Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Molecular Catalysis A: Chemical 249 (2006) 218–222
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Phosphite and thiourea ligand synergy for rhodium catalyzed enantioselective hydroformylation of styrene

Radwan Abdallah, Jérémy A.J. Breuzard, Michel C. Bonnet, Marc Lemaire *

Laboratoire de Catalyse et Synthèse Organique, CPE-CNRS, UMR 5181, UCB-Lyon I, CPE, Bât. 308, 43, Bd du 11 Novembre 1918, 69622 Villeurbanne Cedex, France

Received 28 July 2005; received in revised form 24 November 2005; accepted 20 December 2005
Available online 21 February 2006

Abstract

New non-C_2-symmetric chiral diphosphites have been synthesized and used as ligands in the rhodium catalyzed enantioselective and regioselective hydroformylation of styrene. A synergistic effect improving both activity and enantioselectivity is observed when a chiral dithiourea is introduced as co-ligand in the Rh-diphosphite catalytic system.

Keywords: Enantioselective hydroformylation; Styrene; Phosphites; Thioureas

1. Introduction

Hydroformylation is one of the largest-volume processes of organometallic catalysis [1,2] and is therefore widely studied [3–5]. Moreover, enantioselective hydroformylation of styrene derivatives promises a shortcut access to anti-inflammatory drugs yielding chiral 2-arylpropionic aldehydes, which can be oxidized to pharmaceutically active 2-arylpropionic acids like Naproxen or Ibuprofen [6].

However, efficient catalysts for this reaction are still rare since it requires good chemo, regio and enantioselectivities (Scheme 1). The first example of a highly enantioselective catalyst was reported by Takaya and co-workers 12 years ago and it is based on Rh-BINAPHOS [7]. Many studies on this phosphine-phosphite system lead to a very active and selective olefin hydroformylation catalyst which can be used solvent free in supercritical CO_2 media [8,9] or recovered when polystyrene-supported [10]. In the case of styrene [10] this catalyst allows an enantiomeric excess of 95 and 99% conversion with an *iso*-selectivity of 92.5%.

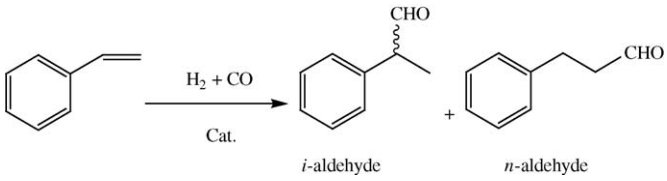
Some rhodium-diphosphite catalysts have been prepared for the enantioselective hydroformylation of styrene based on (2*R*, 4*R*)-pentane-diol with C_2-symmetry [11–13] or on tunable furanoside backbones [14–16]. In these derivatives, all of the chiral centres are not involved in the enantioselective process, but they are sometimes detrimental to it. The rhodium-diphosphite catalytic systems require low temperature and pressure to afford high enantiomeric excesses what is detrimental to their activity. Best results were obtained with [Rh(acac)$(CO)_2$] and a ligand derived from D-(+)-glucose: 90% ee with 98.6% yield on 2-phenylpropanal for a styrene conversion of 83% (48 h at 20 °C, TOF = 18 mol styrene. $Rh^{-1}\,h^{-1}$). Activity can be increased by changing temperature (TOF = 174 mol styrene. $Rh^{-1}\,h^{-1}$ at 40 °C), but enantioselectivity drops to 78% [17]. Claver and co-workers reported that *tert*-butyl groups in the bisphenol moieties also have an important effect on asymmetric induction [18].

As in many other fields of asymmetric catalysis, the use of other heteroatoms such as O, N or S has been investigated for hydroformylation of styrene [3–5,19,20]. The only non-phosphorinated compounds developed for this purpose are indeed sulphur containing ligands: thiols, thioethers and thioureas [5,21–24]. Some enantioselective examples have been reported but ee values remain modest and conversions rather low.

Claver and co-workers prepared chiral thioethers-phosphites analogues to their best furanoside diphosphites. These novel P,S-ligands were used in rhodium catalyzed styrene hydroformylation and led to excellent activities and regioselectivities, but no significant enantioselectivities were detected [25].

* Corresponding author. Tel.: +33 472431407; fax: +33 4 72 43 14 08.
E-mail address: marc.lemaire@univ-lyon1.fr (M. Lemaire).

1381-1169/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2005.12.020



Scheme 1. Hydroformylation of styrene.

Recently, Gladiali et al. reported the use of an heterobidentate P, S version of BINAP in asymmetric catalysis [26,27]. The in situ Rh catalyst formed from the BINAPS (*R*)-methyl sulfide lead to a complete styrene hydroformylation, 96% of isoaldehyde but only 14% ee [26].

