CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200902442

# Copper-Catalyzed Enantioselective Hydrosilylation of Ketones by Using Monodentate Binaphthophosphepine Ligands

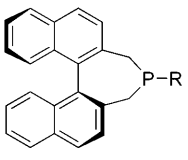
**Kathrin Junge, Bianca Wendt, Daniele Addis, Shaolin Zhou, Shoubhik Das, and Matthias Beller*[a]**

The asymmetric catalytic reduction of carbonyl compounds offers a convenient and efficient preparation of enantiomerically pure chiral alcohols.[1] In the past, various catalytic methods such as precious metal-catalyzed hydrogenation, transfer hydrogenation, and hydrosilylation have been intensively studied. Although asymmetric hydrogenations proceed with high enantioselectivities and good to excellent yields for a wide range of prochiral ketones, often high pressure, elevated temperatures, and special equipment are required. In contrast, asymmetric hydrosilylation offers an attractive alternative due to the smooth reaction conditions and the easy to use reducing agents. Since the first applications of Wilkinson's catalyst in catalytic hydrosilylations[2] three decades ago, much work has been published on the asymmetric hydrosilylation of ketones. In general, Rh-, Ru-, Ir-, Ti-, or Zn-based catalysts have been used and more recently also enantioselective Fe-catalyzed hydrosilylations have been reported.[3]

In the search for cheap and biomimetic catalysts, copper, aside of zinc and iron, offers interesting possibilities. Pioneering work in the field of copper-mediated enantioselective hydrosilylations was carried out by Brunner and co-workers in 1984.[4] Later on, inspired by the potential of Stryker's reagent $[(Ph_3P)CuH]_6$,[5,6] and the work of Buchwald and co-workers,[7] Lipshutz and his group[8] developed a highly effective catalyst system based on CuCl/*t*BuONa and chiral diphosphane ligands for asymmetric hydrosilylations. In the presence of SEGPHOS[8] or BINAP[9] aryl alkyl and heteroaromatic ketones are reduced with excellent enantioselectivities up to 98% *ee*. However, temperatures below −50 °C and addition of base were required for optimal enantiomeric excess. Noteworthy, a base-free and air-accelerating copper catalyst for the hydrosilylation of carbonyl compounds was presented by Riant and co-workers,[10] which was composed of copper(II) salts such as $Cu(OAc)_2$[11] or $CuF_2$[12] and BINAP. The resulting catalysts typically work at mild temperatures (room temperature to −20 °C), and a remarkably low substrate-to-ligand ratio (S/L up to 50000 and 100000) is needed for Xyl-P-Phos[12] for the hydrosilylation of a wide array of aryl alkyl ketones. Finally, it should be mentioned that also heterogeneous copper sources (copper-in-charcoal,[13] copper nanoparticles,[14] and copper–aluminum hydrotalcide[15]) were applied for enantioselective reductions.

Although various copper-based catalysts have been investigated for the asymmetric hydrosilylation of carbonyl compounds, the number of phosphorus ligands applicable in these reactions is rather limited, and many ligands, which are well established in asymmetric hydrogenations, show low chiral induction.[8c,10b]

In recent years, we and others[16] demonstrated the usefulness of monodentate ligands derived from the binaphthophosphepine backbone in asymmetric hydrogenations,[17] transfer hydrogenations,[18] and hydroformylations.[19] Although the potential of chiral monodentate ligands for hydrosilylation reactions has been pointed out in several reviews,[20] to the best of our knowledge there is no reported example of such a copper-catalyzed reaction.[21] Monodentate phosphorus ligands have the advantage of easier syntheses and tuning compared with their bidentate counterparts. Hence, we became interested in testing monodentate phosphepine ligands **1** (Scheme 1) in the hydrosilylation of pro-




**1**

**1a**: $C_6H_5$
**1b**: Et
**1c**: *i*Pr
**1d**: *t*Bu
**1e**: 4-F-$C_6H_4$
**1f**: 4-MeO-$C_6H_4$
**1g**: 4-$CF_3$-$C_6H_4$
**1h**: 4-$Me_2N$-$C_6H_4$
**1i**: 3,5-$Me_2$-$C_6H_3$
**1j**: 2-MeO-$C_6H_4$
**1k**: 3,4,5-$F_3$-$C_6H_2$
**1l**: 2-(1-methyl)-$^1$*H*-pyrrole

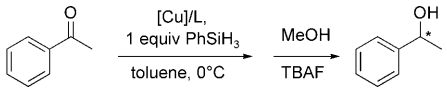
Scheme 1. Structure of monodentate ligands.

