University of Groningen

Enantioselective conjugate addition of diethylzinc to chalcone catalyzed by Co(acac)₂ and chiral amino alcohols

Vries, André H.M. de; Feringa, Bernard

Published in:
Tetrahedron%3A Asymmetry

DOI:
[10.1016/S0957-4166\(97\)00144-4](https://doi.org/10.1016/S0957-4166(97)00144-4)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1997

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Vries, A. H. M. D., & Feringa, B. (1997). Enantioselective conjugate addition of diethylzinc to chalcone catalyzed by Co(acac)₂ and chiral amino alcohols. *Tetrahedron%3A Asymmetry*, 8(9).
[https://doi.org/10.1016/S0957-4166\(97\)00144-4](https://doi.org/10.1016/S0957-4166(97)00144-4)

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

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 α,β -unsaturated compounds are among the most widely used methods for carbon–carbon bond formation in organic synthesis.¹ 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.² Considerable progress has been made with the copper catalyzed conjugate addition of Grignard reagents³ and the nickel catalyzed conjugate addition of diethylzinc.⁴ Also a copper catalyzed 1,4-addition of diethylzinc to cyclohexenone has been reported.⁵ 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.⁵

Although transmetallation reactions of organozinc reagents to several metal salts have been proposed,⁶ Knochel and co-workers recently reported the first synthetically useful transmetallations of organozinc reagents to *cobalt* in acylation and allylation reactions.⁷ The use of organocobalt reagents in conjugate addition reactions has been limited.⁸ 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°C).⁹ No 1,2-addition was observed and chiral HPLC analysis⁹ 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**¹⁰ 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°C)^{4c} 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.¹¹ 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 reactions⁷ 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 Et_2Zn to **1**. In brackets the e.e. of product **2** achieved with the given ligand.

other metal salts.¹² 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) Devasagayaram, 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.; Wingbermühle, D. *Tetrahedron Lett.* **1990**, 31, 511. b) For a recent review on organocobalt reagents derived from alkylolithium 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 α,β -unsaturated ketones is a known process, see: Caporusso, A. M.; Giacomelli, G.; Lardicci, L. *J. Org. Chem.* **1982**, 47, 4640.
12. With $\text{Pd}(\text{OAc})_2$, 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)