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Chiral diethylzinc complexes with diamine ligands: synthesis, crystal structure and enantioselective solvent-free alkylation

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Abstract

In search for conglomerates of stereochemically labile organometallic reagents, three new complexes between diethylzinc and diamine ligands have been synthesized and structurally characterized by single-crystal X-ray diffraction methods. Ligands include *N*,*N*,*N*′,*N*′-tetraethylethylenediamine (teeda), *N*-isopropyl-*N*,*N*′,*N*′-trimethylethylenediamine (itmeda), and (−)-sparteine (spa). Diethylzinc forms monomeric complexes, exhibiting a distorted tetrahedral coordination geometry around zinc in all three complexes, viz. [$ZnEt_2$(teeda)] (**1**), [$ZnEt_2$(itmeda)] (**2**), and [$ZnEt_2$(spa)] (**3**). Both **1** and **2** are stereochemically labile and exhibit chiral complexes, displaying different types of conformational chirality, but they form racemic crystals. By using the chiral crystals of **3** in a nucleophilic addition to benzaldehyde in the absence of solvent at low temperature, an increase in ee from approximately 8 to 10% was obtained (compared to the same reaction in solution). It thus seems feasible, not only to retain the enantioselectivity obtained in solution, but perhaps even to increase the ee by using solventless reactions.

Keywords: Conglomerate; Diethylzinc; *N*-chirogenic; Solid-state reaction; Solvent-free reaction

1. Introduction

Enantioselectivity in asymmetric synthesis can be introduced in different ways, e.g., by using chiral organometallic reagents, such as organozinc complexes [1], organolithium complexes [2], or Grignards reagents [3], and there are two major methods to obtain an optically active organometallic reagent. The first method utilizes coordination of a chiral neutral ligand (e.g., solvent) to the metal center [4–9], while the other method involves modification of the organometallic reagent by protic chiral auxiliaries such as alcohols or amines, giving organometallic alkoxides or amides, respectively [10–13]. Such ligands, neutral or anionic, are usually stereochemically inert in solution, i.e., they have a chirogenic center that does not undergo rapid inversion at the reaction temperature. One drawback with the standard methods is that both enantiomers of the reagent (and consequently, the product) may not be easily accessible. A solution to this problem could be to use auxiliaries or reagents that enantiomerize in solution but retain their optical activity in the solid state. *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, (tmeda) is an achiral ligand that crystallizes as a conformationally chiral complex with $ZnEt_2$ [14]. Depending on the orientation of the ethyl ligands around zinc in such complexes, the molecule can be either achiral (A) or chiral (B) (see Scheme 1). There is, of course, no optical activity in a solution of such a complex, since the ethyl groups are free to change conformation, but in the solid state it would be possible to observe optical activity (provided that a conglomer-

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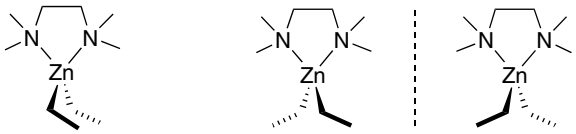
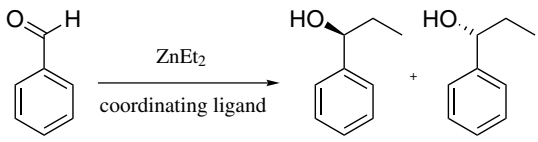


Scheme 1.



Scheme 2.

ate is formed on crystallization) using for example solid-state CD spectroscopy [15].

