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Asymmetric hydroformylation of vinyl acetate with BINAP–rhodium(I) complexes

Dirk Hoegaerts and Pierre A. Jacobs *

Centre for Surface Science and Catalysis - K.U. Leuven, Kardinaal Mercierlaan 92, 3001 Heverlee, Belgium

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Abstract

Complexes of (*R*)-BINAP (BINAP=2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) derived from the available rhodium precursors $Rh(acac)(CO)_2$ and $[Rh(\mu\text{-}OMe)(cod)]_2$ are used for the asymmetric hydroformylation of vinyl acetate. Enantiomeric excesses of up to 60% are achieved with regioselectivities of up to 99%. Only a BINAP/Rh ratio of 2 is required. Effects of pressure and temperature on catalyst stability, enantio- and chemoselectivity are discussed.

1. Introduction

Hydroformylation is one of the most versatile methods for the functionalization of C=C bonds.[1] It is evident that the asymmetric variant represents a potentially powerful synthetic tool for the preparation of optically active aldehydes. In a one-step reaction, the carbon skeleton of an olefin is extended by one C atom and a stereocenter is created. These chiral molecules play an important role in the context of biological activity and are therefore valuable as precursors for drugs, agrochemicals and food additives in enantiomerically pure form.[2] For example, 2-arylpropionic acids, which can be synthesized by oxidation of the corresponding aldehydes, represent an important class of nonsteroidal anti-inflammatory agents.

The development of efficient catalytic systems, that could provide both a high regioselectivity (branched/normal aldehyde ratio) and enantioselectivity, has attracted a lot of research in recent years.[3] The major breakthrough in the rhodium asymmetric hydroformylation was made in 1993 by Takaya and coworkers.[4] They were the first to use BINAPHOS **1** (Fig. 1), a phosphane-phosphite ligand. Rhodium(I) complexes of this ligand gave the highest ees so far reported in the hydroformylation of a broad variety of olefins. Furthermore, excellent chemo- (hydroformylation vs hydrogenation) and regioselectivities were obtained. Although no better catalyst system has yet been discovered, the rather complex synthesis of this kind of ligand is a considerable drawback for practical use.

* Corresponding author. Tel: ++32-16321610; fax: ++32-16321998; e-mail: pierre.jacobs@agr.kuleuven.ac.be

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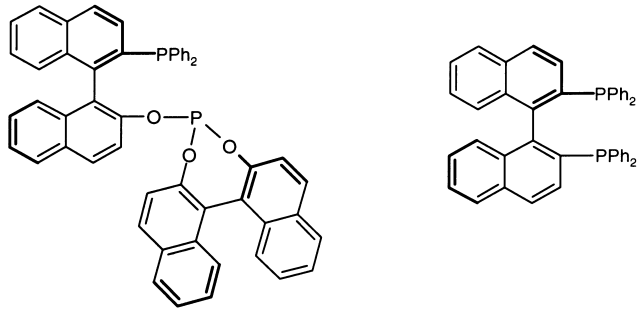

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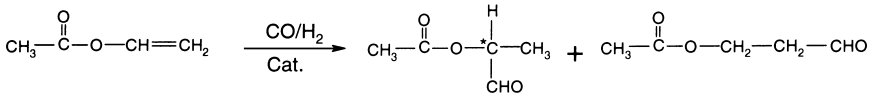
Figure 1.

Instead of synthesizing new and complex chiral ligands, we were interested in the application of existing, commercially available ligands used in other types of chiral reactions. In this paper, we report the use of BINAP **2** (BINAP=2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, Fig. 1) for the rhodium catalyzed conversion of vinyl acetate **3** into 2-acetoxypropanal **4** (Scheme 1). This atropisomeric ligand has already proven to be outstandingly efficient for asymmetric isomerization and hydrogenation reactions.[5]



3 4 5

Scheme 1.

Surprisingly, BINAP was only tested once as a ligand for this reaction, with rather moderate success. Enantiomeric excesses did not exceed 47% and yields were impractically low (6%).[6] By changing the catalyst precursor and by modifying the reaction conditions, we could substantially improve these results and provide higher ees than previously reported for any other simple diphosphane rhodium hydroformylation catalyst.

