Iridium-Catalyzed Enantioselective Hydrogenation of Olefins

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Abstract: Cationic iridium complexes with chiral P,N-ligands and tetrakis[3,5-(trifluoromethyl)phenyl]borate (BAr_F) as the counterion are efficient homogeneous catalysts for the enantioselective hydrogenation of olefins. The complexes are readily prepared, air-stable, and easy to handle. In contrast to chiral rhodium- and ruthenium-phosphine catalysts, they do not require the presence of a polar coordinating group near the C=C bond. In the hydrogenation of unfunctionalized arylolefins, high enantioselectivities of $>95\%$ ee with turnover numbers of up to 5000 and turnover frequencies of $>5000\ h^{-1}$ have been achieved.

Keywords: alkenes; asymmetric hydrogenation; iridium; N,P-ligands; oxazolines

1 Introduction

Enantioselective hydrogenation of olefins with chiral rhodium or ruthenium catalysts is the best established, most widely used method in asymmetric catalysis.[1] Among the huge number of chiral phosphines developed in academic and industrial laboratories, several ligands are available, which exert nearly perfect enantiocontrol in the hydrogenation of various olefins. Nevertheless, there are still many classes of substrates that these catalysts cannot handle. Therefore, the search for new catalysts and ligands continues.

Unfunctionalized olefins are particularly difficult substrates because, in general, a polar group adjacent to the C=C bond, which can coordinate with the rhodium or ruthenium center, is required for high catalyst activity and enantioselectivity. There are very few examples of highly enantioselective hydrogenations of olefins lacking such a polar group.[2–4] Titanocene and zirconocene complexes have been shown by Buchwald et al.[2] to induce high enantiomeric excesses in the hydrogenation of various unfunctionalized tri- and tetrasubstituted arylalkenes. However, the turnover frequencies (TOF) and turnover numbers (TON) are low.

We have recently found a new class of hydrogenation catalysts which overcomes these limitations.[5–9] These catalysts, iridium complexes with chiral P,N-ligands, showed exceptionally high activity with unfunctionalized olefins and in many cases gave excellent enantioselectivity. In addition, promising results were also obtained with certain functionalized alkenes for which no suitable catalysts were available previously. In this account, we discuss the special properties of these chiral iridium catalysts and illustrate their scope by listing the various substrates that have been hydrogenated with high enantioselectivity.

2 Initial Experiments

In the course of our work on chiral phosphinooxazoline (PHOX) ligands,[10] we studied Ir-PHOX complexes as catalysts for the hydrogenation of imines.[11] With *N*-phenylimines derived from aryl methyl ketones, high TON and TOF and enantiomeric excesses of up to 89% could be obtained. The coordination sphere of Ir-PHOX complexes resembles that of the Crabtree catalyst,[12] a cationic achiral Ir(phosphine)(pyridine) complex, which in contrast to Rh or Ru catalysts readily hydrogenates unfunctionalized tri- and tetrasubstituted olefins. Therefore, we thought that the chiral Ir-PHOX complexes might display similar reactivity and could be used for the enantioselective hydrogenation of unfunctionalized olefins.

Indeed, first tests with the iridium-PHOX complex **Ir-A1** and (*E*)-1-phenyl-2-(4-methoxyphenyl)-1-propene

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From left to right: B. Wüstenberg, E. Hörmann, A. Pfaltz, F. Menges, S. P. Smidt, M. Schönleber.

Andreas Pfaltz was born in Basel, Switzerland, in 1948. He received a diploma in natural sciences and a Ph. D. degree from the ETH in Zürich. After completing his thesis under the direction of Albert Eschenmoser in 1978, he joined the research group of Gilbert Stork at Columbia University as a post-doctoral fellow. In 1980 he returned to the ETH where he was appointed 'Privatdozent' (Lecturer) in 1987. From 1990 – 1995 he was Professor of Organic Chemistry at the University of Basel and from 1995 – 1998 director at the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr, Germany. In 1999 he returned to the University of Basel where he is currently Professor of Organic Chemistry. His main interests are in the areas of homogeneous and heterogeneous catalysis, with special emphasis on asymmetric catalysis.

Jörg Blankenstein studied chemistry in Cologne and moved to the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr for his diploma thesis under the supervision of Prof. A. Pfaltz. He stayed with the group for his Ph. D. and obtained his degree in April 2001 at the University of Basel. Subsequently, he worked as a post-doctoral research associate with Jieping Zhu at the Institut de Chimie des Substances Naturelles in Gif-sur-Yvette before joining Sanofi-Synthelabo in 2002.

Robert Hilgraf studied chemistry in Hamburg and Leicester. After his diploma thesis with Prof. W. Francke, he moved to the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr in 1997 for his Ph. D. work with Prof. A. Pfaltz. He obtained his Ph. D. degree in December 2000 at the University of Basel and subsequently moved on to the Scripps Institute as a post-doctoral research associate with Prof. K. B. Sharpless. He recently joined Celgene/ Signal Research Division (San Diego, USA).

Esther Hörmann obtained her B. Sc. in chemistry at the University of Basel in 1990. After three years in the catalysis research group of Hoffmann-La Roche, Basel, a two-year stay in the US, and a family break, she joined Prof. Zuberbühler's research group at the University of Basel in 1999 where she studied binding of molecular oxygen to Cu complexes. She has been a member of the Pfaltz group since fall 2001.

Steven McIntyre was born in Glasgow in 1971. He studied chemistry at the University of Glasgow, where he received a B. Sc. in 1992. After some years at Pfizer and Oxford Asymmetry, he joined the Pfaltz group as a research associate. In 2002, he returned to Glasgow to a position in the pharmaceutical industry.

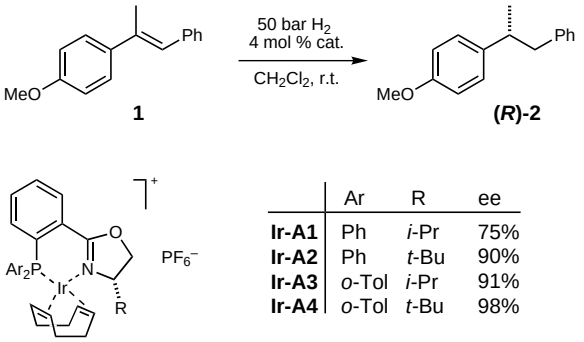
Frederik Menges, born 1974, studied chemistry at the University of Münster and completed his diploma thesis in 2000 under the supervision of Prof. Gerhard Erker. In 2000 he joined the group of Prof. Andreas Pfaltz for his Ph. D. research.