[a] Dr. K. Junge, B. Wendt, D. Addis, S. Zhou, S. Das, Prof. Dr. M. Beller
Leibniz-Institut für Katalyse e.V. an der Universität Rostock
Albert-Einstein-Strasse 29a, 18059 Rostock (Germany)
Fax: (+49) 381-1281-5000
matthias.beller@catalysis

chiral ketones using copper as catalyst metal. As a benchmark reaction, the reduction of acetophenone to 1-phenylethanol with phenylsilane as hydrogen source in the presence of different copper precursors and 4-phenyl-4,5-dihydro-3*H*-dinaphtho[2,1-*c*;1',2'-*e*]phosphepine (**1a**) was chosen. Initially, the copper source was investigated in detail (Table 1). In all experiments the corresponding alcohol is detected in good yield after basic cleavage of the corresponding silyl ether. However, most of the copper(I) and copper(II) precursors showed no or poor enantioselectivity. Nevertheless, promising results were achieved in the presence of copper acetate (Table 1, entries 13 and 14). By applying $Cu(OAc)_2 \cdot H_2O$, 1-phenylethanol is obtained in 83% *ee* after 1 h, which is in the same range as achieved with the diphosphane-based system developed by Yun and Lee[11] (Table 1, entry 15). Interestingly, the use of hydrated $Cu(OAc)_2 \cdot H_2O$ rather than $Cu(OAc)_2$ improved both the product yield as well as the enantioselectivity.

It is known from the work of Chan et al.[12] and Riant et al.[10] that fluoride in the copper precursor is crucial for the generation of the active catalyst. However, for our system we did not observe this effect (Table 1, entry 6).

Table 1. Asymmetric hydrosilylation of acetophenone: Effect of copper precursors.[a]



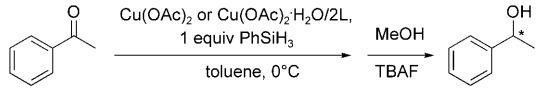

2a 3a

| Entry | Copper precursor | Ligand | Yield [%] | *ee* [%] |
|---|---|---|---|---|
| 1 | CuCl | **1a** | 83 | rac |
| 2 | CuBr | **1a** | 74 | rac |
| 3 | CuI | **1a** | 78 | 7 (*R*) |
| 4 | CuOTf | **1a** | 55 | 5 (*R*) |
| 5 | $Cu_2O$ | **1a** | 80 | rac |
| 6 | $CuF_2$ | **1a** | 79 | rac |
| 7 | $CuCl_2$ | **1a** | 81 | rac |
| 8 | $CuF_2 \cdot H_2O$ | **1a** | 86 | 44 (*R*) |
| 9 | $CuCl_2 \cdot H_2O$ | **1a** | 78 | rac |
| 10 | CuO | **1a** | 81 | 18 (*R*) |
| 11 | $Cu(NO_3)_2 \cdot H_2O$ | **1a** | 79 | 6 (*R*) |
| 12 | $CuSO_4 \cdot 5H_2O$ | **1a** | 89 | rac |
| 13 | $Cu(OAc)_2$ | **1a** | 82 | 78 (*R*) |
| 14[b] | $Cu(OAc)_2 \cdot H_2O$ | **1a** | 91 | **83 (*R*)** |
| 15[c] | $Cu(OAc)_2 \cdot H_2O$ | S-BINAP | 93 | 80 (*S*) |

[a] General conditions: copper salt (3 mol%), **1a** (6 mol%), acetophenone (1 mmol), $PhSiH_3$ (1 equiv), toluene (1 mL), 3 h, 0°C. [b] 1 h, 0°C. [c] Copper salt (3 mol%), S-BINAP (3 mol%), 1 h, 0°C.

