

Substituent-Dependent Formation of Organotransition-Metal Bimetallic Calix[4]arene Inclusion Complexes

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Summary: Reaction of 1,3-di-O-substituted calixarene ligands with Et_2Zn gives new organotransition-metal bimetallic calix[4]arene inclusion complexes when the substituent is larger than methyl. The resulting complexes show strong interactions between the incorporated organometallic fragment and the hydrophobic cavity of the calixarene group.

The unusual three-dimensional properties of calixarene scaffolds have attracted much attention, particularly with regard to molecular recognition and inclusion chemistry.¹ Although the latter is normally associated with organic host–guest interactions, a few examples of metal incorporation into the calixarene cavity have also been reported.^{2,3} There were several recent publications on bimetallic complexation to the fully or partially deprotonated lower (phenolic) rim, with one of the metal centers penetrating the hydrophobic cavity of the calixarene fragment.⁴ While most of this research was performed on alkali-metal and alkaline-earth-metal ions, examples of such inclusion complexes with transition metals remain scarce.^{5,6} Incorporation of an organometallic fragment into the calixarene cavity appears particularly attractive, due to the expected change in the reactivity pattern of the guest. Ishii and co-workers recently communicated the stepwise preparation of a heterobimetallic complex with an organometallic guest fragment coordinated to the lower rim by penetrating the hydrophobic calixarene cavity.⁷ Herein we describe the substituent-dependent formation of bimetallic calixarene inclusion complexes with spontaneous discrimination between the organometallic fragments.

In 1996 Raston and co-workers reported an unusual bimetallic zinc complex formed upon treatment of the calixarene 1,3-dimethyl ether with 2 equiv of diethylzinc.⁸ The solid-state structure of this complex revealed the distorted flattened-cone conformation of the calixarene moiety with two phenolate units lying nearly in the same plane (A, Scheme 1). Each of the Zn atoms is bound to three oxygen atoms and the ethyl group, and the organometallic fragments are equivalent both in solution and in the solid state. As bimetallic zinc complexes are of great importance in catalysis,⁹ we were interested in the possibility of preparing bimetallic zinc calixarene inclusion complexes. We hypothesized that small methyl substituents can be responsible for ring flipping in A (vide infra) and decided to evaluate the reactivity of calixarenes with substituents other than methyl. Interestingly, we discovered that room-temperature stirring of the calixarene 1,3-dibenzyl ether **1a** with 2 equiv of diethylzinc in toluene resulted in the clean formation of the new complex **2a** (Scheme 1), which had two distinctly nonequivalent metal-bound ethyl groups in the ¹H NMR spectrum.¹⁰ These groups give rise to two sets of signals, a quartet (CH_2) and triplet (CH_3), with the $\Delta\delta$ value between the appropriate signals in each set being about 2 ppm (−1.54 ppm vs 0.97 ppm for CH_2 ; −0.11 ppm vs 1.79 ppm for CH_3). The

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(10) See the Supporting Information for full NMR data.