When a racemic solution of chiral metal complexes crystallizes, it normally forms racemic crystals which contain the enantiomers in a 1:1 ratio down to the unit cell level. But in 5–10% of the cases [16], a conglomerate is formed where the enantiomers are separated in different crystals, i.e., each crystal is enantiopure. The total composition of the sample is usually still racemic, since equal amounts of the enantiomorphic crystals are formed. However, if a stereochemically labile complex, which racemizes in solution but is optically active in the solid state, crystallizes as a conglomerate, the result may be exclusive formation of one of the enantiomers by total spontaneous resolution. This rare phenomenon arises when a stereochemically labile complex crystallizes (induced either by seeding with one of the enantiomers or by slow primary nucleation) via secondary nucleation and results in a theoretical yield and enantiomeric excess (ee) of 100%. Total spontaneous resolution can be utilized in absolute asymmetric synthesis where enantioenriched compounds are prepared from achiral (or racemic) starting materials in the absence of optically active catalysts or reagents [17–22]. The [$ZnEt_2$(tmeda)] [14] reagent is conformationally chiral, but it crystallizes in centrosymmetric *C*2/*c*, i.e., both conformers are present in the same crystal and racemic crystals are formed, which cannot undergo total spontaneous resolution. Therefore, in this work we set out to prepare a stereolabile complex between diethylzinc and another bidentate *N*,*N*-ligand. The commercially available *N*,*N*,*N*′,*N*′-tetraethylethylenediamine (teeda) ligand is closely related to the tmeda ligand, and might consequently form a similar (conformationally chiral) complex, which could crystallize as a conglomerate. Such a complex, which is stereochemically labile in solution, but can be optically active in the solid state, can be utilised as a reagent in, for example, alkyl transfer reactions to aldehydes. The reaction of organometallic compounds with carbonyl substrates is one of the most fundamental reactions in synthetic organic chemistry. Monomeric dialkylzinc complexes possessing a sp-hybridized linear geometry are nearly inert to carbonyl compounds, since the alkyl–metal bond is rather nonpolar. However, addition of a ligand generates a bent C–Zn–C coordination geometry, which facilitates alkyl transfer reactions. For example, 1-phenyl-1-propanol can be synthesized from benzaldehyde in an alkyl transfer reaction with diethylzinc and a catalytic amount of ligand, e.g., the teeda ligand (Scheme 2).

If conformationally chiral complexes that are stereochemically labile in solution are to be used as reagents, a solid-state alkylation is necessary so that optical activity is maintained. In order to compare the enantioselectivity of the solid-state reaction with the ee produced by an analogous solution reaction, it is necessary to choose a ligand (responsible for the enantioselectivity of the reaction) that is stereochemically inert in solution. The teeda ligand is obviously not suitable for this purpose. Instead, our intention was to use the commercially available (−)-sparteine as a chiral ligand in the alkyl transfer reaction of diethylzinc with benzaldehyde. It is advantageous to use a ligand that does not give a high ee in solution, since it may be difficult to completely rule out that some of the solid-state reaction actually proceeds in solution. A comparative study between the enantioselectivity in the solid-state and in solution has, to the best of our knowledge, not been attempted before [23].

2. Experimental

2.1. Materials

All manipulations with diethylzinc complexes were carried out under nitrogen, using standard Schlenk techniques. Diethylzinc (Aldrich, 1.0 M in hexane) was used as received, while (−)-sparteine and *N*,*N*,*N*′,*N*′-tetraethylethylenediamine (teeda) was distilled from CaH_2 and stored over 4 Å molecular sieves prior to use.

2.2. Synthesis of *N*-isopropyl-*N*,*N*′,*N*′trimethylethylenediamine (itmeda)

The synthesis followed earlier published procedures [24]. Toluene (100 ml), *N*,*N*-dimethylethylenediamine (20 ml, 0.18 mol) and acetone (30 ml, 0.40 mol) were refluxed for 12 h using a Dean–Stark trap. Evaporation in vacuo yielded a yellow oil. Ethanol (100 ml) and $NaBH_4$ (6.90 g, 0.18 mol) were added in small portions and the solution was stirred for 2 h. The reaction was quenched with water (70 ml) and the remainder was extracted with CH_2Cl_2 (3×100 ml). The combined organic phase was dried over $MgSO_4$. Evaporation in vacuo yielded a bright

