A Novel Tetranuclear [MeZn(μ₃-OCH₂CH₂SMe)Zn(μ-Cl)Me]₂ Adduct Derived from the Interaction of CH₂Cl₂ with an Alkylzinc Complex

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The treatment of 2-(methylthio)ethanol (methioH) with two equivalents of Me₂Zn in CH₂Cl₂ affords a tetranuclear aggregate with two monomeric MeZn(methio) units joined by two MeZnCl moieties. This result demonstrates that transfer of a chloride ion to Zn takes place on the addition of a donor-functionalized alcohol to Me₂Zn in CH₂Cl₂ solution.
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Introduction

Dichloromethane is one of the most commonly used solvents for organic and organometallic reactions involving alkylzinc reagents, especially the Simmons−Smith cyclopropanation of olefins[1] or the enantioselective addition of organozinc reagents to prochiral carbonyl compounds in the presence of catalytic amounts of a chiral ligand,[2] arguably the most important application of organozinc reagents in organic synthesis, as well as other types of reactions involving alkylzinc reagents.[3] The great interest and simple procedure of both reactions have motivated extensive work to better understand the reaction, including detailed mechanistic studies. For instance, very recent theoretical studies on the reaction pathways of the Simmons−Smith reaction have demonstrated that "the Lewis acid coordination to the halogen atom on the halomethyl ligand is likely to be a key event in the cyclopropanation reaction".[4] However, as far as we are aware, an influence of CH₂Cl₂ on the course or outcome of these various reactions has not been considered. Herein we report the isolation and structural characterization of the novel tetranuclear zinc adduct [MeZn(μ₃-OCH₂CH₂SMe)Zn(μ-Cl)Me]₂ (**1**), derived from the reaction of Me₂Zn with a bifunctional alcohol in the presence of CH₂Cl₂.

Results and Discussion

The treatment of 2-(methylthio)ethanol (methioH) with two equivalents of Me₂Zn in toluene/CH₂Cl₂ affords a yellow solution from which a white precipitate deposits after cooling at −15 °C for several hours. The complex could be isolated in moderate yield from the reaction, and it was studied by ¹H NMR spectroscopy and elemental analysis. ¹H NMR spectroscopy revealed two Zn-bonded methyl groups with a 1:1 Me-Zn/ligand ratio.[5] The occurrence of several sets of broad signals due to the O,S-bifunctional ligand indicated the operation of a dynamic process, likely to be the reversible dissociation of the tetranuclear complex, and the inversion of configuration at the sulfur atoms. The obtained ambiguous data of the precipitate led us to carry out a single-crystal X-ray diffraction study to elucidate the product structure. To our surprise, this study revealed **1** to be a tetranuclear aggregate with two monomeric MeZn(methio) units joined by two MeZnCl moieties (Figure 1). Interestingly, in contrast to the commonly observed μ₂-O bonding mode of the alkoxide oxygen atoms in dimeric [RZn(μ-O,N)]₂ complexes,[6] the analogous oxygen atoms of **1** function as μ₃-O donors; this bonding mode is typical for the cubane-type structure of alkylzinc alkoxides [RZn(μ₃-OR)]₄.[7] The aggregate **1** has C_1 symmetry with a central Zn₂(μ₃-O)₂ ring. The chloride acts as a bridge between the two Zn atoms with the formation of Zn₂ClO rings which take up a trans conformation with an angle of 74.92(5)° to the Zn₂O₂ plane [the Zn₂ClO ring is slightly folded about the Zn−Zn vector with a dihedral angle of 168.72(6)°]. The geometry of the O,S-chelate may be described as an open envelope with the S−Me methyl groups trans to each other. The ligand used becomes chiral upon complexation of the SMe group to the zinc atom; the two sulfides have an opposite chirality and the resulting achiral complex possesses C_i symmetry. The geometry about the zinc centers is distorted tetrahedral. Selected bond lengths and bond angles of **1** are given in the legend of Figure 1. The Zn−O bond lengths lie in the range 2.043(2)−2.101(2) Å and are slightly longer than those in dimeric [RZn(μ-O,N)]₂ complexes.[8]

