Tetrahedron 67 (2011) 4358–4363

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of new serine-based phosphinooxazoline ligands and iridium complexes for asymmetric hydrogenations

Axel Franzke [†], Felix Voss, Andreas Pfaltz [*]

Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

ARTICLE INFO

Article history:
Received 14 January 2011
Received in revised form 4 February 2011
Accepted 8 February 2011
Available online 13 February 2011

Keywords:
Asymmetric catalysis
Hydrogenation
Iridium
P,N-Ligands

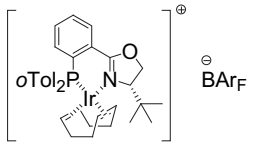
ABSTRACT

A series of serine-based phosphinooxazoline ligands was synthesized and the corresponding iridum complexes were successfully applied in the asymmetric hydrogenation of various unfunctionalized olefines and acetophenone-*N*-phenyl-imine. The results show that these new derivatives are useful substitutes for the standard *tert*-leucine-derived PHOX ligands.

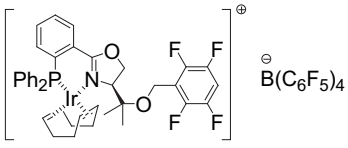
1. Introduction

Iridium complexes with chiral P,N-ligands have considerably enhanced the scope of asymmetric hydrogenation.[1,2] In contrast to rhodium and ruthenium diphosphine complexes, they do not require a coordinating group near the C=C double bond and, therefore, allow the highly enantioselective hydrogenation of a wide range of unfunctionalized tri- and even tetrasubstituted alkenes. In addition, they have also been successfully used for the hydrogenation of various functionalized olefins, heterocycles, such as furans and indoles, and imines.

The first efficient enantioselective iridium catalyst was the phosphinooxazoline (PHOX) complex **1** reported in 1998.[3] The *tert*-butyl substituent at the stereogenic center proved to be essential for achieving high asymmetric inductions, as less sterically demanding groups, such as an *iso*-propyl substituent gave only modest enantiomeric excesses. However, a drawback of the *tert*-butyl moiety is the relatively high cost of *tert*-leucine (especially the (*R*)-enantiomer), which serves as the precursor for this ligand.



1



2

In the course of our studies on the pronounced counterion effects observed with these catalysts,[3,4] we developed a series of zwitterionic complexes and their respective cationic analogs, such as precatalyst **2**.[5] As complex **2** gave encouraging enantioselectivities, we thought that compounds of this type, which are easily accessible from serine as chiral starting material, could be a valuable alternative to *tert*-butyl-substituted phosphinooxazoline catalysts. An attractive feature of these serine-derived ligands is the option to introduce a wide range of sterically demanding moieties at the sterogenic center of the oxazoline ring by synthetic modification of the serine carboxyl group. Although a few examples of

* Corresponding author. Tel.: +41 61 2671108; fax: +41 61 2671103; e-mail address: andreas.pfaltz@unibas.ch (A. Pfaltz).
† Present address: Intermediates Research, BASF SE, D-67056 Ludwigshafen, Germany.

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.02.021

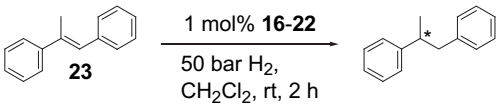
serine-based phosphinooxazoline ligands have been reported,[6,7] their corresponding iridium complexes have not been studied yet.

Herein, we report the synthesis of a library of serine-derived phosphinooxazoline ligands and their evaluation in iridium-catalyzed enantioselective hydrogenation reactions.

2. Results and discussion

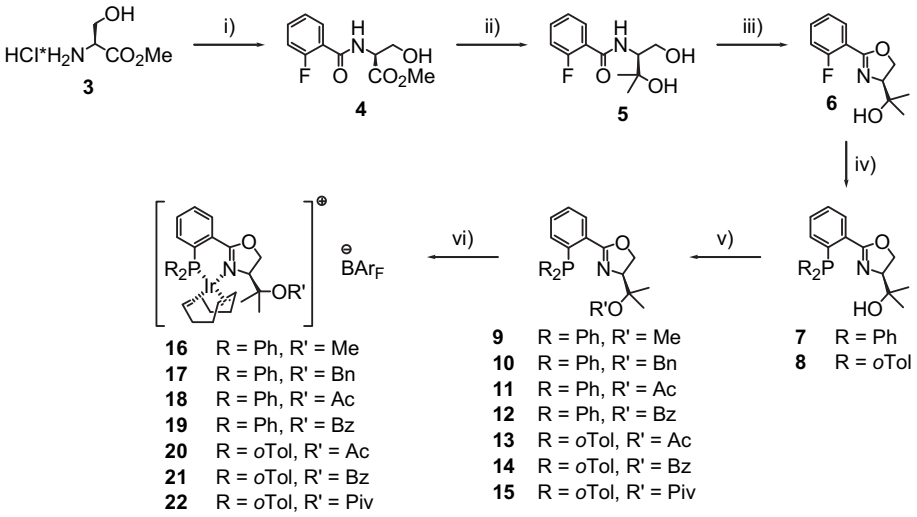
Phosphinooxazoline ligands **9**–**15** were easily accessible in 36–84% yield over two steps from literature-known aryl fluoride **6**,[6] which was prepared by standard procedures starting from (*S*)-serine methyl ester hydrochloride (**3**, Scheme 1). The nucleophilic aromatic substitution to introduce the phosphine donors was accomplished in the presence of the free hydroxyl group, although a second equivalent of *n*-butyl lithium had to be used in the case of the *ortho*-tolyl derivative **8** for the in situ deprotonation of the alcohol. This was necessary because of the higher basicity of the intermediate di-(*ortho*-tolyl)-phosphide compared to the analogous phenyl-substituted reagent.

Table 1
Reduction of (*E*)-1,2-diphenyl-1-propene (**23**)



Entry	Precatalyst	Conversion [%][a]	ee [%][b]
1	**16**	1	n.d.
2	**17**	27	92 (*S*)
3	**18**	90	92 (*S*)
4	**19**	88	92 (*S*)
5	**20**	99	92 (*S*)
6	**21**	99	86 (*S*)
7	**22**	93	97 (*S*)
8[5]	**2**	99	93 (*S*)
9[3]	**1**	> 99	97 (*R*)

n.d. denotes 'not determined'.
[a] Determined by GC.
[b] Determined by HPLC on a chiral stationary phase.



Scheme 1. Preparation of serine-derived iridium precatalysts **16**–**22**: (i) 2-FC_6H_4COCl, NEt_3, MeOH, 0 °C, 2.5 h, 91%; (ii) MeMgBr, THF/Et_2O, 0 °C→rt, 18 h then NH_4Cl, 0 °C, 70%; (iii) TsCl, NEt_3, CH_2Cl_2, rt, 75 h, 92%; (iv) $KPPh_2$, THF, 0 °C, 2 h, 77% (**7**) or $oTol_2PH$, *n*BuLi, THF, −78 °C→0 °C, 2.5 h, 89% (**8**); (v) KH, THF, 0 °C→rt, 2 h then R′X, 0 °C→rt, 15–24 h, 41–94%; (vi) $[Ir(COD)Cl]_2$, CH_2Cl_2, Δ, 2 h then $NaBAr_F$, H_2O, rt, 30 min, 72% to quantitative.

