Pergamon

Tetrahedron Letters, Vol. 35, No. 35, pp. 6521-6524, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01322-5

Application of *N,S*-Chelating Chiral Zinc *bis*(Arenethiolate) Complexes as New Precursor Catalysts in the Enantioselective Addition of Diethylzinc to Aldehydes.

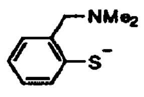
Evelien Rijnberg, Johann T.B.H. Jastrzebski, Maurits D. Janssen, Jaap Boersma and Gerard van Koten.*

Debye Institute, Department of Metal Mediated Synthesis, Utrecht University, Padualaan 8,
3584 CH Utrecht, The Netherlands.

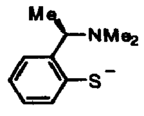
Abstract: The addition of diethylzinc to aldehydes in the presence of a catalytic amount of enantiomerically pure *N,S*-chelated *bis*{2-[(*R*)-1-(dimethylamino)ethyl]phenylthiolato}zinc, afforded the corresponding secondary alcohols in nearly quantitative yields with optical purities of up to 99 % e.e. under mild reaction conditions.

The addition of diethylzinc to benzaldehyde in the presence of a diamino alcohol to give 1-phenyl-1-propanol was first reported by Mukaiyama,[1] while Oguni and Omi[2a] and Noyori *et al.*[2b] reported the first examples of asymmetric induction applying a chiral β-amino-alcohol. Most of the chiral ligands which have been employed since then, including aminoalcohols, quaternary ammonium salts, oxaborolidines and diols, contain two β-positioned hetero-atoms.[3] Noyori nicely demonstrated that such ligands when reacting with diorganozinc compounds give organozinc alkoxides, particularly when potentially coordinating groups are present in positions suitable for the formation of five-membered *N,O*- or *O,O*- chelate rings.[3]

In the course of a study of copper-catalyzed enantioselective conjugate additions of Grignard reagents to α,β-unsaturated ketones, we found that chiral and non-chiral ortho-amino substituted copper(I) arenethiolates are very efficient catalysts.[4] These catalysts, which contain a potentially *N,S*-chelating, mono-anionic ligand as a non-transferable group are also excellent catalysts in cross-coupling reactions[5] and in the 1,6-addition reaction of organometallic reagents to enynesters.[6] In this paper we report the application of these mono-anionic arenethiolate ligands **1a** and (*R*)-**1b** in addition reactions of diorganozinc reagents with aromatic and aliphatic aldehydes.[7]



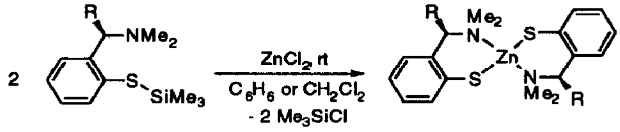
1a



1b

The air-stable zinc *bis*(arenethiolate) complexes **3a** and (*R,R*)-**3b** are easily accessible *via* the reaction of $ZnCl_2$ with two equivalents of 2-[(dimethylamino)methyl]-1-trimethylsilylthiobenzene **2a** and 2-[(*R*)-

(dimethylamino)ethyl]-1-trimethylsilylthiobenzene **2b**, respectively (eqn 1).[8] The novel zinc arenethiolates **3a** and **3b** have been characterized by elemental analysis,[9] ^{1}H and ^{13}C NMR spectroscopy[9] and an X-ray crystal structure determination of **3b**.[10]

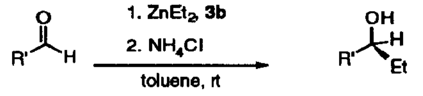


2a R = H
2b R = Me

3a R = H
3b R = Me

(1)

It appears that **3a** and **3b** are very efficient catalysts for the addition of diethylzinc to aldehydes. Moreover, reactions using chiral **3b** proceed with excellent enantioselectivity.[12]



(2)

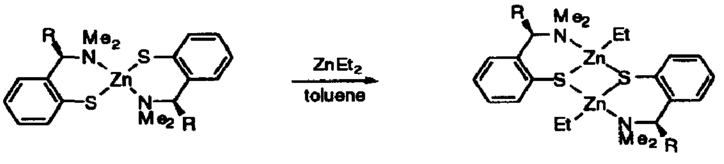
Table 1: Addition of diethylzinc to various aldehydes in the presence of 2 mol % **3a** or (*R*,*R*)-**3b**.

entry	R'	**3a** conversion[a] (%)	**3a** selectivity[a] (%)	(*R*,*R*)-**3b** conversion[a] (%)	(*R*,*R*)-**3b** selectivity[a] (%)	(*R*,*R*)-**3b** e.e. (%)[b] (configuration)
1	C_6H_5	97	97	>99	>99	94(S)
2	4-ClC_6H_4	>99	97	98	>99	95(S)
3	2-ClC_6H_4	98	95	>99	96	96(S)[c]
4	4-MeOC_6H_4	84	97	94	>99	95(S)
5	4-MeC_6H_4	>99	95	>99	>99	99(S)
6	(*E*)-$C_6H_5CH{=}CH$	98	93	>99	95	75(S)
7	2-furyl	>99	>99	>99	>99	89(S)
8	$C_6H_5CH_2CH_2$	>99	>99	>99	>99	69(S)

[a] Determined by GC. [b] Enantiomeric excess determined by HPLC using a Diacel chiralcel OD column unless noted otherwise. Absolute configurations determined from optical rotation. [c] Determined by ^{1}H NMR integration of the characteristic proton signals in the presence of the chiral shift reagent (*tris*[trifluoromethylhydroxymethylene-(+)-camphorato]Eu(III).

