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Hydroformylation of aryloxy ethylenes by Rh/BINAPHOS complex Catalyst deactivation path and application to the asymmetric synthesis of 2-aryloxypropanoic acids

Maurizio Solinas[a,*], Serafino Gladiali[b,*], Mauro Marchetti[a]

[a] *Sezione di Sassari dell'Istituto di Chimica Biomolecolare – CNR, Trav. La Crucca, 3 I-07040 Li Punti-Sassari, Italy*
[b] *Dipartimento di Chimica, Università di Sassari, Via Vienna 2, I-07100 Sassari, Italy*

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Abstract

The behavior of Rh(I)/(*S*,*R*)-BINAPHOS complex in the asymmetric hydroformylation of styrene and other aryloxy substituted ethylenes shows a sharp deterioration in stereocontrol as the conversion increases. This failure is apparently due to an irreversible reaction of the starting complex with the aldehyde which is built up in solution and its extent can be limited operating at short contact times and low temperatures. Under optimized conditions, the hydroformylation of aryloxy substituted ethylenes provides the relevant branched aldehyde in some 70% regioselectivity and in up to 80% ee.

Keywords: Enantioselective catalysis; Hydroformylation; Agrochemicals; Rhodium; BINAPHOS

1. Introduction

As the biological activity of chiral agrochemicals is in most cases dependent on the absolute configuration of the substrate [1–4], the use of racemic mixtures is commercially wasteful and increases the environmental burden to an unacceptable extent.

The herbicidal activity of 2-aryloxypropanoic acids, a class of agrochemicals of wide utility, resides exclusively in the (*R*)-enantiomer [4]. Chiral 2-arylpropionaldehydes, which are obvious precursors of 2-arylpropanoic acids, are easily accessible by Rh-catalyzed asymmetric hydroformylation of arylsubstituted ethylenes.

Asymmetric hydroformylation is one of the most important metal-catalyzed reactions, which provides an efficient synthetic tool for the transformation of cheap olefins into valuable chiral aldehydes through the formation of a new C–C bond. In spite of the great deal of work in this area and of the enormous synthetic potential of this reaction, few examples of Rh-catalyzed hydroformylation of olefins have demonstrated a high efficiency in the enantioselective variant of the reaction [5].

The most significant contribution in the field of enantioselective hydroformylation was given by Takaya, Nozaki and co-workers with the discovery of the BINAPHOS ligand. The hydroformylation of a wide variety of olefins with rhodium(I) complexes containing this chiral modifier or the related BIPHEMPHOS provides consistently high regio- and enantioselectivity under relatively mild conditions [6–11]. More recently, some other chiral bidentate phosphorus ligands have emerged as efficient chiral modifiers for Rh(I)-catalysts in the asymmetric hydroformylation of styrene [12–14] and high stereoselectivities have been

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[*] Corresponding authors. Present address: RWTH-Aachen, Technische Chemie und Makromolekulare Chemie, Worringerweg 1, 52074 Aachen, Germany (M. Solinas). Tel.: +49 241 8026458; fax: +49 241 8022177 (M. Solinas)/Tel.: +39 079 229546; fax: +39 079 212069 (S. Gladiali).

E-mail addresses: solinas@itmc.rwth-aachen.de (M. Solinas), gladiali@uniss.it (S. Gladiali).

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obtained in the asymmetric hydroformylation of vinyl acetate using a chiral Rh(I)-catalyst with a bis(diazophospholidine) ligand [15]. With styrene, however, this last catalyst provides the branched aldehyde in low yield and in racemic form. In spite of these advances, no practical application of asymmetric hydroformylation to the synthesis of chiral fine chemicals is reported in the technical literature to date.

A few years ago, some of us reported that phenyl vinyl ethers can be effectively hydroformylated by rhodium carbonyl complexes with sterically hindered chiral diphosphites or ferrocenyldiphosphines, albeit in very low enantioselectivity [16]. Pursuing our work in this field, we have decided to focus our attention on the synthesis of *Mecoprop* and *Dichlorprop* [17] (Fig. 1). These are two herbicides of wide use of the family of aryloxypropanoic acids, which feature electron-withdrawing substituents on the phenyl ring.

Since Rh(I)/BINAPHOS has found to date the widest application in Rh-catalyzed asymmetric hydroformylation of aryl ethylenes, our first choice was to exploit this catalyst for our purpose. While a large number of olefins have been hydroformylated with this catalyst, the use of enol ethers as prochiral substrates has quite a few precedents [16,18] and, to the best of our knowledge, none of them employ BINAPHOS as the chiral ligand.