yellow oil. Formaldehyde (37% in water, 15 ml, 0.19 mol) and formic acid (7.0 ml, 0.19 mol) was added to the oil and the solution was stirred at 70 °C for 12 h. The reaction flask was put on ice and NaOH (20% in water) was added until pH > 14. The solution was saturated with NaCl, extracted with diethyl ether (3 × 100 ml) and the combined ether phases were dried over K_2CO_3. Evaporation in vacuo gave a yellow oil which was distilled under reduced pressure from CaH_2 (56–59 °C, 32 mbar) to yield *N*-isopropyl-*N*,*N*′,*N*′-trimethylethylenediamine (7.2 g, 27%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (6H, s, CH_3), δ 2.23 (9H, s, CH_3), δ 2.38 (2H, t, CH_2), δ 2.48 (2H, t, CH_2), δ 2.82 (1H, m, C*H*); ^{13}C NMR (400 MHz, $CDCl_3$) δ 30.4, 37.9, 46.1, 51.1, 54.2; IR (KBr) 2950, 2800, 1450, 1380, 1290 cm^{-1}.

2.3. Synthesis of [$ZnEt_2$(teeda)] **1**

Diethylzinc (1.0 ml, 1.0 M in hexane, 1.0 mmol) was added to a Schlenk tube followed by slow addition of teeda (0.21 ml, 1.0 mmol). After stirring at ambient temperature for 1 h, the tube was moved to −80 °C and colourless crystals, suitable for X-ray analysis, formed in 41% (0.12 g) yield after 24 h.

2.4. Synthesis of [$ZnEt_2$(itmeda)] **2**

Diethylzinc (1.0 ml, 1.0 M in hexane, 1.0 mmol) was added to a Schlenk tube followed by slow addition of itmeda (0.15 ml, 1 mmol). After 20 min at ambient temperature, the tube was moved to −30 °C and colourless crystals, suitable for X-ray analysis, formed in 47% (0.13 g) yield after 24 h. The crystals redissolved when the tube was kept at ambient temperature.

2.5. Synthesis of [$ZnEt_2$(spa)] **3**

Diethylzinc (1.0 ml, 1.0 M in hexane, 1.0 mmol) was added to a Schlenk tube followed by slow addition of (−)-sparteine (0.23 ml, 1.0 mmol). After 20 min at ambient temperature colourless crystals started to form, and after several hours, crystals suitable for X-ray analysis had formed in 47% (0.13 g) yield.

2.6. Crystal structure determination

Crystal and experimental data are summarized in Table 1. Crystals of **1** and **2** were selected and mounted under nitrogen in a glass capillary at low temperature and transferred in liquid nitrogen to the Rigaku R-AXIS IIc image plate system [25]. Crystals of **3** were selected and mounted under nitrogen in a glass capillary at low temperature and transferred in liquid nitrogen to the Rigaku AFC6R diffractometer. Diffracted intensities were measured using graphite-monochromated Mo Kα (λ = 0.71073 Å) radiation from a RU200 rotating anode operated at 50 kV and 90 mA (R-AXIS) or 180 mA (AFC6). Using the AFC6 diffractometer, stationary

Table 1
Crystal and refinement data for **1**–**3**

Compound	**1**	**2**	**3**
Formula	[$ZnEt_2$(teeda)]	[$ZnEt_2$(itmeda)]	[$ZnEt_2$(spa)]
Empirical formula	$C_{14}H_{34}N_2Zn$	$C_{12}H_{30}N_2Zn$	$C_{19}H_{36}N_2Zn$
Formula weight	295.80	267.75	357.87
T (K)	123(2)	123(2)	158(2)
λ (Å)	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic	Orthorhombic
Space group	$P2_1cn$	$P2_1/n$	$P2_12_12_1$
a (Å)	7.753(2)	10.555(2)	13.407(3)
b (Å)	13.247(2)	7.257(2)	14.962(5)
c (Å)	16.223(3)	19.277(4)	9.314(4)
β (°)	90.00	101.45(1)	90.00
V (Å^3)	1666(1)	1447.2(6)	1868(1)
Z	4	4	4
δ_{calc} (g cm^3)	1.179	1.229	1.272
μ (mm^{-1})	1.460	1.674	1.315
Crystal size (mm^3)	0.2 × 0.2 × 0.3	0.3 × 0.3 × 0.3	0.2 × 0.2 × 0.3
θ Range (°)	2.0–27.0	2.0–27.0	2.0–25.0
Reflections collected	12,667	10,783	1877
Independent reflection	3454	3125	1877
Parameters	155	136	199
R_1 [$I > 2\sigma(I)$]	0.036	0.027	0.034
wR_2 [$I > 2\sigma(I)$]	0.086	0.068	0.074
R_1 all data	0.041	0.034	0.081
wR_2 all data	0.088	0.070	0.087
Flack parameter	0.47(2)	Centric	0.06(3)
Maximum peak (e Å^{-3})	0.39	0.33	0.50
Minimum hole (e Å^{-3})	−0.99	−0.59	−0.37

