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Enhancement of catalytic reactivity of zinc(II) complex by a cyclotriveratrylene-capped structure

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ABSTRACT

Cyclotriveratrylene (CTV)-capped zinc(II) complex is a covalent molecular capsule that is constructed from a CTV host unit, a tris(2-aminoethylamine) (tren) ligand, and three rigid phenyl spacers. A direct comparison between CTV-capped zinc(II) complex and CTV-uncapped zinc(II) complex based on X-ray crystal structures and the hydrolysis of various activated alkyl carbonates revealed that the 23-membered cap of the complex enhanced its catalytic reactivity.

A cyclotriveratrylene-capped structure enhances the catalytic reactivity of zinc complex.

1. Introduction

Constructing an artificial cavity around the active sites of enzyme models is of fundamental importance for understanding and designing artificial catalysts [1]. Molecular capsules [2–4], which have well-defined artificial cavities, have been studied widely for the enzymatic reactions that they are involved in such as substrate recognition [5–7] and protecting reactive intermediates [8–13]. However, a few examples of molecular capsules that contain a transition metal complex within the internal space for receptors [14–17] and catalysis [18–25] have been reported.

Hemicryptophanes are covalent molecular capsules constructed from a CTV host unit and they are responsible for dissymmetry at the molecular cavity level [26–39]. We recently synthesized hemicryptophane **1** composed of a CTV, a tren ligand, and three rigid phenyl spacers, which provide an appropriate pocket within the cavity, as shown in Fig. 1 [40,41]. We also synthesized its zinc(II) complex [42–45], which contained a zinc(II) cation. The apical ligand exchange site was present within the cavity due to the rigid spacers, as can be seen by X-ray crystal structure analysis in Fig. 2. The CTV-capped $Zn(OAc)_2$·**1** was examined with regard to its ability to catalyze the hydrolysis of methyl para-nitrophenyl carbonate (MPC). A direct comparison between **1** and the uncapped $Zn(OAc)_2$·**2** using kinetic studies of MPC hydrolysis revealed that the cage structure enhanced the catalytic activity of the hydrolysis.

In this paper, we report on a direct comparison between the crystal structure of $Zn(OAc)_2$·**1** and $Zn(OAc)_2$·**2** and a study of $Zn(OAc)_2$·**1** catalyzed hydrolysis of MPC and various activated alkyl carbonate. We shed light on the catalytic reactivity of the zinc(II) complex within the cavity of the complex.

2. Materials and methods

2.1. Synthesis and X-ray crystallography

$Zn(OAc)_2$·**1** and $Zn(OAc)_2$·**2** were synthesized by using the following procedure [40]. Single crystals of $Zn(OAc)_2$·**2** were obtained by slow evaporation from a solution of chloroform. The crystallographic data and the X-ray crystal structure of $Zn(OAc)_2$·**2** are shown in Table 1 and Fig. 3, respectively. Propyl 4-nitrophenyl carbonate **4** [46], isopropyl 4-nitrophenyl carbonate **7** [47], and *tert*-butyl 4-nitrophenyl carbonate **8** [48] were synthesized by the known procedure. The other chemicals that were used in this study were reagent grade and used without further purification.

2.2. Kinetic studies

The rate constants were estimated from kinetic runs that were monitored over a one- or two-day(s) period and were determined

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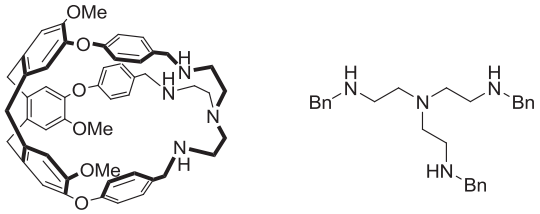


Fig. 1. Structure of hemicryptophane **1** and tris[2-(benzylamino)ethyl]amine **2**.

from the method of initial rates. All the kinetic experiments were run at least twice. The obtained rate constants were reproducible to within 10% with margins of error that were considered acceptable for the purposes of the present study. The complexation reaction of zinc ion and ligand 1 or 2 were completed within 5 min by ^{1}H NMR experiments. These reactions were examined using alkyl carbonate (51 μmol), excess *N*,*N*-diisopropylethylamine (255 μmol), D_2O (510 μmol), $Zn(X)_2$ (5.4 μmol), **1** (5.4 μmol), and DMSO-d_6 (0.60 mL). Each reaction was monitored by using ^{1}H NMR at 295 K.