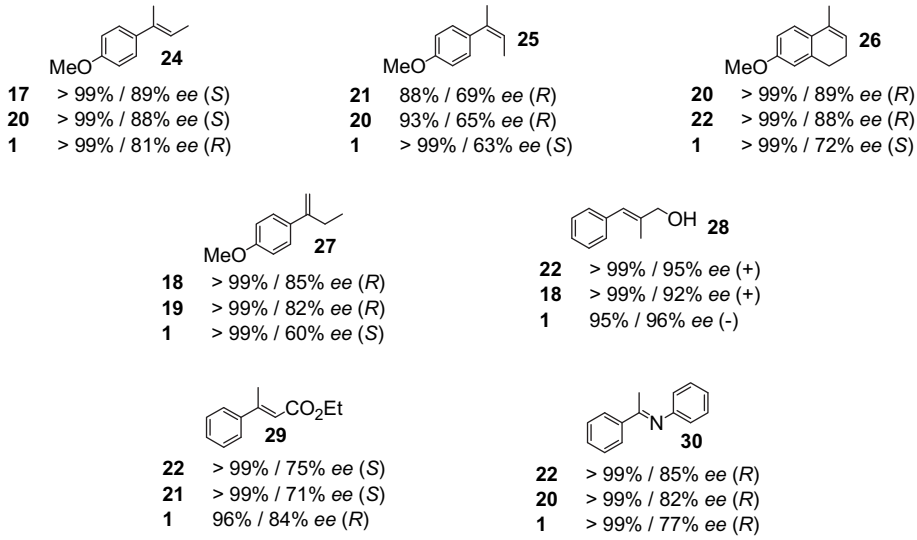
Both activated alkyl halogenides, such as methyl iodide or benzyl bromide and acid chlorides could be used in step (v) with similar efficiencies to furnish the corresponding ethers or esters. The desired iridium complexes **16**–**22** were readily obtained by metalation of the respective phosphinooxazolines **9**–**15** with $[Ir(COD)Cl]_2$ followed by anion exchange. The pathway shown in Scheme 1 offers the advantage that the structural elements, which define the chiral pocket around the catalytically active metal center, namely the substituents at the phosphorus atom and especially in the oxazoline moiety, are introduced in the last two steps of the ligand synthesis. This allows an efficient fine-tuning of the catalysts to meet the specific demands of different substrates.

With the new complexes in hand, the asymmetric hydrogenation of benchmark substrate (*E*)-1,2-diphenyl-1-propene (**23**) was studied. The results are summarized in Table 1 together with the corresponding data for the literature-known, structurally related catalysts **1**[3] and **2**.[5]

While the *O*-alkyl-substituted derivatives **16** and **17** showed very low reactivities, all ester-functionalized complexes **18**–**22** furnished high conversions under standard conditions, which were only slightly lower than the value reported for phosphinooxazoline catalyst **1**. All serine-based complexes yielded good to excellent enantiomeric excesses, with the most selective catalyst **22** matching the asymmetric induction induced by the *tert*-leucine-based derivative **1**.

In Scheme 2 the performance of the new iridium complexes in the enantioselective reduction of other unfunctionalized olefins **24**–**27** as well as allylic alcohol **28**, α,β-unsaturated ester **29** and imine **30** is compared with that of the standard *tert*-butyl phosphinooxazoline catalyst **1**.[1d,3,8,9]

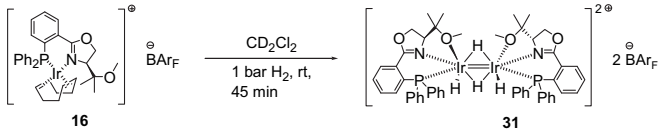
The serine-based complexes yielded significantly higher enantioselectivities in most cases (substrates **24**–**27** and **30**) than the well-known phosphinooxazoline catalyst **1**. For the allylic alcohol **28** the enantiomeric excesses obtained with catalysts **22** and **1** were similar. Only in the hydrogenation of ester **29** the *tert*-butyl derivative **1** performed better. In general, *ortho*-tolyl substituents at the phosphorus donor proved to be advantageous for achieving high asymmetric inductions. Overall, the pivalate **22** was the most effective precatalyst. However, most of the unfunctionalized olefins gave better results with other complexes. Like this, higher selectivities were obtained for the three substrates **24**, **26**, and **27** with acetate-substituted catalysts **18** and **20**, furnishing 88% ee, 89% ee and 85% ee, respectively, while with 89% ee the best result for **24** was provided by benzyl ether **17**. Since the ligand synthesis is



Scheme 2. Conversions and enantioselectivities for the asymmetric hydrogenation of substrates **24**–**30** (conditions: 50 bar H_2, CH_2Cl_2, rt, 2 h except for **27** (1 bar H_2, 30 min) and **30** (4 h)). For the data of catalyst **1** see Ref. 1d (**24**–**27**), Ref. 3 (**28**, **29**), and Ref. 8 (**30**).

highly flexible with the introduction of the *P*- and *O*-substituents in the last two steps, structural optimization can be accomplished easily and very efficiently.

To find an explanation for the unexpectedly low reactivity of the methoxy-substituted catalyst **16**, it was treated with hydrogen gas in the absence of substrate (Scheme 3). Subsequent analysis of the crude reaction mixture indicated a quantitative, selective transformation of **16** into a new species. The latter was unequivocally identified as hydride-bridged dimeric iridium complex **31** by NMR spectroscopy and X-ray crystallography (Fig. 1).[10]



Scheme 3. Preparation of the dimeric iridium hydride complex **31**.

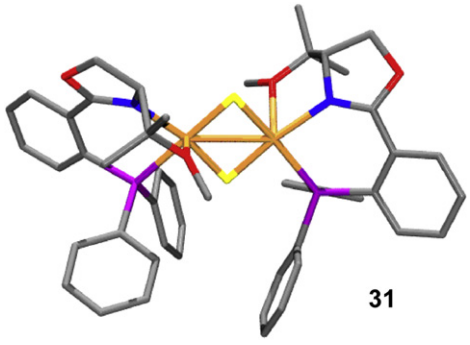


Fig. 1. Crystal structure of the dimeric iridium hydride complex **31**. The counterions as well as all hydrogen atoms (except of the two bridging hydrides) and solvent molecules have been omitted for clarity.

In contrast to the two bridging hydrides the terminal hydrides in the apical positions of the distorted coordination octahedrons around the metal centers were not located in the refinement of the structure, but these were assigned by NOESY NMR spectroscopy. The distance between the two iridium atoms (2.62 Å) is slightly shorter than Ir–Ir distances in analogous complexes (2.66 Å and 2.70 Å, respectively).[11] The more reactive acetate derivative **18** furnished an analogous dimeric complex **32** according to NMR spectroscopy, when it was stirred under the conditions shown in Scheme 3. However, formation of this complex was slower.

Remarkably, this class of precatalysts does not form trinuclear complexes with an Ir_3 core and a single bridging hydride upon deactivation,[12] as this is the case for complexes derived from other amino acids like valine or *tert*-leucine.[13] This can be explained by the observed coordination of the methoxy groups in the crystal structure of **31**, which stabilizes the dimeric complex. In contrast, no bonding Ir–O interactions can be detected in the solid state structures of the cyclooctadiene derivatives **16**, **21**, and **22** with a stable square-planar coordination geometry characteristic of a d^8 16-electron configuration.[14] Obviously, the iridium atoms in these complexes show no tendency to coordinate additional ligands for electronic and steric reasons.