Next, the influence of the silane was investigated in the presence of both hydrated and water-free copper acetate. As illustrated in Table 2, the catalytic activity and stereoselectivity depends to a large extent on the nature of the reducing agent. The highest yields and enantioselectivities are obtained by using monoaryl- and diarylsilanes such as $PhSiH_3$ and $Ph_2SiH_2$ (Table 2, entries 1 and 2), while depletion of the reaction rate and lower *ee* values were observed with alkyl- and alkyl(aryl)silanes or polysiloxanes (Table 2, entries 3–7).

Table 2. Asymmetric hydrosilylation of acetophenone: Effect of silanes.[a]

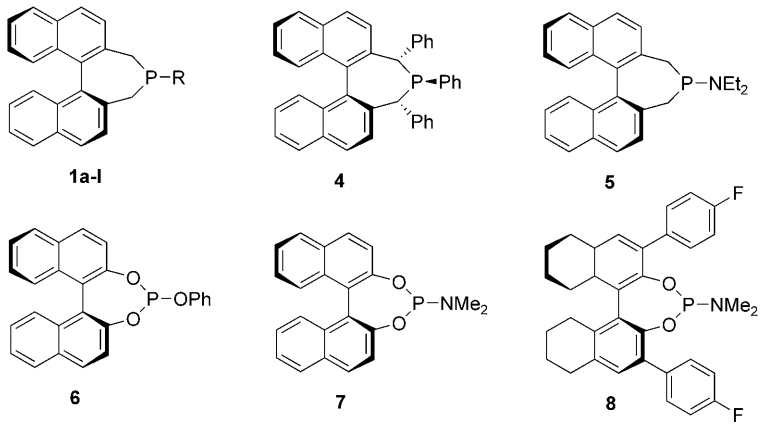



2a 3a

| Entry | Silane | $Cu(OAc)_2$ | | $Cu(OAc)_2 \cdot H_2O$ | |
|---|---|---|---|---|---|
| | | yield [%] | *ee* [%] (*R*) | yield [%] | *ee* [%] (*R*) |
| 1 | $Ph_2SiH_2$ | 86 | 78 | 85 | **83** |
| 2 | $PhSiH_3$ | 91 | **83** | 90 | **84** |
| 3 | $Me_2PhSiH$ | 24 | 12 | 25 | 12 |
| 4 | $MeEt_2SiH$ | 12 | 19 | 15 | 2 |
| 5 | $Et_2SiH_2$ | 87 | 17 | 64 | 14 |
| 6 | $(EtO)_2MeSiH$ | 46 | 62 | 36 | 44 |
| 7 | PMHS | 61 | 21 | 52 | 15 |
| 8 | $Cl_3SiH$ | 38 | 80 | 38 | 80 |

[a] General conditions: copper salt (3 mol%), **1a** (6 mol%), acetophenone (1 mmol), silane (1 equiv), toluene (1 mL), 3 h, 0°C.

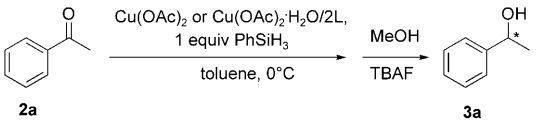
Interestingly, the economically attractive trichlorosilane furnished up to 80% *ee*, but only moderate amounts of product were obtained. Hence, phenylsilane was chosen for further studies. Within the process of optimization of the reaction parameters, we also explored the influence of the ligand structure (Scheme 2). Here, 13 different monodentate phosphepines **1a–l** and **4**, phosphoramidites **5**, **7**, and **8**, and phosphite **6** were tested in the hydrosilylation of acetophenone with copper acetate. As shown in Table 3, the phenyl-substituted phosphepine ligand **1a** showed the best performance. After 3 h, yields up to 92% and enantioselectivities




Scheme 2. Selected monodentate ligands tested in the asymmetric hydrosilylation.