Marc Schönleber was born in 1974 in Basel, Switzerland. He received the Diploma in chemistry from the University of Basel in 2000. Since then he is working as a Ph. D. student under the direction of Prof. A. Pfaltz.

Sebastian P. Smidt studied chemistry in Freiburg i. Br., Edinburgh, and Erlangen. After his diploma thesis with Prof. L. Dahlenburg in 1998, he worked for one year in the group of Prof. J. A. Osborn in Strasbourg in the field of oxidation catalysis. He joined Prof. A. Pfaltz's group at the University of Basel for his Ph. D. research in December 1999.

Bettina Wüstenberg was born in Hamburg, Germany in 1972. She studied chemistry at the Carl von Ossietzky University in Oldenburg, Germany. After graduating in 1999 with a diploma thesis under the direction of Prof. J. Martens, she then joined the group of Prof. A. Pfaltz at the University of Basel, where she is currently working on her Ph. D. thesis.

Nicole Zimmermann studied chemistry in Hamburg and Leicester. After her diploma thesis with Prof. W. Francke, she did her Ph. D. thesis under the direction of Prof. A. Pfaltz at the Max-Planck-Institut für Kohlenforschung in Mülheim and at the University of Basel from November 1997 to January 2001. After post-doctoral studies with Peter G. Schultz at the Scripps Research Institute (La Jolla, USA), she recently joined Vertex Pharmaceuticals (San Diego, USA).



	Ar	R	ee
Ir-A1	Ph	*i*-Pr	75%
Ir-A2	Ph	*t*-Bu	90%
Ir-A3	*o*-Tol	*i*-Pr	91%
Ir-A4	*o*-Tol	*t*-Bu	98%

Scheme 1. Hydrogenation of (*E*)-1-phenyl-2-(4-methoxyphenyl)-1-propene.

as substrate gave encouraging results (Scheme 1). With 4 mol % of catalyst at 50 bar hydrogen pressure, 75% ee and 78% conversion were obtained. Introduction of a bulky *tert*-butyl group at the stereogenic center in the oxazoline ring and *ortho*-tolyl substituents at the phosphorus atom led to a significant increase in the enantioselectivity. Thus, with ligand **A4**, containing a bis(*ortho*-tolyl)phosphino and a 4-*tert*-butyloxazoline group, the enantioselectivity could be improved to 98% ee.[5]

Kinetic studies with (*E*)-1,2-diphenyl-1-propene showed that the reaction is extremely fast.[6] With 4 mol % of catalyst in a 0.3 M solution of olefin at 7 bar hydrogen pressure the reaction reached completion within less than one minute. Lower catalyst loadings resulted in decreased conversion. Although the initial rate was still high using 1 mol % of catalyst or less, rapid and essentially complete deactivation of the catalyst was observed before 50% of the olefin was consumed. Deactivation is a known problem of the Crabtree catalyst, which is thought to be caused by the formation of inactive hydride-bridged trimers.[12] In our case, too, NMR analysis of reaction mixtures suggested the presence of such hydride-bridged trimers. Recently, we could isolate a trimeric Ir(PHOX)-hydride complex after treating the corresponding Ir(COD) complex with hydrogen.[13] The structure of this catalytically inactive compound, which was elucidated by NMR and X-ray analysis, is similar to those of analogous hydride-bridged trimeric Ir complexes reported in the literature.[14]

3 Catalyst Optimization: an Unexpected Anion Effect

Attempts to increase the conversion by varying the solvent, the hydrogen pressure, or the catalyst and substrate concentration were unsuccessful. Coordinating solvents or additives such as amines, as well as coordinating anions such as halides or carboxylates were found to inhibit the reaction. The best results were obtained in anhydrous dichloromethane or 1,2-dichloroethane using cationic Ir(PHOX) complexes with hexafluorophosphate or hexafluoroantimonate as counterion. Rigorous exclusion of moisture and oxygen resulted in increased conversion. When the reaction was set up in dry dichloromethane under argon, full conversion could be achieved with only 0.5 mol % of catalyst. However, at such low catalyst loadings it was usually difficult to consistently avoid deactivation.

Surprisingly, a simple solution for the problem of deactivation was found by exchanging the counterion with tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BAr_F).[15] Iridium complexes with this special anion proved to be much more robust and full conversion could be routinely obtained with catalyst loadings as low as 0.02 mol %. Compared to the corresponding hexafluorophosphates or hexafluoroantimonates, the complexes containing BAr_F as the counterion were much less sensitive to moisture. The origin of this unexpected counterion effect remains unclear and is currently under investigation.[16] Other fluorinated tetraarylborates such as tetrakis(pentafluorophenyl)borate had a similar effect, although in terms of TON, TOF, and conversion, the BAr_F anion proved to be the best choice.[6,17] Catalysts with tetraphenylborate, tetrafluoroborate, and triflate as counterion gave only low conversion.

4 Practical Aspects

Iridium(COD) complexes with PHOX or related P,N-ligands, which are used as precatalysts, are readily prepared by refluxing a solution of $[Ir(COD)Cl]_2$ and the P,N-ligand in dichloromethane. For the exchange of the chloride ion with BAr_F, the complexes are treated with $NaBAr_F$ in a two-phase dichloromethane-water system. The resulting orange BAr_F salts can be purified by column chromatography on silica gel. The complexes are stable against oxygen and moisture and, therefore, can be easily handled in the laboratory atmosphere. Also, the catalytic reactions can be set up in the air with no need to purge the autoclave with an inert gas.

Hydrogenations are usually carried out in dichloromethane at room temperature at 50 bar hydrogen pressure. 1,2-Dichloroethane and toluene can also be used with similar results. However, high pressures are not necessary, as fast reactions and almost the same enantioselectivities are obtained under 5–10 bar of hydrogen pressure. In general, only a weak pressure dependence of the ee was observed [with (*E*)-1,2-diphenyl-1-propene: 96.2% ee at 5 bar, 97.8% ee at 100 bar]. One exception are terminal olefins such as 2-phenyl-1-butene (see Scheme 14), which react with significantly higher enantioselectivity at low pressure. The effect of temperature was not systematically studied. In one case [hydrogenation of (*E*)-1,2-diphenyl-1-propene at 14 bar] the ee remained essentially constant between 98.0–98.3% when the temperature

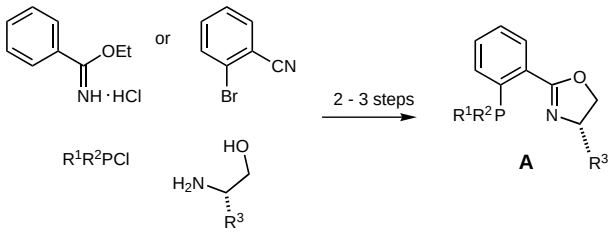
was raised from −6 to 25 °C, whereas at 40 °C it dropped to 96.7%.