3. Conclusion

A series of iridium complexes with serine-derived P,N-ligands was readily synthesized in six steps from commercially available starting materials in 18–49% overall yields. The catalysts were evaluated in the enantioselective hydrogenation of representative olefins and an imine, where they generally outperformed previously developed, structurally similar phosphinooxazoline complexes.

A significant advantage of the serine-based ligands over the *tert*-leucine-derived analogs is their flexible synthesis, which allows the introduction of a wide range of sterically demanding substituents at the stereogenic center in the oxazoline ring. In this way the ligand structure can be optimized for a specific application. In addition, enantiomerically pure (*S*)- and (*R*)-serine are much less expensive precursors than (*S*)- and especially (*R*)-*tert*-leucine. Thus, it seems worthwhile to evaluate serine-based phosphinooxazolines as cheap alternatives for their *tert*-butyl-substituted analogs in other reactions.

4. Experimental section

4.1. General

All reactions were performed in flame-dried glassware under argon using Schlenk techniques. Solvents and NEt_3 were dried employing standard procedures and distilled under nitrogen or argon.[15] All other commercial reagents were used as received. Deuterated solvents for NMR spectroscopy were degassed by three freeze-

pump-thaw cycles, dried over 4 Å molecular sieves and stored under argon. Solvents for workup and chromatographic purification of air-sensitive compounds were purged with a stream of argon for at least 15 min prior to use. Catalytic hydrogenations were set up under a nitrogen atmosphere in a MBraun Labmaster 130 glovebox using absolute solvents purchased from Fluka. Chromatographic separations were performed on Merck silica gel 60 (Darmstadt, 40–63 nm). For TLC analyses pre-coated Macherey–Nagel Polygram SIL G/UV$_{254}$ plates were used, and the compounds were visualized with the help of UV light. NaBAr$_F$[16] and *o*Tol$_2$PH (**33**)[17] were prepared following modified literature procedures.

NMR experiments were performed on Bruker Avance 400 or 500 spectrometers. ^{1}H and ^{13}C spectra were referenced relative to SiMe$_4$ using the solvent residual peaks and the solvent signals, respectively, as internal standards.[18,19] ^{31}P, ^{19}F, and ^{11}B spectra were calibrated using H_3PO_4 (85%), $CFCl_3$ and $BF_3\cdot OEt_2$ as external standards. All NMR shifts are given in parts per million (ppm). Mass spectra were measured on VG70-250, Finnigan MAT 95Q (EI), Finnigan MAT 312, Finnigan MAR 8400 (FAB) or Finnian MAT LCQ apparatus (ESI). Elemental analyses were performed by the Micro Analysis Laboratory of the University of Basel. IR spectra were measured on a Perkin–Elmer 1600 FTIR spectrometer. Melting points were determined on a Büchi 535 apparatus and are uncorrected. Specific rotations were measured on a Perkin–Elmer 314 polarimeter. HPLC analyses were performed on a Shimadzu system, GC measurements on equipment from Carlo Erba Instruments. The abbreviation BAr$_F$ refers to the tetrakis[3,5-bis(trifluoromethyl)phenyl]borate anion, whilst Ar$_F$ denotes the 3,5-bis(trifluoromethyl)phenyl substituent in general.

4.2. Introduction of phosphine donors by nucleophilic aromatic substitution

*4.2.1. (4′S)-2-[2′-(2″-Diphenylphosphanylphenyl)-4′,5′-dihydro-oxazol-4′-yl]-propan-2-ol (**7**)*[5]. To oxazoline **6** (2.23 g, 10.0 mmol) in absolute THF (15 mL) $KPPh_2$ in THF (0.5 M, 20.0 mL, 10.0 mmol) was slowly added at 0 °C. After the red solution had been stirred for 2 h at this temperature, H_2O (50 mL) was added. The mixture was extracted with CH_2Cl_2 (3×70 mL), the combined organic phases were dried over $MgSO_4$, filtrated, and evaporated under reduced pressure. Purification of the yellow crude product by column chromatography under argon (silica gel, 5×19 cm, hexanes/EtOAc 3:2) yielded PHOX **7** (3.01 g, 77%) as colorless, foamy solid. R_f (hexanes/EtOAc 3:2) 0.25; $[\alpha]_D^{20}$ +97.5 (*c* 1.14 in $CHCl_3$); $\tilde{\nu}$ (KBr) 3424, 3054, 2971, 2902, 1953, 1887, 1824, 1760, 1650, 1584, 1473, 1433, 1354, 1293, 1246, 1174, 1134, 1092, 1034, 960, 906, 871, 745, 696, 579, 503 cm^{-1}; δ_H (400.1 MHz, $CDCl_3$, 300 K) 0.97 (3H, s, CH_3), 1.15 (3H, s, CH_3), 1.74 (1H, br s, OH), 4.16 (1H, dd, *J* 10.0, 8.4 Hz, Ox-4′-H), 4.23 (1H, t, *J* 8.2 Hz, Ox-5′-H), 4.31 (1H, dd, *J* 10.0, 8.0 Hz, Ox-5′-H), 6.91 (1H, dddd, *J* 7.7, 3.9, 1.4, 0.5 Hz, Ar-3″-H), 7.20–7.29 (4H, m, Ar-H), 7.29–7.37 (7H, m, Ar-H), 7.41 (1H, td, *J* 7.5, 1.3 Hz, Ar-H), 7.94 (1H, ddd, *J* 7.7, 3.7, 1.3 Hz, Ar-6″-H); δ_C (100.6 MHz, $CDCl_3$, 300 K) 24.4 (s, CH_3), 27.6 (s, CH_3), 68.6 (s, Ox-5′-CH_2), 71.0 (s, $C(CH_3)_2OH$), 76.4 (s, Ox-4′-CH), 128.5–128.8 (m, several Ar-CH), 129.8 (d, *J* 3 Hz, Ar-CH), 130.9 (s, Ar-CH), 131.8 (br d, *J* 22 Hz, Ar-1″-C), 133.4 (d, *J* 20 Hz, PPh_2-*o*-CH), 134.4 (d, *J* 20 Hz, PPh_2-*o*-CH), 134.7 (s, Ar-3″-CH), 138.0 (d, *J* 10 Hz, Ar-C), 138.5–138.8 (m, several Ar-C), 164.2 (br s, Ox-2′C); δ_P (162.0 MHz, $CDCl_3$, 300 K) −6.1; *m*/*z* (FAB, NBA) 390 (100, $[M+H]^+$), 330 (79, $[M-CMe_2OH]^+$), 302 (21), 183 (14), 59 (14%, Me_2COH^+); $C_{24}H_{24}NO_2P$ requires: C, 74.02; H, 6.21; N, 3.60; found: C, 73.63; H, 6.24; N, 3.55%.