Table 3. Asymmetric hydrosilylation of acetophenone: Effect of ligands.[a]




2a 3a

| Entry | Ligand | $Cu(OAc)_2$ | | $Cu(OAc)_2 \cdot H_2O$ | |
|---|---|---|---|---|---|
| | | yield [%] | *ee* [%] | yield [%] | *ee* [%] |
| 1 | **1a** | 91 | 83 (*R*) | 90 | 84 (*R*) |
| 2[b] | **1a** | 92 | **87** (*R*) | 88 | **86** (*R*) |
| 3 | **1b** | 90 | 37 (*R*) | 53 | 31 (*R*) |
| 4 | **1c** | 48 | 29.5 (*S*) | 80 | 28 (*S*) |
| 5 | **1d** | 5 | rac | 29 | 3 (*R*) |
| 6 | **1e** | 83 | 78 (*R*) | 83 | 71 (*R*) |
| 7 | **1f** | 92 | 82.5 (*R*) | 90 | 82.5 (*R*) |
| 8[b] | **1f** | 84 | **86** (*R*) | 87 | **85** (*R*) |
| 9 | **1g** | 75 | 83 (*R*) | 87 | 83 (*R*) |
| 10[b] | **1g** | 89 | 82 (*R*) | – | – |
| 11 | **1h** | 88 | 76 (*R*) | 86 | 65 (*R*) |
| 12 | **1i** | 88 | 66 (*R*) | 80 | 51 (*R*) |
| 13 | **1j** | 25 | 52 (*S*) | 78 | 44 (*S*) |
| 14 | **1k** | <2 | n.d.[c] | 70 | 77 (*R*) |
| 15 | **1l** | 11 | 67 (*S*) | 56 | 72 (*S*) |
| 16 | **4** | 5 | 44 (*R*) | <1 | n.d.[c] |
| 17 | **5** | 3 | 57 (*S*) | – | – |
| 18 | **6** | 18 | 5 (*S*) | – | – |
| 19 | **7** | 3 | rac | – | – |
| 20 | **8** | 2 | 11 (*S*) | – | – |

[a] General conditions: copper salt (3 mol%), **1**, **4**–**8** (6 mol%), acetophenone (1 mmol), $PhSiH_3$ (1 equiv), toluene (1 mL), 3 h, 0°C. [b] 5 h, −20°C. [c] Not determined.

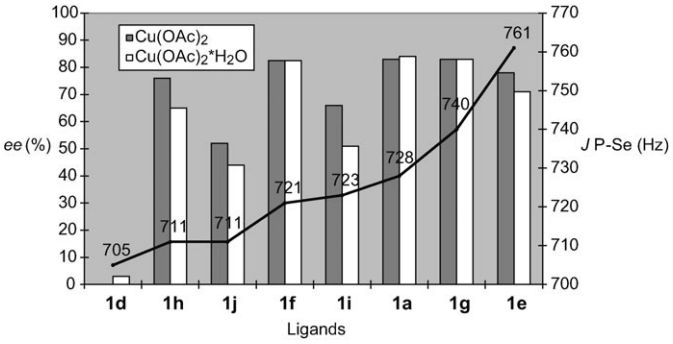



Figure 1. Graphical representation of selectivity in hydrosilylation of acetophenone in relation to the coupling constant $^1J_{P-Se}$ of binaphthophosphenines **1**.

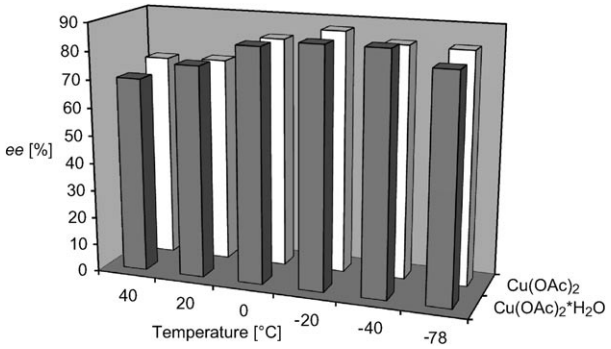



Figure 2. Graphical representation of relation between temperature and enantioselectivity for the hydrosilylation of acetophenone with [Cu]/**1a**.

up to 84% *ee* are obtained (Table 3, entry 1). Two other aryl-substituted phosphepines (**1f** and **1g**) provided comparable enantioselectivities to **1a** (Table 3, entries 7 and 9). In general, alkyl-substituted phosphepines gave less favorable results (Table 3, entries 3–5).