background counts were recorded on each side of a reflection, the ratio of peak counting time to background counting time being 2:1. Weak reflections ($I < 10.0\sigma(I)$) were rescanned up to three times and counts accumulated to improve counting statistics. The intensities of three reflections were monitored regularly after measurement of 150 reflections and indicated crystal stability during the diffraction experiment. Cell constants were obtained by least-squares refinement from the setting angles of 20 reflections. With the R-AXIS IIc detector, 90 oscillation photos with a rotation angle of 2° were collected and processed using the CrystalClear software package [26]. An empirical absorption correction was applied using the REQAB program under CrystalClear. All structures were solved by direct methods, SIR-92 [27], and refined using full-matrix least-squares calculations on F^2, SHELXL-97 [28], operating in the WINGX program package [29]. Complex **1** was refined as a racemic twin. Anisotropic thermal displacement parameters were refined for all the non-hydrogen atoms. Hydrogen atoms were included in calculated positions and refined using a riding model. Structural illustrations have been drawn with ORTEP-III [30] and PLUTON [31] under WinGX.

2.7. Typical reaction of *3* with benzaldehyde in hexane

To a solution of diethylzinc (1.0 M in hexane, 2.0 ml, 2.0 mmol) was added (−)-sparteine (23 μl, 0.1 mmol, 5 mol%) and hexane (0.877 ml) (a total reaction volume of 3.0 ml) and the mixture was stirred at ambient temperature for 20 min. Benzaldehyde (0.1 ml, 1.0 mmol) was then slowly added. The reaction mixture was stirred at ambient temperature for 1 h, and then quenched with NH_4Cl (saturated solution in water). The mixture was extracted with dichloromethane and the extract was dried over anhydrous sodium sulfate. The enantiomeric excess and the conversion were determined by chiral GC analysis carried out on a Varian Star 3400 CX gas chromatograph. All GC analyses were run on a chiral stationary phase column (CP-Chirasil-DEX CB, 25 m, 0.32 mm) from Chrompack. All analyses were performed isothermal at 115 °C (injector: 225 °C; detector: 250 °C) with helium as carrier gas. (t_R(benzaldehyde) = 1.82 min, t_R((*R*)-1-phenyl-1-propanol) = 8.09 min, t_R((*S*)-1-phenyl-1-propanol) = 8.64 min).

2.8. Solvent-free reaction of *3* with benzaldehyde

Diethylzinc (2.0 ml, 1.0 M in hexane, 2.0 mmol) was added to a Schlenk tube followed by slow addition of (−)-sparteine (0.46 ml, 2.0 mmol). Crystals formed after 1 h. After 3 h, the solvent was removed by a syringe, and the remaining solution was evaporated in vacuo. Benzaldehyde (0.02 g, 0.2 mmol) was added and the resulting mixture was allowed to stir for 24 h. A saturated NH_4Cl solution was added extremely slowly, and to the quenched reaction dichloromethane (2 ml) was added. The organic phase was dried with $NaSO_4$ and transferred to a vial. The conversion of the aldehyde to its corresponding alcohols and the enantiomeric outcome of the alkylation reaction were measured by chiral GC analysis as described above.