*4.2.2. (4′S)-2-{2′-[2″-(Di-ortho-tolylphosphanyl)-phenyl]-4′,5′-dihydrooxazol-4′-yl}-propan-2-ol (**8**).* To oxazoline **6** (1.12 g, 5.00 mmol) and (*o*Tol)$_2$PH (**33**, 1.18 g, 5.50 mmol) in absolute THF (20 mL) was added *n*BuLi in hexanes (1.6 M, 6.41 mL, 10.3 mmol) dropwise within 14 min at −78 °C. After the dark red solution had been stirred for 2.5 h at 0 °C, H_2O (40 mL) was added and the mixture extracted with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over $MgSO_4$, filtrated, and all volatiles removed under reduced pressure. Purification of the brownish residue by column chromatography under argon (silica gel, 5×17 cm, hexanes/EtOAc 3:2) yielded PHOX **8** (1.86 g, 89%) as colorless solid. R_f (hexanes/EtOAc 3:2) 0.28; $[\alpha]_D^{20}$ +126 (*c* 1.01 in $CHCl_3$); $\tilde{\nu}$ (KBr) 3462, 3053, 2972, 2905, 1653, 1586, 1465, 1351, 1288, 1249, 1202, 1170, 1135, 1095, 1038, 964, 868, 785, 753, 718, 674, 582, 554, 524, 461 cm^{-1}; δ_H (400.1 MHz, $CDCl_3$, 300 K) 0.99 (3H, s, $C(CH_3)(CH_3)OH$), 1.09 (3H, s, $C(CH_3)(CH_3)OH$), 2.32 (3H, s, *o*Tol-CH_3), 2.38 (3H, s, *o*Tol-CH_3), 4.18 (1H, dd, *J* 9.7, 8.4 Hz, Ox-4′-H), 4.25–4.35 (2H, m, Ox-5′-H), 6.75 (1H, dd, *J* 7.3, 4.2 Hz, *o*Tol-6‴-H), 6.79 (1H, ddd, *J* 7.6, 4.3, 1.2 Hz, *o*Tol-6‴-H), 6.95 (1H, ddd, *J* 7.7, 3.7, 0.8 Hz, Ar-3″-H), 7.08 (2H, m_c, *o*Tol-5‴-H), 7.16–7.29 (4H, m, *o*Tol-3‴-H and *o*Tol-4‴-H), 7.32 (1H, td, *J* 7.6, 1.4 Hz, Ar-4″-H), 7.42 (1H, td, *J* 7.6, 1.3 Hz, Ar-5″-H), 7.91 (1H, br s, Ar-6″-H) (despite prolonged data aquisition time, the signal for the exchangeable proton OH was not detected); δ_C (100.6 MHz, $CDCl_3$, 300 K) 21.2 (d, *J* 14 Hz, *o*Tol-CH_3), 21.4 (d, *J* 12 Hz, *o*Tol-CH_3), 24.3 (s, $C(CH_3)(CH_3)OH$), 27.5 (s, $C(CH_3)(CH_3)OH$), 68.4 (s, Ox-5′-CH_2), 71.0 (s, $C(CH_3)_2OH$), 76.7 (s, Ox-4′-CH), 126.1 (s, *o*Tol-5‴-CH), 126.4 (s, *o*Tol-5‴-CH), 128.6–128.9 (m, oTol-4‴-CH and Ar-5″-CH), 129.7 (br s, Ar-CH), 130.1 (d, *J* 5 Hz, *o*Tol-3‴-CH), 130.5 (d, *J* 5 Hz, *o*Tol-3‴-CH), 130.9 (s, Ar-CH), 132.6 (s, Ar-CH), 133.6 (s, Ar-CH), 134.9 (s, Ar-CH), 135.7 (d, *J* 10 Hz, Ar-C), 136.3 (br s, Ar-C), 137.0 (br s, Ar-C), 137.2 (br s, Ar-C), 142.0 (br s, *o*Tol-2‴-C), 142.2 (br s, *o*Tol-2‴-C), 164.0 (s, Ox-2′-C); δ_P (162.0 MHz, $CDCl_3$, 300 K) −21.4; *m*/*z* (FAB, NBA) 418 (100, $[M+H]^+$), 402 (12, $[M-Me]^+$), 358 (33, $[M-CMe_2OH]^+$), 333 (13), 326 (35, $[M-o\text{Tol}]^+$), 316 (11%); $C_{26}H_{28}NO_2P$ requires: C, 74.80; H, 6.76; N, 3.36; found: C, 74.30; H, 6.62; N, 3.42%.

4.3. Preparation of ligands by ether or ester formation

*4.3.1. (4S)-4-(1′-Methoxy-1′-methylethyl)-2-(2″-diphenylphosphanylphenyl)-4,5-dihydrooxazole (**9**).* To a suspension of KH (44.1 mg, 1.10 mmol) in absolute THF (10 mL) PHOX **7** (389 mg, 1.00 mmol) was added at 0 °C and the mixture was stirred at room temperature, until no further gas evolution was detected (about 2 h). After MeI (filtered over basic Al_2O_3 directly before use, 75 μL, 1.20 mmol) had been added at 0 °C, the mixture was stirred for 24 h at room temperature. The resulting yellow suspension was treated with aqueous $Na_2S_2O_3$ (5%, 20 mL) and the mixture was extracted with CH_2Cl_2 (4×20 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated to dryness under reduced pressure. The yellowish crude product was purified by column chromatography under argon (silica gel, hexanes/EtOAc 4:1) to yield ligand **9** (263 mg, 65%) as colorless, waxy solid. R_f (hexanes/EtOAc 4:1) 0.15; $[\alpha]_D^{20}$ +40.7 (*c* 0.935 in $CHCl_3$); $\tilde{\nu}$ (KBr) 3043, 2969, 2933, 2889, 2823, 1965, 1828, 1768, 1647, 1582, 1562, 1470, 1432, 1340, 1305, 1254, 1154, 1087, 1031, 960, 902, 850, 748, 699, 580, 552, 501 cm^{-1}; δ_H (500.1 MHz, $CDCl_3$, 295 K) 0.77 (3H, s, $C(CH_3)(CH_3)O$), 1.10 (3H, s, $C(CH_3)(CH_3)O$), 3.13 (3H, s, OCH_3), 4.11–4.21 (2H, m, Ox-4-H and Ox-5-H), 4.25 (1H, br t, *J* 6.2 Hz, Ox-5-H), 6.87 (1H, ddd, *J* 7.7, 4.0, 1.0 Hz, Ar-3″-H), 7.21–7.35 (11H, m, PPh_2-H and Ar-4″-H), 7.37 (1H, t, *J* 7.5 Hz, Ar-5″-H), 7.96 (1H, br s, Ar-6″-H); δ_C (125.8 MHz, $CDCl_3$, 295 K) 18.9 (s, $C(CH_3)(CH_3)O$), 23.0 (s, $C(CH_3)(CH_3)O$), 49.6 (s, OCH_3), 68.6 (br s, Ox-5-CH_2), 74.7 (br s, Ox-4-CH), 76.6 (s, $C(CH_3)_2O$), 128.3 (s, Ar-CH), 128.4–128.6 (m, several Ar-CH), 128.8 (s, Ar-CH), 130.1 (br s, Ar-6″-CH), 130.7 (br s, Ar-CH), 133.7 (d, *J* 20 Hz, PPh_2-*o*-CH), 134.4 (s, Ar-3″-CH), 134.5 (d, *J* 21 Hz, PPh_2-*o*-CH), 138.4–139.2 (br m, several Ar-C) (despite prolonged data aquisition time, the signal for Ox-2-C was not detected); δ_P (202.5 MHz, $CDCl_3$, 295 K) −5.4; *m*/*z* (FAB, NBA) 404 (66, $[M+H]^+$), 372 (12, $[M-OMe]^+$), 330 (62, $[M-CMe_2OMe]^+$), 304 (27), 220 (11), 183 (15), 57 (100%); $C_{25}H_{26}NO_2P$ requires: C, 74.43; H, 6.50; N, 3.47; found: C, 74.47; H, 6.64; N, 3.55%.

