

Catalytic Enantioselective Conjugate Addition of Diethylzinc using Ni^{II}-DAIB complexes.

Johan F.G.A. Jansen, Ben L. Feringa*,

Department of Organic Chemistry, University of Groningen,
Nijenborgh 16, 9747 AG, Groningen, The Netherlands.

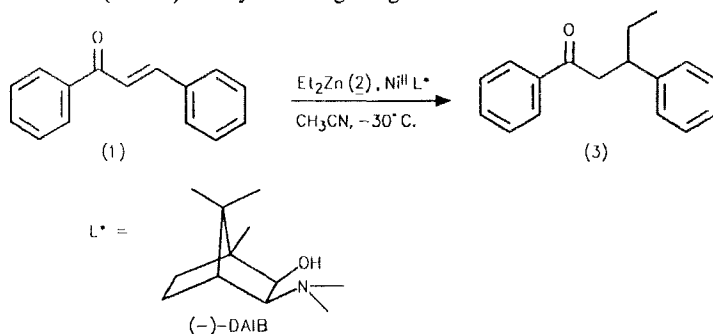
Key Words: enantioselective catalysis, conjugate addition, diethylzinc, enones.

(Received 3 March 1992)

Abstract : The conjugate addition of diethylzinc to chalcone, catalyzed by a Ni^{II} complex of the chiral amino-alcohol (-)-DAIB, resulted in the formation of (R)-1,3-diphenyl-penta-1-one with enantiomeric excess up to 85%.

Although there are numerous reports on catalytic asymmetric 1,2-additions¹, only a limited number of catalytic enantioselective 1,4-addition reactions of organometallic reagents are known. Excellent selectivities have however been reached in the synthesis of β -substituted ketones using stoichiometric or excess amounts of chiral organocopper reagents². Realizing these facts the design of an efficient chiral catalyst for this important carbon-carbon formation is a challenging goal. Enantioselective additions of *Grignard reagents* to cyclohexenone using catalytic amounts of a chiral copper complex (ee 14-78%)³ or various chiral zincates (ee \leq 33%)⁴ have been demonstrated. Furthermore it has been shown that the use of *dialkylzinc reagents* and Ni^{II} complexes, based on norephedrine⁵ or a substituted bipyridine⁶, as chiral catalysts resulted in modest to high enantioselectivities (up to 90%).

As a result of our studies on the conjugate addition of organozinc reagents⁷ we now report a Ni^{II}-(-)-dimethylaminoisoborneol (DAIB) catalyst for high regio- and enantio-selective diethylzinc additions to enones.



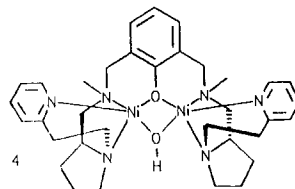
The reaction of diethylzinc with chalcone in CH_3CN using a Ni-catalyst (7 mol%), in situ prepared from Nickel acetylacetonate ($\text{Ni}(\text{acac})_2$) and (-)-DAIB (1:2.4 ratio), afforded R-(-)-1,3-diphenylpentan-1-one (**3**) in 94% isolated yield and 59% ee⁸ (scheme, Table).

Table: Enantioselective 1,4-addition using $\text{Ni}(\text{II})$ -(-)-DAIB complex and an achiral additive

entry	achiral additive ^a	$\gamma(\%)^b$	ee (%) ^c	configuration ^d
1	---	94	59	R
2	2,4,6-trimethylpyridine	83	65	R
3	2,2'-bipyridine	75	85	R
4	morpholine	88	56	R
5	piperidine	77	70	R

a) ratio; 1 : 2 : $\text{Ni}(\text{acac})_2$: (-)-DAIB : additive 1 : 1.1 : 0.07 : 0.17 : 0.07 ; b) isolated yield of **3** ; c) determined by HPLC ; d) based on reported elution order⁶ of (R)- and (S)-**3**

The addition of achiral amine ligands led to a substantial improvement of the enantioselectivity although yields are slightly lower. Thus addition of 2,2'-bipyridine (1 eq. with respect to Ni^{II}) raised the enantiomeric excess to 85% (75% yield of **3**). Although less effective some monodentate ligands also improve the selectivity (entries 2,5). The promoting effect on the stereoselectivity of additional achiral ligands (*achiral ligand control*) is in excellent agreement with recent results described by Soai⁵ and coworkers. It should be emphasized that in contrast to the observation of low enantioselectivities in previous studies using bidentate aminoalcohols⁵ the (-)-DAIB derived Ni-catalyst gives already a remarkable enantiomeric excess of 59% without additional achiral ligands. Preliminary investigations with the well characterized⁹ pentacoordinated chiral Ni^{II} -complex **4** showed high activity (84% yield) but poor selectivity (ee 10%) so far in the formation of **3**.



references and notes:

- For a review, see: Noyori, R.; Kitamura, M.; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49.
- a) Leyendecker, F.; Laucher, D.; *Nouv. J. Chim.* **1985**, *9*, 13. b) Dieter, K.R.; Tokles, T.; *J. Am. Chem. Soc.* **1987**, *109*, 2040. c) Rossiter, B.E.; Eguchi, M.; *Tetrahedron Lett.* **1990**, *31*, 965. d) Corey, E.J.; Neaf R.; Hannon, F.J.; *J. Am. Chem. Soc.* **1986**, *108*, 7114.
- a) Villacorta, G.M.; Rao, Ch.P.; Lippard, S.J. *J. Am. Chem. Soc.* **1988**, *110*, 3175. b) Ahn, K.H.; Klassen, B.; Lippard S.J. *Organometallics* **1990**, *9*, 3178.
- a) Jansen, J.F.G.A.; Feringa, B.L. *J. Chem. Soc., Chem. Commun.* **1989**, 741. b) Jansen, J.F.G.A.; Feringa, B.L. *J. Org. Chem.* **1990**, *55*, 4168.
- a) Soai, K.; Hayasaka, T.; Ugajin, S.; Yokoyama, S. *Chem. Lett.* **1988**, 1571. b) Soai, K.; Yokoyama, S.; Hayasaka, T.; Ebihara, K. *J. Org. Chem.* **1988**, *53*, 4149. c) Soai, K.; Hayasaka, T.; Ugajin, S. *J. Chem. Soc., Chem. Commun.* **1989**, 516. d) Soai, K.; Okudo, M.; Okamoto, M. *Tetrahedron Lett.* **1991**, *32*, 95.
- a) Bolm, C.; Ewald, M. *Tetrahedron Lett.* **1990**, *31*, 5011. b) Bolm, C. *Tetrahedron: Asymmetry* **1991**, *2*, 701.
- Jansen, J.F.G.A.; Feringa, B.L.; *Tetrahedron Lett.* **1988**, *29*, 3593.
- The ee was determined by HPLC analysis: chiral colum: CHIRACEL OD; 0.25% iPrOH in hexane, flow rate 1.0 ml/min, UV detector (254 nm), ret. times: (S) 16.3 min, (R) 19.0 min.
- The crystal and molecular structure as determined by X-ray analysis will be reported elsewhere.