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Introduction

Metal-organic polyhedrons (MOPs), discrete molecular architectures constructed through the coordination of metal ions and organic linkers, have attracted considerable attention due to their high symmetry, stability and rich chemical/physical properties.^{1,2} Driven by the ultimate goal of enzyme mimetics, their applications in the reactivity modulation of bound guests, molecular recognition and catalysis are rife with allusions and direct comparisons to natural enzymes.^{3,4} The MOPs have shown excellent advantages in the rational building of microenvironments isolated from bulk solution, with size and shape-selective recognition of the substrate.⁵ Although the constructing strategy of MOPs with controllable configurations has been well established,⁶ a few "artificial enzymes" have achieved the levels of catalysis of natural enzymes. The challenge in this field remains the introduction of more kinds of guest-accessible sites into the well-defined cavity of the molecular flasks to expand their application in molecular recognition and catalysis.7

Cerium-based M₄L₄ tetrahedrons containing hydrogen bond groups as functional molecular flasks for selective reaction prompting⁺

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The application of metal-organic polyhedrons as "molecular flasks" has resulted in a surge of interest in the reactivity and properties of molecules within their well-defined cavity. Inspired by the structures of the natural enzymatic pockets, two neutral metal-organic tetrahedrons, Ce-**TBMN** and Ce-**TBAS**, were achieved *via* self-assembly by incorporating triamine-triazine and amide groups as hydrogen bond sites into the fragments of the ligands respectively. Both of them could act as molecular flasks to prompt the Knoevenagel condensation reactions of salicylaldehyde derivatives and cyanosilylation reactions of aromatic aldehydes. Experiments of catalysts with different cavity radii and substrates with different sizes and shapes, as well as competitive experiments using nonreactive guests as inhibitors demonstrated that the tetrahedrons exhibited enzymatically catalytic behavior and the catalytic reactions occurred in the "molecular flasks". Control experiments with the **H**₆**TMBN** or **H**₆**TBAS** ligands themselves as the catalyst in the Knoevenagel condensation were carried out under the same conditions. For the smaller substrates, their conversions catalyzed by the ligands were significantly lower than those catalyzed by Ce-**TBMN** or Ce-**TBAS**, respectively, suggesting that metal-organic polyhedrons could effectively fix multi hydrogen bond groups to avoid the "self-quenching" effect, enhancing the catalytic activity of the multi-hydrogen bond groups in the homogeneous state.

On the other hand, homogeneous hydrogen bond-donating catalysis has emerged as a biomimetic alternative to Lewis acid activation in excellent yield and selectivity.^{8,9} However, the competency of H-bond donors presenting in these catalysts was often significantly attenuated as a result of "self-quenching" through the hydrogen bonding of catalyst molecules to each other.¹⁰ Consequently, if these catalytically active sites were incorporated into a defined environment with a larger cavity, the self-quenching might be avoided.¹¹

We have reported the assembly of Werner-type capsules containing amide groups as multiple hydrogen bonding trigger sites for the selective recognition of biomolecules.¹² The incorporation of amide groups as guest-accessible sites within the metal–organic cages is a powerful approach to achieve functional flasks for prompting several important reactions, because the amide group possesses two types of hydrogen bonding sites¹³ and can act as a base-type catalytic driving force.¹⁴ However, in the homogeneous state, simple molecule catalysts containing amide groups may not show excellent catalytic behavior due to the self-quenching effect.¹⁵ We reasoned that fixing multi-hydrogen bonding catalytic groups into MOPs containing inner cavities with rigid conformation might lead to a new class of materials with significant potential.

To enrich the hydrogen bonding catalytic activity of the MOPs, through the construction strategy we have established,



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here we introduced a functional group, triamine-triazine (melamine), which has showed interesting multi-hydrogen bonding formation properties¹⁶ in Ce-based molecular tetrahedron Ce-**TBMN**-containing amide groups. Additionally, the catalytic behavior of the Ce-**TBAS** molecular tetrahedron containing two types of amide groups with different sizes was also investigated. The catalytic behavior of the two molecular tetrahedrons containing many hydrogen bonded groups was examined with several aldehyde substrates of various sizes and shapes. The tetrahedrons showed interesting enzymatically catalytic behavior in the chemical transformations of the Knoevenagel condensation reaction of salicylaldehyde derivatives and the cyanosilylation reactions of aromatic aldehydes.