*4.3.2. (4′S)-1-Methyl-1-{2′-[2″-(di-ortho-tolylphosphanyl)-phenyl]-4′,5′-dihydrooxazol-4′-yl}-ethyl pivalate (**15**).* In analogy to the

synthesis of **9**, PHOX **8** (1.04 g, 2.50 mmol) was reacted with KH (110 mg, 2.75 mmol) and PivCl (369 μL, 3.00 mmol) in absolute THF for 22 h at room temperature. In contrast to the preparation of **9**, half-saturated aqueous $NaHCO_3$ (20 mL) was added during workup. Purification of the yellowish crude product by column chromatography under argon (silica gel, 4×19 cm, hexanes/EtOAc 5:1) furnished ligand **15** (1.19 g, 94%) as colorless, foamy solid. R_f (hexanes/EtOAc 5:1) 0.33; $[\alpha]_D^{20}$ +36.9 (*c* 0.990 in $CHCl_3$); $\tilde{\nu}$ (KBr) 3055, 2971, 1725, 1650, 1588, 1468, 1356, 1289, 1247, 1174, 1135, 1093, 1031, 968, 901, 841, 749, 718, 677, 556, 521, 455 cm^{-1}; δ_H (400.1 MHz, $CDCl_3$, 300 K) 1.08 (12H, s, $C(CH_3)_3$ and $C(CH_3)(CH_3)O$), 1.40 (3H, s, $C(CH_3)(CH_3)O$), 2.36 (3H, d, *J* 1.9 Hz, *o*Tol-CH_3), 2.37 (3H, d, *J* 1.6 Hz, *o*Tol-CH_3), 4.18 (1H, dd, *J* 10.1, 8.8 Hz, Ox-5′-H), 4.27 (1H, dd, *J* 8.6, 7.3 Hz, Ox-5′-H), 4.44 (1H, dd, *J* 10.2, 7.2 Hz, Ox-4′-H), 6.71 (2H, ddd, *J* 7.6, 4.0, 0.9 Hz, *o*Tol-6‴-H), 6.92 (1H, dddd, *J* 7.7, 3.5, 1.3, 0.4 Hz, Ar-3″-H), 7.03 (2H, m_c, *o*Tol-5‴-H), 7.14–7.27 (4H, m, *o*Tol-3‴-H and *o*Tol-4‴-H), 7.31 (1H, td, *J* 7.6, 1.4 Hz, Ar-4″-H), 7.39 (1H, td, *J* 7.6, 1.3 Hz, Ar-5″-H), 7.96 (1H, dd, *J* 7.2, 3.2 Hz, Ar-6″-H); δ_C (100.6 MHz, $CDCl_3$, 300 K) 20.5 (s, $C(CH_3)(CH_3)O$), 21.2 (s, *o*Tol-CH_3), 21.5 (s, *o*Tol-CH_3), 23.9 (s, $C(CH_3)(CH_3)O$), 27.2 (s, $C(CH_3)_3$), 39.5 (s, $C(CH_3)_3$), 68.2 (s, Ox-5′-CH_2), 75.3 (s, Ox-4′-CH), 82.5 (s, $C(CH_3)_2O$), 126.1 (s, *o*Tol-5‴-CH), 126.3 (s, *o*Tol-5‴-CH), 128.3 (s, Ar-5″-CH), 128.6 (s, *o*Tol-4‴-CH), 128.6 (s, *o*Tol-4‴-CH), 130.1 (m, several Ar-CH), 130.9 (s, Ar-CH), 132.3 (br d, *J* 24 Hz, Ar-1″-C), 133.1 (s, *o*Tol-6‴-CH), 133.5 (s, *o*Tol-6‴-CH), 134.6 (s, Ar-3″-CH), 136.4–136.7 (m, *o*Tol-1‴-C), 138.0 (d, *J* 25 Hz, Ar-2″-C), 142.2 (d, *J* 27 Hz, *o*Tol-2‴-C), 142.6 (d, *J* 27 Hz, *o*Tol-2‴-C), 164.1 (br s, Ox-2′-C), 177.6 (s, CO_2); δ_P (162.0 MHz, $CDCl_3$, 300 K) −21.2; *m*/*z* (EI, 70 eV) 501 (7, M^+), 486 (9, $[M-Me]^+$), 410 (50, $[M-o\text{Tol}]^+$), 400 (43, $[M-OPiv]^+$), 358 (65, $[M-CMe_2OPiv]^+$), 332 (100), 316 (39), 308 (46), 57 (27%, $^tBu^+$); $C_{31}H_{36}NO_3P$ requires: C, 74.23; H, 7.23; N, 2.79; found: C, 73.94; H, 7.24; N, 2.87%.