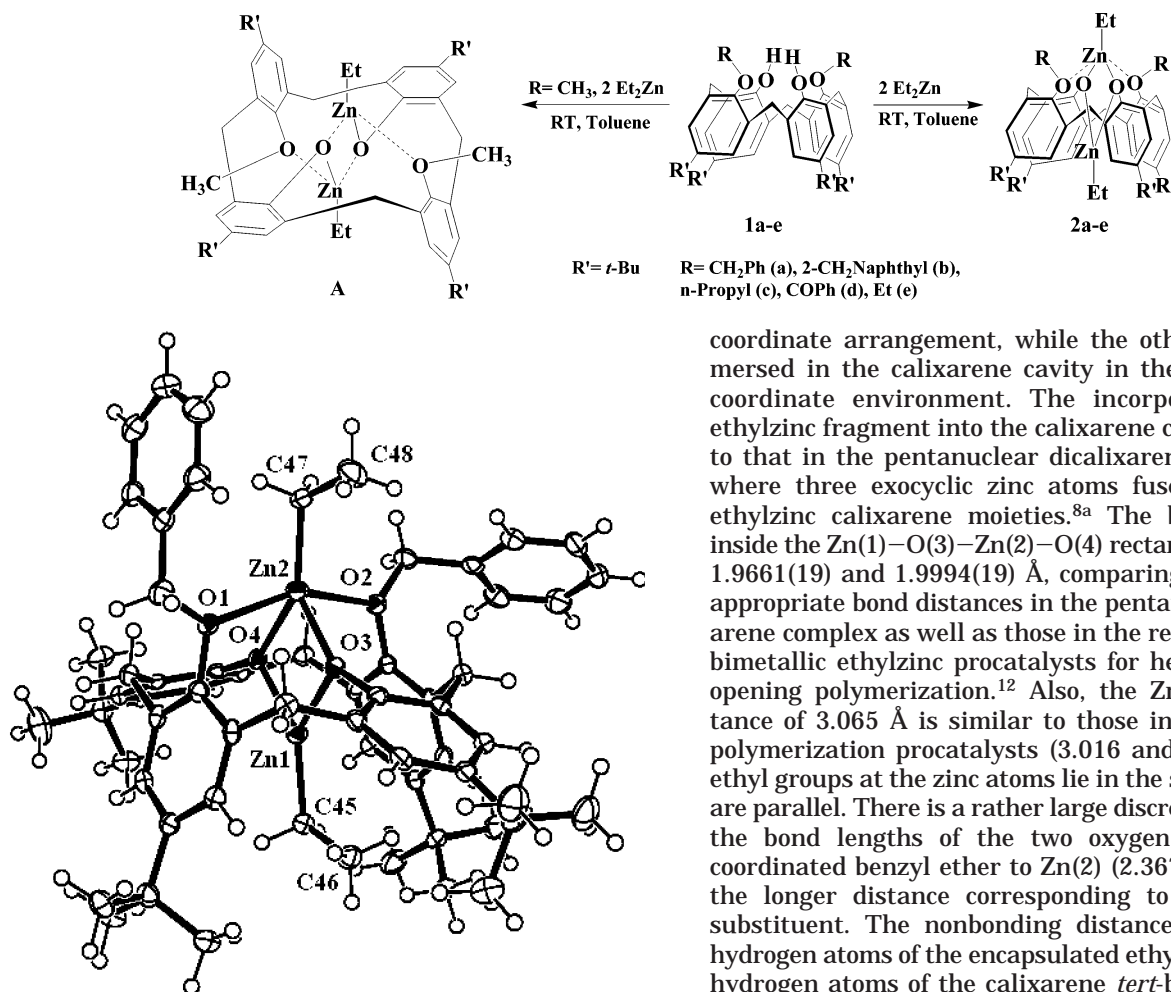
Scheme 1. Reaction of 1,3-Disubstituted Calixarene Ligands with Et₂Zn

Figure 1. ORTEP view of a molecule of **2a** with thermal ellipsoids shown at 50% probability.

chemical shifts for the same signals in the symmetrical **A** (−0.21 ppm for CH₂ and 0.92 ppm for CH₃) fall between the two sets in **2a**. Two sets of signals were also observed in the ¹³C NMR spectrum of **2a**: −1.88 and −6.22 ppm for the CH₂ carbon atoms (cf. −2.14 ppm in **A**). In light of this difference, it was crucial to determine the structure of **2a** by a single-crystal X-ray analysis.