2.9. Solid-state reaction of *3* with benzaldehyde

Diethylzinc (2.0 ml, 1.0 M in hexane, 2.0 mmol) was added to a Schlenk tube followed by slow addition of (−)-sparteine (0.46 ml, 2.0 mmol). Crystals formed after 1 h. After 3 h, the solvent was removed by a syringe, and the remaining solution was evaporated in vacuo. The Schlenk tube was submerged into a −78 °C EtOH/CO_2 bath and pre-frozen benzaldehyde (0.02 g, 0.2 mmol) was added and the resulting mixture of solids was allowed to stir for 24 h. A saturated NH_4Cl solution was added extremely slowly. To the quenched reaction dichloromethane (2 ml) was added and the organic phase was dried with $NaSO_4$ and transferred to a vial. (In a blind test, quenching and work-up was performed directly after mixing the solid substrate and reagent. No adduct could be identified, showing that reaction indeed occurs without solvent at −78 °C, and not in solution during quenching). The conversion of the aldehyde to its corresponding alcohols and the enantiomeric outcome of the alkylation reaction were measured by chiral GC analysis as described above.

3. Results and discussion

The preparation of a complex between diethylzinc and teeda is straightforward; addition of an equimolar amount of diamine to a solution of diethylzinc in hexane results in deposition of colorless crystals in good yield upon cooling. A crystal structure determination shows that [$ZnEt_2$(teeda)] (**1**) crystallizes as monomeric species in orthorhombic $P2_1cn$ (Fig. 1). The conformation of the ethyl groups around zinc in **1** is the same as in [$ZnEt_2$(tmeda)], i.e., the complex is conformationally chiral and the molecule displays C_2 symmetry. Moreover, another element of conformational chirality can be identified when considering the orientation of the amine ethyl groups, see Scheme 3. The $P2_1cn$ space-group is acentric, but since it is polar, both enantiomers of the complex are present in the same crystal and no conglomerate is formed. Weak intermolecular interactions, such as CH/π interactions, are capable of transferring stereochemical information and has been shown to be a characteristic of many conglomerates [32]. It may thus be symptomatic that short intermolecular interactions cannot be found in **1**.

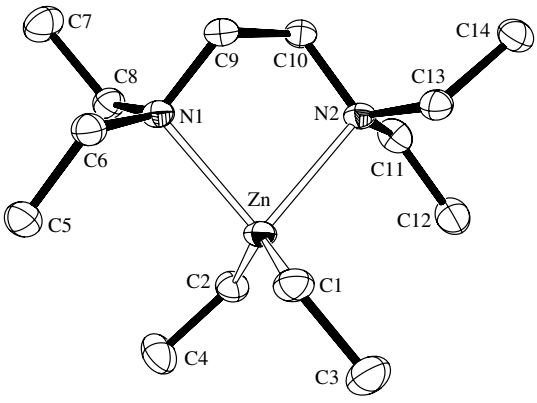
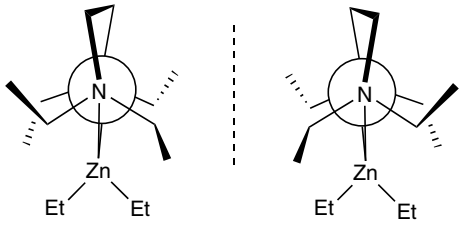


Fig. 1. ORTEP plot of [ZnEt(teeda)] (**1**) showing the crystallographic numbering, with displacement ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity.



Scheme 3.

The coordination geometry around Zn in **1** is distorted tetrahedral, i.e., the N(1)–Zn–N(2) angle is 82.16(8)°. Similar structures have been reported for tmeda complexes of diethyl- [14], dimethyl- [33], dichloro- [34] and chloroethylzinc [14]. In the two complexes containing chloride ligands the N–Zn–N bond angles are larger (86.73° in [$ZnCl_2$(tmeda)] and 84.4° for [ZnClEt(tmeda)]), while in [$ZnEt_2$(tmeda)] and [$ZnMe_2$(tmeda)] the N–Zn–N bond angles are smaller (80.7° and 79.8°, respectively), as compared to the corresponding angle in **1** (Table 2). Diethylzinc, as well as dimethylzinc, is linear as characterized by electron diffraction [35]. However, when diethylzinc coordinates teeda in **1**, the linear metal–alkyl unit is bent by 43.1(1)°. A slightly more bent coordination figure is observed in [$ZnMe_2$(tmeda)], 44.2(3)°, while the C–Zn–C angle of 118.1(1)° in [$ZnEt_2$(tmeda)] indicates near tetrahedral geometry. The Zn–C bond distance in diethylzinc is 1.950(2) Å in vapour phase [35], while the Zn–C bond distances in **1** are 2.012(3) and 2.013(3) Å.