Results and discussion

Structural study of the tetrahedrons

The ligand H₆TBMN was easily synthesized through the Schiff base reaction of 4,4',4"-(1,3,5-triazine-2,4,6-triyl)tris(azanediyl)tribenzohydrazide and 2-hydroxy-1-naphthaldehyde in ethanol solution. Mixing the ligand H₆TBMN and Ce(NO₃)₃·6H₂O in DMF solution gave black solid Ce-TBMN in a yield of 78%. Single crystal X-ray structural analysis revealed the formation of a face-driven molecular tetrahedron Ce-TBMN with four cerium ions on the vertex and the four ligands on the face (Scheme 1). The compound was crystallized in the C2 space group. The tetrahedral cage exhibited a 2-fold axial symmetry with two cerium ions and two ligands presented in an unsymmetrical unit. Each cerium was nine-coordinated to three ligands as found in the similar Ce-based polyhedron.¹⁷ The average Ce-O (amide), Ce-N (amide) and Ce-O (phenyl) distances were 2.42, 2.62 and 2.21 Å respectively, within the normal ranges reported in the literature.¹⁸ The edge Ce...Ce separations were about 18.0 Å and the inner volume of the tetrahedron was 630 Å³ with the opening size of the windows on the edge being about 18.0 imes7.6 $Å^2$, allowing the substrate molecules of suitable size to ingress and egress through the opening to interact with the active sites of the tetrahedron. Each triamine-triazine moiety was sited on the centre of each face, with three NH groups being fixed in a C_3 symmetrical configuration. In total, 12 NH groups and 12 coordinated amide groups in the tetrahedron cage could act as hydrogen bond active sites. The complementary hydrogen bonding and the potential stacking interaction, in cooperation with the spatial effects of the tetrahedron nanocage, will benefit the enzymatically catalytic behavior to specific reactions. One DMF solvent molecule was encapsulated in the cage and several DMF solvent molecules were found outside of the cage, while neither the triamine-triazine groups nor the amide groups were found to form any hydrogen bonds with each other or with the solvent molecules. It could be anticipated that these groups could act as guest-binding sites to activate corresponding substrates. The electrospray ionization mass spectrometry (ESI-MS) data of Ce-TBMN (DMF solution) in the presence of KOH exhibited an intense peak at m/z 1136.46 and a moderate peak at m/z 1515.59, which can be assigned to the negative



Scheme 1 Structures of the M_4L_4 tetrahedrons Ce-TBMN, Ce-TBAS and Ce-TBBS, as well as their constitutive/constructional fragments. The cerium, nitrogen, oxygen and carbon atoms are represented by green, blue, red and grey, respectively. Hydrogen atoms and solvent molecules are omitted for clarity. Average bond distances (Å): Ce-TBMN: Ce-O (amide) 2.42, Ce-N (amide) 2.62 and Ce-O (phenyl) 2.21; Ce-TBAS: Ce-O (amide) 2.40, Ce-N (amide) 2.66 and Ce-O (phenyl) 2.20; Ce-TBBS: Ce-O (amide) 2.42, Ce-N (amide) 2.70 and Ce-O (phenyl) 2.20.

charged species $[(Ce-TBMN-5H)+K]^{4-}$ and $[(Ce-TBMN-4H)+K]^{3-}$, demonstrating that the compound Ce-TBMN is substantially stable in solution.

The tetrahedron cage Ce-TBAS was synthesized according to the literature method.^{17a} The structure of Ce-TBAS is similar to that of Ce-TBMN. For Ce-TBAS, the four triamine-triazine moieties were displaced by four 1,3,5-triamide benzene moieties. The Ce---Ce separation of the tetrahedron is ca. 21.0 Å, and the inner volume is about 1000 Å³, with the opening size is about 21.0 \times 11.1 Å², which are all larger than those of Ce-TBMN. In total, 12 uncoordinated and 12 coordinated amide groups sited on the faces of the tetrahedron also did not form any hydrogen bonds with the solvent molecule or with each other. The different kinds of amide groups ensure the ability of the tetrahedron to be applied in various catalytic applications. The ESI-MS of Ce-TBAS exhibited an intense peak at m/z = 1057.41 which is assigned to the [Ce-TBAS-4H]⁴⁻ species, revealing the stability of the M4L4 tetrahedron in the solution.