Typically, 0.02–1 mol % of catalyst is used in a 0.1–2 M solution of substrate. Kinetic studies[6,17] with the standard substrate (*E*)-1,2-diphenyl-1-propene showed that the reaction is very fast at room temperature. Under the experimental conditions used, the rate was found to be limited by hydrogen diffusion between the gas and liquid phase. Therefore, the TOF of 7200 h^{-1}, measured under these conditions, should be taken as a lower limit. At 4 °C and less than 0.1 mol % of catalyst, the reaction was no longer diffusion-limited and relevant kinetic data with TOF of 5500 h^{-1} could be recorded.[17]

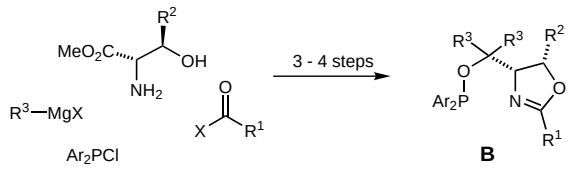
5 Survey of Chiral Ligands

Although very high enantioselectivities could be obtained in the hydrogenation of (*E*)-1,2-diphenyl-1-propene and related trisubstituted diarylalkenes using Ir(PHOX) catalysts, the range of substrates proved to be limited. For many alkenes the enantioselectivities remained unsatisfactory, even after extensive variation of the substituents at the P atom and the oxazoline ring. Therefore, we decided to extend our studies to other types of oxazoline-derived P,N-ligands with different backbones (see Schemes 3–6). Like the original PHOX ligands (Scheme 2), all these new ligands are modular and can be readily assembled from simple, commercially available precursors.

The phosphinite-oxazolines of type **B** (Scheme 3), which are derived from serine or threonine, proved to be an especially promising class of ligands.[7,9] In contrast to the PHOX ligands, the phosphorus unit is attached to the stereogenic center next to the oxazoline nitrogen atom. For the R^1 substituent, located adjacent to the coordination site, almost unlimited variations are possible, because it stems from a carboxylic acid. Serine (R^2 = H) as well as threonine (R^2 = Me), which serve as precursors for the backbone, are available in both enantiomeric forms. Using a different synthetic route,[18] or starting from *allo*-threonine instead of threonine,[9] diastereomeric ligands with inverted configuration next to the oxazoline oxygen atom can be synthesized. Variation of the Grignard reagent and the chlorophosphine makes it possible to prepare a highly diverse library of ligands.

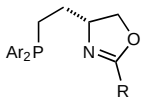


Scheme 2. Synthesis of PHOX ligands **A**.



Scheme 3. Synthesis of phosphinite-oxazoline ligands **B**.

Closely related ligands have been recently reported by Burgess[19] (JM-Phos) and Richards[20] (structure **B** with $R^2 = R^3 = H$). Although these ligands are structurally very similar, the enantioselectivities they induce in Ir-catalyzed hydrogenations are not as high as those obtained with the most effective derivatives of structure **B** (R^3 = alkyl).



***JM*-Phos**

Comparison of the crystal structures of an Ir-PHOX complex **Ir-A1** and an analogous complex **Ir-B1** derived from a phosphinite-oxazoline reveals two distinct differences (Figure 1).[7] In contrast to the typical axial-equatorial disposition of the two P-phenyl groups in Ir-PHOX complexes, the two P-Ph bonds in complex **Ir-B1** form a nearly symmetrical arrangement with respect to the P-Ir-N coordination (dihedral angles N-Ir-P-C: 111° and 126°). In the PHOX complex, the substituent at the stereogenic center is quite remote from the Ir atom, whereas the bis(*tert*-butyl)phenyl group in complex **Ir-B1** extends towards the coordination sphere and, therefore, is expected to interact with reactants bound at the adjacent coordination sites. This implies that the chiral environment of the Ir-atom is substantially different in the two complexes and, therefore, it is not surprising that different results are obtained with these two types of catalysts.

Another very useful, readily available class of phosphinite-oxazoline ligands is shown in Scheme 4.[21] The synthesis is very short and convenient. Refluxing *tert*-leucinol and 2-hydroxy-2-methylpropionic acid in xylene leads to the corresponding oxazolinyl alcohol in high yield, which has been converted to a series of ligands **C** by deprotonation and reaction with chlorophosphines.

The same oxazolinyl alcohol also serves as a precursor for diaminophosphine- and phosphite-oxazoline ligands **D** (Scheme 5).[22–24] Starting from chiral 1,2-diamines or TADDOLs,[25] libraries of ligands with high structural diversity can be built. In addition to Ir-catalyzed hydro-

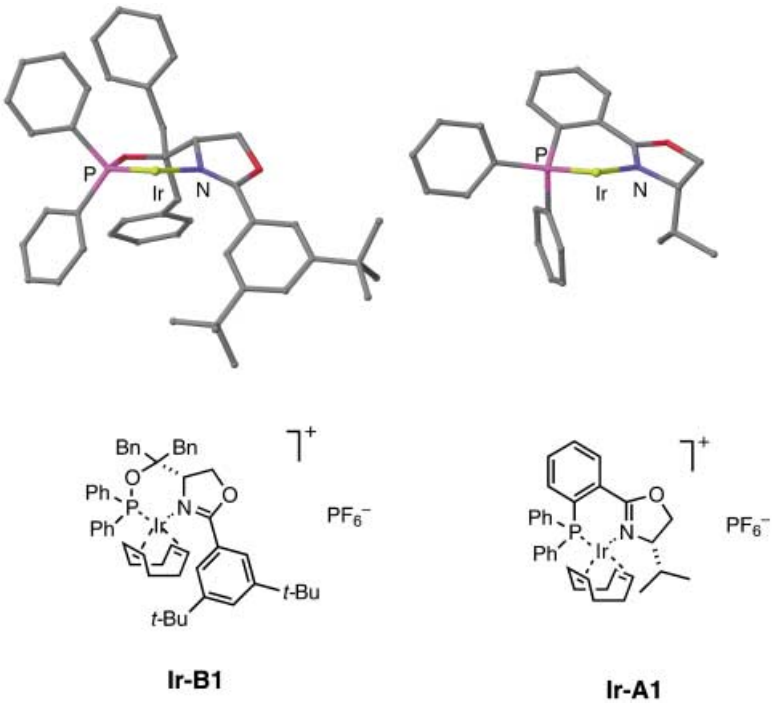
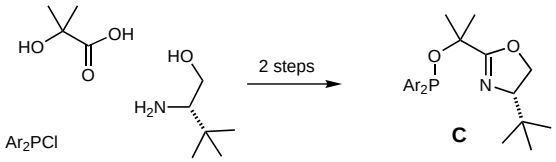
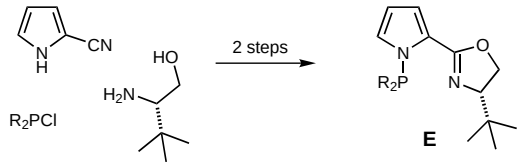


Figure 1. Crystal structures of **Ir-B1** and **Ir-A1**. The anion and cyclooctadiene are omitted for clarity.