In our quest for a conglomerate comprised of a stereochemically labile diethyl reagent, we next considered chirogenic amine ligands. We synthesized the *N*-isopropyl-*N*,*N*′,*N*′-trimethylethylenediamine (itmeda) ligand, which formed [$ZnEt_2$(itmeda)] (**2**) when coordinated by diethylzinc (Fig. 2), and determined its crystal structure. The itmeda ligand has a bulky isopropyl substituent on the chirogenic nitrogen donor, but the chirogenic center may still exhibit rapid inversion. The energy barrier restricting inversion for ammonia is 5.58 and 7.46 kcal/mol for trimethylamine which results in approximately 2×10^{11} inversions each seconds [36,37]. So, even though the energy barrier increases with larger substituents on nitrogen, the inversion of nitrogen in alkylamines will not be stopped at normal reaction temperatures, unless special structural features of the molecule, as in bicyclic and polycyclic amines, are introduced. When itmeda is coordinated by diethylzinc, a stereochemically labile complex should form, which racemizes in solution but can be optically active in the solid state. It should be possible to obtain an enantiopure product by total spontaneous resolution if such a complex would crystallize as a conglomerate.

The crystal structure determination of [$ZnEt_2$(itmeda)] (**2**) reveals distorted tetrahedral monomers with a N(1)–Zn–N(2) bond angle of 82.10(5)°. As in **1**, a bending from the linear C–Zn–C structure in diethylzinc of 42.8(6)° is observed in **2**. The Zn–N bond distances in **2** of 2.334(2) Å (N1) and 2.291(2) Å (N2),

Table 2
Selected bond distances and angles in **1–3**

Compound	Zn–C(1), Zn–C(2) (Å)	Zn–N(1), Zn–N(2) (Å)
[$ZnEt_2$(teeda)] **1**	2.012(3), 2.013(3)	2.250(2), 2.276(2)
[$ZnEt_2$(itmeda)] **2**	2.006(2), 2.009(2)	2.334(2), 2.291(2)
[$ZnEt_2$(spa)] **3**	2.003(6), 2.017(7)	2.238(5), 2.265(4)
[$ZnEt_2$(tmeda)][14]	2.17(2)	2.294(5)
[$ZnMe_2$(tmeda)][31]	1. 989(9), 1.974(9)	2.260(8), 2.278(8)
[$ZnMe_2$(spa)][34]	2.008(8), 2.016(8)	2.222(5), 2.256(6)

Compound	C(1)–Zn–C(2) (°)	N(1)–Zn–N(2) (°)	C–Zn–N (°)
[$ZnEt_2$(teeda)] **1**	136.9(1)	82.16(8)	106.7(1), 105.3(1), 107.3(1), 105.0(1)
[$ZnEt_2$(itmeda)] **2**	137.20(6)	82.10(5)	105.98(6), 104.62(6), 109.03(6), 104.19(6)
[$ZnEt_2$(spa)] **3**	130.0(3)	80.5(2)	110.1(2), 106.0(2), 101.6(2), 117.7(2)
[$ZnEt_2$(tmeda)][14]	118.08(1)	80.7(2)	111.1(6), 115.1(6)
[$ZnMe_2$(tmeda)][31]	135.8(3)	79.8(3)	106.4(4), 106.9(4), 106.7(4), 107.1(4)
[$ZnMe_2$(spa)][34]	128.2(4)	80.4(2)	109.2(4), 105.9(3), 104.6(4), 118.0(3)

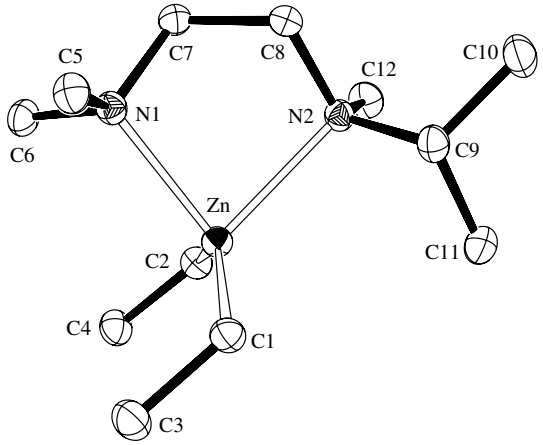


Fig. 2. ORTEP plot of [ZnEt(itmeda)] (**2**) showing the crystallographic numbering, with displacement ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted.