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The chloride bridges are essentially symmetrical with Zn−Cl distances of 2.365(1) Å and 2.370(1) Å and this fact indicates that the formation of these bridges is geometrically favorable. The Zn−C bond length of the bridging MeZnCl moiety does not differ from the value for the terminal Zn−Me group.
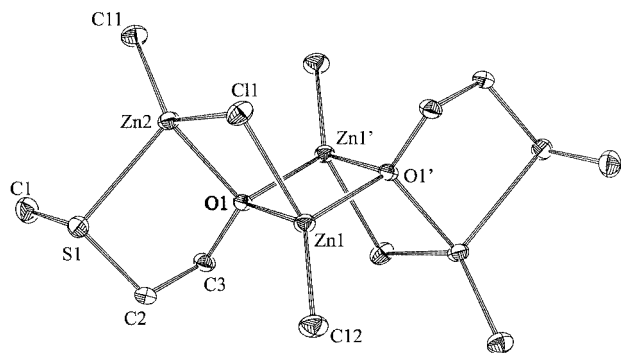

Figure 1. Molecular structure of **1** with thermal ellipsoids drawn at the 30% probability level; selected bond lengths [Å] and angles [°]: C12−Zn1 1.956(3), Zn1−O1 2.101(2), Zn1′−O1 2.043(2), Zn1−Cl1 2.370(1), Zn2−Cl1 2.365(1), Zn2−O1 2.072(2), Zn2−S1 2.475(2), Zn2−C11 1.960(3); C12−Zn1−Cl1 123.97(8), Zn1′−O1−Zn1 96.38(6), O1−Zn2−Cl1 87.59(4), Zn2−Cl1−Zn1 84.70(2)

Compound **1**, apart from being a novel organozinc aggregate, may also serve as a useful model compound for the donor-functionalized-alcohol promoted addition of dialkylzinc reagents to carbonyl compounds (vide infra). So, can related tetranuclear aggregates be formed and observed in the reaction without additional stabilization provided by the chloride bridges? In order to answer this question we conducted an analogous reaction of methioH with two equivalents of Et$_2$Zn in benzene as a solvent. Cryoscopic weight measurements on the post reaction mixture indicated the presence of some higher aggregated species in solution [MW found 270; for example, calcd. 309 for EtZn(methio)ZnEt$_2$]. The ^{1}H NMR spectrum of the same solution showed several multiple resonances, presumably due to dynamic processes and skeletal rearrangement of the resulting products in solution. Unfortunately, the above studies only confirm that zinc alkoxides have a tendency to form higher aggregates.

The reported studies revealed several important aspects of various transformations involving alkylzinc reagents. Of particular importance is the fact that on the addition of a bifunctional alcohol to R$_2$Zn in CH$_2$Cl$_2$ solution, the transfer of a chloride ion to Zn takes place. In this regard, our studies demonstrate that CH$_2$Cl$_2$ seems to be the least desirable solvent for reactions involving alkylzinc reagents supported by donor-functionalized alcohols and a large number of investigations reported in the literature may be invalid.[9] Furthermore, in our opinion adduct **1** mimics a potential intermediate in the donor-functionalized-alcohol promoted addition of dialkylzinc to aldehydes (especially in the case of the *O,X*-bifunctional auxiliary ligand with sterically non-encumbered alkyl substituents at the α-carbon atom). The commonly accepted mechanism for the lat-