In order to draw conclusions about possible structure–activity relationships and to estimate the steric and electronic properties of ligands **1a–l**, the first-order coupling constant between the phosphorus and selenium atom of the corresponding selenides was analyzed.[19] The magnitude of the $^{77}Se$–$^{31}P$ coupling constants reveals the σ character of the phosphorus lone-pair orbital. The greater the coupling constants between $^{31}P$ and $^{77}Se$, the stronger the σ bond between the two, which in turn indicates a less basic phosphane.[22] In Figure 1, the $^{77}Se$–$^{31}P$ coupling constants are correlated with the enantioselectivity reported for the asymmetric hydrosilylation of acetophenone with [Cu]/**1** (Table 3). In fact, there is no clear trend observed: binaphthophosphepine ligands **1g** ($J = 740$ Hz) and **1f** ($J = 721$ Hz), which vary electronically, both show high enantiomeric excess. Hence, we believe that the enantioselectivity in this copper-catalyzed reduction is controlled more by steric than by electronic factors.

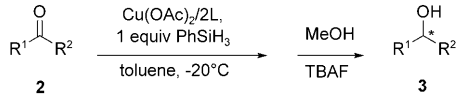
Next, the influence of the temperature on the hydrosilylation of acetophenone in the presence of **1a** was investigated. As stated before the copper catalysts developed by Lipshutz et al.[8] gave the best enantioselectivities from −50 to −78°C. Similarly, Riant et al.[10] reported improved enantioselectivities at −20°C. Our results are depicted in Figure 2. With both catalyst systems at −20°C an optimal enantioselectivity up to 86% *ee* for $Cu(OAc)_2 \cdot H_2O$ and 87% *ee* for $Cu(OAc)_2$ is obtained, respectively (Table 3, entry 2).

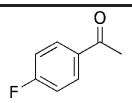
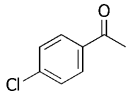
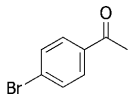
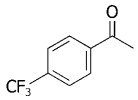
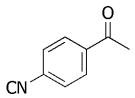
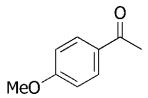
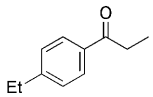
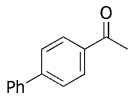
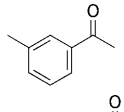
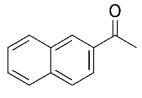
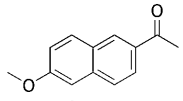
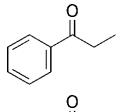
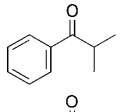
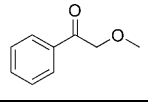
Finally, the general applicability of our protocol was tested for a broad range of aryl alkyl, cyclic, heterocyclic, and aliphatic substrates (Table 4 and Table 5). Complete hydrosilylation of most substrates is achieved with $PhSiH_3$ in the presence of anhydrous $Cu(OAc)_2$/**1a** at −20°C within 5 h. Introduction of electron-withdrawing groups at the *para* position of acetophenone resulted in increased enantioselectivity (Table 4, entries 1, 7, and 9), giving 89% *ee* for **2b**, 91% *ee* for **2g**, and 90% *ee* for **2i**, respectively. With respect to 4-haloacetophenones, the enantiomeric excess decreased in the sequence F > Cl > Br according to the decreasing induction effect. Electron-donating groups at the *ortho* and *meta* position of the aryl group led to high enantioselectivity (Table 4, entry 10–12).