Diphosphites are selective ligands for the rhodium catalyzed hydroformylation, but their activities should be improved. The combination of P and S heterodonor ligands with rhodium give highly active catalysts for this reaction, but the obtained chiral inductions are low with the reported systems. It is worthy to evaluate if there is any synergetic effects between chiral diphosphites and chiral thioureas. This is the goal of the present study in which we first describe the synthesis of novel chiral diphosphites and their use in rhodium catalyzed styrene hydroformylation. The effect of chiral thiourea ligands on the rhodium-diphosphite catalyst is then reported.

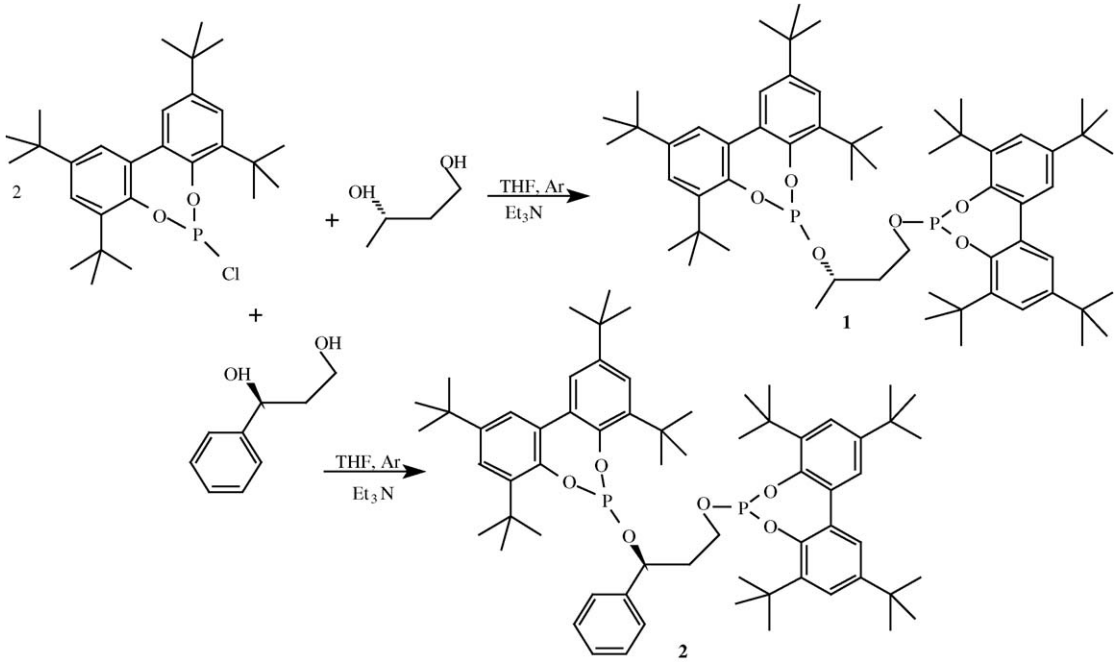
2. Experimental

2.1. General procedures

All the organic and organometallic reagents are pure commercial products. The solvents are reagent grade and are dried and distilled by standard techniques before use. Melting points (m.p.), uncorrected, are determined with an Electrothermal 9100 apparatus. Elemental analyses are obtained from the Service Central d'Analyse of the CNRS (Solaize). High-resolution mass spectra: HR liquid secondary ionisation mass spectrometry (LSIMS: Thioglycerol), HR CIMS (Isobutan) and were carried out on a Finnegan MAT 95×L by the UCBL Centre de Spectroscopie de Masse. $[\alpha]_D$ were determined with a Perkin-Elmer 241 polarimeter (l = 1 dm; 25 °C; concentration *c* in g/100 mL). ^1H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker AC-200 (200.13 MHz for ^1H, 50.32 MHz for ^{13}C); δ values are given in ppm and *J* in Hz. GC analysis (styrene conversion, aldehyde yields and enantioselectivities) were determined with a Shimadzu (SE-54) chromatograph equiped with a chiral column (Supelco β-DEX-225, 60 m, i.d. 0.25 mm), using decane as internal standard.

2.2. General procedure for the synthesis of diphosphite ligands

The chiral diphosphites **1** and **2** were synthesized from (*S*)-methyl or phenyl-1,3-butanediol and the corresponding phosphochloridite (Scheme 2), which was prepared according to the procedure published by van Leeuwen and co-workers [13]. The diols (1 mmol) were dissolved in THF (25 mL) and triethylamine (2.5 mL) and added dropwise to a phosphochloridite (5 mmol) solution in THF (25 mL), at 0 °C. The reaction mixture was heated to reflux overnight. The resulting triethylamine salts were filtered off. Evaporation of the solvent gave white foams, which were purified by washing several times with acetonitrile to give white solids which were then dried under vacuum for 24 h. The diphosphites were obtained in good yields (>70%).



Scheme 2. Diphosphite synthesis.