	Ce-TBMN	Ce- TBAS ^a	Ce-TBBS
Formula	$Ce_4(C_{228}H_{156}N_{48}O_{24})\cdot9C_3H_7NO \cdot CH_3OH\cdot8H_2O$	Ce ₄ (C ₅₁ H ₃₅ N ₉ O ₉) ₄ ·8C ₃ H ₇ NO· 9CH ₃ OH·7H ₂ O	$\begin{array}{c} Ce_4(C_{144}H_{100}N_{24}O_{24})\cdot9C_3H_7NO\cdot\\ CH_3OH\cdot2H_2O \end{array}$
Formula weight	5346.52	5231.26	3836.90
T/K	200(2)	200(2)	200(2)
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	C2	Fddd	C2/c
a/Å	42.6162(16)	18.303(4)	29.074(4)
b/Å	23.0136(9)	46.917(11)	22.851(3)
c/Å	21.8331(8)	91.25(2)	33.440(6)
β (°)	117.460(2)	_	112.605(2)
$V/Å^3$	19000.3(12)	78 360(32)	20 510(5)
Ζ	2	8	4
$D_{\rm c}/{\rm g~cm^{-1}}$	0.935	0.887	1.243
μ/mm^{-1}	0.526	0.511	0.942
F(000)	5484	21 504	7816
Flack parameter	0.595(13)	_	_
No. ref. measured	50 323	62 007	49704
No. unique ref.	29 828	12729	18 005
R _{int}	0.0893	0.1247	0.0632
$R_1[I > 2\sigma(I)]$	0.0694	0.0959	0.0593
wR_2 (all data)	0.1610	0.2497	0.1832
Goodness of fit	1.024	0.953	1.044
CCDC ref.	973898	987459	973899
$R_1 = \Sigma F_0 - F_c / \Sigma F_0 \cdot \mathbf{w} R_2 =$	$= [\Sigma w (F_o^2 - F_c^2)^2 / \Sigma (F_o)^2]^{1/2}$. ^{<i>a</i>} The crystal data	of Ce-TBAS has been reported previously,	^{17<i>a</i>} the CCDC ref. code is 987459.

Table 1 Crystallographic data of compounds Ce-TBMN, Ce-TBAS and Ce-TBBS

The Ce-based tetrahedron analogue Ce-**TBBS** was obtained by mixing a smaller ligand **H**₆**TBBS** and Ce(NO₃)₃·6H₂O in DMF solution with a yield of 53%. Compared to the former two ligands, there is only one benzene group inserted into one of the three arms of the central benzene ring of ligand **H**₆**TBBS**. The compound was crystallized in the *C*2/*c* space group. In the molecular tetrahedron of Ce-**TBBS**, the Ce···Ce distance in the long edges was 13.5 Å and in the short edges was 11.4 Å, and the inner volume and the opening size of the tetrahedron were quite a bit smaller than the two cages mentioned above. The crystallographic data of each compound were listed in Table 1. The ESI-MS of Ce-**TBAS** also revealed its stability in DMF solution with the intense peak at m/z = 1034.22 assigned to the [Ce-**TBBS**–3H]^{3–} species.

Catalytic study of Knoevenagel condensation

The triamine–triazine moieties of Ce-**TBMN** and free amide groups of Ce-**TBAS** could act as basic catalysis sites to promote the Knoevenagel condensation reaction that requires the formation of an active methylene anion under weak base-catalyzed conditions.¹⁹ Firstly, the recognition of Ce-**TBMN** to the various salicylaldehyde substrates was investigated. As shown in Fig. 1 (above), the emission intensity of Ce-**TBMN** exhibited about a 25-times enhancement when *o*-Vanillin (5×10^{-4} M) was added into the solution. The Hill-plot profile²⁰ of the fluorescence titration curves at 478 nm demonstrated the 1:1 stoichiometric host–guest complexation behavior, with the association constant (log K_{ass}) calculated as 4.08 ± 0.06. The addition of other aldehydes (4-benzoxyl-salicylaldehyde (**BOS**) or 4-*N*,*N'*-dimethylsalicylaldehyde (**NMS**), listed in Table 2) gave association constants (log K_{ass}) of 3.51 and 3.44 respectively.

Under the conditions of Ce-**TBMN** (2 mol%), *o*-Vanillin (0.08 M) and cyanoacetonitrile (0.20 M) in 2 mL DMF–benzene (v/v = 1:99)



Fig. 1 Top: spectra of compound Ce-**TBMN** (5×10^{-6} M) in DMF solution upon the addition of a standard solution of *o*-Vanillin. The inset exhibits the responses of Ce-**TBMN** to other aldehydes for the Knoevenagel condensation. The samples were excited at 385 nm and the emission intensities were recorded at 478 nm. Bottom: time dependence of the integral area (IA) ratio variations of the reaction of *o*-Vanillin catalyzed by Ce-**TBMN** based on ¹H NMR detection in DMF-CDCl₃. IA_P and IA_R represent the NMR integral areas at 4.32 ppm and 9.83 ppm respectively.

