Pergamon

Tetrahedron Letters 39 (1998) 9419–9422

TETRAHEDRON
LETTERS

Chiral *o*-Hydroxyarylphosphine Oxides : a New Family of Efficient Catalysts in Asymmetric Addition of Diethylzinc to Benzaldehyde

Olivier Legrand, Jean-Michel Brunel and Gérard Buono[1*]

Ecole Nationale Supérieure de Synthèses, de Procédés et d'Ingénierie Chimiques d'Aix Marseille, UMR CNRS 6516, Faculté de St Jérôme, Av. Escadrille Normandie Niemen, 13397 Marseille, Cedex 20, France.

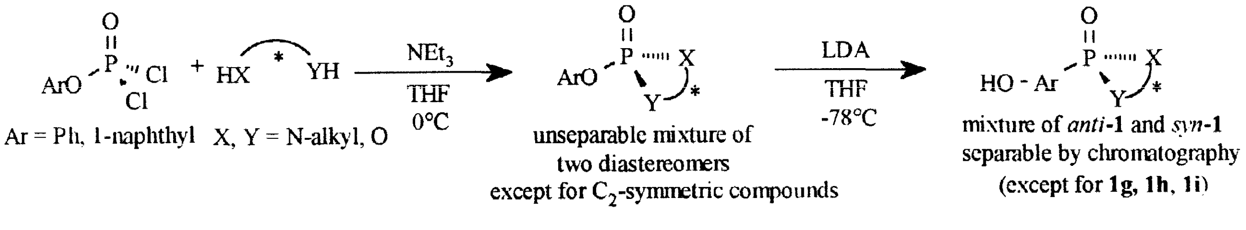
Received 2 September 1998; accepted 2 October 1998

Abstract : A serial of new chiral *o*-hydroxyarylphosphine oxides has been used as catalysts (5 mol%) in the asymmetric addition of diethylzinc to benzaldehyde. 1-Phenylpropanol is obtained in high chemical yields with good to excellent enantiomeric excesses up to 98%. The influence of the structural features on the enantioselectivity has been investigated. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords : Asymmetric Reactions ; Chiral Catalyst ; *o*-Hydroxyarylphosphine Oxides ; Diethylzinc

Enantioselective alkylation of aldehydes is one of the most useful methods to obtain optically active secondary alcohols.[1] Thus, in the last decade, more and more attention has been focused on the addition of organozinc compounds to aldehydes catalyzed by various chiral ligands.[2] In this area, the synthesis and use of new aminoalcohols[3] and their parent compounds such as aminothiols,[4] diamines,[5] diaminodiols[6] or diols[7] have been extensively developped. Soai *et al.* were the first to describe the enantioselective addition of diethylzinc to aldehydes using chiral phosphoramidates leading to enantiomeric excesses (ee) up to 98%.[8] Recently, we have described the synthesis of a new chiral *o*-hydroyphenyldiazaphospholidine oxide **1a** and its use as a catalyst in the enantioselective addition of diethylzinc to various aromatic aldehydes.[9] In this paper, we will report the ability of new *o*-hydroxyarylphosphine oxides to catalyze the enantioselective addition of diethylzinc to benzaldehyde.

The preparation of various new chiral *o*-hydroxyaryldiazaphospholidine oxides, *o*-hydroxyaryloxazaphospholidine oxides and *o*-hydroxyarylphosphonates has been recently achieved in a two steps sequence involving a totally diastereoselective rearrangement key step (Scheme 1).[10]



Scheme 1

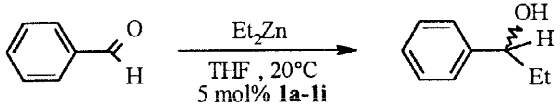
Under the best previously depicted experimental conditions[9] (solvent : THF, room temperature, 5 mol% of catalyst), compounds **1a-1i** have been successfully employed as catalysts in the asymmetric addition of diethylzinc to benzaldehyde.[11] The results are summarized in Table 1.