ter reaction assumes the participation of the monomeric three-coordinate zinc species **II** as the sole reactive species, which exists in equilibrium with the inactive dimer **I** (Scheme 1).[2] Some uncertainties, however, in the mechanistic analysis of this reaction have been observed,[10] which are probably introduced by the presence of multiple equilibria of different Zn aggregates, and in this regard the question as to whether the reaction can proceed through different pathways arises. All the above facts indicate that a more in-depth understanding of this reaction is necessary to better interpret the results from the experiments and raises the question as to whether the reaction can proceed through different pathways. However, alternative structural models for the dormant and active species present within the donor-functionalized-alcohol promoted addition of dialkylzinc to aldehydes are lacking.
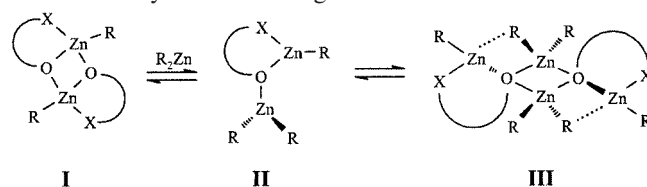
Scheme 1

Based on the isolation of **1**, we suggest that higher aggregate species, such as the tetrametallic dimer of type **III**, are possible primary reactants in the reaction. The speculated structures of the dimer **III** are presented in Scheme 1. As far as we are aware, in all the recent mechanistic discussions, as well as in the field of zinc alkoxide chemistry, such a possibility has never been taken into consideration. The considered tetrametallic species can be easily stabilized by weak intramolecular interactions resulting from metal-alkyl agostic interactions or the formation of a relatively stable carbon-bridge between zinc atoms. There is no relevant experimental evidence for this hypothesis, however, we can anticipate that both the increased nucleophilicity of the alkyl group of the R$_2$Zn fragment (due to the Zn coordination to two alkoxide centers) and the presence of the unsaturated three-coordinate Zn atom of the monometallic RZn(O,X) subunit will favour these types of interactions.[11] The symmetrical strong chloride bridges observed for **1** also indicate that such interactions are geometrically favorable. In our opinion further studies should require serious consideration of the contribution of the associative mechanism in the case of less sterically encumbered reaction systems than the "DAIB system".[12] It seems likely that the monomeric dimetallic adduct or dimeric tetrametallic aggregate may be the active catalyst in the latter reaction depending on the nature of the auxiliary ligand and reaction conditions.[13] We fully intend to investigate this problem further based on these preliminary studies.

The reported results should be helpful for a rational catalyst design and stimulate further experimental and theoretical investigations to clarify the correlation between the structure and activity of organozinc species. Further studies on the factors controlling the degree of aggregation of

SHORT COMMUNICATION

alkylzinc chelate complexes and the extent to which CH$_2$Cl$_2$ reacts with various organozinc reagents are in progress.

Conclusion

The reported studies revealed that the transfer of a chloride ion to the zinc atom takes place upon the addition of a bifunctional alcohol to R$_2$Zn in CH$_2$Cl$_2$ solution. In this regard, CH$_2$Cl$_2$ seems to be the least-desirable solvent for reactions involving alkylzinc reagents supported by donor-functionalized alcohols. The reaction results in the formation of the novel tetrametallic adduct [MeZn(μ_3-OCH$_2$CH$_2$SMe)Zn(μ-Cl)Me]$_2$ (**1**). In our opinion, the latter compound mimics a new potential intermediate in the donor-functionalized-alcohol promoted addition of dialkylzinc to aldehydes.

Experimental Section

General Remarks: All reactions were carried out under dry nitrogen using standard Schlenk techniques. Solvents were dried and distilled prior to use. NMR spectra were recorded on a Varian Mercury 400 spectrometer.