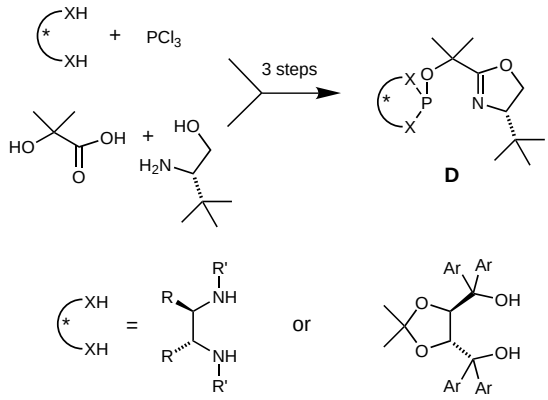
Scheme 4. Synthesis of phosphinite-oxazoline ligands **C**.



Scheme 6. Synthesis of PyrPHOX ligands **E**.

genation, these ligands have also been successfully applied to Pd-catalyzed allylic substitution.[22]

In collaboration with Cozzi, we studied the PyrPHOX ligands **E** (Scheme 6).[8] The free ligands are sensitive to hydrolysis and cannot be chromatographed on silica gel,



Scheme 5. Synthesis of diaminophosphine- and phosphite-oxazoline ligands **D**.

in contrast to the corresponding [Ir(PyrPHOX)(COD)]BAr_F complexes, which could be obtained as analytically pure crystalline solids after chromatography.

We were interested in these ligands because we expected that replacing the phenyl backbone of PHOX ligands by a pyrrole ring would result in different electronic and structural properties. Comparison of the crystal structures of an iridium-PyrPHOX and an analogous PHOX complex indeed revealed some distinct differences (Figure 2). The angle constraints imposed by the pyrrole ring result in a flattening of the chelate ring. The plane defined by the pyrrole ring forms a smaller angle with the P-Ir-N coordination plane than the corresponding plane defined by the phenyl backbone in the PHOX complex (20° *vs.* 42°). As a consequence, the geometries of the P-substituents differ substantially. The P-C bond to the equatorial phenyl group in the PHOX complex, which is thought to play a crucial role in the chirality transfer from the ligand to the substrate,[10] is located approximately in the coordination plane, whereas the corresponding P-C bond to the

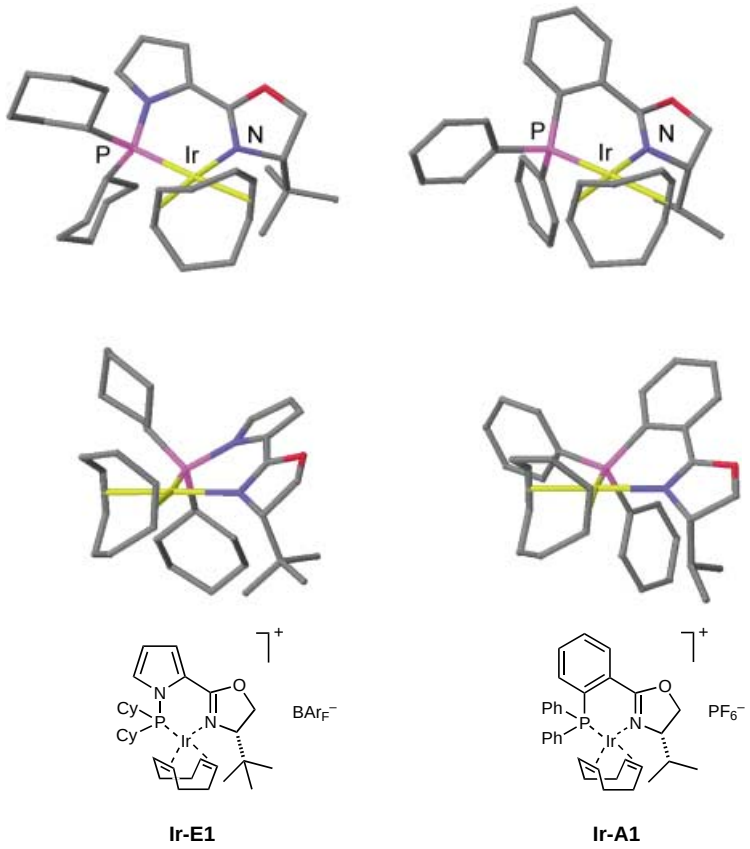
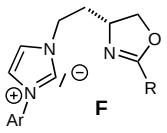


Figure 2. Crystal structures of **Ir-E1** and **Ir-A1**. Anions omitted for clarity.

cyclohexyl group in the PyrPHOX complex sticks out of the coordination plane. Thus the steric effects of PyrPHOX and PHOX ligands are expected to be quite different even if the substituents at the oxazoline ring and the P atom are identical.

Interesting new phosphinooxazoline analogues, in which the phosphorus unit has been replaced by a heterocyclic carbene, have been developed by Burgess and tested in Ir-catalyzed hydrogenations.[26] The best results have been obtained with the (1-adamantyl)oxazoline ligand **F**. For the standard substrate, (*E*)-1,2-diphenyl-1-propene, this ligand induced 98% ee, while for monoarylalkenes the ee values were significantly lower than those recorded for the best phosphinooxazolines.



