Catalysis Letters 41 (1996) 111–112

Homogeneous asymmetric hydrogenation of *o*-chloroacetophenone to enantiomerically pure *o*-chloro-(1-phenyl)ethanol catalyzed by BINAP–Ru(II) complex

Vilas H. Rane, Diedrik Tas [1], Rudy F. Parton and Peter A. Jacobs

Department Interfasechemie, Centrum voor Oppervlaktechemie en Katalyse, KU Leuven, Kardinaal Mercierlaan 92, B-3001 Heverlee, Belgium

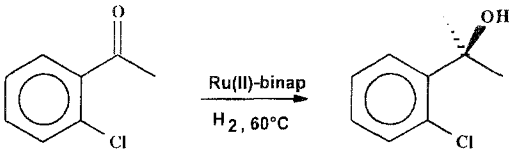
Received 23 April 1996; accepted 11 June 1996

The BINAP–Ru(II) catalyst (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)chloro(*p*-cymene)ruthenium chloride is found to be highly active and enantioselective for homogeneous asymmetric hydrogenation of *o*-chloroacetophenone to optically pure *o*-chloro-(1-phenyl)ethanol. In contrast to results of Noyori and coworkers, no organic and inorganic bases are required to obtain high activities and enantioselectivities

Keywords: enantioselective hydrogenation; *o*-chloroacetophenone; BINAP–Ru

1. Introduction

For more than a decade the production of optically pure compounds is of great practical importance because its need in pharmaceutical, agrochemical and fine chemical industries. There are several methods available to obtain enantiomerically pure products but among them asymmetric synthesis is a most desirable and challenging method. It is well known that BINAP–Ru(II) complexes ((BINAP = 2, 2′-bis(diphenylphosphino)-1,1′-binaphthyl) are found to be among the most efficient complexes to convert functionalized ketones to functionalized alcohols with high activity and enantioselectivity [1–4]. There are few reports available on enantioselective conversion of simple aromatic ketones to corresponding alcohols catalyzed by BINAP–Ru(II)–diamine–inorganic base [5,6]. Recently, Noyori and coworkers [7] have reported that simple aromatic ketones can be hydrogenated homogeneously at room temperature by a BINAP–Ru(II)–chiral diamine–KOH ternary system with high enantioselectivity. Because of the importance of this reaction, we carried out an investigation on homogeneous reduction of aromatic ketones by BINAP–Ru(II) complex and are able to obtain enantiomerically pure products. In this communication, we report our preliminary results on the asymmetric homogeneous hydrogenation of *o*-chloroacetophenone to optically pure *o*-chloro-(1-phenyl)ethanol by Ru(II)–BINAP catalyst (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)chloro(*p*-cymene)ruthenium chloride) with high enantiomeric excess and good turnover number:



2. Experimental

The homogeneous asymmetric hydrogenation reaction was carried out in a 10 ml stainless steel autoclave. In a typical experiment, 0.0023 g of (R) or (S)-2,2′-bis (diphenylphosphino)-1,1′-binaphthyl)chloro(*p*-cymene) ruthenium chloride catalyst, 1.7 g of *o*-chloroacetophenone and 7.5 g of methanol or 2-propanol were used. The autoclave was pressurized upto 30 or 60 atm initial hydrogen pressure and reaction was carried out at 60°C. During reaction, the mixture was stirred continuously using a magnetic stirrer at constant 1000 rpm. The products were analyzed by HP 5890A gas chromatograph with flame ionization detector (FID) using a Chiraldex GTA column and also identified by the gas chromatography–mass spectrometry (GCMS) technique. The enantiomeric excess (%) is defined as ([R] − [S])/([R] +[S]) × 100. All the experimental procedures were carried out in N_2 atmosphere.

3. Results and discussion

The catalytic results obtained in the asymmetric hydrogenation of *o*-chloroacetophenone at different hydrogen pressures and in various solvents are presented in table 1. The results show that with the (R)-enantio-

---

[1] To whom correspondence should be addressed.