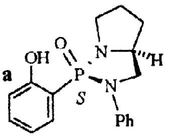
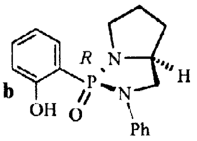
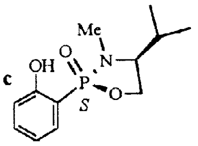
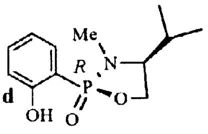
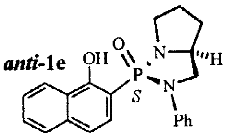
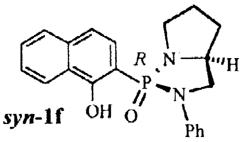
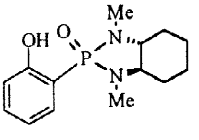
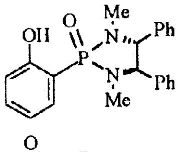
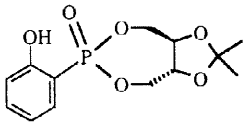
---

[1] E-mail : buono@spi-chim.u-3mrs.fr ; fax : 04-91-02-77-76

PII: S0040-4039(98)02140-6

Table 1. Enantioselective Addition of Diethylzinc to Benzaldehyde in Presence of 5 mol% of **1a-1i**

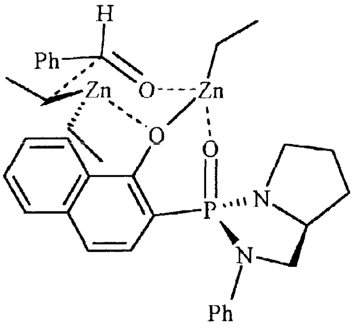


Entry[a]	Catalyst	Conversion (%)[b]	Ee (%)[b]	Configuration[c]
1	*anti*-**1a** 	100	73	*R*
2	*syn*-**1b** 	100	82	*R*
3	*anti*-**1c** 	100	73	*R*
4	*syn*-**1d** 	100	86	*R*
5	*anti*-**1e** 	100	98	*R*
6	*syn*-**1f** 	100	92	*R*
7	**1g** 	100	73	*R*
8	**1h** 	100	84	*S*
9	**1i** 	100	0	-

[a] Experiment performed at 1 mmol scale. [b] Conversion and ee determined by HPLC analysis on a Daicel Chiralcel OD-H column at λ = 254 nm, eluent : hexane/*i*-PrOH = 90/10, flow rate 0.9 mL/min. [c] Absolute configuration determined by comparison of reported optical rotation.

In all cases, a total conversion of benzaldehyde into 1-phenylpropanol and enantioselectivities varying from good to excellent (entries 1-8, 73 to 98% ee) were encountered. Furthermore, the (*R*)-1-phenylpropanol was formed as the major enantiomer whatever the stereochemistry beared at the phosphorus atom (entries 1-6). The best result was obtained using *o*-hydroxyarylphosphine oxide **1e**, probably due to the presence of a naphthyl group increasing the steric hindrance of the catalyst (entry 5, 98% ee). Phosphonate **1i** led to the exclusive formation of racemic 1-phenylpropanol but in an excellent chemical yield (entry 9, 92% yield).

Although the actual active species in this reaction are unclear, a plausible mechanism may be envisioned. Thus, assuming the mechanism proposed by Noyori *et al.*,[12] the reaction in the presence of catalyst **1e** can proceed through a six-centre transition state **A** (Figure 1).[13]



Transition State **A**

Figure 1

In this paper, we have clearly demonstrated that chiral *o*-hydroyarylphosphine oxides are a new class of efficient catalysts for the enantioselective addition of diethylzinc to benzaldehyde. Further investigations of their catalytic ability including modifications to aldehydes and catalysts design are still in progress.

References and Notes

(1)Noyori, R. *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York **1994**, Ch. 5.

(2) Soai, K. ; Niwa, S. *Chem. Rev.* **1992**, *92*, 833-856.

