ELSEVIER

Journal of Molecular Catalysis A: Chemical 157 (2000) 79–82

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

Rhodium catalysed enantioselective hydrogenation in water using pyrphos bound to poly-acrylic acid as ligand

Torsten Malmström, Carlaxel Andersson *

Inorganic Chemistry 1, Chemical Center, Lund University, P.O. Box 124, S-22100 Lund, Sweden

Received 15 June 1999; received in revised form 30 November 1999; accepted 24 December 1999

Abstract

Coupling of pyrphos ((*R*,*R*)-3,4-bis-diphenylphosphino-pyrrolidine) to poly-acrylic acid (PAA) furnish a new water-soluble ligand (PAA–pyrphos), which can be successfully applied as a ligand in biphasic (H_2O/EtOAc) rhodium catalysed enantioselective hydrogenation of acetamido cinnamic acid. Contrary to the PAA–PPM (PPM = (2*S*,4*S*)-4-diphenylphosphino-2-diphenylphosphino-methylpyrrolidine) ligand system the enantioselectivity of catalysts based on the PAA–pyrphos ligand system is virtually unaffected by changes in reaction parameters which influence the local phosphine concentration.

Keywords: Water-soluble; Chiral; Hydrogenation; Rhodium; Biphasic; Phosphine

1. Introduction

Catalytic asymmetric hydrogenation of dehydroamino acids is one of the most important advances in homogeneous catalysis, and enantioselectivities approaching 100% have been reported [1,2]. The difficulty in separating the catalyst from the products is the main drawback with homogeneous catalysts. This problem can, however, be solved by performing the catalytic reaction under biphasic conditions, i.e., having the catalyst substituted with water-soluble phosphines in an aqueous phase and the substrate/products in a nonmiscible organic phase [3–5]. An easy recovery and reuse of expensive enantioselective hydrogenation catalysts is of course very desirable, and water-soluble bidentate chiral phosphines are therefore desirable chiral ligands in biphasic asymmetric hydrogenations [6,7].

Herein we report on the preparation of a new ligand, PAA–pyrphos, comprised of (*R*,*R*)-3,4-bis-diphenylphosphino-pyrrolidine coupled to the sodium salt of poly-acrylic acid, and its use in rhodium catalysed biphasic enantioselective hydrogenations [8]. The study is aimed at comparing how the different chelate ring sizes in PAA–pyrphos and PAA–PPM ((2*S*,4*S*)-4-diphenylphosphino-2-diphenylphosphino-methylpyrrolidine bound to PAA), affects the enantioselectivity [9,10].

* Corresponding author. Tel.: +46-46-222-81-04; fax: +46-46-222-81-04.

E-mail address: carlaxel.andersson@inorg.lu.se (C. Andersson).

1381-1169/00/$ - see front matter
PII: S1381-1169(99)00451-3

2. Results and discussion

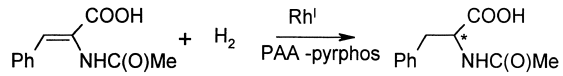

Fig. 2. Hydrogenation of α-acetamido cinnamic acid to *N*-acetyl phenylalanine.

Dicyclohexylcarbodiimine (DCC) mediated couplings of amino-substituted phosphines to PAA have been described previously [9,11], and this reaction proceeds smoothly also in the case of pyrphos and the three different ligands, A–C, containing different amounts of phosphorus were straightforwardly synthesised and isolated as their sodium salts (Fig. 1). Ligand A contained 3.9% P while B and C contained 1.6% and 0.95% P, respectively. The ^{31}P NMR spectra of these ligands only revealed one resonance at 10.8 ppm for the free ligand and no phosphineoxide was detected. The IR spectra exhibited absorbtions for the amid carbonyl at 1612 cm^{-1} and for the carboxylate anion at 1584 and 1406 cm^{-1}.

For the PAA–PPM ligand system, we have previously noted that the factors which affect the local concentration of phosphine groups, that is the phosphine loading on the polymer, the ionic strength and the polymer concentration in the aqueous phase also affects the enantioselectivity of the catalysts based on the PAA–PPM ligands [10]. Tentatively we suggested that the main cause for this local concentration effect could be ascribed to the type of complexes formed; a high local concentration promotes the formation of complexes in which the rhodium atom coordinates two phosphorus atoms from different phosphine moieties while a low local concentration promotes the formation of an authentic chelate complex, and that these two type of complexes give rise to different enantioselectivities. The seven-membered chelat ring which is formed by the PAA–PPM ligand upon coordination to a metal centre is for reasons of ring-size less stable than the five-membered ring formed by the PAA–pyrphos ligand. Consequently, the PAA–pyrphos ligand system should give an opportunity to verify or reject the hypothesis regarding local concentration effects.

