Available online at www.sciencedirect.com
ScienceDirect
C. R. Chimie 10 (2007) 178–187
COMPTES RENDUS CHIMIE
http://france.elsevier.com/direct/CRAS2C/

Account / Revue

Recent advances in iridium-catalysed asymmetric hydrogenation of unfunctionalised olefins

Stephen J. Roseblade, Andreas Pfaltz*

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

Received 23 August 2006; accepted after revision 1 December 2006
Available online 9 January 2007

Abstract

In this account, the recent advances which have been made in asymmetric iridium-catalysed hydrogenation are reviewed. The first part focuses on our own studies of bicyclic pyridine–phosphinite ligands. These ligands have greatly enhanced the application range of asymmetric hydrogenation and, for the first time, have allowed highly enantioselective hydrogenation of simple, alkyl-substituted olefins and substituted furans. In the second part of this account, experimental and computational mechanistic studies are discussed. Whether the catalytic cycle proceeds via Ir(I)–Ir(III) intermediates or via Ir(III)–Ir(V) intermediates is still the subject of debate. ***To cite this article: Stephen J. Roseblade, A. Pfaltz, C. R. Chimie 10 (2007).***

Keywords: Catalysis; Asymmetric hydrogenation; Iridium; Ligand synthesis; Density functional theory

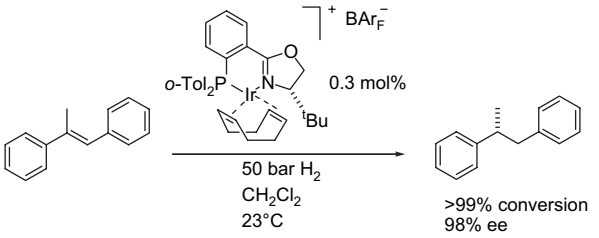
Since Crabtree and co-workers discovered that [Ir(pyridine)(PCy_3)(COD)]PF_6 catalyses the hydrogenation of unfunctionalised olefins with high turnover frequencies in non-coordinating solvents [1], subsequent studies have focused on investigations into the mechanism of iridium-catalysed hydrogenation [2], applications in stereoselective organic synthesis [3] and, most recently, enantioselective hydrogenations using chiral P, N ligands [4].

Our interest in developing chiral analogues of Crabtree's catalyst stemmed from the fact that whilst asymmetric hydrogenation is clearly an attractive synthetic method [5], the Monsanto -L-DOPA process being a well-known example from industry [6], the range of olefins that can be hydrogenated with high enantiomeric excess is limited. Rhodium and ruthenium catalysts require the presence of a polar functional group next to the C=C bond which can coordinate to the metal centre and help in achieving high levels of activity and stereocontrol [5,7].

Some years ago, we introduced cationic iridium complexes with chiral P, N ligands as catalysts that overcome these limitations. The original ligand was a phosphino-oxazoline (PHOX) [8] and the optimal counter-anion was found to be the large, weakly coordinating tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BAr_F). These catalysts allowed the hydrogenation of stilbenes to be carried out with high levels of enantioselectivity [9]. The nature of the anion proved to be crucial in avoiding catalyst deactivation and reducing the moisture-sensitivity of the reactions. Under optimised conditions turnover numbers of >5000 could be achieved (Scheme 1) [10].

* Corresponding author.
E-mail address: andreas.pfaltz@unibas.ch (A. Pfaltz).

1631-0748/$ - see front matter © 2006 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.crci.2006.12.001



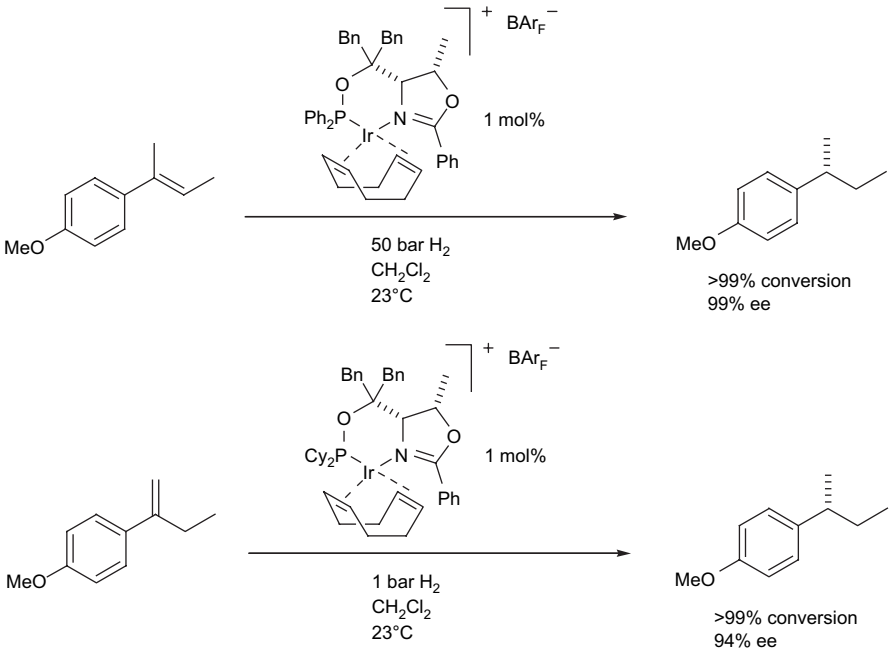
Scheme 1. Highly enantioselective hydrogenation of a stilbene.

Subsequent studies in these laboratories have extended the range of substrates which can be hydrogenated with high levels of enantioselectivity by systematic variation of the structure of the P, N ligands [11]. The threonine-derived phosphinite P, N ligands (ThrePHOX) have proven to be especially versatile for highly efficient and enantioselective hydrogenations of a wide range of unfunctionalised and certain functionalised olefins (Scheme 2) [12].

Other research groups have also become interested in asymmetric hydrogenation of unfunctionalised olefins using chiral analogoues of Crabtree's catalyst and, during the last few years, have reported a number of efficient ligands [13].

Until recently, highly enantioselective hydrogenation of purely alkyl-substituted olefins has not been possible. From a synthetic point of view, a catalyst which is able to hydrogenate the C=C double bond of a substrate without the need for any specific functional group or aryl substituent would allow the reaction to be applied to a much wider range of substrates. In view of the encouraging results obtained with pyridine–phosphinites of type **1** [14], we prepared a series of bicyclic analogues **2**, since we expected the more rigid geometry imposed by the additional ring to raise enantioselectivity (Fig. 1). Iridium complexes incorporating the five- and six-membered ring derivatives **2** ($n = 1,2$) proved to be efficient catalysts, inducing enantioselectivities generally higher than those of the analogous ligands **1** and we have found that bicyclic pyridine–phosphinite complexes of this type are highly selective catalysts for hydrogenation of simple, purely alkyl-substituted olefins [15].

Initially, we used the (*E*)- and (*Z*)-olefins **3** as test substrates, the methoxyphenyl group having been introduced to facilitate product analysis by GC or HPLC on chiral columns. Most ligands that had given high enantioselectivities with alkenes containing an aryl substituent at the C=C bond performed poorly with (*E*)- and (*Z*)-**3**. Pyridine-based ligands **4**, **5** and **6** were exceptions, giving full conversion and ee values between 83% and 98%. Among a series of oxazoline- and imidazoline-derived ligands, two derivatives **7** and **8** induced reduction with almost 90% ee. However, these two ligands performed well only with one of the two



Scheme 2. Highly enantioselective hydrogenations using IrThrePHOX catalysts.