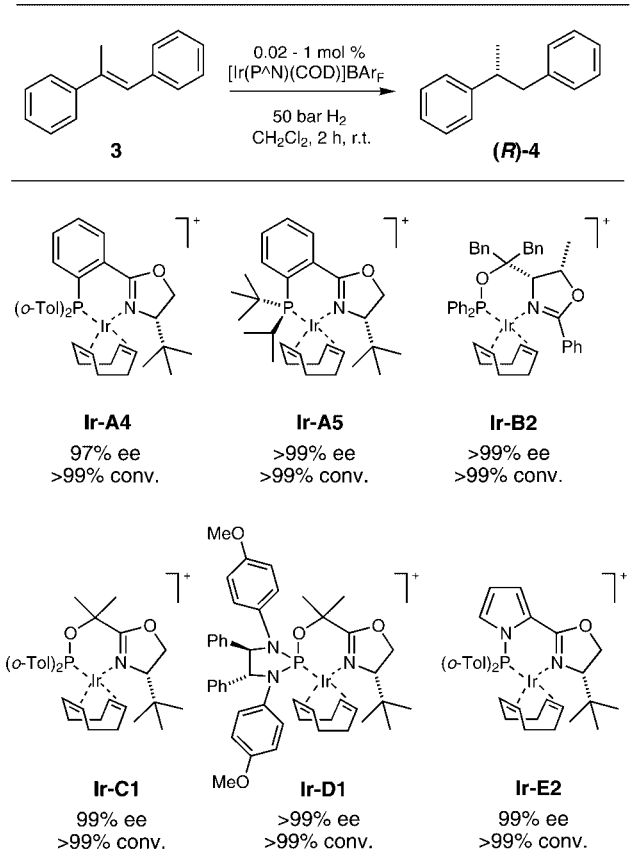
F

R = 1-Adamantyl
Ar = 2,6-(*i*-Pr)$_2$Ph

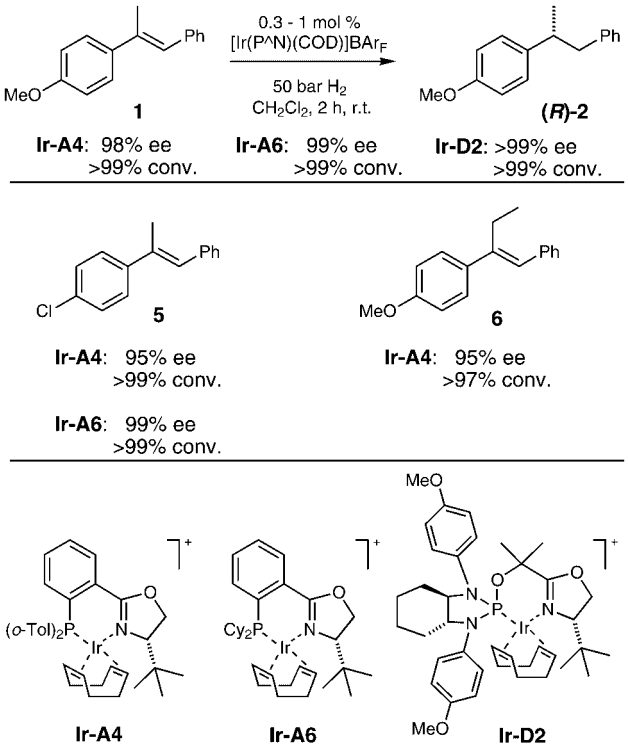
6 Survey of Reactions

Trisubstituted olefins with two aryl groups in a *trans* arrangement such as (*E*)-1,2-diphenyl-1-propene are unproblematic substrates, reacting with high enantioselectivity with many different catalysts (Scheme 7). Among the PHOX ligands, the bis(*ortho*-tolyl)phosphino-*tert*-butyloxazoline derivative **A4** is often the ligand of choice because it is easily synthesized and gives high enantiomeric excesses for a range of different diarylalkenes (Scheme 8). Although other PHOX derivatives, such as the *tert*-butyl-isopropylphosphinooxazoline **A5** with a stereogenic P atom or the dicyclohexylphosphinooxazoline **A6** can induce even higher enantiomeric excesses, they are somewhat more difficult to synthesize. Phosphinite-oxazolines (structures **B** and **C**) are also very effective, readily available ligands for this class of substrates. As shown in Scheme 8, the *para*-methoxy and *para*-chloro derivatives give very similar results as the unsubstituted methylstilbene **3**.

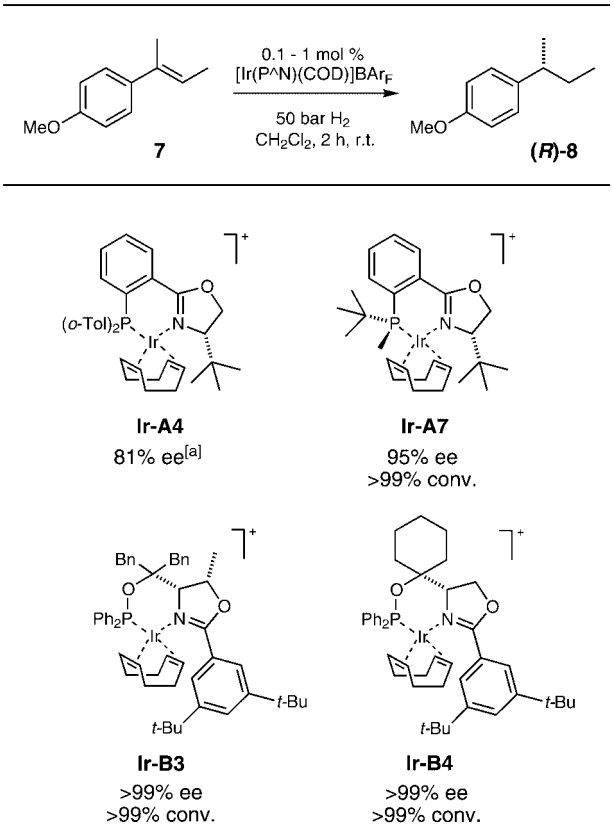
(*E*)- and (*Z*)-2-aryl-2-butenes are more difficult to hydrogenate with high enantioselectivity (Schemes 9 and 10). For this class of substrates, phosphinite-oxazolines of type **B** are the most versatile ligands. Variation of the substituents at the oxazoline ring and the backbone makes it possible to systematically optimize the enan-



Scheme 7. Hydrogenation of (*E*)-1,2-diphenyl-1-propene.



Scheme 8. Hydrogenation of 1,2-diarylalkenes.