The catalysts were generated in situ by stirring $[Rh(NBD)_2]O_3SCF_3$ with PAA–pyrphos

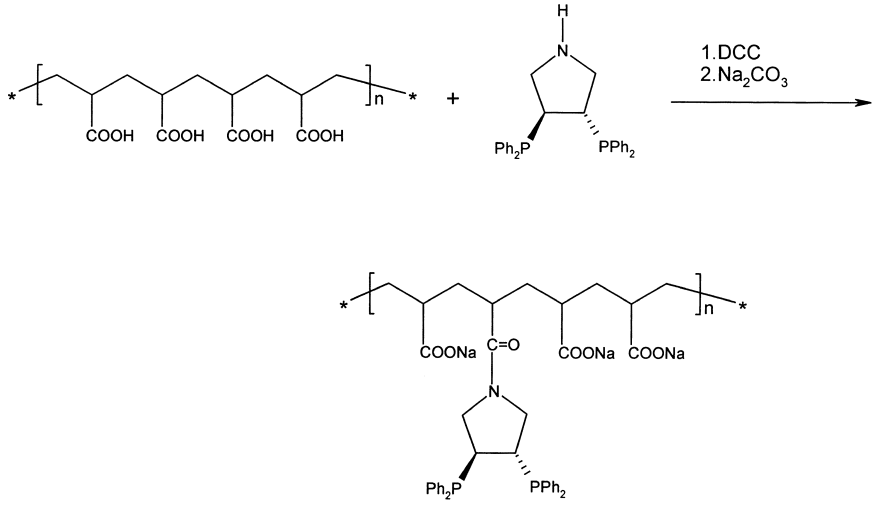

Fig. 1. Preparation of PAA–pyrphos.

Table 1
Hydrogenation of α-acetamido cinnamic acid using catalysts prepared by reacting $[Rh(NBD)_2]O_3SCF_3$ with PAA–pyrphos

Entry	Ligand[a]	Yield[b] (time)	ee[c] (configuration)	Additive
1	A	76 (6)	82 (S)	
2	A	63 (8)	77 (S)	70 mM $NaClO_4$
3	B	70 (6)	76 (S)	
4	B	81 (6)	79 (S)	70 mM $NaClO_4$
5	C	71 (6)	78 (S)	
6	C	81 (6)	83 (S)	70 mM $NaClO_4$

[a] [Rh] = 1.5 mM.
[b] Determined by ^{1}H NMR.
[c] Determined by polarimetry.

(ligand A–C), giving a orange aqueous phase containing $[Rh(P–P)NBD)]^+$ (P–P = PAA–pyrphos) and a colourless EtOAc phase. Hydrogenations of α-acetamidocinnamic acid (Fig. 2) with the in situ prepared catalysts gave *N*-acetyl-(*S*)-phenylalanine with only small variations in the enantioselectivity, around 80% (Table 1). Performing the hydrogenations at a $NaClO_4$ concentration of 70 mM decreased the chiral induction for the PAA–PPM based catalysts, while the PAA–pyrphos based catalysts only varied slightly. The enantioselectivity is generally lower in water than in organic solvents [12] and thus the lower enantioselectivity obtained for the PAA–pyrphos compared to catalysts based on the parent pyrphos ligand is not surprising.

3. Conclusion

The small and unsystematic variations in enantioselectivity observed for the PAA–pyrphos based catalysts, by changing the ligand loading or the ionic strength and hence the local phosphine concentration around the polymer, can be taken as a confirmation that the formation of complexes other than the authentic seven-membered chelate complex is the cause for the variations in enantioselectivity obtained for the PAA–PPM based catalysts.

4. Experimental

All reactions were performed under an inert atmosphere and double distilled water and EtOAc (A.R.) were used throughout the study. PAA was used as supplied (Merck, 63% H_2O-solution). α-Acetamido cinnamic acid was purchased from Acros and recrystallised from EtOH prior to use. $[Rh(NBD)_2]O_3SCF_3$ was synthesised according to the literature [13]. High grade H_2 (5.7) was supplied by AGA, Sweden. The enantiomeric excess was determined polarimetrically using a Perkin-Elmer 241 polarimeter. The pyrphos ligand was supplied by Novartis, Basel, Switzerland. ^{31}P NMR spectra were recorded on a Varian 300 Unity spectrometer. ^{31}P NMR shifts are given relative to H_3PO_4, positive values downfield. Elemental analysis were performed by Mikro Kemi Uppsala, Sweden.

