



## Enantioselective conjugate addition of diethylzinc to chalcone catalyzed by $\text{Co}(\text{acac})_2$ and chiral amino alcohols

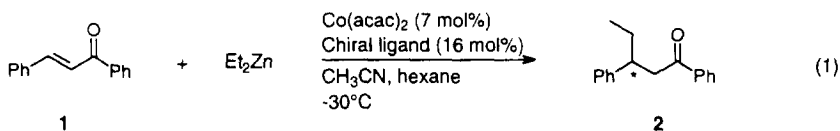
André H. M. de Vries and Ben L. Feringa \*

Department of Organic and Molecular Inorganic Chemistry, Groningen Center for Catalysis and Synthesis, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

**Abstract:**  $\text{Co}(\text{acac})_2$  in the presence of chiral ligands has been employed as catalyst for the enantioselective conjugate addition of diethylzinc to chalcone. With chiral amino alcohols derived from (+)-camphor, enantioselectivities up to 83% were achieved. © 1997 Elsevier Science Ltd

Conjugate addition reactions of carbon nucleophiles to  $\alpha,\beta$ -unsaturated compounds are among the most widely used methods for carbon–carbon bond formation in organic synthesis.<sup>1</sup> Asymmetric conjugate addition reactions, however, still lack the ‘ideal chiral catalyst’ which promotes enantioselective conjugate addition of readily available organometallic reagents to a wide variety of substrates.<sup>2</sup> Considerable progress has been made with the copper catalyzed conjugate addition of Grignard reagents<sup>3</sup> and the nickel catalyzed conjugate addition of diethylzinc.<sup>4</sup> Also a copper catalyzed 1,4-addition of diethylzinc to cyclohexenone has been reported.<sup>5</sup> Recently, we and others have found the first catalytic system capable of the enantioselective conjugate addition of dialkylzinc reagents to *both* cyclic and acyclic substrates.<sup>5</sup>

Although transmetallation reactions of organozinc reagents to several metal salts have been proposed,<sup>6</sup> Knochel and co-workers recently reported the first synthetically useful transmetallations of organozinc reagents to *cobalt* in acylation and allylation reactions.<sup>7</sup> The use of organocobalt reagents in conjugate addition reactions has been limited.<sup>8</sup> Herein we describe catalytic enantioselective conjugate addition reactions of diethylzinc to chalcone using  $\text{Co}(\text{acac})_2$  and chiral amino alcohols (Equation 1).

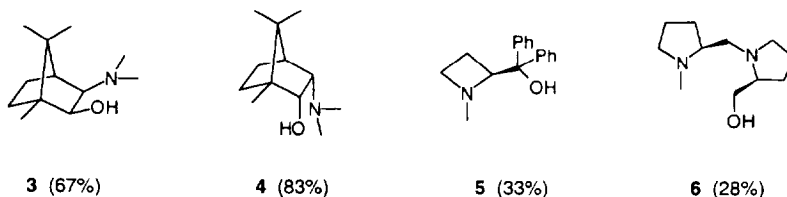


When  $\text{Co}(\text{acac})_2$  (7 mol%) and chiral amino alcohol **3** (16 mol%) were employed in the model reaction the 1,4-product **2** was isolated in 61% yield (70% conversion according to GC analysis, after 16 h at  $-30^\circ\text{C}$ ).<sup>9</sup> No 1,2-addition was observed and chiral HPLC analysis<sup>9</sup> revealed an enantioselectivity of 67%.

Three other chiral amino alcohol ligands **4–6** were also examined in the model reaction. With ligand **4** product **2** was isolated in 73% yield with an e.e. of 83%. Ligands **5**<sup>10</sup> and **6** gave substantial lower conversions to the 1,4-product (~50%) and moderate e.e.'s (see Figure 1).