Colorless crystals of **2a** were obtained by slow crystallization from pentane at −30 °C.¹¹ The X-ray structure of **2a** (Figure 1) shows coordination of two ethylzinc groups to a single calixarene unit in the pinched-cone conformation. Interestingly, the two ethylzinc fragments demonstrate different binding modes, with one of the zinc atoms capping the calixarene cone in the five-

coordinate arrangement, while the other is fully immersed in the calixarene cavity in the formal three-coordinate environment. The incorporation of the ethylzinc fragment into the calixarene cavity is related to that in the pentanuclear dicalixarene zinc system, where three exocyclic zinc atoms fuse together two ethylzinc calixarene moieties.^{8a} The bond distances inside the Zn(1)–O(3)–Zn(2)–O(4) rectangle lie between 1.9661(19) and 1.9994(19) Å, comparing well with the appropriate bond distances in the pentanuclear dicalixarene complex as well as those in the recently reported bimetallic ethylzinc procatalysts for heterocycle ring-opening polymerization.¹² Also, the Zn(1)–Zn(2) distance of 3.065 Å is similar to those in the bimetallic polymerization procatalysts (3.016 and 3.084 Å). The ethyl groups at the zinc atoms lie in the same plane and are parallel. There is a rather large discrepancy between the bond lengths of the two oxygen atoms of the coordinated benzyl ether to Zn(2) (2.367 and 2.576 Å), the longer distance corresponding to the diverging substituent. The nonbonding distances between the hydrogen atoms of the encapsulated ethyl group and the hydrogen atoms of the calixarene *tert*-butyl group are almost within the sum of two hydrogen atom van der Waals radii (2.499 and 2.506 Å for the CH₃ and CH₂ groups, respectively). A similar close distance is observed for the CH₂ group hydrogen atom of the second ethyl group and one of the CH₂ group hydrogen atoms of the benzyl ether (2.402 Å).

The close proximity of the ethyl hydrogen atoms to the hydrogens of the calixarene scaffold in **2a** was further evaluated by ¹H NOESY solution studies. The 2D spectrum in C₆D₆ (Figure 2) clearly shows strong interactions between the entrapped ethyl group protons and one set of the *tert*-butyl groups, as well as an interaction between the CH₃ of this ethyl group and the meta protons of the calixarene aromatic ring. Similarly, the CH₂ fragment of the second ethyl group interacts with the methylene hydrogens of the benzyl ether group. Therefore, the whole ethylzinc fragment remains fully immersed in the calixarene cavity, both in solution and in the solid state. The intercalation of the ethyl group inside the hydrophobic calixarene cavity is strongly manifested by the aromatic shielding of the ethyl hydrogen atoms as well as through-space interactions.

As the structure of **A** does not indicate any steric barriers toward having a bulkier benzyl group in the similar environment, we were puzzled as to the cause of such different behaviors of two closely related calix-

(11) X-ray structure data for **2a**: C₆₂H₇₆O₄Zn₂, *M_r* = 1015.97, 0.35 × 0.2 × 0.15 mm³, monoclinic, space group *P*2₁/*c*, *a* = 12.3180(3) Å, *b* = 42.2240(15) Å, *c* = 11.1870(4) Å, β = 112.691(2)°, *V* = 5368.2(3) Å³, *Z* = 4, ρ_{calcd} = 1.257 g cm^{−3}, 2θ_{max} = 25.0°, Nonius KappaCCD diffractometer, Mo Kα radiation (λ = 0.710 73 Å), graphite monochromator, *T* = 110(2) K, 19 500 collected reflections, 9162 unique reflections (*R*_{int} = 0.036). The structure was determined by direct methods (SIR-97) and refined anisotropically by least squares on *F*² data (SHELXL-97, 627 parameters with no restraints). The structure of **2a** at ca. 110 K is fully ordered and characterized by a relatively high precision, with *R*₁ = 0.041 and *wR*₂ = 0.097 for 6966 data with *I* > 2σ(*I*) and *R*₁ = 0.062 and *wR*₂ = 0.109 for all unique data. The file CCDC-226862 (Cambridge Crystallographic Data Base) contains full crystallographic data for this compound.

