Pergamon

Tetrahedron Letters, Vol. 36, No. 43, pp. 7897-7900, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01627-9

Catalytic Asymmetric Synthesis Promoted by a Chiral Zirconate: Highly Enantioselective Allylation of Aldehydes

Paolo Bedeschi, Sonia Casolari, Anna L. Costa, Emilio Tagliavini* and Achille Umani-Ronchi

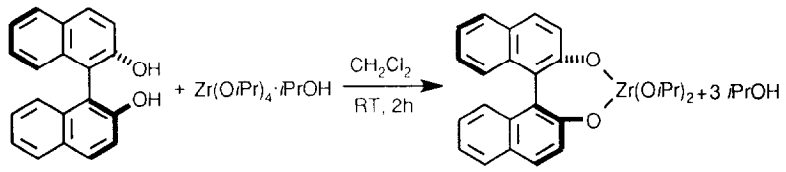
Dipartimento di Chimica "G. Ciamician", Università di Bologna, Via Selmi, 2, 40126-Bologna, Italy.

Abstract: A new chiral Lewis acid catalyst, [BINOL-Zr(O*i*Pr)$_2$], is prepared from *(R)* or *(S)*-BINOL and commercially available Zr(O*i*Pr)$_4$·*i*PrOH; it efficently promotes the enantioselective allylation of aldehydes by allyltributyltin in shorter times and at lower temperatures with respect to related catalysts.

In the last few years asymmetric catalysis by means of chiral Lewis acids has led to highly enantioselective protocols for a variety of synthetic transformations including some important C—C bond forming processes. We have recently contributed to such development, reporting the catalytic asymmetric allylation of aldehydes by allyltributyltin in the presence of BINOL-$TiCl_2$ **1** (BINOL = 1,1'-binaphtalene-2,2'-diol **2**), which affords highly enantiomerically enriched homoallylic alcohols.[1]

The most successful chiral Lewis acids for catalyzing enantioselective C—C bond formation contain B(III), Al(III), Ti(IV), Sn(II) and rare earth metals,[2] but few reports have appeared with chiral Zr(IV) complexes.[3] With the aim of exploiting these less popular chiral catalysts we have prepared complex **3** [4] from commercially available Zr(O*i*Pr)$_4$·*i*PrOH **4** and BINOL according to Scheme 1. Since the synthesis of homoallylic alcohols promoted by **1**, or by the closely related BINOL-Ti(O*i*Pr)$_2$ **1'**,[5] suffers from very long reaction times, our goal was to find a more reactive allylation catalyst.

Scheme 1



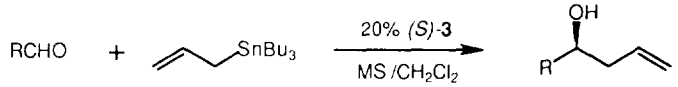
(S)-**2** **4** *(S)*-**3**

Scheme 1. Synthesis of catalyst **3**.

Complex **3** effectively catalyzes the addition of allyltributyltin **5** to aldehydes **6a-e** in the presence of 4Å molecular sieves (MS) to give 1-alken-4-ols **7a-e** in good yield and enantiomeric excess (Table 1). The enantiopreference showed **3** matches that of **1**: the *Si* face of the aldehyde is attacked if *(S)-(-)*-**2** is used in the preparation of the catalyst.

Indeed a high reaction rate is characteristic of this new system in comparison with that of the Ti complexes **1** and **1'**. Such behaviour is of particular concern for aromatic and unsaturated aldehydes whose allylation requires very long times under catalysis from **1** or **1'**. Nevertheless a decrease in chemical yields was observed for the less reactive substrates, **6a** and especially **6c**. This effect can be partially attributed to the formation of the primary alcohol, probably by a Meerwein-Ponndorf-Verley like reduction of the aldehyde by the isopropanol formed in the preparation of the catalyst. In the case of benzaldehyde an increase of enantioselectivity is also observed. The two catalysts are thus complementary, **1** being superior for aliphatic substrates and the Zr complex **3** for aromatic ones. We believe that the less crowded complex **3** can better accommodate the more sterically demanding aromatic aldehydes.[6]

Table 1: Allylation of aldehydes catalyzed by *(S)*- **3**[a]