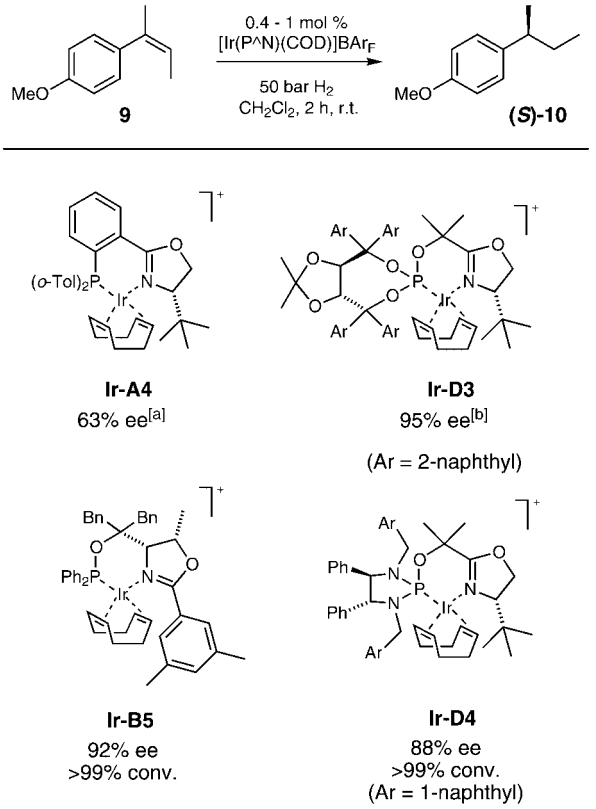


Scheme 9. Hydrogenation of (*E*)-2-(4-methoxyphenyl)-2-butene.
[a] This value, which was obtained with freshly purified substrate, is higher than the previously published ee (ref.[5]).

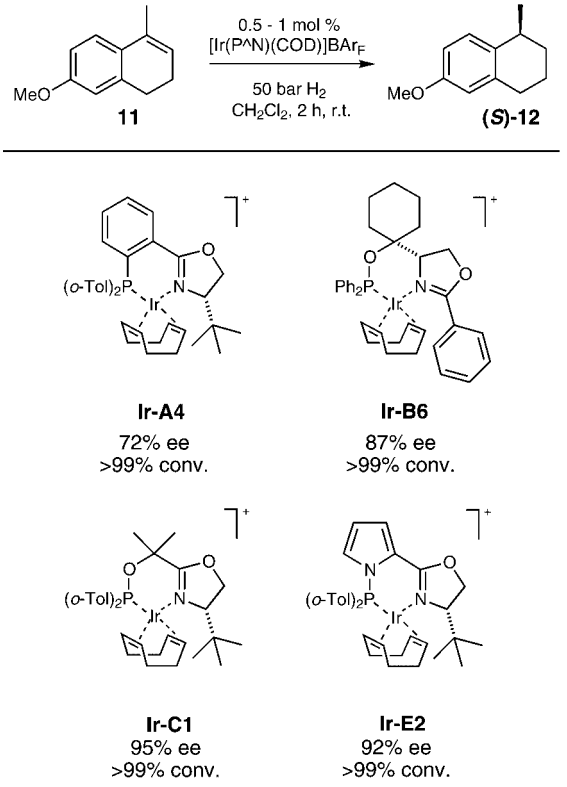
tioselectivity for each substrate. For (*E*)-2-(4-methoxyphenyl)-2-butene **7** the enantiomeric excess could be increased to >99% ee, using ligands **B3** or **B4**, whereas for the corresponding (*Z*)-isomer, complex **Ir-B5** proved to be the best catalyst. The (*E*)- and the (*Z*)-isomers afforded products of opposite configuration. PHOX ligands were less suited in this case, with the exception of derivative **A7** containing a chiral methyl-*tert*-butylphosphino group. High enantioselectivities were also obtained with complexes derived from ligands **D3** and **D4**, however, with **Ir-D3** much higher catalyst loadings of 4 mol % were necessary to achieve full conversion. The purity of the alkenes proved to be crucial for obtaining reproducible results (see footnote [a]) in Schemes 9 and 10).

Hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene (**11**) gave only moderate enantioselectivities with most ligands. In this case, catalyst **Ir-C1** containing a bis(*ortho*-tolyl)phosphinite group and the PyrPHOX complex **Ir-E2** afforded the best results with >90% ee (Scheme 11).

Alkenes bearing heterocyclic substituents such as furyl, thiophenyl, or pyrrolyl groups could be hydrogenated with high efficiency and enantiomeric excesses



Scheme 10. Hydrogenation of (*Z*)-2-(4-methoxyphenyl)-2-butene.
[a] This value, which was obtained with freshly purified substrate, is higher than the previously published ee (ref.[5]).
[b] 4 mol % of metal complex/100 bar H_2.



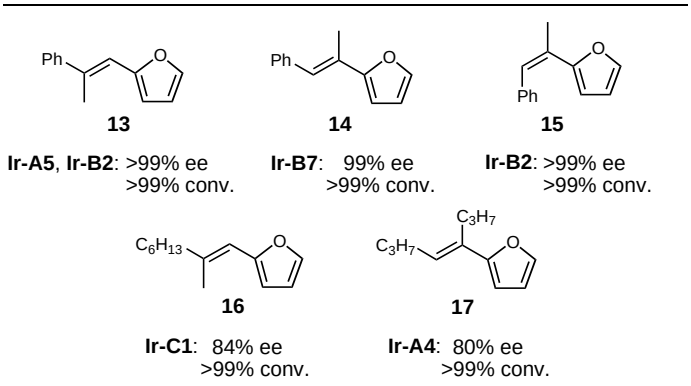
Scheme 11. Hydrogenation of 6-methoxy-1-methyl-3,4-dihydronaphthalene.

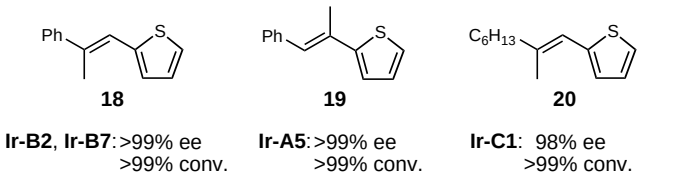
of >99% ee (Scheme 12). Remarkably, even the unprotected pyrrole derivative **21** reacted smoothly, giving quantitative conversion and outstanding enantioselectivity. Pyridyl substituents, on the other hand, were found to completely inhibit the reaction. The heterocyclic π-systems in the thiophene and pyrrole derivatives are resistant to hydrogenation, whereas in some reactions of the furan derivatives **13**–**15** small amounts of the corresponding tetrahydrofurylalkanes were formed as side products (2–6%). With the furylalkenes **15** and **17**, *cis/trans*-isomerization was observed in some cases (5–20%, depending on the catalyst), whereas for all other substrates shown in Scheme 12, no evidence for isomerization was found.[27]

