Pergamon

Tetrahedron Letters 39 (1998) 7321-7322

TETRAHEDRON
LETTERS

Remarkable Ligand Effect on the Enantioselectivity of the Chiral Lanthanum Complex-Catalyzed Asymmetric Epoxidation of Enones

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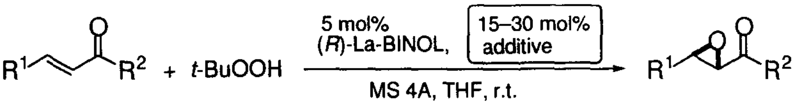
Received 11 June 1998; revised 21 July 1998; accepted 23 July 1998

Abstract: The addition of triphenylphosphine oxide significantly enhanced the degree of asymmetric induction (up to 96% ee) in the chiral La-BINOL-complex-catalyzed epoxidation of enones using *tert*-butyl hydroperoxide as the oxidant. The new protocol is highly general and practical. © 1998 Elsevier Science Ltd. All rights reserved.

The development and utilization of new lanthanoid complex catalysts in asymmetric synthesis are currently of intense interest.[1] We have recently found that the addition of an external ligand to the chiral ytterbium complex [Yb-(*R*)-$(BNP)_3$] not only solubilizes the catalyst but also largely enhances the enantioselectivity of the catalytic hetero Diels-Alder reaction.[2] This suggested the importance of coordinative saturation of the lanthanoid with appropriate ligands for the deoligomerization of lanthanoid complexes and prompted us to examine the effect of additives on the lanthanoid complex-catalyzed asymmetric epoxidation of enones recently developed by Shibasaki and co-workers.[3,4] We report here the realization of the asymmetric epoxidation in high optical yields simply by adding an achiral ligand to the chiral La-BINOL complex which was prepared from La(*O*-*i*-Pr)$_3$ and (*R*)-BINOL (1 molar equiv) in the presence of molecular sieves 4A (MS 4A, 1 g for 1 mmol of substrate).[3,5]

The epoxidation of chalcone (R^1=R^2=Ph) was first examined using 5 mol% of the La-BINOL-complex and 1.5 molar equivalents of *tert*-butyl hydroperoxide (TBHP) in the presence of various achiral additives (15-30 mol%). (Eq. 1)



(1)

Some selected results are shown in Table 1. Among the additives tested, triphenylphosphine oxide gave the best result with a record of 96% ee showing a notable ligand-acceleration (entry 5).[6] The observed ee jump from 73% ee to 96% ee indicates that there exists ca. 1.3 kcal/mol of free energy difference in the enantioselection stage. One plausible explanation for such a remarkable ligand effect, which is also our working hypothesis, is that the ligation by Ph_3P=O would produce a non-polymeric catalyst having a uni-structure. The epoxidation would then take place on the coordination sphere of the lanthanum where the reaction site might become closer to the chiral binaphthyl ring due to the phosphine oxide ligand with suitable steric bulkiness. However, the precise structure of the real catalyst of the present epoxidation is not clear at present.

The method was found to be quite general; the substituents (R^1 and R^2 in Eq 1) can be either aryl or alkyl

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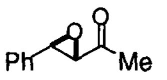
PII: S0040-4039(98)01569-X

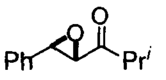
Table 1. Effect of Additives on the Enantioselectivity in the Epoxidation of Chalcone[a]

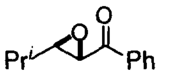
Entry	Additive (15 mol%)	Time / h	Product	
			Yield / %[b]	Ee / %[c]
1	None	3 (0.5)[d]	86 (90)[d]	73 (62)[d]
2	Lutidine-N-Oxide	3	96	74
3	DMEU[e]	3	97	68
4	(*n*-Bu)$_3$P=O	3	88	73
5	Ph$_3$P=O	0.5	99	96
6	(*p*-Tolyl)$_3$P=O	1.0	95	94
7	(*o*-Tolyl)$_3$P=O	1.5	96	73
8	(Me$_2$N)$_3$P=O	1.5	99	86

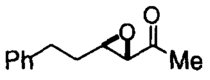
a) See the text. b) Isolated yield. c) Determined by chiral HPLC using a chiral OB-H. Absolute configuration: ($\alpha S,\beta R$) (See ref. 3). d) The reported data in parentheses (ref. 3). e) 1,3-Dimethyl 2-imidazolidinone (30 mol%).

with some examples shown below. In addition, all of the reagents required for this asymmetric epoxidation are commercially available thus making the protocol highly practical.


(6 h, 92%, 93% ee)


(12 h, 67%, 96% ee)


(1 h, 89%, 93% ee)


(1 h, 92%, 87% ee)

Further study of the ligand effects on the asymmetric epoxidation as well as on other chiral lanthanoid complex-catalyzed reactions is underway in this laboratory.[7]

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Culture, and Sports, Japan and also by the Nagase Science and Technology Foundation. We thank Professors Sasai and Shibasaki for the information from their unpublished results.

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5. The amount of MS4A largely influenced the product's ee: 53% ee (with 200 mg) and 66% ee (with 500 mg); *cf.* entry 1 in Table 1. The use of 1 g of MS4A was found to be enough to reproduce the high ees.
6. To a mixture of (*R*)-BINOL (7.2 mg), Ph$_3$P=O (21.1 mg), and MS4A (506 mg) in dry THF (1 ml) was added a mixture of La(*O*-*i*-Pr)$_3$ (8.0 mg) in THF (1.5 ml) and the mixture was stirred for 1 h, and then a decane solution of TBHP (5M, 0.15 ml) was added. After stirring for 0.5 h, a solution of chalcone (105.4 mg) in THF (1 ml) was added and the whole mixture was stirred at room temperature for 0.5 h.
7. A part of this work was presented at the 74th Meeting of the Chemical Society of Japan, Kyoto, March, 1998 and the 15th Meeting of the Rare Earth Society of Japan, Tokyo, May, 1998.