3. Results and discussion

3.1. X-ray crystallography

The X-ray crystallographic analysis showed that $Zn(OAc)_2$·**2** crystallized in the triclinic space group $P\bar{1}$ and had a C_3-symmetric conformational structure. The zinc ion was surrounded by four nitrogen atoms and an acetate anion in a slightly distorted trigonal bipyramidal configuration. The three benzyl groups adopted equatorial positions to shield themselves from the acetate anion. The tertiary amine nitrogen N(1) and the acetate oxygen O(1) were located at apical positions, and the three secondary amine nitrogen atoms N(2), N(3) and N(4) were located at equatorial positions. The Zn–N average distances for the trigonal base of the pyramid were 2.105 Å. The tertiary nitrogen atom was more loosely bound to the metal ion [d(Zn(1)–N(1)) = 2.289 Å] than was the acetate anion [d(Zn(1)–O(1)) = 1.965 Å] as well as $Zn(OAc)_2$·**1** ([d(Zn(1)–N(1)) = 2.150 Å] and [d(Zn(1)–O(1)) = 1.957 Å]). The bond angle for $Zn(OAc)_2$·**2** [O(1)–Zn(1)–N(1) = 165.84°] was more wide than the bond angle for $Zn(OAc)_2$·**1** [O(1)–Zn(1)–N(1) = 151.77°] due to the caged structure of $Zn(OAc)_2$·**1**.

3.2. Kinetic studies of MPC hydrolysis

Table 2 summarizes the observed rate constants (k_{obs}) for the solvents and zinc(II) salts for the hydrolysis of MPC. The reactions were first-order reactions for MPC (Fig. 3). The hydrolysis reaction proceeded slowly in solvents such as $CDCl_3$, CD_3CN, d_6-acetone, and d_8-THF. A 1:1 mixture of $CDCl_3$ and DMSO-d_6 solvent accelerated the reaction. DMSO-d_6 solvent was the best choice for the hydrolysis probably because of the solubility of the zinc catalyst and D_2O in the solvent. Counter anion effects were examined for DMSO-d_6 solvent and the same reaction conditions. The reactions were first-order for MPC with $Zn(OTf)_2$ and $Zn(ClO_4)_2$, the same as for $Zn(OAc)_2$, and the reactions rates with ligand **1** were higher than with ligand **2**.

Kinetic studies of various alkyl carbonate hydrolysis were performed and the results are summarized in Table 3. The reaction rate of MPC **3** hydrolysis in the presence of $Zn(OAc)_2$·**1** was higher than that for $Zn(OAc)_2$·**2** (Table 3 entries 1and 2). Despite the benzyl group being bigger than the size of the cavity, the reaction rates for **4** hydrolysis in the presence of $Zn(OAc)_2$·**1** or **2** were lower than those for **5**. The benzyl and *p*- nitrophenoxy groups were bigger than the 23-membered cap over the $Zn(OAc)_2$·**1** cavity. The host–guest complexes $Zn(OAc)_2$·**1** and **3**, **4** or **5** were not detected by NMR spectroscopy at 295 K. These results indicate that no encapsulation of these alkyl groups in the cavity occurred throughout the course of the reaction. For the hydrolysis of **6** and **7** in the presence of $Zn(OAc)_2$·**1** and **2**, respectively, the reaction rates for $Zn(OAc)_2$·**1** and **2** ($k_{ligand\ 1}/k_{ligand\ 2}$) were bigger than the hydrolysis rates for **3**, **4**, and **5** (Table 3 entry 7–10). In the case of hydrolysis **8** in the presence of $Zn(OAc)_2$·**1** and **2**, the reaction rates were slower, indicating that the *t*-Bu group hindered access to the inner catalytic zinc site. The mechanism of the hydrolysis by a zinc tren complex required the active participation of zinc-coordinated water molecule [43]. DFT gas-phase structure optimization and frequency calculations were performed at the B3LYP/6-31G level of

Table 1
Crystallographic data of uncapped $Zn(OAc)_2$·**2**.

Empirical formula	$C_{124}\ H_{156}\ N_{16}\ O_{17}\ Zn_4$
Formula weight	2404.21
Crystal system	triclinic
Space group	P-1
Z	1
a (Å)	11.0746(3)
b (Å)	11.5315(3)
c (Å)	24.7665(6)
α (°)	82.1600(7)
β (°)	81.6450(7)
γ (°)	81.1200(7)
μ(MoKα) mm^{-1}	0.085
*R*1	0.0645
wR_2	0.1924
Goodness of fit (GOF) for F^2	1.055

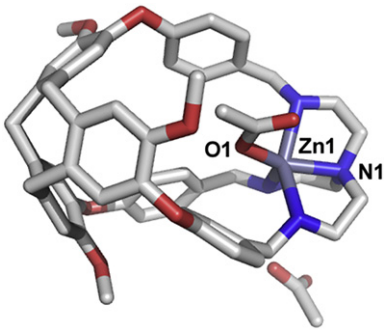


Fig. 2. X-ray crystal structure of CTV-capped (II) $Zn(OAc)_2$·**1** [40]. All the hydrogen atoms and solvents of crystallization are omitted for clarity.