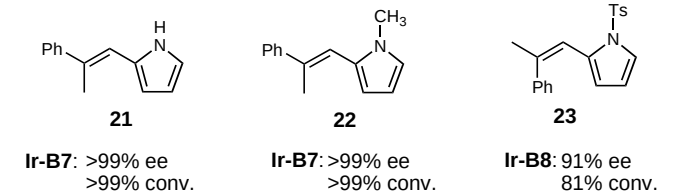
Tetrasubstituted alkenes such as **24** are much more difficult to hydrogenate than the trisubstituted alkenes discussed above. The only catalysts that react with high yields and enantioselectivities with these substrates are the zirconocene complexes reported by Buchwald.[2b] Initial experiments with iridium-PHOX complexes gave disappointing results. The bis(*ortho*-tolyl)phosphino-*tert*-butyloxazoline ligand **A4**, which was one of the most effective PHOX derivatives for the hydrogenation of trisubstituted olefins, gave essentially racemic product. However, using less bulky derivatives such as the diphenylphosphino-isopropyloxazoline **A1** or the diphenylphosphino-(2,2-dimethylpropyl)oxazoline **A8**, high conversion and enantioselectivities of up to 81% ee could be accomplished (Scheme 13). Although these results are encouraging, further work will be necessary to develop practical catalysts for this class of substrates.

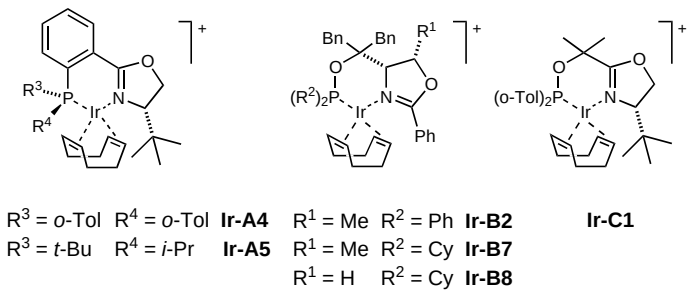
Terminal olefins such as 2-phenyl-1-butene are much more reactive than the substrates discussed so far. They are readily hydrogenated with Rh- or Ru-diphosphine catalysts at ambient pressure.[3a] With most catalysts, however, only moderate to low enantioselectivities are obtained (<70% ee). An exception is the Ru-(MeDuPhos) system, recently reported by Noyori et al.,[4] which in the presence of *t*-BuOK afforded 81–89% ee for 2-phenylbutene and several *meta*- and *para*-substituted derivatives. Chiral metallocenes have also been used in this reaction. With titanocenes up to 77% ee could obtained at −75 °C, while at room temperature the enantioselectivities were low.[3a] The highest ee for 2-phenylbutene has been achieved with an *ansa*-bis(cyclopentadienyl)lanthanide catalyst at very low temperature (96% ee at −80 °C; 64% ee at 25 °C).[3b]

Unfortunately, no other method besides polarimetry is available for determining the ee of 2-phenylbutane.[3,4] Therefore, we chose 2-(4-methoxyphenyl)-1-butene





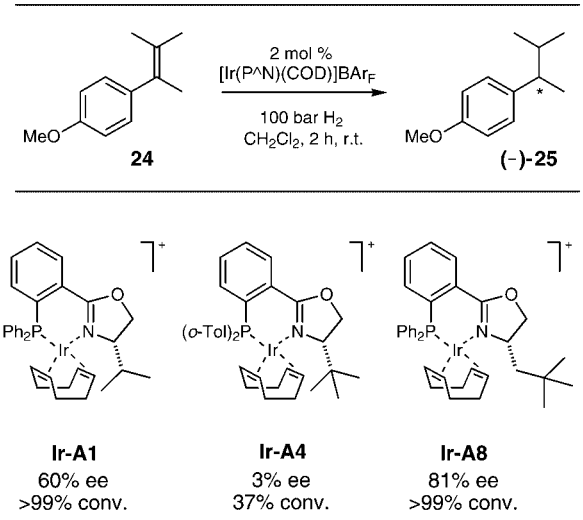




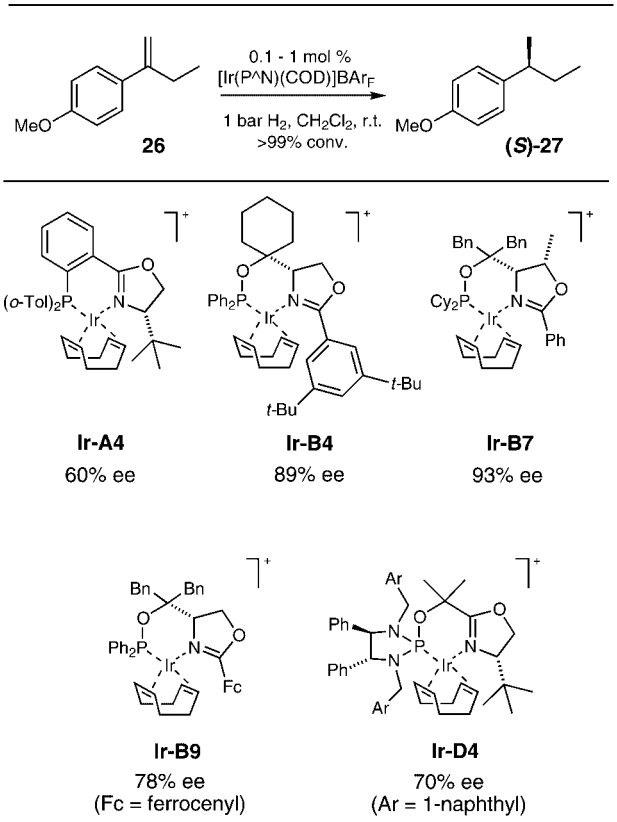
Scheme 12. Hydrogenation of heteroaromatic alkenes **13**–**23**.

(**26**) as a test substrate, because the ee of the hydrogenation product can be determined by HPLC or GC on chiral columns.[28] PHOX ligands of type **A** gave only low to moderate enantioselectivities with this olefin (Scheme 14). However, with phosphinite-oxazolines of structure **B** up to 93% ee could be obtained at 1 atm of hydrogen pressure. At higher pressures the enantioselectivity decreased significantly.