6a-e **5** **7a-e**

Entry	R	MS[b]	T(°C)	t(h)	7 (Yield %)[c,d]	e.e.%[e]
1	nC_7H_{15}	Y	0	6	**7a** (58)	87.2
2	nC_7H_{15}	N	0	20	**7a**(53)	71.0
3	nC_7H_{15}	A	-20	20	**7a**(61)	88.0
4	nC_7H_{15}	N	0	2[f]	**7a** (15)	85.0
5	nC_5H_{11}	Y	0	10	**7b** (84)	89.0
6	cC_6H_{11}	Y	-20	6	**7c** (34)	90.3
7	*(E)*-PhCH=CH	Y	-20	3	**7d** (81)	91.0
8	Ph	Y	-40	6	**7e** (79)	92.8
9	Ph	N	-30	4	**7e** (64)	87.4

[a] All the reactions were carried out with a **6** : **5** : **3** = 1 : 2 : 0.2 molar ratio. [b] Y: MS were present during the formation of the catalyst **3** and for the whole reaction course; N: MS were absent; A: MS were added after the formation of the catalyst and immediately before the addition of the reagents. [c] Yields of purified products. [d] Octanol was formed in entries 1 (6%), 2 (15%), 3 (3%); cyclohexanemethanol was formed in entry 6 (15%). [e] Determined by GC of the alcohols (**7a-d**) or of the corresponding TMS-ether (**7e**) on a chiral MEGADEX 5 column. [f] The reaction was stopped at 15% conversion.

The preparation of the colorless catalyst **3** resembles that of orange-brown **1**, but *the role of MS is different* as we could guess from ^{1}H-NMR analysis. In fact, while a mixture of $TiCl_2(OiPr)_2$ and **2** consists manily of «free» BINOL, the corresponding spectrum of an equimolar solution of $Zr(OiPr)_4$·*i*PrOH and BINOL shows only traces of the uncomplexed ligand, completely new signals being present in the aromatic region. Thus the complex **1** forms in high yield only if prepared in the presence of MS; in the case of **3** no significant difference can be seen in the spectra obtained from samples prepared either in the presence or in the absence of MS.

Although not essential for the formation of the catalyst **3**, MS play some role in the control of enantioselectivity at least in the case of the allylation of **6a** (entries 1 and 2). Probably they inhibit some non enantioselective catalysis. The developing of this effect should occur *during the course of the reaction*, since the addition of MS *after the formation of 3* restores the original enantioselectivity (entry 3). In fact the enantiomeric excess of product **7a** formed *in the early stage* of the reaction performed in the absence of MS (entry 4) is very similar to that obtained *in the presence* of MS.

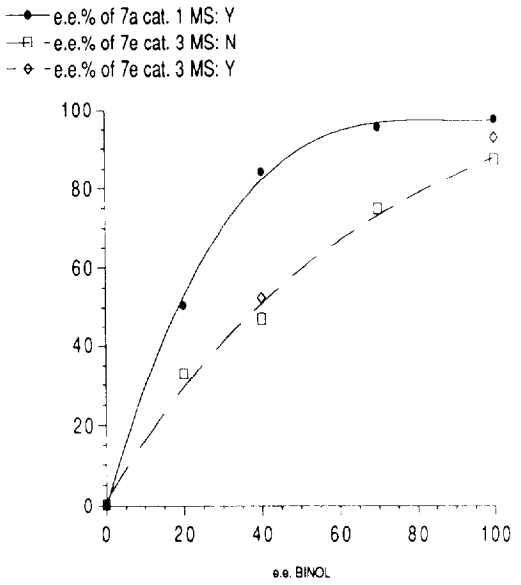


Fig. 1. NLE data for complexes **1** and **3**. E.e.% of homoallylic alcohols **7a** (for catalyst **1**) and **7e** (for catalyst **3**) obtained by catalysis from complexes of different enantiomeric purity. For catalyst **1** the reactions were carried out according to ref. 1.