2. Results and discussion

Initially, $Rh(acac)(CO)_2$ (acac=acetylacetonate) was used as the catalyst precursor for the asymmetric hydroformylation of vinyl acetate. In all experiments (except run 11, Table 1), an excess of diphosphane was used to exclude the formation of $[RhH(CO)_4]$. The latter is a highly active achiral hydroformylation catalyst and forms predominantly linear aldehydes.[7] No hydrogenation or isomerization products were observed (except run 8, Table 1). The results are given in Table 1.

In all cases, using (*R*)-BINAP leads to the formation of an excess of (*R*)-2-acetoxypropanal. A substrate/catalyst ratio of 250 seems best to provide acceptable yields. Higher reaction temperatures cause a decrease in ee after longer reaction times (runs 6, 13 and 15). When decreasing the phosphane/rhodium ratio, comparable ees are obtained after 24 h (runs 9 and 10). Longer reaction times, however, result in a loss of enantioselectivity, probably due to racemization of the branched aldehydes.

Using a 1:1 mixture of CO and H_2 and thereby decreasing the total pressure causes a significant enhancement of the reaction rate in the pressure range of 50 to 10 atm (runs 2–4). However, no significant change in the regio- or enantioselectivity is observable within this range. It is known that carbon monoxide and the chelating diphosphane ligand can compete for coordination around the rhodium metal

Table 1
Hydroformylation of vinyl acetate using $Rh(acac)(CO)_2$ as rhodium precursor[a]

Run	*P/Rh* [b]	*T*. °C	*p*, bar	*t*, h	*S/C* [c]	*% Yield* [d]	*Br/Lin* [e]	*% ee* [d]
1	3/1	60	10	24	100	25	97/3	58
2	3/1	60	10	48	250	45	97/3	56
3	3/1	60	30	48	250	25	95/5	60
4	3/1	60	50	48	250	17	94/6	54
5	3/1	65	10	48	250	55	99/1	52
6	3/1	70	10	6 (24)	250	15 (56)	97/3	54 (36)
7[f]	3/1	60	10	48	250	12	98/2	45
8[g]	3/1	60	10	48	250	4[h]	99/1	35
9	2/1	60	10	24 (48)	250	27 (42)	99/1	55 (44)
10	1.2/1	60	10	24 (48)	250	10 (26)	98/2	50 (18)
11	1/1	60	10	24	250	58	92/8	3
12	3/1	60	10	48	500	22	98/2	57
13	3/1	70	10	24 (48)	500	40 (65)	99/1	53 (36)
14	3/1	60	10	72	1000	19	97/3	60
15	3/1	80	10	3 (24)	1000	12 (35)	98/2	53 (34)

[a] All reactions were carried out in toluene under H_2/CO atmosphere (1/1). *(R)*-BINAP was used as the chiral ligand. [b] Phosphane/Rhodium ratio. [c] Substrate/Catalyst ratio. [d] Determined by GC (Chiraldex G-TA column). [e] Ratio branched to linear aldehyde. [f] $CO/H_2 = 5/1$. [g] $CO/H_2 = 1/5$. [h] Ethylacetate is the major product (65% yield)

and can afford different species.[3] In our case, a higher CO partial pressure obviously slows down the reaction rate (run 7). This inverse dependence was also observed by Horiuchi et al, when studying the mechanistic effects of the rhodium catalyzed hydroformylation of olefins, using BINAPHOS as the chiral ligand.[8] Not surprisingly, as BINAP is a typical hydrogenation ligand, increasing the hydrogen partial pressure results in a predominant reduction of the substrate into ethyl acetate (65% yield) (run 8). Only a small amount of 2-acetoxypropanal was formed (4%).

In a second series of experiments, $[Rh(\mu\text{-OMe})(cod)]_2$ (cod=cycooctadiene) was used as rhodium precursor. The results are summarized in Table 2.