Table 1
Enantioselective hydrogenation of *o*-chloroacetophenone catalyzed by BINAP–Ru(II) complex (reaction conditions: substrate/catalyst ratio = 740, reaction temperature = 60°C and reaction time = 65 h)

Run	Solvent	H_2 pressure (atm)	Conversion (%)	ee (%)	Conf.
1 (R)	methanol	60	85.0	86.6	S
2 (S)	methanol	60	85.3	86.7	R
3 (R)	2-propanol	60	16.3	45.7	S
4 (R)	methanol	30	91.0	86.5	S
5 (R)	2-propanol	30	19.2	33.2	S

meric form of the Ru(II)–BINAP catalyst and methanol as solvent, a very high conversion with 86.5% enantiomeric excess for (S)-*o*-chloro-(1-phenyl)ethanol was obtained (entry 1). When the reaction was carried out under the same reaction conditions with the (S)-enantiomeric form of the Ru(II)–BINAP complex, reproducible results were obtained (entry 2). To compare these results, another reaction was performed in 2-propanol at the same reaction conditions. For this reaction very low activity as well as enantioselectivity were obtained (entry 3) compared to methanol as solvent. Similar catalytic results were obtained when the reaction was carried out at 30 atm H_2 pressure and at 60°C in methanol and 2-propanol. The hydrogen pressure does not show any influence on the activity and enantioselectivity, indicating that this system is not much sensitive to hydrogen pressure. Also when the reaction was carried out at room temperature in methanol and 2-propanol and at similar reaction conditions, no activity and enantioselectivty was observed.

For determination of the reaction rate, the hydrogenation reactions were performed in methanol and 2-propanol under similar reaction conditions but at different reaction time. Fig. 1 shows the effect of reaction rate in solvents in the hydrogenation of *o*-chloroacetophenone to (S)-*o*-chloro-(1-phenyl)ethanol. It can be seen that the reaction rate in methanol is much higher than in 2-propanol. This clearly indicates the important role of the solvent for this catalytic system. Therefore, methanol is a good solvent for this reaction. The results are in contrast with the results observed by Noyori and coworkers [7] with a Ru(II)–BINAP–chiral diamine–KOH ternary system. They observed higher reaction rates in 2-propanol than in methanol. Moreover, they used additional chiral diamine and KOH to achieve high enantiomeric excess, whereas, for our system, high enantioselectivity was obtained without addition of chiral diamime and KOH. In this respect our catalytic system has more advantages compared to the above system.

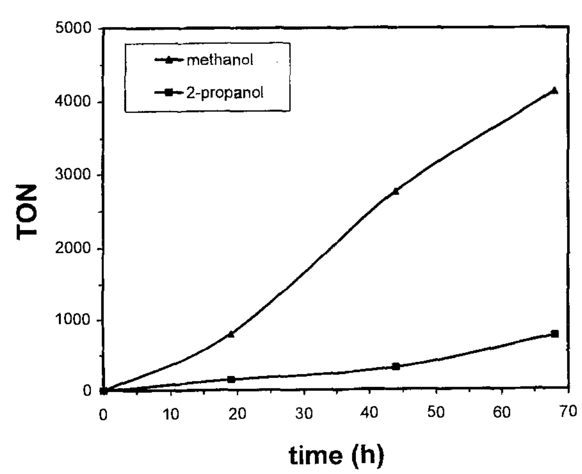


Fig. 1. Effect of solvent on reaction rate in the homogeneous hydrogenation of *o*-chloroacetophenone (substrate/catalyst ratio = 740, hydrogen pressure = 60 atm, T = 60°C).

4. Conclusions

In conclusion, Ru(II)–BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)chloro(*p*-cymene)ruthenium chloride is an excellent catalyst for homogeneous asymmetric hydrogenation of *o*-chloroacetophenone to optically pure *o*-chloro-(1-phenyl)ethanol with respect to activity and enantioselectivity. The addition of strong bases is not necessary to obtain high turnover number and/or enantioselectivities.

Acknowledgement

We are grateful to the Belgian Government for the support in the frame of a IUAP-PAI grant on Supramolecular Catalysis. VHR thanks the KU Leuven for a post-doctoral fellowship. DT thanks the Belgian National Fund of Scientific Research (NFWO) for a grant as aspirant research fellow and RFP is indebted to the NFWO for a fellowship as post doctoral research assistant.

References

[1] R. Noyori, Chem. Soc. Rev. 18 (1989) 187.
[2] H. Takaya, T. Ohta and R. Noyori, in: *Catalytic Asymmetric Synthesis*, ed. I. Ojima (VCH, Weinheim, 1993).
[3] R. Noyori and H. Takaya, Acc. Chem. Res. 23 (1990) 345.
[4] R. Noyori, CHEMTECH 22 (1992) 360.
[5] H. Takaya, S. Akutagawa and R. Noyori, Org. Synth. 67 (1989) 20.
[6] S. Pikul and E.J. Corey, J. Org. Synth. 71 (1993) 22.
[7] T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya and R. Noyori, J. Am. Chem. Soc. 117 (1995) 2675.