(3) For recent examples see : (a) Bringmann, G. ; Breuning, M. *Tetrahedron : Asymmetry* **1998**, *9*, 667-679. (b) Tae Cho, B. ; Sung Chun, Y. ; *Tetrahedron : Asymmetry* **1998**, *9*, 1489. (c) Aurich, H. G. ; Soeberdt, M. *Tetrahedron Lett.* **1998,** *39*, 2553-2554. (d) Vidal-Ferran, A. ; Moyano, A. ; Pericàs, M. A. ; Riera, A. *J. Org. Chem.* **1997**, *62*, 4970. (e) Solà, L. ; Vidal-Ferran, A. ; Moyano, A. ; Pericàs, M. A. ; Riera, A. *Tetrahedron : Asymmetry* **1997**, *8*, 1559-1568. (f) Wilken, J. ; Gröger, H. ; Kossenjans, M. ; Martens, J. *Tetrahedron : Asymmetry* **1997**, *8*, 2761-2771. (g) Nakano, H. ; Kumagai, N. ; Matsuzaki, H. ; Kabuto, C. ; Hongo, H. *Tetrahedron : Asymmetry* **1997**, *8*, 1391-1401. (h) Bolm, C. ; Fernandez, K. M. ; Seger, A. ; Raabe, G. *Synlett* **1997,** 1051-1052. (i) Zhang, H. ; Xue, F. ; Mark, T. C. W. ; Chan, K. S. *J. Org. Chem.* **1996**, *61*, 8002-8003.

(4) (a) Anderson, J. C. ; Harding, M. *J. Chem. Soc., Chem. Commun.* **1998**, 393-394. (b) Kossenjans, M. ; Martens, J. *Tetrahedron : Asymmetry* **1998**, *9*, 1409-1417.

(5) Asami, M. ; Inoue, S. *Bull. Chem. Soc. Jpn* **1997**, *70*, 1687-1690.

(6) Williams, D. R. ; Fromhold, M. G. *Synlett* **1997**, 523-524.

(7) Kitajima, H. ; Ito, K. ; Aoki, Y. ; Katsuki, T. *Bull. Chem. Soc. Jpn* **1997**, *70*, 207-217.

(8) Soai, K. ; Ohno, Y. ; Inoue, Y. ; Tsuruoka, T. ; Hirose, Y. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 145-152.

(9) Brunel, J. M. ; Constantieux, T. ; Legrand, O. ; Buono, G. *Tetrahedron Lett.* **1998**, *39*, 2961-2964.

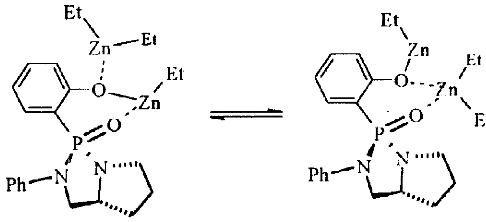
(10) Legrand, O. ; Brunel, J. M. ; Constantieux, T. ; Buono, G. *Chem. Eur. J.* **1998**, *4*, 1061-1067.

(11) General procedure for asymmetric addition of diethylzinc to benzaldehyde : In a 25 mL two necked round bottomed flask was successively introduced under argon atmosphere at 0°C, 4.72 10^{-5} mol of ligand (5 mol % with respect to substrate) in 5 mL of freshly distilled THF, 100 mg of benzaldehyde (9.43 10^{-4} mol) and 2 equiv. of Et_2Zn (1.1 M in hexane solution). The reaction mixture was allowed to warm up and stirred at room temperature for 48 hours. After quenching by addition of 3 mL of saturated NH_4Cl solution, the aqueous layer was extracted with 3 x 10 mL of diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel column (eluent : diethylether/pentane 50/50) to afford the corresponding pure 1-phenylpropanol.

(12) (a) Kitamura, M. ; Okada, S. ; Suga, S. ; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028-4036. (b) Noyori, R. ; Kitamura, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49-69. (c) Kitamura, M. ; Suga, S. ; Niwa, M. ; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 4832-4842. (d) Knochel, P. ; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117.

(13) ^{31}P NMR analysis of ligand **1a** exhibits a signal at 33.2 ppm. Addition of one equivalent of Et_2Zn revealed several signals due to the formation of numerous complexes. Addition at r.t. or –78°C of two equivalents of Et_2Zn led to a single signal at 35.8 ppm, probing that the catalytic active species **2** or **3** probably exist both in equilibrium as a monomeric complex according to the previously reported results.[14]

2



3

(14) (a) Soai, K. ; Yokoyama, S. ; Hayasaka, T. *J. Org. Chem.* **1991**, *56*, 4264-4268. (b) Kitamura, M. ; Yamakawa, M. ; Oka, H. ; Suga, S. ; Noyori, R. *Chem. Eur. J.* **1996**, *2*, 1173-1181.