Compared to the results shown in Table 1, Table 2 shows that this catalyst provides significantly higher yields to 2-acetoxypropanal, while maintaining the same regio- and enantioselectivities. Furthermore, using $[Rh(\mu\text{-OMe})(cod)]_2$ as the precursor allows the use of only a small excess of phosphane relative to rhodium (runs 19 and 20). Only a small decrease in activity is observed. Moreover, the catalyst seems to be more stable than when $Rh(acac)(CO)_2$ is used as precursor (runs 9 and 10). However, longer reaction times still result in a slight decrease of ee in the case of a 1.2/1 ratio (run 20). Similar temperature and pressure effects are observable as in the case of $Rh(acac)(CO)_2$. Low pressures are favorable for the catalytic activity and using higher temperatures results in a small loss of enantioselectivity at longer reaction times (runs 17 and 18).

In a final experiment, we tested (*R*)-tolBINAP as a chiral hydroformylation ligand ((*R*)-tolBINAP= 2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl). Although enantio-, chemo- and regioselectivities are comparable to those achieved with (*R*)-BINAP, yields were rather low.

Table 2
Hydroformylation of vinyl acetate using [Rh(μ-OMe)(cod)]$_2$ as rhodium precursor[a]

run	*P/Rh*	*T*, °C	*p*, bar	*t*, h	*S/C*	*% Yield*	*Br/Lin*	*% ee*
16	3/1	60	10	48	250	55	97/3	58
17	3/1	60	50	48	250	33	92/8	56
18	3/1	65	10	24 (48)	250	44 (65)	97/3	55 (47)
19	2/1	60	10	48	250	42	98/2	53
20	1.2/1	60	10	24 (48)	250	22 (40)	95/5	57 (45)
21	1/1	60	10	24	250	62	98/2	3
22[b]	3/1	60	10	48	250	13	99/1	57

[a] All reactions were carried out under same conditions as in Table 1.

[b] *(R)*-tolBINAP was used as catalyst ligand

3. Conclusion

BINAP–rhodium(I) complexes are active catalysts in the asymmetric hydroformylation of vinyl acetate. These chiral phosphanes provide a better enantioselectivity than previously reported for any other chiral diphosphane–rhodium system. Enantiomeric excesses of up to 60% are achieved. Applying 10 bar of a 1:1 CO:H_2 mixture seems appropriate in order to obtain good activities and selectivities. Furthermore, the reaction rate is inversely dependent on the CO partial pressure, while increasing the H_2 partial pressure leads to an important hydrogenation of the substrate. In addition, using [Rh(μ-OMe)(cod)]$_2$ as rhodium precursor allows to work at a lower BINAP:Rh ratio (2:1). (*R*)-tolBINAP, a derivative of BINAP, is far less active but also provides good regio-, chemo- and enantioselectivities.

4. Experimental

4.1. General

The diphosphanes (*R*)-BINAP and (*R*)-tolBINAP, and the Rh(acac)(CO)$_2$ precursor were of commercial origin. The [Rh(μ-OMe)(cod)]$_2$ complex was prepared using standard literature methods.[9] Vinyl acetate was obtained from Acros Organics. Solvents were distilled before use. Gas chromatographic analyses were carried out on a Hewlett–Packard Model 5890 gas chromatograph. This instrument was equipped with a FID detector and a 30 m×0.32 mm Astec Chiraldex G-TA (G: γ-cyclodextrin; TA: trifluoroacetyl) column. Hydroformylation experiments were performed in home-made stainless steel 10 ml autoclaves with magnetic stirring. The reactors are equipped with a heating control unit, a ‘micro-sampling’ unit and an analogue manometer.

4.2. General procedure for the asymmetric hydroformylation of vinyl acetate

A solution of the substrate (typically 6.25 mmol), the catalyst precursor (0.025 mmol) and the phosphorus compound (in the appropriate ratio) in anhydrous toluene (5 ml) was introduced into the reactor. After flushing three times with nitrogen, the autoclave was heated. When the desired temperature

was reached, the premixed gas mixture was introduced. The reaction progress was followed by GC analysis.

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