solution stirred at room temperature, the *o*-Vanillin almost completely reacted after 3 hours. As shown in Table 2, under the same conditions, when the size of the salicylaldehyde derivatives increased, the relative conversion of the Knoevenagel condensation of malononitrile decreased significantly. The conversions of

Table 2 Results for the Knoevenagel condensation reaction catalyzed by various catalysts

		$R_{1} \sim CN \xrightarrow{Ce-base MOP_{S}} (1) \sim R_{1} \qquad R_{1} \rightarrow R_{1} \rightarrow R_{1} \rightarrow R_{2} \xrightarrow{Ce-base MOP_{S}} (1) \rightarrow R_{0} \rightarrow R_{1} \rightarrow R$,
			Conversion (%)					
Entry	Substrates		Ce-TBMN	Ce - TBMN + G^a	H ₆ TBMN	Ce-TBAS	Ce - TBAS + Suc^b	H ₆ TBAS
1		NC^CN	>95	55	28	>95	39	24
2	ССОНО	NC^CN	43	24	26	54	31	19
3		NC^CN	15	11	22	17	13	18
4		NC^CN	13	9.4	20	14	10	15
5	ОН	NC TO~	25	15	26	34	18	23
6		\sim γ γ γ \sim	19	13	25	27	16	20

Reaction conditions: cyanoacetonitrile (0.20 M), aldehyde (0.08 M), M_4L_4 tetrahedron (1.6 mM)/ligand(6.4 mM) at room temperature under N_2 for 3 hours in 2 mL DMF-benzene (v/v = 1:99) solution. ^{*a*} The value is the related conversion of the respective reaction in the presence of guanosine (0.16 M) as the inhibitor. ^{*b*} The value is the related conversion of the respective reaction in the presence of sucrose (0.16 M) as the inhibitor.

ethyl cyanoacetate and diethyl malonate with *o*-Vanillin were about 25% and 19%, respectively. Despite there being many factors influencing the conversion of the reactions, the sizeselective catalytic properties as well as the same sequence of the reactivity and the response efficiency partly demonstrated that the recognition process seems to be an important step for these reactions.

The special microenvironment of the tetrahedron nanocage will benefit the enzymatically catalytic behavior. The reactions were monitored by a ¹H NMR tracing process. The product formation was pseudo-zeroth-order with the rate constant being 0.6 M h^{-1} (bottom of Fig. 1, black line), in the case of the reaction of o-Vanillin with high concentration (0.40 M). With the concentration decreased to 0.04 M, the dependence of the rate on the substrate concentration tended to the first order (bottom of Fig. 1, green line), and the combined kinetic data followed the overall rate law: kinetic rate = k_2 [guest \subset Ce-**TBMN**]. The kinetic rate of reaction depends on the concentration of the host-guest complexation species rather than the total concentration of the substrate, suggesting that the substrate and "enzyme" participated in a reversible equilibrium with an enzyme/complex.²¹ The catalysis behavior is described in the Michaelis-Menten mechanism in which substrate binding is the first equilibrium prior to the rate-limiting step of the reaction.²²

Although it could not be proved conclusively that the catalyzed reactions were displayed within the cavities of the tetrahedron Ce-**TBMN**, the size-selective catalytic properties and the kinetic study of the catalytic reactions all supported this hypothesis. To further validate whether the catalytic behavior either occurred within the cavity of Ce-**TBMN** or was just

displayed through a normal homogeneous system, the inhibition of the catalytic reaction was displayed through the addition of a nonreactive species. In this case, the biomolecule guanosine with the associate constant ($\log K_{ass}$) of 5.78 was chosen as the inhibitor for this enzymatic system. As expected, in the presence of 0.16 M of guanosine, the catalytic action by Ce-**TBMN** decreased significantly. These results gave further proof that Ce-**TBMN** is an interesting molecular flask, within which the salicylaldehyde substrates were activated.

The size-selective effect of the Knoevenagel condensation reaction was also exhibited by Ce-TBAS. The association constants $(\log K_{ass})$ of the salicylaldehyde derivatives calculated by fluorescence titration were 4.77, 3.59 and 3.45 for o-Vanillin, BOS and NMS respectively. Under the same conditions as Ce-TBMN, o-Vanillin and cyanoacetonitrile almost completely reacted in 3 hours. As shown in Table 2, the conversion of the larger salicylaldehyde derivatives with malononitrile catalyzed by Ce-TBAS also decreased significantly. The conversion of the corresponding entries were higher than those catalyzed by Ce-TBMN, suggesting the better sizesuitability of Ce-TBAS with larger windows and inner space for the larger substrates. In addition, the conversion of 4-(benzyloxy)salicylaldehyde in the two cases are both low, indicating that the size of this substrate excesses the encapsulation ability of both two cages. The inhibition experiments of the related reactions in Ce-TBAS were also carried out by using sucrose, which was found to be well encapsulated by Ce-TBAS in our previous study,^{17a} as the inhibitor. In the presence of 0.16 M sucrose, the catalytic action of Ce-TBAS decreased significantly.