4.4. Synthesis of iridium complexes

*4.4.1. (4S)-[(η^4-1,5-Cyclooctadiene)-{4-(1′-methoxy-1′-methylethyl)-2-(2″-diphenylphosphanylphenyl)-4,5-dihydrooxazole}-iridium(I)] tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (**16**).* To a solution of $[Ir(COD)Cl]_2$ (73.9 mg, 0.110 mmol) in absolute CH_2Cl_2 (3 mL) ligand **9** (80.7 mg, 0.200 mmol) in absolute CH_2Cl_2 (2 mL) was added dropwise at room temperature. After the resulting red solution had been stirred in a closed vessel for 2 h at 50 °C, the mixture was cooled to room temperature and $NaBAr_F$ (230 mg, 0.260 mmol) was added. The slightly turbid solution was stirred for 5 min and then treated with H_2O (5 mL). After the mixture had vigorously been stirred for 30 min at room temperature, the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic phases were dried over $MgSO_4$, filtered, and evaporated under reduced pressure. Purification of the crude product by column chromatography under argon (silica gel, CH_2Cl_2) furnished precatalyst **16** (227 mg, 72%) as red solid. Single crystals suitable for X-ray analysis were obtained by layering a concentrated solution of **16** in $CDCl_3$ with hexane at room temperature. R_f (CH_2Cl_2) 0.74 (tailing); $[\alpha]_D^{20}$ +173 (*c* 0.225 in $CHCl_3$); $\tilde{\nu}$ (KBr) 2976, 2839, 1603, 1566, 1484, 1437, 1356, 1279, 1127, 967, 889, 839, 778, 743, 710, 677, 564, 510, 440 cm^{-1}; δ_H (500.1 MHz, $CDCl_3$, 295 K) 0.64 (3H, s, $C(CH_3)(CH_3)O$), 0.79 (3H, s, $C(CH_3)(CH_3)O$), 1.42 (1H, m_c, COD-CHH), 1.64 (1H, m_c, COD-CHH), 2.01 (2H, m_c, COD-CHH), 2.33–2.62 (4H, m, COD-CH_2), 2.95 (1H, m_c, COD-CH), 3.01 (3H, s, OCH_3), 3.28 (1H, br s, COD-CH), 4.12 (1H, dd, *J* 9.3, 3.1 Hz, Ox-4-H), 4.39 (1H, t, *J* 9.6 Hz, Ox-5-H), 4.59 (1H, dd, *J* 9.9, 3.0 Hz, Ox-5-H), 4.99 (1H, br s, COD-CH), 5.39 (1H, quint, *J* 7.0 Hz, COD-CH), 7.09 (2H, br s, PPh_2-*o*-H), 7.34–7.58 (13H, m, Ar-H and Ar_F-*p*-H), 7.61 (2H, m_c, Ar-4″-H and Ar-5″-H), 7.73 (8H, s, Ar_F-*o*-H), 8.19 (1H, dd, *J* 9.0, 4.3 Hz, Ar-6″-H); δ_C (125.8 MHz, $CDCl_3$, 295 K) 18.0 (s, $C(CH_3)(CH_3)O$), 19.8 (s, $C(CH_3)(CH_3)O$), 26.0 (d, *J* 2 Hz, COD-CH_2), 28.6 (s, COD-CH_2), 32.5 (s, COD-CH_2), 36.7 (d, *J* 5 Hz, COD-CH_2), 49.1 (s, OCH_3), 61.0 (s, COD-CH), 62.2 (s, COD-CH), 70.2 (s, Ox-5-CH_2), 73.7 (s, Ox-4-CH), 75.9 (s, $C(CH_3)_2O$), 95.5 (d, *J* 13 Hz, COD-CH), 97.7 (d, *J* 11 Hz, COD-CH), 117.6 (sept, *J* 4 Hz, Ar_F-*p*-CH), 122.7 (d, *J* 58 Hz, PPh_2-*i*-C), 124.7 (q, *J* 273 Hz, CF_3), 128.4 (d, *J* 47 Hz, Ar-2″-C), 128.6–129.4 (m, Ar_F-*m*-C, PPh_2-*m*-CH and Ar-1″-C), 129.6 (d, *J* 11 Hz, PPh_2-*m*-CH), 130.1 (d, *J* 52 Hz, PPh_2-*i*-C), 132.1 (d, *J* 2 Hz, PPh_2-*p*-CH), 132.5 (d, *J* 2 Hz, Ar-5″-CH), 132.6 (d, *J* 2 Hz, PPh_2-*p*-CH), 133.3 (d, *J* 10 Hz, PPh_2-*o*-CH), 134.1 (d, *J* 8 Hz, Ar-6″-CH), 134.3 (d, *J* 7 Hz, Ar-4″-CH), 134.7–134.9 (m, Ar_F-*o*-CH, PPh_2-*o*-CH and Ar-3″-CH), 161.8 (q, *J* 50 Hz, Ar_F-*i*-C), 164.9 (d, *J* 6 Hz, Ox-2-C); δ_F (376.5 MHz, $CDCl_3$, 300 K) −62.7; δ_P (202.5 MHz, $CDCl_3$, 295 K) 17.0; *m*/*z* (ESI^+, CH_2Cl_2) 704 (100%, $[M-BAr_F]^+$); $C_{65}H_{50}BF_{24}IrNO_2P$ requires: C, 49.82; H, 3.22; N, 0.89; found: C, 49.91; H, 3.30; N, 1.09%.

*4.4.2. (4′S)-[(η^4-1,5-Cyclooctadiene)-(1-methyl-1-{2′-[2″-(di-ortho-tolylphosphanyl)-phenyl]-4′,5′-dihydrooxazol-4′-yl}-ethyl pivalate)-iridium(I)] tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (**22**).* In analogy to the synthesis of **16**, ligand **15** (150 mg, 0.300 mmol) was reacted with $[Ir(COD)Cl]_2$ (111 mg, 0.165 mmol), and $NaBAr_F$ (346 mg, 0.390 mmol). Purification of the crude product by column chromatography under argon (silica gel, 4×20 cm, CH_2Cl_2) yielded precatalyst **22** (503 mg, quantitative) as orange-red solid. According to ^{31}P NMR spectroscopy **22** is in equilibrium between two conformers in a ratio of 5:1 at 295 K, when it is dissolved in $CDCl_3$. Single crystals suitable for X-ray analysis were obtained by layering a concentrated solution of **22** in $CDCl_3$ with hexane at room temperature. R_f (CH_2Cl_2) 0.74 (tailing); $[\alpha]_D^{20}$ +114 (*c* 0.215 in $CHCl_3$); $\tilde{\nu}$ (KBr) 2975, 1731, 1598, 1565, 1480, 1356, 1279, 1128, 974, 889, 839, 751, 713, 677, 567, 533, 454 cm^{-1}; δ_H (500.1 MHz, $CDCl_3$, 295 K, main conformer) 0.28 (3H, br s, $C(CH_3)(CH_3)O$), 1.06 (9H, br s, $C(CH_3)_3$), 1.51 (1H, br s, COD-CHH), 1.57–1.74 (4H, br m, $C(CH_3)(CH_3)O$ and COD-CHH), 2.02–2.22 (2H, br m, COD-CHH), 2.26–2.52 (7H, br m, COD-CH_2 and *o*Tol-CH_3), 3.04 (1H, br s, COD-CH), 3.15 (3H, br s, *o*Tol-CH_3), 3.40 (1H, br s, COD-CH), 4.38 (1H, br t, *J* 9.6 Hz, Ox-5′-H), 4.71 (1H, br d, *J* 9.5 Hz, Ox-5′-H), 4.88 (1H, br s, COD-CH), 5.02 (2H, br s, COD-CH and Ox-4′-H), 6.47 (1H, br m_c, *o*Tol-6‴-H), 6.80 (1H, br dd, *J* 11.1, 7.8 Hz, *o*Tol-6‴-H), 7.07 (1H, br s, *o*Tol-5‴-H), 7.18–7.32 (2H, br m, Ar-H), 7.33–7.69 (10H, br m, Ar-H and Ar_F-*p*-H), 7.73 (8H, s, Ar_F-*o*-H), 8.19 (1H, br s, Ar-6″-H); δ_C (125.8 MHz, $CDCl_3$, 295 K, main conformer) 19.2 (s, $C(CH_3)(CH_3)O$), 23.3 (s, $C(CH_3)(CH_3)O$), 24.7 (d, *J* 5 Hz, *o*Tol-CH_3), 25.6 (s, COD-CH_2), 25.8 (d, *J* 7 Hz, *o*Tol-CH_3), 26.9 (s, $C(CH_3)_3$), 28.3 (s, COD-CH_2), 32.6 (s, COD-CH_2), 35.6 (d, *J* 3 Hz, COD-CH_2), 39.5 (s, $C(CH_3)_3$), 67.6 (s, COD-CH), 67.6 (s, COD-CH), 69.6 (s, Ox-4′-CH), 70.0 (s, Ox-5′-CH_2), 80.9 (s, $C(CH_3)_2O$), 91.6 (d, *J* 13 Hz, COD-CH), 95.9 (d, *J* 10 Hz, COD-CH), 117.6 (br s, Ar_F-*p*-CH), 119.2 (d, *J* 53 Hz, *o*Tol-1‴-C), 124.7 (q, *J* 273 Hz, CF_3), 127.4–127.6 (m, *o*Tol-5‴-CH), 128.6 (d, *J* 49 Hz, Ar-2″-C), 129.0 (q, *J* 32 Hz, Ar_F-*m*-C), 129.9 (d, *J* 47 Hz, *o*Tol-1‴-C), 132.5–132.9 (m, several Ar-CH), 133.7 (d, *J* 10 Hz, *o*Tol-6‴-CH), 134.0 (d, *J* 3 Hz, *o*Tol-6‴-CH), 134.3 (d, *J* 8 Hz, Ar-6″-CH), 134.6–134.9 (m, Ar_F-*o*-CH and several Ar-CH), 141.0 (d, *J* 11 Hz, *o*Tol-2‴-C), 142.8 (d, *J* 16 Hz, *o*Tol-2‴-C), 161.8 (q, *J* 50 Hz, Ar_F-*i*-C), 165.7 (s, Ox-2′-C), 178.1 (s, CO_2) (despite prolonged data aquisition time, the signal for Ar-1″-C was not detected); δ_F (376.5 MHz, $CDCl_3$, 300 K) −62.7; δ_P (202.5 MHz, $CDCl_3$, 295 K) 10.7 and 18.7 (in a ratio of 5:1); *m*/*z* (ESI^+, CH_2Cl_2) 802 (100%, $[M-BAr_F]^+$); $C_{71}H_{60}BF_{24}IrNO_3P$ requires: C, 51.21; H, 3.63; N, 0.84; found: C, 51.33; H, 3.71; N, 1.01%.