As summarized in Table 1, the alkylation reactions of the aldehydes in the presence of 2 mol % (*R*,*R*)-**3b** predominantly give the corresponding optically active (*S*)-secondary alcohols. Thus, **3b** having the (*R*)-configuration at the benzylic carbon atoms obeys the configurational rules found by Noyori for the β-amino-alcohols.[3b] The amount of chiral induction clearly depends on the nature of the aldehyde: while both the α,β-unsaturated and the aliphatic aldehydes (entry 6 and 8) give moderate e.e.'s of 75 % and 69 %, respectively, heterocyclic 2-furylaldehyde (entry 7) is converted in 89 % e.e. and all aromatic aldehydes tested gave excellent e.e.'s of ≥ 94 %.

It is likely that the zinc *bis*(arenethiolate) complexes **3a** and **3b** themselves are not the actual catalysts in these addition reactions, but instead the ethylzinc arenethiolate complexes **4a** and **4b**, which are readily formed from the reaction of **3a** and **3b** with $ZnEt_2$ present in large excess in the reaction medium (Eqn. 3). Indeed, the use of separately prepared **4a** and **4b** in the zinc-catalyzed addition of diethylzinc to benzaldehyde gave the same results as obtained with **3a** and **3b**.



(3)

3a R = H
3b R = Me

4a R = H
4b R = Me

Ethylzinc arenethiolates **4a** and **4b** are white crystalline solids, which were characterized by ^{1}H and ^{13}C NMR.[13] We presume that **4a** and **4b** are dimeric in the solid state *via* Zn-S bridging of the two mono-anionic sulphur atoms as depicted in eqn. 3. This is supported by the molecular structure of the analogous methylzinc arenethiolate, which is a dimer with a central Zn_2S_2 core in the solid state.[8]

An attractive aspect of the present results is the ready accessibility and simplicity of the chiral arenethiolate-anion (*R*)-**1b**. Yet, the chemoselectivity and enantiomeric excesses are similar to or even exceed those earlier reported.[3b] We are currently extending the application of this ligand in the zinc-catalyzed addition of various dialkylzinc reagents to aldehydes as well as to *N*-diphenylphosphinoylimines.[14] Further studies concerning mechanistic details are in progress.

Acknowledgement

This work was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (NWO).

References and Notes

1 Mukaiyama, K.; Soai, K.; Shimizu, H.; Suzuki, K. *J. Am. Chem. Soc.* **1979**, *101*, 1455.

2 a) Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823. b) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071.

3 Reviews: a) Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M.; Oguni, N.; Hayashi, M.; Kaneko, T.; Matsuda,Y. *J. Organomet. Chem.* **1990**, *382*, 19. b) Noyori, R.; Kitamura, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49. c) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833.

4 a) Knotter, D. M.; Van Maanen, H. L.; Grove, D. M.; Spek, A. L.; Van Koten, G. *Inorg. Chem.* **1991**, *30*, 3309. b) Lambert, F.; Knotter, D. M.; Janssen, M. D.; Van Klaveren, M.; Boersma, J.; Van Koten, G. *Tetrahedron Asymm.* **1991**, 2, 1097. c) Van Klaveren, M.; Lambert, F.; Eijkelkamp, D. J. F. M.; Var Koten, G. To be published.

5 Van Klaveren, M.; Persson, E. S. M.; Bäckvall, J. -E.; Van Koten, G. To be published.

6 Haubrich, A.; Van Klaveren, M.; Van Koten, G.; Handke, G.; Krause, N. *J. Org. Chem.* **1993**, *58*, 5849.

7 While this manuscript was in preparation, enantioselective addition of diethylzinc to benzaldehyde promoted by sulphur derivatives of ephedrine (5 mol %) was reported to afford 1-phenyl-1-propanol with

optical purities of up to 90 % e.e. See Hof, R. P.; Poelert, M. A.; Peper, N. C. M. W.; Kellogg, R. M. *Tetrahedron Asymm.* **1994**, *5*, 31.

8 Knotter, D. M.; Janssen, M. D.; Grove, D. M.; Smeets, W. J. J.; Horn, E.; Spek, A. L.; Van Koten, G. *Inorg. Chem.* **1991**, *30*, 4361.