The results obtained in this study and some comments on the stability of the Rh(I)/BINAPHOS catalyst under the reaction conditions are reported in this paper.

2. Experimental

2.1. General methods and chemicals

(a*R*)-(+)-1,1′-binaphthalene-2,2′-diol ((*R*)-BINOL), (a*S*)-(+)-1,1′-binaphthalene-2,2′-diol ((*S*)-BINOL), $Rh(CO)_2$(acac), $[Rh(COD)Cl]_2$, phenol, 2,4-dichlorophenol, 2-methyl-4-chlorophenol, 1,2-dibromoethane and styrene were of commercial quality and used as purchased or after further purification. BINAPHOS was prepared according to literature procedure [6]. Phosphorus trichloride (PCl_3) was distilled before use and stored under argon atmosphere. Triethylamine (Et_3N) was distilled over KOH. All reactions were carried out under a positive pressure of argon. Toluene was used freshly distilled over sodium.

^1H NMR and ^{31}P NMR spectra were recorded with a Varian VXR 5000 spectrometer at 299.94 and 121.42 MHz, respectively. ^{31}P NMR chemical shifts are relative to H_3PO_4 (external standard) in $CDCl_3$. Mass spectra were recorded using a HP 5971 series mass spectrometer. Elemental analyses were performed using an elemental analyzer Perkin Elmer model 240 C. Optical rotations were measured with a Perkin Elmer 241 spectropolarimeter. The purity of all compounds was judged to be >98% by ^1H NMR and ^{31}P NMR spectral determination.

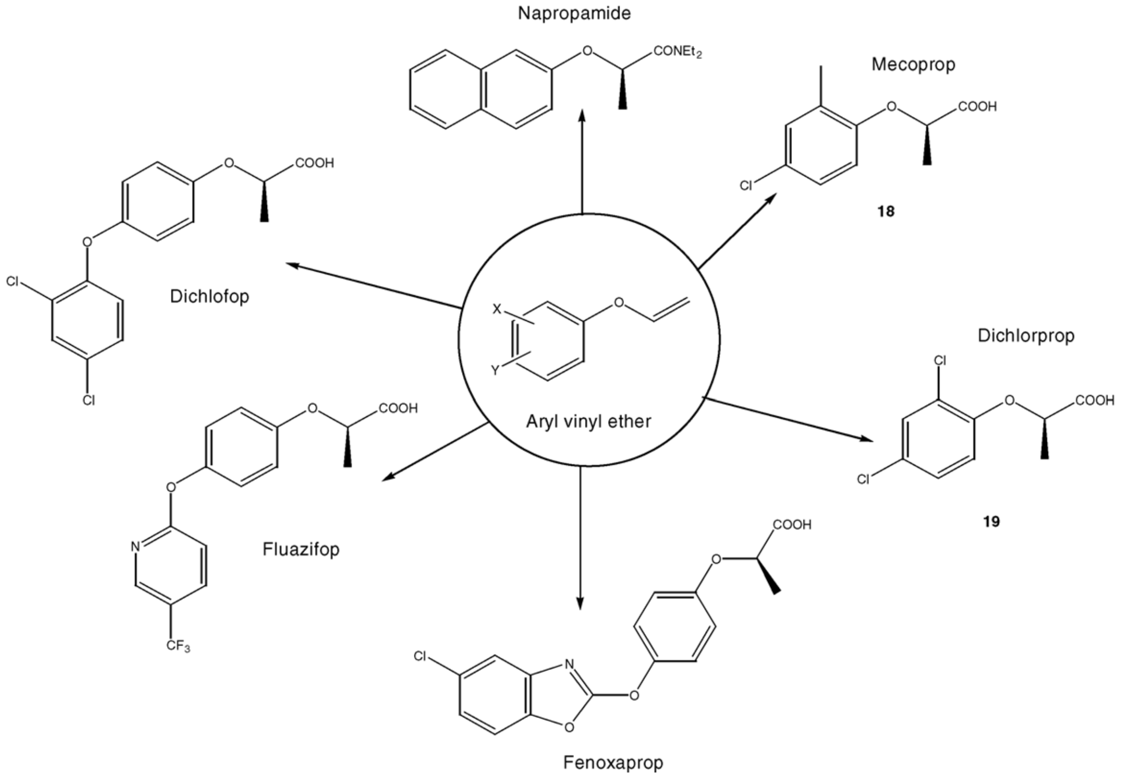

Fig. 1. Example of chiral agrochemicals, possible target molecules for the enantioselective hydroformylation of the corresponding aryl vinyl ethers.