Unfortunately, sterically more demanding aryl alkyl ketones were inert, despite running the reaction at ambient temperature (Scheme 3). However, high yields (83–99%) are determined for cyclic and heterocyclic ketones (Table 5, entries 1, 6, and 7), while the level of enantioselectivity ranges between 14% and 88% *ee*. In the case of cyclohexenylethanone, regioselective hydrosilylation of the carbonyl group and no reaction of the C=C double bond takes place (Table 5, entry 3). Notably, with our catalyst system the

Table 4. Asymmetric hydrosilylation of different ketones catalyzed by $Cu(OAc)_2$/**1a**.[a]

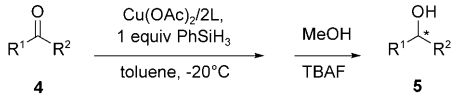


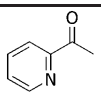
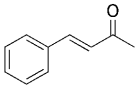
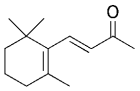
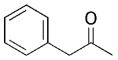
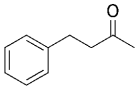

| Entry | Substrate | | Yield [%] | *ee* [%] |
|---|---|---|---|---|
| 1 |  | **2b** | 94 | 89 (*R*) |
| 2[b] | | | 99 | 90 (*R*) |
| 3 |  | **2c** | 79 | 80 (*R*) |
| 4 |  | **2d** | 82 | 76 (*R*) |
| 5 |  | **2e** | 83 | 37 (*R*) |
| 6 |  | **2f** | 78 | 35 (*R*) |
| 7 |  | **2g** | 57 | **91** (*R*) |
| 8 |  | **2h** | 99 | 87 (+) |
| 9 |  | **2i** | 75 | **90** (*R*) |
| 10 |  | **2j** | 72 | 80 (*R*) |
| 11 |  | **2k** | 73 | 89 (*R*) |
| 12[b] | | | 99 | **90** (*R*) |
| 13 |  | **2l** | 72 | 82 (*R*) |
| 14 |  | **2m** | 40 | 89 (*R*) |
| 15 |  | **2n** | 90 | 84 (*R*) |
| 16 |  | **2o** | 91 | 39 (*R*) |
| 17 |  | **2p** | 88 | 19 (*S*) |

[a] General conditions: copper salt (3 mol%), **1a** (6 mol%), ketone **2** (1 mmol), $PhSiH_3$ (1 equiv), toluene (1 mL), 5 h, −20°C. [b] 5 h, −40°C.

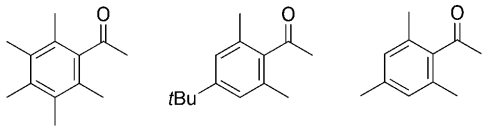
highest enantiomeric excess (>96% *ee*) ever reported for this ketone is obtained. Interestingly, this result represents

Table 5. Asymmetric hydrosilylation of different heterocyclic, cyclic and aliphatic ketones catalyzed by $Cu(OAc)_2$/**1a**.[a]




| Entry | Substrate | | Yield [%] | *ee* [%] |
|---|---|---|---|---|
| 1 |  | **4a** | 90 | 51 (*S*) |
| 2 |  | **4b** | 90 | 47 (*R*) |
| 3 |  | **4c** | 82 | **96** (*R*) |
| 4 |  | **4d** | C–C(O) 10<br>C=C 22<br>C–C 24 | –-<br>60 (−)<br>28 (*S*) |
| 5 |  | **4e** | 92 | 84 (*R*) |
| 6 |  | **4f** | 83 | 14 (*S*) |
| 7 |  | **4g** | 92 | 88 (*S*) |
| 8 |  | **4h** | 40 | 12 (*R*) |
| 9 |  | **4i** | >99 | 20 (*S*) |
| 10 |  | **4j** | 99 | 9 (*S*) |
| 11 |  | **4k** | 83 | 3 (n.d.[b]) |
| 12 |  | **4l** | 99 | 22 (*R*) |

[a] General conditions: copper salt (3 mol%), **1a** (6 mol%), ketone **4** (1 mmol), $PhSiH_3$ (1 equiv), toluene (1 mL), 5 h, −20°C. [b] Not determined.



**2q** **2r** **2s**

Scheme 3. Sterically demanding ketones showing no reaction with [Cu]/**1a**.

no general trend regarding α,β-unsaturated aliphatic ketones (Table 5, entries 3–5). Similarly, ketone **4e** is reduced with both chemo- and enantioselectivity (Table 5, entry 5). Also various aliphatic ketones could be reduced with good activity but low to moderate enantiomeric excess (Table 5, entries 9–12).