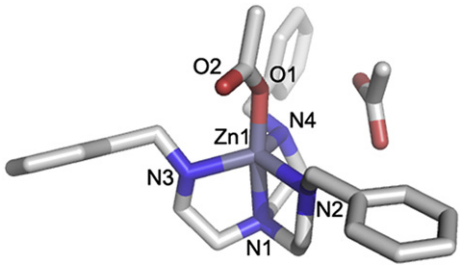
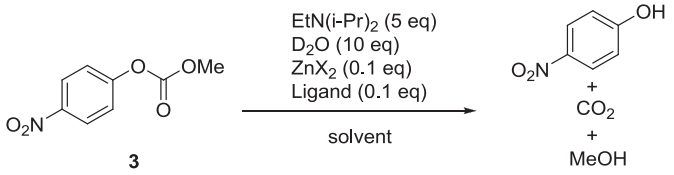


Fig. 3. X-ray crystal structure of uncapped $Zn(OAc)_2$·**2**. All the hydrogen atoms and solvents of crystallization are omitted for clarity. Selected bond lengths (Å) and angles (°): Zn(1)–N(1) 2.289(3); Zn(1)–N(2) 2.107(3); Zn(1)–N(3) 2.100(3); Zn(1)–N(4) 2.108(3); Zn(1)–O(1) 1.965(6); O(1)–Zn(1)–N(1) 165.84(18); N(1)–Zn(1)–N(2) 79.58(11); N(1)–Zn(1)–N(3) 81.03(11); and N(1)–Zn(1)–N(4) 80.71(11).

Table 2
Solvent and counter anion effects.[a]

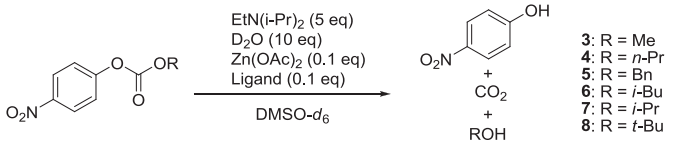


3

Entry	Ligand	X	Solvent	$k_{obs}(10^{-3}\ h^{-1})$
1	**1**	OAc	$CDCl_3$	5.1
2	**1**	OAc	CD_3CN	9.1
3	**1**	OAc	d_6-acetone	5.9
4	**1**	OAc	d_8-THF	9.9
5	**1**	OAc	$CDCl_3$ + DMSO-d_6	16
6	**1**	OAc	DMSO-d_6	35
7	**2**	OAc	DMSO-d_6	16
8	**1**	OTf	DMSO-d_6	33
9	**2**	OTf	DMSO-d_6	16
10	**1**	ClO_4	DMSO-d_6	37
11	**2**	ClO_4	DMSO-d_6	15

[a] Conditions: 85 μM MPC, 5.0 equivalents of EtN(i-Pr)$_2$, 10 equivalents of D_2O, and 0.1 equivalent of catalyst in DMSO-d_6 at 295 K.

Table 3
Zinc-catalyzed hydrolysis of various alkyl carbonates.[a]



Entry	Substrate	Ligand	$k_{obs}(10^{-3}\ h^{-1})$	$k_{ligand\ 1}/k_{ligand\ 2}$
1	**3**	**1**	35	2.2
2	**3**	**2**	16	
3	**4**	**1**	18	1.8
4	**4**	**2**	10	
5	**5**	**1**	27	1.8
6	**5**	**2**	15	
7	**6**	**1**	6.2	2.6
8	**6**	**2**	2.4	
9	**7**	**1**	9.2	3.5
10	**7**	**2**	2.6	
11	**8**	**1**	4.4	0.8
12	**8**	**2**	5.4	

[a] Conditions: 85 μM substrate, 5.0 equivalents EtN(i-Pr)$_2$, 10 equivalents D_2O and 0.1 equivalent catalyst in DMSO-d_6 at 295 K.

theory [49]. The optimized structure of $[ZnOH_2\cdot\mathbf{1}]^{2+}$ is shown in Fig. 4. The structure indicates that the coordinated water molecule exists within the cavity. These results show that the higher catalytic reactivity of $Zn(OAc)_2\cdot\mathbf{1}$ is due to not only a proximity effect owing to substrate encapsulation within the cavity but also control of solvent access owing to the inhibition of DMSO coordination with the zinc complex in the cavity. We reported recently on CTV-capped azaphosphatrane where the reactivity of its endohedral proton was highly suppressed as a result of being protected by the CTV-capped structure [50]. These differences in reactivity within the cavity caused difference in covalent P–N bonds and coordinate Zn–N bonds and difference in the size of the phosphorous atom and zinc ion, respectively.

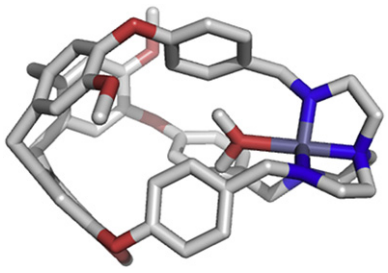


Fig. 4. Optimized structure of $[ZnOH_2\cdot\mathbf{1}]^{2+}$; hydrogen atoms of **1** were omitted for clarity.

4. Conclusions

In this paper, we reported a direct comparison of the crystal structures of **1** and **2**, and hydrolysis reactions of various activated alkyl carbonates that were catalyzed by **1**. Kinetic studies on MPC hydrolysis catalyzed by **1** and **2** were also performed. A direct comparison between **1** and **2** revealed that the 23-membered cap enhanced the catalytic activity.

Acknowledgments

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Appendix. Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2012.01.006.

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