Tetrahedron: Asymmetry Vol. 4, No. 8, pp. 1783-1784, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Enantioselectivity for Hydrophosphonylation of Aromatic Aldehydes Catalyzed by Lanthanum Binaphthol Complex. Remarkable Electronic Effect of Aromatic Substituents

Tsutomu Yokomatsu, Takehiro Yamagishi, and Shiroshi Shibuya*

Tokyo College of Pharmacy, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

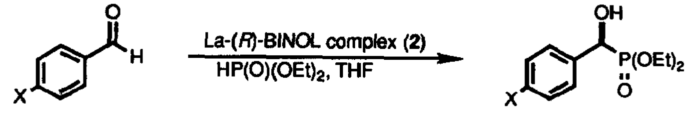
(*Received in UK* 14 *May* 1993)

Abstract: Hydrophosphonylation of aromatic aldehydes with diethyl phosphite in the presence of catalytic amount of La-BINOL complex (2) proceeded enantioselectively to give the corresponding α-hydroxyphosphonates in good yield. Enantioselectivity was found to depend on the electronic nature of *para*-substituents.

In the preceding paper,[1] we have described the catalytic enantioselective hydrophosphonylation of aromatic aldehydes with diethyl phosphite using a chiral titanium alkoxide as a catalyst. In this reaction decreasing the Lewis acidity of the catalyst by tuning the donor ability of the solvent used was found to be effective for obtaining chiral α-hydroxyphosphonate enantioselectively. Changing the metal in the catalyst to a more basic one was also considered to be an alternative method for the achievement of high enantioselectivity. In this context the modified binaphthol-derived lanthanum alkoxide, recently developed by Shibasaki,[3] should be a suitable catalyst for the hydrophosphonylation reactions because of its inherent basic character[2] and potential usefulness for asymmetric synthesis.[3] We now describe the enantioselective hydrophosphonylation of aromatic aldehydes using chiral lanthanum binaphthol complex[3] as a catalyst and findings on a remarkable electronic effect of aromatic substituents to the reaction in this paper.

Reactions of several aromatic aldehydes (1) with diethyl phosphite (1.2 equiv.) were examined in the presence of a catalytic amount (20 *mol* %) of the catalyst (2), prepared from $LaCl_3 \cdot 7H_2O$ and dilithium (*R*)-binaphthoxide according to the method of Shibasaki,[3b] in THF at the range of -20 to -78 °C for 15 h. The results are summarized in Table 1. All reactions gave the corresponding (*S*)-(-)-α-hydroxyphosphonates (3)[4] in generally excellent yield (>90%) at -40 °C (Table 1, entries 3 to 6). The yield of the product decreased from 95 to 67%, when the reaction was conducted at -78 °C (Table 1, entry 2). The results show the catalytic reaction works effectively around at -40 °C. The degree of enantioselectivity for the reactions strongly depends on the electronic nature of the substituent in the *para* position on the aromatic ring. The reactions with *p*-anisaldehyde and *p*-tolualdehyde proceeded in enantioselectivities of 82 and 57% *ee*, respectively under the conditions (Table 1, entries 3 and 4). On the contrary, low enantioselectivity was observed in the reaction with benzaldehyde and *p*-chlorobenzaldehyde (Table 1, entries 5 and 6). In order to obtain information about the origin of the enantioselectivity, we examined the correlation between the Hammett aromatic substituent constants (σ_p) and the *ee*. A linear Hammett plot with a relatively large negative ρ value (-1.30, r=0.92) was observed as shown in Fig. 1. From these data and the above results, the following two steps-mechanism was considered: diethyl phosphite was easily incorporated onto the chiral lanthanum complex (2) *via* its phosphite tautomer owing to the basicity of the catalyst to form intermediate (4), then the coordination of an aldehyde to the metal in 4 followed by addition of the phosphorus to aldehydes gave 3 (Fig. 2). Relatively a large negative ρ value suggests the coordination step should be involved in at least the enantiodeterminating step.

In conclusion this study has demonstrated that the Lewis acidity of **1** *as well as its basicity was also* **important to give a high degree of the enantioselectivity.**



1 **3**

Fig. 1 Hammett plot for enantioselective hydrophosphonylation of substituted benzaldehydes with diethyl phosphite catalyzed by **2** at -40°C

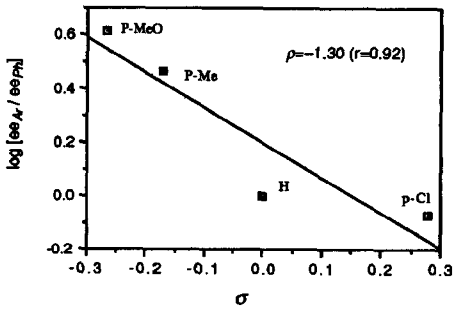


Fig. 2

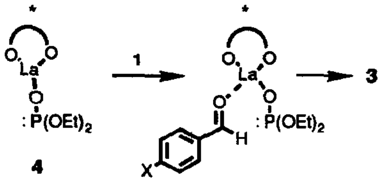


Table 1. Reaction of aromatic aldehydes (**1**) with diethyl phosphite catalyzed by **2**[a]

				3		
Entry	X	Temp.(°C)	Yield (%)	Ee (%)[b]	mp	[α]D[c]
1	MeO	-20	87	74	120-121	-26.1
2	MeO	-78	67	79		-30.3
3	MeO	-40	95	82		-31.1
4	Me	-40	94	58	93-94	-20.0
5	H	-40	98	20	74-76	-6.6
6	Cl	-40	99	17	67-70	-5.5

[a] All reactions were carried out on 2mmol scale for 15 h. [b] Determined by ^{1}H-NMR(300 MHz) analysis of the corresponding Mosher esters. [c] Measured in $CHCl_3$ (c 1.0) at 20 °C.

References and Notes

1. T. Yokomatsu, T. Yamagishi, and S. Shibuya, *Tetrahedron Asymmetry*, preceding communication.
2. A. Lebrun, J.-L. Namy, and H. B. Kagan, *Tetrahedron Lett.*, **1991**, *32*, 2355; H. Ohno, A. Mori, and S. Inoue, *Chem. Lett.*, **1993**, 375.
3. a) H. Sasai, T. Suzuki, S. Arai, T. Arai, and M. Shibasaki, *J. Am. Chem. Soc.*, **1992**, *114*, 4418; b) H. Sasai, T. Suzuki, N. Itoh, and M. Shibasaki, *Tetrahedron Lett.*, **1993**, *34*, 851; c) H. Sasai, N. Itoh, T. Suzuki, and M. Shibasaki, *ibid*, **1993**, *34*, 855.
4. Absolute stereochemistry was determined based on their cotton effects in CD spectra and the colleration with authentic samples prepared as described in the accompanying report.