz, Acc. Chem. Res. 33 (2000) 336;
(g) L. Haughton, J.M.J. Williams, J. Chem. Soc., Perk. Trans. 1 20 (2000) 3335, For Heck reaction, see:;
(h) O. Loiseleur, M. Hayashi, M. Keenan, N. Schmees, A. Pfaltz, J. Organomet. Chem. 576 (1999) 16, For hydrosilylation, see:;
(i) H. Nishiyama, in: E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive Asymmetric Catalysis, 1, Springer, Berlin, 1999, p. 267, For hydroboration, see:;
(j) F.Y. Kwong, Q. Yang, T.C.W. Mak, A.S.C. Chan, K.S. Chan, J. Org. Chem. 67 (2002) 2769, and references therein. For hydroformylation, see:;
(k) C. Abu-Gnim, I. Amer, J. Organomet. Chem. 516 (1996) 235;
(l) C. Basoli, C. Botteghi, M.A. Cabras, G. Chelucci, M. Marchetti, J. Organomet. Chem. 488 (1995) C20, For transfer hydrogenation to ketones, see:;
(m) P. Braunstein, F. Naud, A. Pfaltz, S.J. Rettig, Organometallics 19 (2000) 2676;
(n) P. Braunstein, C. Graiff, F. Naud, A. Pfaltz, A. Tiripicchio, Inorg. Chem. 39 (2000) 4468.

[4] A. Schnyder, L. Hintermann, A. Togni, Angew. Chem., Int. Ed. Engl. 34 (1995) 931.

[5] (a) E. Drent, P. Arnoldy, P.H.M. Budzelaar, J. Organomet. Chem. 455 (1993) 247;
(b) G.P.C.M. Dekker, A. Buijs, C.J. Elsevier, K. Vrieze, P.W.N.M. Van Leeuwen, W.J.J. Smeets, A.L. Spek, Y.F. Wang, C.H. Stam, Organometallics 11 (1992) 1937.

[6] (a) E. Shirakawa, Y. Nakao, Y. Murota, T. Hiyama, J. Organomet. Chem. 670 (2003) 132;
(b) M. Koprowski, R.M. Sebastián, V. Maraval, M. Zablocka, V. Cadierno, B. Donnadieu, A. Igau, A.M. Caminade, J.P. Majoral, Organometallics 21 (2002) 4680;
(c) A. Scrivanti, U. Matteoli, V. Beghetto, S. Antonaroli, B. Crociani, Tetrahedron 58 (2002) 6881;
(d) E. Shirakawa, T. Hiyama, J. Organomet. Chem. 576 (1999) 169.

[7] (a) E.K. van den Beuken, W.J.J. Smeets, A.L. Spek, B.L. Feringa, Chem. Commun. 2 (1998) 223;
(b) Z. Guan, W.J. Marshall, Organometallics 21 (2002) 3580.

[8] (a) K.S. Coleman, M.L.H. Green, S.I. Pascu, N.H. Rees, A.R. Cowley, L.H. Rees, J. Chem. Soc., Dalton Trans. 22 (2001) 3384;
(b) K.R. Reddy, C.L. Chen, Y.H. Liu, S.M. Peng, J.T. Chen, S.T. Liu, Organometallics 18 (1999) 2574.

[9] K.R. Reddy, K. Surekha, G.H. Lee, S.M. Peng, S.T. Liu, Organometallics 19 (2000) 2637.

[10] (a) P. Crochet, J. Gimeno, J. Borge, S. García-Granda, New J. Chem. 27 (2003) 414;
(b) P. Crochet, J. Gimeno, S. García-Granda, J. Borge, Organometallics 20 (2001) 4369;
(c) J.X. Gao, T. Ikariya, R. Noyori, Organometallics 15 (1996) 1087.

[11] S. Doherty, J.G. Knight, T.H. Scanlan, M.R.J. Elsegood, W. Clegg, J. Organomet. Chem. 650 (2002) 231.

[12] (a) M. Zablocka, M. Koprowski, B. Donnadieu, J.P. Majoral, M. Achard, G. Buono, Tetrahedron Lett. 44 (2003) 2413;
(b) A. Saitoh, K. Achiwa, K. Tanaka, T. Morimoto, J. Org. Chem. 65 (2000) 4227;
(c) A. Saitoh, T. Morimoto, K. Achiwa, Tetrahedron Asymm. 8 (1997) 3567.

[13] A. Caiazzo, S. Dalili, A.K. Yudin, Org. Lett. 4 (2002) 2597.

[14] A. Caiazzo, A.J. Lough, A.K. Yudin, Acta Cryst. E 59 (2003) m399.

[15] T. Suzuki, M. Rude, K.P. Simonsen, M. Morooka, H. Tanaka, S. Ohba, F. Galsbøl, J. Fujita, Bull. Chem. Soc. Jpn. 67 (1994) 1013.

[16] (a) B.M. Trost, D.L. Vranken, Chem Rev. 96 (1996) 395;
(b) B.M. Trost, D.J. Murphy, Organometallics 4 (1985) 1143.

[17] D.S. Clyne, Y.C. Mermet-Bouvier, N. Nomura, T.V. RajanBabu, J. Org. Chem. 64 (1999) 7601.

[18] (a) The terms endo and exo related to these kind of complexes were used for the first time by Faller for the description of diastereomeric π-allyl complexes: R.D. Adams, D.F. Chodosh, J.W. Faller, A.M. Rosan, J. Am. Chem. Soc. 101 (1979) 2570;
(b) J.W. Faller, K.H. Chao, J. Am. Chem. Soc. 105 (1983) 3893.

[19] G. Helmchen, J. Organomet. Chem. 576 (1999) 203.

[20] A. Pfaltz, Acc. Chem. Res. 26 (1993) 339.

[21] (a) Z. Otwinowski, W. Minor, Meth. Enzymol. 276 (1997);
(b) C.W. Carter, R.M. Sweet (Eds.), Macromolecular Crystallography, Part A, Academic press, London, pp. 307–326.

[22] R.H. Blessing, Acta Cryst. A 51 (1995) 33–38.

[23] G.M. Sheldrick, SHELXTL/PC. Version 6.1 Windows NT Version, Bruker AXS Inc., Madison, USA, 2001