[MeZn(μ_3-OCH$_2$CH$_2$SMe)Zn(μ-Cl)Me]$_2$ (1): 2-(Methylthio)-ethanol (2 mmol, 0.17 mL, 0.18 g) was added at −78 °C to a stirred toluene/CH$_2$Cl$_2$solution of Me$_2$Zn (2 M, 2 mL, 4 mmol). The reaction mixture was then allowed to warm to room temperature and stirred for 4 h. The solvents were then removed under vacuum, leaving a white solid that was crystallized from toluene at −15 °C. Yield 42% (0.24 g). C$_{10}$H$_{26}$Cl$_2$O$_2$S$_2$Zn$_4$ (574.9): calcd. C 20.89, H 4.56, Cl 12.33; found C 20.75, H 4.62, Cl 12.43. ^{1}H NMR: δ = −0.30 (s, 6 H, Zn-CH_3), 2.10 (s, 3 H, S-CH_3), 2.58 (t, 2 H, CH_2-O), 3.83 (t, 3 H, S-CH_2) ppm.

X-ray Crystallographic Study: A single crystal of **1** suitable for X-ray diffraction studies was placed in a thin-walled capillary tube (Lindemann glass 0.5 mm) under an inert atmosphere. The tube was plugged with grease, then flame-sealed and mounted on a goniometer head.

Crystal Data for 1: M = 574.86, crystal dimensions 0.40 × 0.36 × 0.16 mm^3, monoclinic, space group $P2_1/c$ (no. 14), a = 7.0040(3), b = 13.0070(6), c = 11.7400(6) Å, β = 104.5840(18)°, U = 1035.07(8) Å^3, Z = 4, F(000) = 576, D_c = 1.844 g m^3, T = 293(2) K, Mo-K_α radiation (λ = 0.71073 Å), Nonius Kappa-CCD diffractometer, θ_{max} = 27.48°, 2357 unique reflections which were used in all calculations. The structure was solved by direct methods[14] and refined by full-matrix least-squares on F^2.[15] H atoms were included in idealized positions and refined isotropically. Refinement converged at $R1$ = 0.0340, $wR2$ = 0.0624 for all data and 91 parameters [$R1$ = 0.0274, $wR2$ = 0.0606 for 2083 reflections with $I_o > 2\sigma(I_o)$]. The goodness-of-fit on F^2 was equal to 1.083. A weighting scheme w = [$\sigma^2(F_o^2 + (0.0418P)^2 + 3.1964P$]$^{-1}$ where P = ($F_o^2 + 2F_c^2$)/3 was used in the final stage of refinement; residual electron density = 0.42/−0.48 e·Å^{-3}. CCDC-197262 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[9] For example, it may concern a large body of work concerning a highly enantioselective addition of diethylzinc to aldehydes with the catalysis of racemic amino alcohols in the presence of chiral additives, through an asymmetric deactivation strategy with a combinatorial approach, where the reactions were carried out in CH$_2$Cl$_2$/hexane solution for 48 h; J. Long, K. L. Ding, *Angew. Chem. Int. Ed.* **2001**, *40*, 544. The same concern can be raised about other recent work using a high-throughput screening technique to find the most efficient catalyst for asymmetric reactions: R. Angelaud, Y. Matsumoto, T. Korenaga, K. Kudo, M. K. Senda. Mikami, *Chirality* **2000**, *12*, 544.

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[11] There are only two structurally characterized dimeric compounds which incorporate unsaturated hydrocarbon bridges between zinc atoms, R. S. Dickson, G. D. Fallon, Q.-Q. Zhang, *J. Chem. Soc., Dalton Trans.* **2000**, 1973; E. A. Jeffery, T. Mole, J. K. Saunders, *Aust. J. Chem.* **1968**, *21*, 137.

[12] The extensive mechanistic studies carried out by Noyori et al. were supported by detailed kinetic studies involving sterically demanding camphor-derived chiral amino alcohols as auxiliary ligands, 3-*exo*-dimethylamino-*iso*-borneol (DAIB), see ref.[7]

[13] One of the most striking features of the reaction is the strong asymmetric amplification in product enantioselectivity and the central problem concerns the origin of the nonlinear effect in this catalytic reaction. The proposed novel intermediate **III** corresponds well to the theoretical idea of the ML$_2$ model system involving the catalytically active dimer: C. Girard, H. B. Kagan, *Angew. Chem. Int. Ed.* **1998**, *37*, 2923.

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