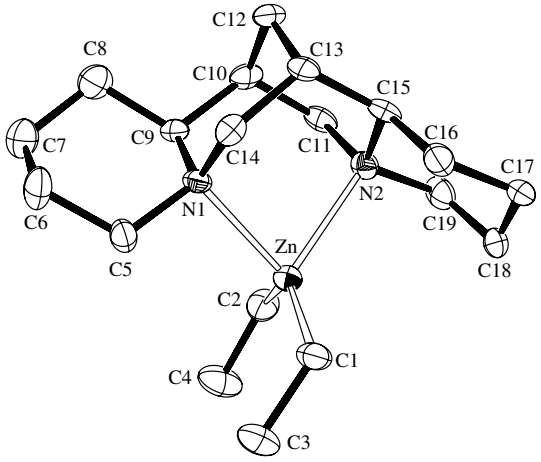


Fig. 3. ORTEP plot of [ZnEt(spa)] (**3**) showing the crystallographic numbering, with displacement ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted.

respectively, are similar to those reported for [$ZnEt_2$-(tmeda)], but the Zn–C bond distances of 2.006(2) Å (C1) and 2.009(2) Å (C2), respectively, are somewhat shorter than the same bond distances in [$ZnEt_2$(tmeda)] of 2.17(2) Å. The C–Zn–C bond angle of 137.20(6)° in **2** is much larger than the same bond angle of 118.08(1) in [$ZnEt_2$(tmeda)], but it is similar to that angle in **1** (136.9(1)°). Overall, the Zn–N and Zn–C bond distances as well as the C–Zn–C, N–Zn–N and C–Zn–N bond angles are similar in **1** and **2**, as can be seen from Table 2.

Apart from the chirogenic N atom, complex **2** displays another element of chirality: the five-membered itmeda-zinc chelate ring is conformationally chiral, and the (*S*)-configuration at nitrogen corresponds to the δ-conformation of the five-membered chelate, and vice versa. However, when crystals of **2** are assembled, the enantiomers alternate and the (*R*)- as well as the (*S*)-enantiomer (with respect to the chirogenic N atom) are present in the same crystal, which results in racemic crystals that crystallize in a centrosymmetric space group ($P2_1/n$). Moreover, the ethyl groups now adopt the achiral conformation shown in Scheme 1. No short intermolecular interactions are observed in **2**.

Crystals of **1** or **2** cannot be used in an asymmetric synthesis since they are achiral, but by using a ligand that is enantioenriched, i.e., the alkaloid (−)-sparteine (spa), chiral crystals must form. Such complexes are not stereochemically labile and cannot undergo total spontaneous resolution, but in order to compare the enantioselectivity of a solid-state reaction with the ee produced by an analogous solution reaction, it is necessary to choose a ligand that does not enantiomerize in solution. Addition of sparteine to a solution of diethylzinc in hexane yields [$ZnEt_2$(spa)] (**3**), which crystallizes as distorted tetrahedral monomers in orthorhombic $P2_12_12_1$ (Fig. 3). The orientation of the ethyl ligands is similar to what is observed in **2**. In the [$ZnMe_2$(spa)] complex,[38] which also crystallized in $P2_12_12_1$, the Zn–N and the Zn–C bond distances are similar to those in **3**, and the N–Zn–N, N–Zn–C and C–Zn–C bond angles are also similar (Table 2). The N–Zn–N bond angle of 80.5(2) in **3** is somewhat smaller than the same angles in **1** and **2** (82.16(8)° and 82.10(5)°, respectively), which may be a result of the rigidity of the sparteine ligand. The [$ZnMe_2$(spa)] complex is reported to be unusually air stable, with no apparent sign of decomposition after 3–4 days exposed to air. This was not observed with **3**, which started to decompose after a few minutes exposed to air. No drastic differences in the crystal packing patterns of [$ZnMe_2$(spa)] versus [$ZnEt_2$(spa)] can be discerned, which otherwise could have rationalized the variance in air-sensitivity.