*4.4.3. (4S,4S)-{Diiridium(III)-bis(μ_1-hydrido)-bis(μ_2-hydrido)-bis[4-(1′-methoxy-1′-methylethyl)-2-(2″-diphenylphosphanylphenyl)-4,5-dihydrooxazole]} bis{tetrakis[3,5-bis(trifluoromethyl)phenyl]borate} (**31**).* Precatalyst **16** (16.8 mg, 10.7 μmol) in absolute CD_2Cl_2 (1.0 mL) was stirred under an atmosphere of dihydrogen (about 1 bar) at room temperature for 45 min. The NMR spectroscopic analysis of the now yellowish solution revealed the complete, selective transformation of **16** into iridium dimer **31**. Layering this mixture with absolute hexane (3.0 mL) at room temperature furnished

crystals, some of which were suitable for X-ray analysis. After removal of the mother liquor these were washed with pentane (2×1 mL) and dried under high vacuum. Like this, complex **31** (8.4 mg, 50%) was isolated as yellow solid. $\tilde{\nu}$ (KBr) 2990, 1639, 1487, 1438, 1357, 1280, 1127, 1023, 936, 890, 838, 776, 744, 712, 677, 553, 506, 444 cm^{-1}; δ_H (500.1 MHz, CD_2Cl_2, 295 K) −31.29 (2H, m_c, μ_1-Ir-H), −25.17 (1H, sept, *J* 4.7 Hz, μ_2-Ir-H_{cisP}), −0.95 (1H, tt, *J* 78.5, 2.4 Hz, μ_2-Ir-H_{transP}), 0.14 (6H, s, C(CH_3)(CH_3)O), 1.14 (6H, s, C(CH_3)(CH_3)O), 3.35 (6H, s, OCH_3), 4.32–4.39 (4H, m, Ox-4-H and Ox-5-H), 4.75 (2H, t, *J* 10.8 Hz, Ox-5-H), 6.62 (4H, dd, *J* 11.9, 7.2 Hz, PPh_2-*o*-H), 7.16 (4H, br s, PPh_2-*o*-H), 7.22 (2H, dd, *J* 10.9, 7.6 Hz, Ar-3″-H), 7.38 (4H, t, *J* 7.2 Hz, PPh_2-*m*-H), 7.45 (4H, br t, *J* 7.0 Hz, PPh_2-*m*-H), 7.55 (8H, s, Ar_F-*p*-H), 7.58 (4H, t, *J* 7.4 Hz, PPh_2-*p*-H), 7.62–7.76 (18H, m, Ar_F-*o*-H and Ar-4″-H), 7.78 (2H, t, *J* 7.6 Hz, Ar-5″-H), 8.18 (2H, dd, *J* 7.7, 2.1 Hz, Ar-6″-H); δ_C (125.8 MHz, CD_2Cl_2, 295 K) 14.4 (s, C(CH_3)(CH_3)O), 21.4 (s, C(CH_3)(CH_3)O), 54.3 (s, OCH_3), 70.8 (s, Ox-5-CH_2), 80.7 (s, Ox-4-CH), 81.4 (s, C(CH_3)$_2$O), 118.0 (sept, *J* 4 Hz, Ar_F-*p*-CH), 125.1 (q, *J* 272 Hz, CF_3), 128.2–128.3 (m, several Ar-C), 129.0–129.8 (m, PPh_2-*m*-CH and Ar_F-*m*-C), 130.1 (m_c, PPh_2-*m*-CH), 132.6–132.8 (m, PPh_2-*o*-CH, Ar-6″-CH and Ar-C), 133.3–133.4 (m, PPh_2-*o*-CH and PPh_2-*p*-CH), 133.8 (s, Ar-5″-CH), 135.0 (m_c, Ar-C), 135.2–135.3 (m, Ar_F-*o*-CH, Ar-3″-CH and Ar-4″-CH), 162.0 (br s, Ox-2-C), 162.3 (q, *J* 50 Hz, Ar_F-*i*-C); δ_F (376.5 MHz, CD_2Cl_2, 300 K) −63.1; δ_P (162.0 MHz, CD_2Cl_2, 300 K) −1.5; *m*/*z* (ESI$^+$, CH_2Cl_2) 598 (100%, $[M-2\cdot BAr_F]^{2+}$).

4.5. General procedure for enantioselective hydrogenations

Precatalyst (usually 1.0 μmol) and substrate (usually 100 μmol) were weighed in a 2 mL screw cap glass vial equipped with a magnetic stir bar and the desired solvent was added (usually 0.5 mL absolute CH_2Cl_2). In this connection, stock solutions of the iridium complexes and alkenes were sometimes used leaving the overall concentrations unchanged. Four vessels were placed in a 60 mL autoclave (Premex), which was closed under an inert atmosphere. After pressurizing the autoclave with hydrogen (usually 50 bar) the transformation was initiated by switching on the stirrer (700 min^{-1}). After the target reaction time the hydrogen was released and hexanes (2 mL) added. The resulting suspension was filtered over a pad of silica gel, which was washed with Et_2O/hexanes 1:1. The eluate was concentrated under reduced pressure, the residue dissolved in heptane (3 mL) and the conversion and enantioselectivity were directly determined by GC and HPLC analyses.[3,20,21]

Acknowledgements

A. F. thanks the 'Fonds der Chemischen Industrie' (Frankfurt) and the German Federal Ministry for Science and Technology (BMBF) for a Kekulé Fellowship. Financial support by the Swiss National Science Foundation is gratefully acknowledged. We also thank Markus Neuburger and Dr. Sylvia Schaffner for the crystal structure analyses as well as Dr. Daniel Häussinger for the help with the NMR measurements.

Supplementary data

Supplementary data contain additional experimental procedures and hydrogenation results as well as X-ray structure analyses of complexes **16**, **21**, and **22**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.02.021.