Using chiral amino alcohols the cobalt catalyzed conjugate addition is relatively slow compared to the nickel catalyzed reaction (>95% conversion to the 1,4-product **2** after 2 h at  $-30^\circ\text{C}$ )<sup>4c</sup> and a considerable amount (5% with ligands **3** and **4**, 20% with ligands **5** and **6**) of the reduced by-product 1,3-diphenylpropan-1-one has been detected.<sup>11</sup> However, relatively high enantioselectivities were found in this reaction and moreover transmetallation processes of organozinc reagents to cobalt seem to have a greater applicability in (enantioselective) organic reactions<sup>7</sup> than transmetallation to

\* Corresponding author. E-mail: Feringa@chem.rug.nl



**Figure 1.** Chiral amino alcohols used in the  $\text{Co}(\text{acac})_2$  catalyzed addition of  $\text{Et}_2\text{Zn}$  to **1**. In brackets the e.e. of product **2** achieved with the given ligand.

other metal salts.<sup>12</sup> Therefore, further studies involving enantioselective cobalt mediated reactions of organozinc reagents are in progress in our laboratories.

### Acknowledgements

We are grateful to Prof. J. Martens, University of Oldenburg, for a gift of chiral ligand **5**.

### References

1. Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis* Tetrahedron Organic Chemistry Series, No. 9, Pergamon, Oxford, 1992.
2. a) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771. b) Feringa, B. L.; de Vries, A. H. M. in *Advances in Catalytic Processes, Vol 1: Asymmetric Chemical Transformations* Doyle, M. P., Ed., JAI Press, Connecticut, 1995, p. 151.
3. a) Zhou, Q.-L.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467. b) van Klaveren, M.; Lambert, F.; Eijkelkamp, D. J. F. M.; Grove, D. M.; van Koten, G. *Tetrahedron Lett.* **1994**, *35*, 6135. c) Spescha, M.; Rihs, G. *Helv. Chim. Acta* **1993**, *76*, 1219. d) Kanai, M.; Tomioka, K. *Tetrahedron Lett.* **1995**, *36*, 4275.
4. a) Soai, K.; Hayasaka, T.; Ugajin, S. *J. Chem. Soc., Chem. Commun.* **1989**, 516. b) Bolm, C.; Ewald, M.; Felder, M. *Chem. Ber.* **1992**, *125*, 1205. c) de Vries, A. H. M.; Jansen, J. F. G. A.; Feringa, B. L. *Tetrahedron* **1994**, *50*, 4479. d) Corma, A.; Iglesias, M.; Martín, V.; Rubio, J.; Sánchez, F. *Tetrahedron: Asymmetry* **1992**, *3*, 845.
5. a) Alexakis, A.; Frutos, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1993**, *4*, 2427–2430. b) de Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2374.
6. a) Boersma, J. In *Comprehensive Organometallic Chemistry* Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds., Pergamon, Oxford, 1982, Vol. 2, Chapter 16. b) Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117.
7. a) Devasagayaraj, A.; Knochel, P. *Tetrahedron Lett.* **1995**, *36*, 8411. b) Reddy, C. K.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1700.
8. a) Kauffmann, T.; Hopp, G.; Laarmann, B.; Stegemann, D.; Wingbermhühle, D. *Tetrahedron Lett.* **1990**, *31*, 511. b) For a recent review on organocobalt reagents derived from alkyllithium or Grignard reagents, see: Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 386.
9. For a typical experimental procedure, see: de Vries, A. H. M.; Imbos, R.; Feringa, B. L. *Tetrahedron: Asymmetry* **1997**, *8*, 1467.
10. Kindly provided by Prof. J. Martens, see: Behnen, W.; Mehler, T.; Martens, J. *Tetrahedron: Asymmetry* **1993**, *4*, 1413.
11. Confirmed by GCMS analysis. Nickel catalyzed conjugate reduction of  $\alpha,\beta$ -unsaturated ketones is a known process, see: Caporusso, A. M.; Giacomelli, G.; Lardicci, L. *J. Org. Chem.* **1982**, *47*, 4640.
12. With  $\text{Pd}(\text{OAc})_2$ ,  $\text{PdCl}_2$ , and  $\text{Fe}(\text{acac})_3$  as catalyst in the model reaction only traces of the 1,4-product were determined.

(Received in UK 19 February 1997; accepted 25 March 1997)