A distinctive feature of complex **1** is the strongly nonlinear relationship between the enantiomeric purity of the catalyst and that of the product (NLE effect).[7] We have compared the NLE trends of **1** and **3** in the catalysis of homoallylic alcohol formation (Fig. 1), finding a less pronounced deviation from linearity for **3** (either in the presence or in the absence of MS) than for **1**. The origin of the NLE effect is generally attributed to a nonmonomeric nature of the catalysts coupled with a strong difference in the reactivities of the heterochiral and homochiral species. According to Kagan,[8] we have performed a regresson analysis of these data finding $g = 0.01$ for complex **1** and $g = 0.6$ for complex **3**, where g represents the ratio of the kinetic constants for the reactions carried out with hetero- and homochiral catalysts respectively. Indeed the allylation of **6e** promoted by *rac*-**3** is complete in 10 h at -30°C, while *rac*-**1** works extremely sluggishly in the allylation reaction.

We believe that our new catalyst based on Zr(IV) and BINOL can improve the efficency of the asymmetric allylation of aldehydes, expecially in the case of sterically hindered substrates. Furthermore it

represents novelty in the field of chiral Lewis acids and exhibits a peculiar behaviour requiring further investigations.

Acknowledgements: This work was supported by a grant from the Progetto Strategico C.N.R. and M.U.R.S.T. (Rome).

REFERENCES AND NOTES

1. A. L.Costa, M. G. Piazza, E. Tagliavini, C. Trombini, A. Umani-Ronchi, *J. Am. Chem. Soc.* **1993**, *115*, 7001.
2. Recent works: K. Ishihara, M. Mouri, Q. Gao, T. Maruyama, K. Furuta, H. Yamamoto, *J. Am. Chem. Soc.*, **1993**, *115*, 11490; Q. Gao, K. Ishihara, T. Maruyama, M. Mouri, H. Yamamoto, *Tetrahedron*, **1994**, *50*, 979; E. J. Corey, A. Guzman-Perez, T. P. Loh, *J. Am. Chem. Soc.*, **1994**, *116*, 3611; N. Imai, H. Takahashi, S. Kobayashi, *Chem. Lett.*, **1994**, 177; E. J. Corey, S. Sarshar, D. H. Lee, *J. Am. Chem. Soc.*, **1994**, *116*, 12089; S. Kobayashi, T. Kawasuji, N. Mori, *Chem. Lett.*, **1994**, 217; K. Mikami, S. Matsukawa, *J. Am. Chem. Soc.*, **1994**, *116*, 4077; B. Weber, D. Seebach, *Tetrahedron*, **1994**, *50*, 7473; S. Kobayashi, *Synlett* , 1994, 689; H. Sasai, T. Arai, M. Shibasaki, *J. Am. Chem. Soc.*, **1994**, *116*, 1571.
3. *Ansa*-Zirconocene complexes: G. Guerra, L. Cavallo, G. Moscardi, M. Vacatello, P. Corradini, *J. Am. Chem. Soc.*, **1994**, *116*, 2988; Y. Hong, B. A. Kuntz, S. Collins, *Organometallics*, **1993**, *12*, 964; J. P. Morken, M. T. Dudiuk, A. H. Hoveyada, *J. Am. Chem. Soc.*, **1993**, *115*, 6997; J. P. Morken, M. T. Didiuk, M. S. Visser, A. H. Hoveyda, *J. Am Chem. Soc.*, **1994**, *116*, 3123. Chiral aminol-Zr complex: W. A. Nugent, *J. Am. Chem. Soc.*, **1992**, *114*, 2768.
4. The structure of complex **3** as well as that of complexes **1** or **1'**, has not been established. Thus formulas and drawings are only indicative.
5. G. E. Keck, K. H. Tarbet, L. S. Geraci, *J. Am. Chem. Soc.*, **1993**, *115*, 8467.
6. Zr-OAr bonds are significantly longer than Ti-OAr bonds in homologous complexes. For example see: Cozzi, P. G.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Inorg. Chem.* **1995**, *34*, 2921.
7. K. Mikami, M. Terada, *Tetrahedron* , **1992**, *48*, 5671.
8. D. Guillaneux, S. Zhao, O. Samuel, D. Rainford, H. B. Kagan, *J. Am. Chem. Soc.*, **1994**, *116*, 9430.

(*Received in UK* 2 *August* 1995; *accepted* 25 *August* 1995)