In summary, the first copper-catalyzed asymmetric hydrosilylation of carbonyl compounds by using chiral monodentate ligands is presented. Under comparably mild conditions, high yields and enantioselectivities (up to 96% *ee*) are achieved for a broad range of carbonyl compounds such as aryl alkyl, cyclic, heterocyclic, and aliphatic ketones. Compared to other known asymmetric hydrosilylation catalysts, advantageously no base or fluoride activation is necessary.

## Experimental Section

**General procedure**: A mixture of the silane (1 mmol), copper precursor ($3\times10^{-2}$ mmol), and ligand ($6\times10^{-2}$ mmol) in toluene (0.5 mL) was purged with argon in a Schlenk tube and stirred for 20 min at −20 °C. A solution of acetophenone (1 mmol) in toluene (0.5 mL) was transferred by syringe to the in situ generated catalyst. The reaction mixture was stirred for 3 or 5 h at −20 °C and quenched with methanol (2 mL) or distilled water (2 mL) and TBAF (1.2 mL; 1 M in THF). After the reaction mixture had been stirred for 2 h, hexadecane was added as standard. The yield was determined by GC (30 m HP 5 Agilent Technologies 50–300 °C) and the enantioselectivity was determined by HPLC or GC.

**2a**: *ee* values were determined by GC (50 m Lipodex E), (*S*)-**3a** 35.7 min and (*R*)-**3a** 36.9 min (85/35–6–180/2–8–200/15).

**2b**: *ee* values were determined by HPLC (Chiracel OD-H), (*S*)-**3b** 44.5 min and (*R*)-**3b** 52.7 min (eluent: *n*-heptane/ethanol 99:1; flow: 1.0 mL min$^{-1}$).

**2c**: *ee* values were determined by HPLC (Chiralcel OD-H), (*S*)-**3c** 26.4 min and (*R*)-**3c** 28.7 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.5 mL min$^{-1}$).

**2d**: *ee* values were determined by HPLC (Chiralcel OD-H), (*S*)-**3d** 30.9 min and (*R*)-**3d** 33.7 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.5 mL min$^{-1}$).

**2e**: *ee* values were determined by HPLC (Reposil 100), (*S*)-**3e** 32.0 min and (*R*)-**3e** 33.7 min (eluent: *n*-heptane/ethanol 99.75:0.25; flow: 0.5 mL min$^{-1}$).

**2f**: *ee* values were determined by GC (50 m Chiraldex ß-PM), (*R*)-**3f** 42.1 min and (*S*)-**3f** 43.0 min (120/30–6–180/15).

**2g**: *ee* values were determined by HPLC (Chiralcel OD-H), (*R*)-**3g** 21.7 min and (*S*)-**3g** 24.7 min (eluent: *n*-heptane/ethanol 98:2; flow: 1.0 mL min$^{-1}$).

**2h**: *ee* values were determined by HPLC (Chiralpak AD-H), (+)-**3h** 29.3 min and (−)-**3h** 31.7 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.4 mL min$^{-1}$).

**2i**: *ee* values were determined by HPLC (Chiralpak AD-H), (*S*)-**3i** 19.4 min and (*R*)-**3i** 23.3 min (eluent: *n*-heptane/ethanol 97:3; flow: 1.0 mL min$^{-1}$).

**2j**: *ee* values were determined by HPLC (Chiralcel OJ-H), (*S*)-**3j** 34.4 min and (*R*)-**3j** 36.8 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.5 mL min$^{-1}$).

**2k**: *ee* values were determined by HPLC (Chiralcel OD-H), (*R*)-**3k** 42.8 min and (*S*)-**3k** 54.3 min (eluent: *n*-heptane/ethanol 97:3; flow: 0.2 mL min$^{-1}$).

**2l**: *ee* values were determined by HPLC (Chiralcel OD-H), (*S*)-**3l** 19.0 min and (*R*)-**3l** 21.0 min (eluent: *n*-heptane/ethanol 97:3; flow: 1.0 mL min$^{-1}$).