References and notes

1. Reviews: (a) Church, T. L.; Andersson, P. G. *Coord. Chem. Rev.* **2008**, *252*, 513–531; (b) Roseblade, S. J.; Pfaltz, A. *Acc. Chem. Res.* **2007**, *40*, 1402–1411; (c) Cui, X.; Burgess, K. *Chem. Rev.* **2005**, *105*, 3272–3296; (d) Pfaltz, A.; Blankenstein, J.; Hilgraf, R.; Hörmann, E.; McIntyre, S.; Menges, F.; Schönleber, M.; Smidt, S. P.; Wüstenberg, B.; Zimmermann, N. *Adv. Synth. Catal.* **2003**, *345*, 33–43.
2. Selected, recent examples: (a) Verendel, J. J.; Zhou, T.; Li, J.-Q.; Paptchikhine, A.; Lebedev, O.; Andersson, P. G. *J. Am. Chem. Soc.* **2010**, *132*, 8880–8881; (b) Zhu, Y.; Fan, Y.; Burgess, K. *J. Am. Chem. Soc.* **2010**, *132*, 6249–6253; (c) Baeza, A.; Pfaltz, A. *Chem.—Eur. J.* **2010**, *16*, 4003–4009; (d) Baeza, A.; Pfaltz, A. *Chem.—Eur. J.* **2010**, *16*, 2036–2039; (e) Woodmansee, D. H.; Müller, M.-A.; Neuburger, M.; Pfaltz, A. *Chem. Sci.* **2010**, *1*, 72–78; (f) Zhao, J.; Burgess, K. *J. Am. Chem. Soc.* **2009**, *131*, 13236–13237; (g) Mazuela, J.; Verendel, J. J.; Coll, M.; Schäffner, B.; Börner, A.; Andersson, P. G.; Pàmies, O.; Diéguez, M. *J. Am. Chem. Soc.* **2009**, *131*, 12344–12353; (h) Cheruku, P.; Paptchikhine, A.; Church, T. L.; Andersson, P. G. *J. Am. Chem. Soc.* **2009**, *131*, 8285–8289; (i) Schrems, M. G.; Pfaltz, A. *Chem. Commun.* **2009**, 6210–6212; (j) Paptchikhine, A.; Cheruku, P.; Engman, M.; Andersson, P. G. *Chem. Commun.* **2009**, 5996–5998; (k) Baeza, A.; Pfaltz, A. *Chem.—Eur. J.* **2009**, *15*, 2266–2269; (l) Diéguez, M.; Mazuela, J.; Pàmies, O.; Verendel, J. J.; Andersson, P. G. *J. Am. Chem. Soc.* **2008**, *130*, 7208–7209; (m) Zhu, Y.; Burgess, K. *J. Am. Chem. Soc.* **2008**, *130*, 8894–8895; (n) Wang, A.; Wüstenberg, B.; Pfaltz, A. *Angew. Chem.* **2008**, *120*, 2330–2332; *Angew. Chem., Int. Ed.* **2008**, *47*, 2298–2300; (o) Diéguez, M.; Mazuela, J.; Pàmies, O.; Verendel, J. J.; Andersson, P. G. *Chem. Commun.* **2008**, 3888–3890; (p) Zhu, Y.; Burgess, K. *Adv. Synth. Catal.* **2008**, *350*, 979–983.
3. Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem.* **1998**, *110*, 3047–3050; *Angew. Chem., Int. Ed.* **1998**, *37*, 2897–2899.
4. Smidt, S. P.; Zimmermann, N.; Studer, M.; Pfaltz, A. *Chem.—Eur. J.* **2004**, *10*, 4685–4693.
5. Franzke, A.; Pfaltz, A. *Chem.—Eur. J.* in press, doi:10.1002/chem.201003314.
6. Helmchen and coworkers synthesized ligand **7** and the related THP ether: Peer, M.; de Jong, J. C.; Kiefer, M.; Langer, T.; Rieck, H.; Schell, H.; Sennhenn, P.; Sprinz, J.; Steinhagen, H.; Wiese, B.; Helmchen, G. *Tetrahedron* **1996**, *52*, 7547–7583.
7. Ligand **10** and the corresponding TBDMS ether were reported by Stoltz and coworkers. In a palladium-catalyzed enantioselective decarboxylative protonation the TBDMS derivative was found to be inferior to the *tert*-butyl phosphinooxazoline ligand: (a) Marinescu, S. C.; Nishimata, T.; Mohr, J. T.; Stoltz, B. M. *Org. Lett.* **2008**, *10*, 1039–1042; (b) Tani, K.; Behenna, D. C.; McFadden, R. M.; Stoltz, B. M. *Org. Lett.* **2007**, *9*, 2529–2531; (c) Further example of serine-based PHOX ligands: Caprioara, M.; Fiammengo, R.; Engeser, M.; Jäschke, A. *Chem.—Eur. J.* **2007**, *13*, 2089–2095.
8. Stohler, R. Ph.D. Thesis, University of Basel, **2006**.
9. For reaction conditions and additional asymmetric hydrogenation experiments see the Supplementary data.
10. Crystal data for **31** (from CD_2Cl_2/hexane): $C_{114}H_{78}B_2F_{48}Ir_2N_2O_4P_2\cdot 2.75\ CD_2Cl_2$, *M*=3153.36, triclinic, *a*=12.9269(1), *b*=15.8510(1), *c*=16.7145(2) Å, *α*=73.0026(4), *β*=73.5387(4), *γ*=89.7452(5)°, *U*=3129.52(5) Å^3, *T*=173 K, space group *P* 1, *Z*=1, 35,894 reflections measured, 35,886 unique (R_{int}=0.00), 29,618 used in all calculations. The final w*R* was 0.0500 (all data). For a selection of bond lengths and angles see the supplementary data. Crystallographic data (excluding structure factors) for **31** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-805973. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
11. (a) Schnabel, R. C.; Carroll, P. S.; Roddick, D. M. *Organometallics* **1996**, *15*, 655–663; (b) Esteruelas, M. A.; García, M. P.; Lahoz, F. J.; Martín, M.; Modrego, J.; Oñate, E.; Oro, L. A. *Inorg. Chem.* **1994**, *33*, 3473–3480.
12. (a) Wang, H. H.; Pignolet, L. H. *Inorg. Chem.* **1980**, *19*, 1470–1480; (b) Crabtree, R. *Acc. Chem. Res.* **1979**, *12*, 331–337.
13. Smidt, S. P.; Pfaltz, A.; Martínez-Viviente, E.; Pregosin, P. S.; Albinati, A. *Organometallics* **2003**, *22*, 1000–1009.
14. For details of the X-ray crystallograhic investigations see the Supplementary data.
15. Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon: Oxford, 1988.
16. Reger, D. L.; Wright, T. D.; Little, C. A.; Lamba, J. J. S.; Smith, M. D. *Inorg. Chem.* **2001**, *40*, 3810–3814.
17. Grim, S. O.; Yankowsky, A. W. *J. Org. Chem.* **1977**, *42*, 1236–1239.
18. Gottlieb, H. E.; Kotylar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512–7515.
19. For CD_2Cl_2 the solvent shifts *δ*=5.32 (^{1}H) and 54.0 (^{13}C) ppm, respectively, were used to calibrate the spectra.
20. (a) Blankenstein, J.; Pfaltz, A. *Angew. Chem.* **2001**, *113*, 4577–4579; *Angew. Chem., Int. Ed.* **2001**, *40*, 4445–4447; (b) Schnider, P.; Koch, G.; Prétôt, R.; Wang, G.; Bohnen, F. M.; Krüger, C.; Pfaltz, A. *Chem.—Eur. J.* **1997**, *3*, 887–892.
21. The conversion of **28** was determined by GC (Restek Rtx 1701, 60 kPa He, 100 °C/2 min/7 °C min^{-1}/250 °C/10 min): t_R 14.2 (product) and 16.1 (substrate) min.