5. Preparation of PAA–pyrphos

Three different PAA–pyrphos ligands, with different phosphorus content, have been prepared and the following describes the synthesis of ligand A (3.9% P).

PAA (0.470 g, 63% H_2O solution) was dissolved in THF:H_2O (14 ml, 5:1). Pyrphos (0.190 g), dissolved in THF (4 ml), was added followed by dropwise addition (30 min) of DCC (0.126 g) dissolved in THF (4 ml). After stirring the reaction mixture overnight, THF was evaporated and water (5 ml) added to the remaining slurry. The pH was adjusted to 8 by addition of Na_2CO_3 (s) to ensure complete dissolution of the product. The remaining slurry was stirred for 30 min and the precipitated dicyclohexylurea (DHU) was separated by filtration and washed twice with 3 ml portions of water. The combined aqueous phases were evaporated to dryness under high vacuum giving a white powder (0.510 g).

^{31}P NMR (D_2O): −10.8 ppm.

FT-IR (KBr): 1612, 1584, 1406 cm^{-1}.

Elemental analysis: ligand A: 3.9% P, 1.1% N; ligand B: 1.6% P, 0.4% N; ligand C: 0.95% P, 0.25% N.

6. Hydrogenations

All catalysts were generated in situ by reaction of $[Rh(NBD)_2]O_3SCF_3$ and the ligands A–C. The hydrogenations were performed at a constant rhodium concentration of 1.5 mM and a Rh:P ratio of 1:2.1.

The ligand (A–C: A 8.6 mg, B 21.7 mg, C 35.6 mg) dissolved in water (3.5 ml) $[Rh(NBD)_2]O_3SCF_3$ (2.3 mg) was added and the resulting slurry was stirred till all the Rh-precursor had dissolved, whereafter EtOAc (3.5 ml) and α-acetamido cinnamic acid (108 mg) were added. The reaction flask was evacuated and filled with H_2 twice. The hydrogenation reaction was commenced by starting the stirrer and the H_2 pressure was kept constant by keeping a low H_2 flow through the system. After the selected time (6 h) the hydrogenation was stopped and the aqueous phase washed twice with EtOAc and Et_2O, respectively. The combined organic phases were dried over Na_2SO_4, filtered and finally evaporated to dryness.

The conversion was determined by ^{1}H NMR and the optical yield with polarimetry (Table 1).

N-acetyl-(*S*)-phenylalanine **1**: (CD_3OD); s, 1.89, CH_3C(O); dd 2.95 CH(H)-CH; dd, 3.10, C H(H)-CH; dd, 4.63, CH-CH_2; m, 7.20, C_6H_5-. polarimetry $[\alpha]_D^{20} = +46.0°$ ($c = 1$, EtOH)[6].

Acknowledgements

Financial support from TFR (Swedish Research Council for Engineering Sciences) and the gift of the pyrphos ligand by Novartis is gratefully acknowledged.

References

[1] H.B. Kagan, Asymmetric synthesis using organometallic catalysts, in: G. Wilkinson, F.G. Stone, E.N. Abel (Eds.), Comprehensive Organometallic Chemistry Vol. 8 Pergamon, Oxford, 1982, p. 463.
[2] H. Takaya, T. Ohta, R. Noyori, Asymmetric hydrogenation, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, VCH Publ., New York, 1993, p. 1.
[3] P. Kalck, F. Monteil, Adv. Organomet. Chem. 34 (1992) 219.
[4] W.A. Herrmann, C.W. Kohlpainter, Angew. Chem. Int. Ed. Engl. 32 (1993) 1524.
[5] F. Joo, A. Katho, J. Mol. Catal. A 116 (1997) 3.
[6] Y. Amrani, L. Lecomte, D. Sinou, J. Bakos, I. Toth, B. Heil, Organometallics 8 (1989) 542.
[7] I. Toth, B.E. Hanson, M.E. Davis, Tetrahedron: Asymmetry 1 (1990) 913.
[8] U. Nagel, E. Kinzel, J. Andrade, G. Prescher, Chem. Ber. 119 (1986) 3326.
[9] T. Malmström, C. Andersson, Chem. Commun. (1996) 1135.
[10] T. Malmström, C. Andersson, J. Mol. Catal. 139 (1999) 259.
[11] Y.S. Klausner, M. Bodansky, Synthesis (1972) 453.
[12] L. Lecomte, D. Sinou, J. Bakos, I. Toth, B. Heil, J. Organomet. Chem. 370 (1989) 277.
[13] R. Uson, L. Oro, M.A. Gerralda, M.C. Claver, P. Lahuerta, Trans. Met. Chem. 4 (1979) 55.