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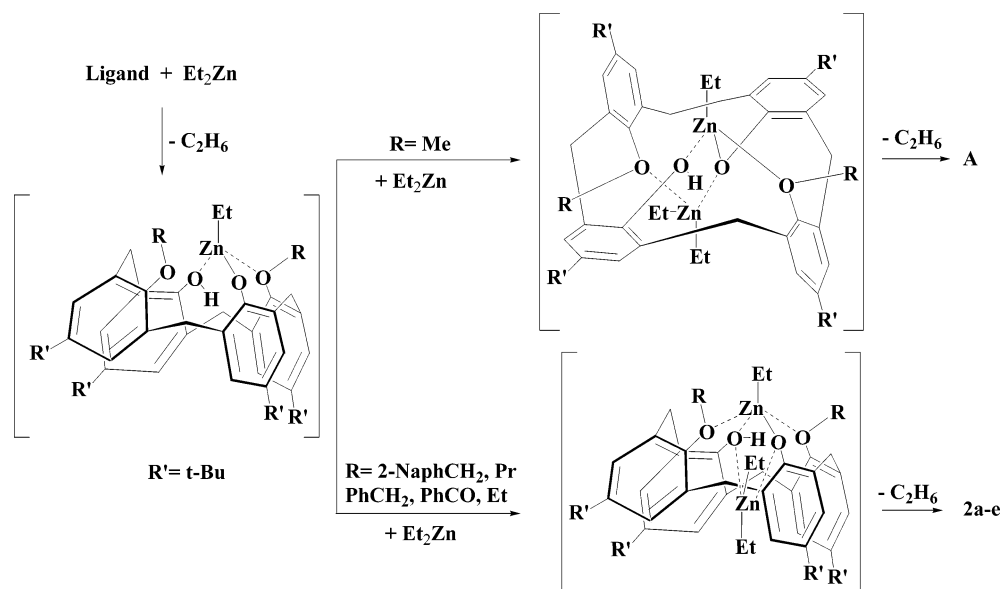
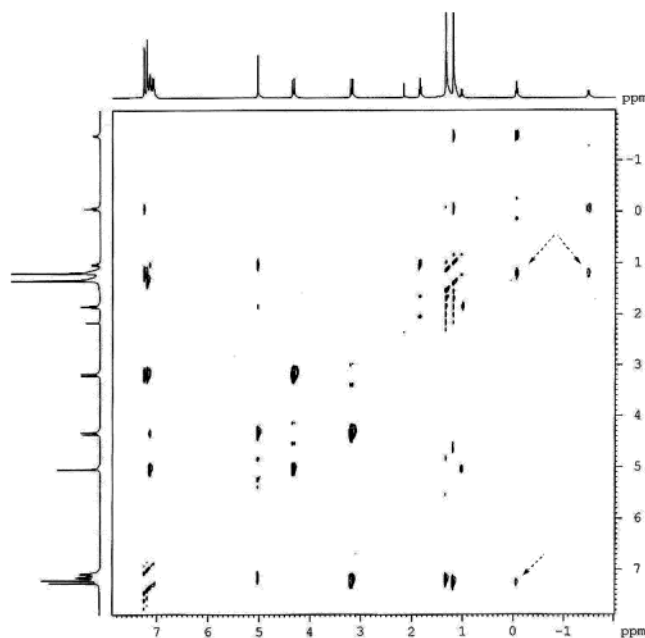
Scheme 2. Proposed Mechanism of Reaction between Diethylzinc and the Calixarene Ligand**Scheme 3. Synthesis of the Phenylzinc Inclusion Complexes**

Figure 2. NOESY spectrum of complex **2a** in benzene- d_6 . Through-space interactions of the endo-cavity $\text{Zn}-\text{CH}_2\text{CH}_3$ fragment with the calixarene are shown by arrows.