9 The ^{1}H NMR spectra of **3a** and **3b** are temperature dependent. The ^{1}H NMR spectrum for **3a** at ambient temperature contains an AB pattern for the benzylic protons and two distinct signals for the dimethylamino groups, indicating that Zn-N coordination is also present in solution. Compound **3b** shows broad signals, even at 332 K. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 MHz spectrometer in chloroform-*d*. **3a**: ^{1}H NMR (291 K): δ 7.57 (d, 2H, Ar-H$_{ortho}$); 7.1-6.9 (m, 6H, Ar-H); 3.99 (d, 2H, $^2J_{HAHB}$ = 11.0 Hz, CH_AH$_B$); 3.21 (d, 2H, $^2J_{HBHA}$ = 11.0 Hz, CH$_A$$H_B$); 2.49 (s, 6H, NMe); 1.82 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (327 K): δ 143.9 (C$_{ipso}$); 135.4, 134.8, 131.1, 128.9, 123.2 (Ar-C); 67.2 (CH_2N); 46.5 (br, $N(CH_3)_2$). **3b**: ^{1}H NMR (338 K): δ 7.53 (d, 2H, Ar-H$_{ortho}$); 7.0-6.9 (m, 6H, Ar-H); 4.08 (br s, 2H, CH); 2.18 (br s, 12H, $N(CH_3)_2$); 1.48 (d, 6H, CH_3). ^{13}C NMR (332 K): δ 142.8, 139.3, 135.4, 128.6, 127.8, 123.0 (Ar-C); 66.4 (br CH); 45.3 (br, $N(CH_3)_2$); 11.3 (br CH_3). Anal. Calcd for $C_{20}H_{28}N_2S_2Zn$: C, 56.40; H, 6.63; N, 6.58. Found: C, 56.44; H, 6.66; N, 6.63.

10 An X-ray crystal structure determination of **3b** revealed that **3** is a monomer, in which both dimethylamino groups of the arenethiolate ligands coordinate intramolecularly to the zinc atom. Important bonding distances and angles defining the geometry at zinc: Zn–S1 2.284(3), Zn–S2 2.260(3), Zn–N1 2.146(8), Zn–N2 2.096(6) Å S1–Zn–S2 119.6(1), S1–Zn–N1 99.7(2), S1–Zn–N2 108.7(2), S2–Zn–N1 110.6(2), S2–Zn–N2 101.3(2), N1–Zn–N2 117.9(3) °. Full details will be reported in a forthcoming paper.[11]

11 Rijnberg, E.; Kleij, A. W.; Jastrzebski, J. T. B. H.; Janssen, M. D.; Boersma, J.; Spek, A. L.; Van Koten, G. Manuscript in preparation.

12 In a typical experiment $ZnEt_2$ (11.0 mL of a 1.0 Molar solution in toluene, 11.0 mmol) was added to a stirred solution containing (*R*,*R*)-**3b** (4.0 mL of a 0.05 Molar solution in toluene, 0.20 mmol) in dry toluene (25 mL) at room temperature. After 5 min 10.0 mmol of the appropriate aldehyde in toluene (20 mL) was added and the reaction mixture was stirred for 17 h at room temperature. The reaction mixture was quenched with 20 mL of a saturated NH_4Cl solution. The organic layer was separated and the water layer was extracted with dichloromethane (2 x 20 mL), the combined organic layers were dried on Na_2SO_4 and concentrated *in vacuo*, isolated yields 72-96%. The organic products were analyzed by ^{1}H and ^{13}C NMR spectroscopy and GC-MS.

13 ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200 MHz spectrometer in benzene-d_6. **4a**: ^{1}H NMR (320 K): δ 7.73 (d, 2H, Ar-H$_{ortho}$); 7.0-6.7 (m, 6H, Ar-H); 3.51(br s, 4H, CH_2); 2.06 (s, 12 H, $N(CH_3)_2$); 1.39 (t, 6H, ZnCH$_2$CH_3); 0.40 (q, 4H, ZnCH_2CH$_3$). ^{13}C NMR (320 K): δ 139.4, 136.3, 135.2, 132.3,128.9, 124.6 (Ar-C); 66.2 (CH_2); 47.1 ($N(CH_3)_2$); 13.6 (ZnCH$_2$$CH_3$); 1.0 (Zn$CH_2CH_3$). **4b**: ^{1}H NMR (346 K): δ 7.72 (d, 2H, Ar-H$_{ortho}$); 7.0-6.7 (m, 6H, Ar-H); 3.35 (br s, 2H, CH); 2.15 (s, 12H, $N(CH_3)_2$); 1.42 (d, 6H, CH_3); 1.32 (t, 6H, ZnCH$_2$CH_3); 0.36 (q, 4H, ZnCH_2CH$_3$). ^{13}C NMR (346 K): δ 140.4, 137.8, 137.1, 130.1, 128.0, 124.6 (Ar-C); 70.0 (br CH); 45.6 (br $N(CH_3)_2$); 16.2 (br CH_3); 13.3 (ZnCH$_2$$CH_3$); 1.4 (Zn$CH_2CH_3$).

14 Soai, K.; Hatanaka, T.; Miyazawa, T. *J. Chem. Soc., Chem. Comm.* **1992**, 1097.

(*Received in UK* 20 *April* 1994; *revised* 6 *July* 1994; *accepted* 8 *July* 1994)