Having access to chiral crystals of [$ZnEt_2$(spa)] (**3**), the difference in enantioselectivity between the solvent-free reaction and the solution reaction can now be investigated. Benzaldehyde freezes at −56 °C, so two different situations must be considered. At ambient temperature, the benzaldehyde is a liquid so the term solid-state reaction is obviously not appropriate and we refer to this reaction as solvent-free. However, at −78 °C benzaldehyde is frozen so a solid-state reaction is possible. It can be argued that it does not have to be a true solid-state reaction since an eutectic melt could form when the reactants are mixed [39,40]. Although the relatively high conversion (60%) obtained (Table 3) could indicate mass transport via melting, the case is not clear-cut since the zinc reagent is present in tenfold excess and new surfaces are opened by constant grinding and mixing with the stirring bar for 24 h. It is thus not easy to determine if local melting is taking place, so we have adopted the utilitarian view of Braga [41] and referred to the reaction at −78 °C as "solid-state" since both reactants and the product (zinc alkoxide) are solid.

Table 3
Alkyl transfer reactions to benzaldehyde

mol% Sparteine	Temperature (°C)	% Conversion[a]	% ee[a]
Solution reaction			
5	0	>99	7.8
10	0	>99	7.9
50	0	>99	8.2
100	0	>99	7.9
5	Amb.	>99	8.3
10	Amb.	>99	8.5
50	Amb.	>90	8.4
100	Amb.	>20	8.5
Reagent	Temperature (°C)	% Conversion[a]	% ee[a]
Solvent-free reaction			
3	Amb.	>88	9.0
Solid-state reaction			
3	−78	>60	10.4

[a] Determined by GC analysis using chiral column.

When benzaldehyde was treated with diethylzinc in hexane at ambient temperature in the presence of (−)-sparteine (5 mol%), optically active (*R*)-1-phenyl-1-propane-1-ol was obtained with >99% conversion and about 8% ee after 1 h (Table 3). The ee did not change markedly with larger amounts of (−)-sparteine or by lowering the temperature. When benzaldehyde was treated with chiral crystals of **3** at ambient temperature in a solvent-free reaction, the optically active alcohol was obtained with >99% conversion and 9% ee after 24 h. When a solid-state reaction was performed by keeping the reactants at −78 °C, the enantiomeric excess increased to 10.4%. To prove that all of the benzaldehyde was alkylated during solventless conditions and not at the time of (or after) the quenching with ammonium chloride, blind tests were performed. They showed that if quenching was performed directly after mixing the solid reagents, no alcohol was obtained, so it is therefore safe to conclude that the bulk of the reaction takes part under solventless conditions.

4. Conclusions

Diethylzinc forms monomeric complexes, exhibiting a distorted tetrahedral coordination geometry around zinc, with the *N*,*N*-bidentate teeda, itmeda and (−)-sparteine ligands, viz. [$ZnEt_2$(teeda)] (**1**), [$ZnEt_2$(itmeda)] (**2**), and [$ZnEt_2$(spa)] (**3**). Both **1** and **2** are stereochemically labile and exhibit chiral complexes, displaying different types of conformational chirality, but they form racemic crystals. It is still unclear how to design a reagent that will form a conglomerate, but it is likely that weak intermolecular (supramolecular) interactions are necessary for the transfer of stereochemical information. By using the chiral crystals of **3** in nuclephilic addition to benzaldehyde in the absence of solvent at low temperature, a small increase in ee was obtained (compared to the same reaction in solution). It thus seems feasible, not only to retain the enantioselectivity obtained in solution, but perhaps even to increase the ee by using solventless reactions.

5. Supplementary material

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publications Nos. CCDC 264401 for compound **1**, CCDC 264402 for compound **2**, and CCDC 264403 for compound **3**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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