arene ligands. To that end, we prepared a series of disubstituted calixarene ligands **1b–d** and studied their reactivity toward diethylzinc (Scheme 1). Replacing the ether ligand in **1a** with the ester in **1d** led to dramatic changes in both the ^1H and ^{13}C NMR spectra of the external ethyl group, while only slightly influencing the

internal group. In all cases, however, the bimetallic Zn complexes, similar to **2a**, were isolated, indicating that the inclusion of the organometallic fragment into the calixarene cavity is independent of the electronic or steric (*n*-propyl and larger) nature of the substituent. Reaction of **1a** with diethylzinc in the coordinating THF did not affect the formation of **2a**, indicating that it is the thermodynamic product. Since **1a–d** and their dimethyl analog exist in the cone conformation as the most stable form, it is conceivable that the different structures obtained from the dimethyl ether and the rest of the ligands are the result of *conformational differences at the stage prior to the formation of the bimetallic complexes*. As the propyl group is the smallest one known to prevent the phenolic ring flipping in the calixarene system to form a partial cone or 1,3-alternate conformers,¹³ this process must be responsible for the formation of different products in the cases of the dimethyl and dipropyl calixarene ligands. It is noteworthy that the reaction of the 1,3-diethyl calixarene ether **1e** with 2 equiv of diethylzinc resulted in a mixture of products, in which **2e** could be identified as the major product (Scheme 1). Scheme 2 illustrates the proposed mechanism for the formation of **A** and **2a–d**. In a stepwise approach, the monoethylzinc calixarene intermediate is initially formed. When the substituent is small, this intermediate undergoes ring flipping. Reaction with the second diethylzinc molecule results in arresting of the calixarene fragment in the 1,3-alternate conformation to form **A**. When no ring flipping is

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possible, due to the steric bulk of the substituents, the second diethylzinc molecule must approach the remaining phenolic group by penetrating the hydrophobic calixarene cavity.

Further evidence to support this stepwise mechanism came from the reaction of the calixarene ligands with diphenylzinc. Treatment of **1d** with 2 equiv of Ph_2Zn in toluene resulted in the bimetallic inclusion complex **3** (Scheme 3). Due to aromatic shielding, two protons of the guest phenylzinc fragment appear in the ^1H NMR spectrum as a doublet at 5.46 ppm. Importantly, when a 1:1 mixture of Et_2Zn and Ph_2Zn was reacted with 1 equiv of **1d**, the formation of **2d** and **3** was observed along with complex **4**. Complex **4** has the external ethylzinc fragment with the phenylzinc fragment bound through the hydrophobic cavity. This coordination mode is manifested in the overlapped ^1H NMR signals of the external ethylzinc protons as well as the overlapped proton signals of the aromatic groups at 8.31 ppm in **2d** and **4**. The overlapping signal integration corresponds well with the doublet at 5.46 ppm of the internal phenylzinc. No formation of another isomer of **4**, which would have the ethylzinc guest fragment and the external phenylzinc group, was observed. The ^{13}C NMR spectrum of the reaction mixture also showed exclusively the signals of the external ethyl group. Therefore, it is likely that, in the stepwise process, the more reactive Et_2Zn occupies the easily accessible external position, leaving the remaining Et_2Zn and Ph_2Zn molecules to compete for the calixarene cavity to form **2d** and **4**, respectively.

In summary, the unusual self-assembly of organotransition-metal bimetallic calixarene inclusion complexes has been described. This transformation is strongly dependent on the steric properties of the substituent at the calixarene lower rim, with larger ones favoring the discrimination between the equivalent organometallic fragments. These findings allow the preparation of stable organometallic calixarene inclusion complex to become a *predictable* process. This predictability factor remains strikingly missing in calixarene–metal chemistry. The reactivity studies of the new complexes are currently underway.

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Supporting Information Available: Text giving experimental details for compounds **2–4** and a CIF file giving X-ray data for **2a**. The material is available free of charge via the Internet at <http://pubs.acs.org>. The CIF file is also available from the Cambridge Crystallographic Data Base as the file number CCDC-226862.

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