**2m**: *ee* values were determined by HPLC (Chiralpak AD-H), (*S*)-**3m** 18.0 min and (*R*)-**3m** 20.0 min (eluent: *n*-heptane/ethanol 99:1; flow: 0.5 mL min$^{-1}$).

**2n**: *ee* values were determined by HPLC (Chiralcel OD-H), (*R*)-**3n** 8.4 min and (*S*)-**3n** 9.7 min (eluent: *n*-heptane/ethanol 97:3; flow: 1.0 mL min$^{-1}$).

**2o**: *ee* values were determined by HPLC (Chiralpak AD-H), (*R*)-**3o** 9.4 min and (*R*)-**3o** 10.4 min (eluent: *n*-heptane/ethanol 99.5:0.5; flow: 1.0 mL min$^{-1}$).

**2p**: *ee* values were determined by HPLC (Chiralcel OB-H), (*R*)-**3p** 5.1 min and (*S*)-**3p** 5.85 min (eluent: *n*-heptane/ethanol 95:5; flow: 1.0 mL min$^{-1}$).

**4a**: *ee* values were determined by HPLC (Chiralcel OD-H), (*R*)-**5a** 29.4 min and (*S*)-**5a** 31.4 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.5 mL min$^{-1}$).

**4b** *ee* values were determined by GC (50 m Chiraldex ß-PM), (*R*)-**5b** 62.4 min and (*S*)-**5b** 63.5 min (80/60–6–180/30).

**4c** *ee* values were determined by GC (50 m Lipodex E), (*S*)-**5c** 66.4 min and (*R*)-**5c** 67.3 min (70/75–6–180).

**4d**: *ee* values were determined by HPLC (Chiralcel OB-H), (−)-**5d** 14.5 min and (+)-**5d** 16.1 min (eluent: *n*-heptane/2-propanol 98:2; flow: 0.6 mL min$^{-1}$).

**4e**: *ee* values were determined by HPLC (Chiralpak AS-H), (*S*)-**5e** 19.8 min and (*R*)-**5e** 24.4 min (eluent: *n*-heptane/2-propanol 99:1; flow: 0.2 mL min$^{-1}$).

**4f**: *ee* values were determined by HPLC (Chiralcel OJ-H), (*S*)-**5f** 13.7 min and (*R*)-**5f** 16.4 min (eluent: *n*-heptane/ethanol 95:5; flow: 0.7 mL min$^{-1}$).

**4g**: *ee* values were determined by HPLC (Chiralcel OJ-H), (*S*)-**5g** 13.8 min and (*R*)-**5g** 19.3 min (eluent: *n*-heptane/ethanol 95:5; flow: 0.7 mL min$^{-1}$).

**4h**: *ee* values were determined by HPLC (Chiralcel OD-H), (*S*)-**5h** 21.4 min and (*R*)-**5h** 24.9 min (eluent: *n*-heptane/ethanol 99:1; flow: 1.0 mL min$^{-1}$).

**4i**: *ee* values were determined by HPLC (Chiralcel OB-H), (*R*)-**5i** 16.0 min and (*S*)-**5i** 17.2 min (eluent: *n*-heptane/ethanol 98:2; flow: 0.3 mL min$^{-1}$).

**4j**: *ee* values were determined by GC (50 m Lipodex E), (*S*)-**5j** 25.9 min and (*R*)-**5j** 29.4 min (40/35–6–180/2–8–200).

**4k**: *ee* values were determined by GC (50 m Chiraldex ß-PM), **5k** 13.7 min and **5k** 14.2 min (130/30–6–200/30).

**4l**: *ee* values were determined by GC (50 m Chiraldex ß-PM), (*S*)-**5l** 33.1 min and (*R*)-**5l** 33.5 min (40/30–10–180/5).

## Acknowledgements

The authors thank Dr. C. Fischer, S. Buchholz, S. Schareina, and A. Kammer (all at the Leibniz-Institut für Katalyse e.V.) for analytical and technical support.

**Keywords:** copper · homogeneous catalysis · hydrosilylation · ketones · P ligands

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Received: September 3, 2009
Published online: November 27, 2009

  