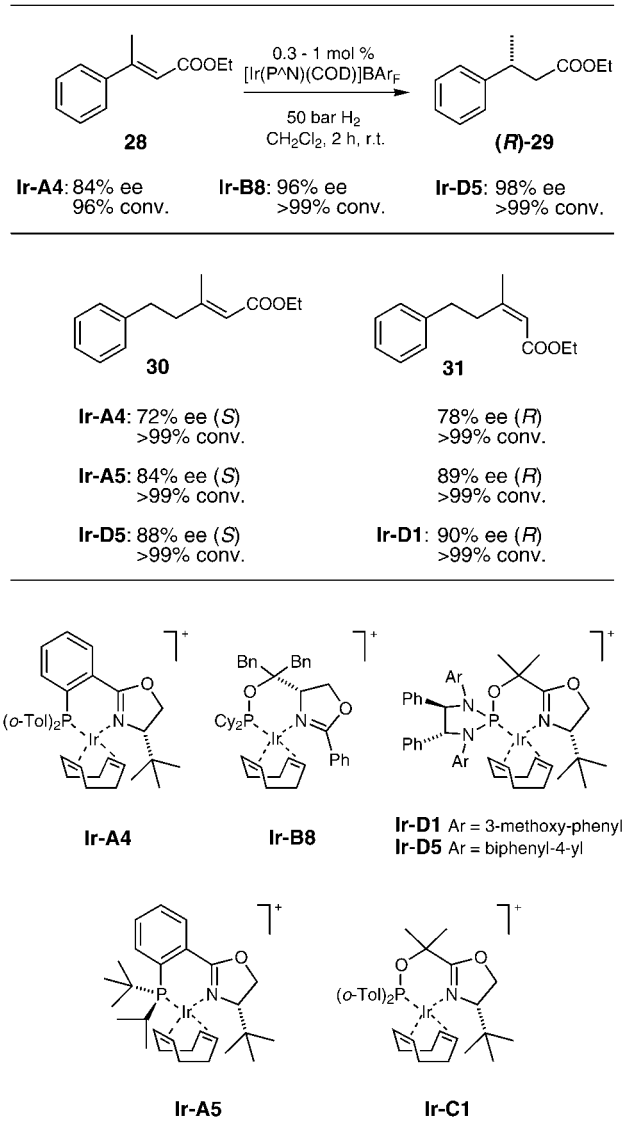
α,β-Unsaturated carboxylic acids can be hydrogenated with high enantioselectivity using Ru catalysts.[1] However, for analogous esters, no suitable catalysts have been reported yet, with the exception of cobalt-semicorrin complexes in combination with sodium borohydride as reducing agent.[29] Preliminary experiments with Ir-phosphinooxazoline complexes gave encouraging results. (*E*)-2-Methylcinnamic acid ethyl ester **28** could be reduced to the corresponding saturated ester **29** with up to 97% ee, while the (*E*)- and (*Z*)-alkenoic esters **30** and **31** gave enantioselectivities around 90% ee using ligands of types **C** or **D**



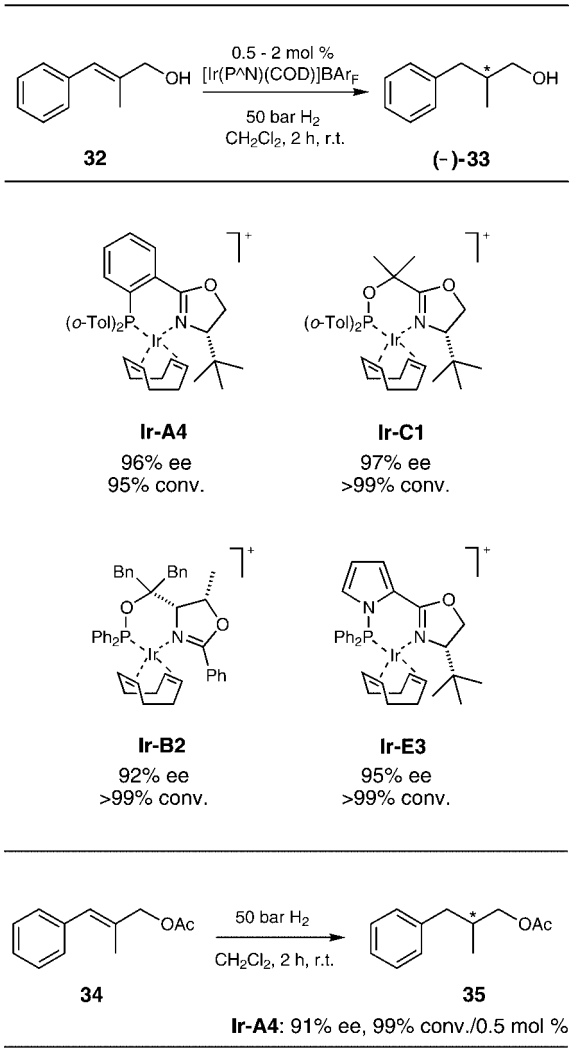
Scheme 13. Hydrogenation of 2-(4-methoxyphenyl)-3-methyl-2-butene.



Scheme 14. Hydrogenation of 2-(4-methoxyphenyl)-1-butene.



Scheme 15. Hydrogenation of α,β-unsaturated carboxylic esters **28**, **30**, and **31**.



Scheme 16. Hydrogenation of (*Z*)-2-methyl-3-phenyl-prop-2-enol and the corresponding allylic acetate **34**.

(Scheme 15).[23] For this class of substrates with an electron-poor double bond, dialkylphosphino-oxazolines with an electron-rich P atom proved to be superior to the corresponding diarylphosphino-substituted ligands.

Allylic alcohols like **32** were also briefly investigated. Enantiomeric excesses between 92–97% could be obtained with several ligands (Scheme 16). Early experiments had suggested that with this polar substrate, the PF_6 salts were superior to the catalysts with BAr_F as counterion.[5] However, more recent studies showed that with 0.5 mol % of catalyst, [Ir(COD)**A4**]BAr_F gave higher conversion than the PF_6 salt (100% *vs.* 88%). In contrast to ruthenium-BINAP catalysts[1] which require a free hydroxy group for high enantioselectivity, the corresponding allylic acetate **34** could be hydrogenated with 91% ee using an Ir-PHOX catalyst. No reductive cleavage of the allylic C-O bond was observed in this case.

7 Conclusion

With iridium complexes derived from chiral P,N-ligands, we have introduced a new class of hydrogenation catalysts that significantly expand the application range of enantioselective hydrogenation. Several types of olefins, for which no suitable catalysts were previously available, can now be hydrogenated with high efficiency and good to excellent enantioselectivity. The iridium complexes used as precatalysts are air-stable and easy to handle. A further attractive feature is the modular nature of the chiral ligands, which makes it possible to tailor the catalyst structure for a specific substrate.

Acknowledgements

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