Control experiments with the ligands H₆TMBN or H₆TBAS themselves as the catalyst were carried out under the same conditions. For the small substrates *o*-Vanillin and 1-hydroxyl-2-napthylaldehyde, the conversions were significantly lower than those catalyzed by Ce-**TBMN** and Ce-**TBAS** respectively. The results suggest that for the free ligand, their triamine–triazine and amide groups might form intermolecular hydrogen bonding among themselves, deceasing their catalytic efficiency, and the fixation of these multi-hydrogen bond moieties into the rigid MOPs is a promising way to avoid self-quenching in the homogeneous state. Meanwhile, for the other substrates with larger size, the conversions were a little higher than those catalyzed by the tetrahedron cage. In all the cases, there was no significant difference in the conversion between each entry, also supporting that the reaction occurred within the cavity of the tetrahedron. We also checked that no reaction occurred with Ce(NO₃)₂·6H₂O as the catalyst.

Catalytic study of the cyanosilylation reaction

The similar Ce-based tetrahedron reported previously in our group has shown good activity in promoting the cyanosilylation reaction,²³ a convenient route to cyanohydrins which are key derivatives in the synthesis of fine chemicals and pharmaceuticals.²⁴ The recognition between Ce-**TBMN** and the various nitrobenzaldehyde substrates for the cyanosilylation was investigated. As shown in Fig. 2 (top), the emission intensity of Ce-**TBMN** exhibited about a 1.7 times enhancement when 2-nitrobenzaldehyde (2-**NBA**, 2×10^{-4} M) was added into the solution. The Hill-plot profile of the fluorescence titration curves at 478 nm demonstrated the 1:1 stoichiometric host-guest



Fig. 2 Top: the luminescence response of compound Ce-TBMN (red column) and Ce-TBAS (blue column) in DMF solution upon the addition of a standard solution of various nitrobenzaldehydes. The samples were excited at 385 nm and the emission intensities were recorded at 478 nm. Bottom: time dependence of the integral area (IA) ratio variations of the reaction of 2-nitrobenzaldehyde catalyzed by Ce-TBMN, based on ¹H NMR detection in DMF-CDCl₃. IA_P and IA_R represent the NMR integral areas at 6.22 ppm and 10.42 ppm, respectively.

complexation behavior, with the association constant $(\log K_{ass})$ calculated as 4.17 \pm 0.24. The addition of other aldehydes (3-NBA and 4-NBA) led to a 1.35 or 1.33 times fluorescence enhancement of the solution, with the association constants $(\log K_{ass})$ calculated as 3.95 and 3.68, respectively. Compared with the Ce-based tetrahedron Ce-TTS which exhibited a luminescence decrease towards the corresponding aldehydes due to the photoinduced electron transfer from its triphenylamine moiety to the guest molecules,^{13b} the different luminescence enhancement recognition occurring for Ce-TBMN should be attributed to the formation of hydrogen bonding between the guests and the NH groups, which blocks the PET process from the NH groups to the naphthyl moieties in Ce-TBMN. The strongest association constant for 2-NBA might be due to the formation of multi-hydrogen bonds between the o-position nitrobenzaldehyde and the NH donor. The recognition between the Ce-TBAS and the other nitrobenzaldehyde substrates was also investigated. The association constants ($\log K_{ass}$) of 2-, 3-, and 4-NBA calculated by fluorescence titration were 3.99, 4.13 and 4.36 respectively. The different recognition sequence compared with that of Ce-TBMN might be due to the free amide groups being sited in a more steric hindrance microenvironment in the cavity of Ce-TBAS, and hence were more difficult to interact with o- and m-nitrobenzaldehyde to form the hydrogen bond.

Under the conditions of Ce-TBMN (2 mol%), 2-nitrobenzaldehyde (0.08 M) and (CH₃)₃SiCN (0.20 M) in 2 mL DMF- $CHCl_3$ (v/v = 1:99) solution stirred at room temperature, the 2-nitrobenzaldehyde almost completely reacted after 1 hour. Also, the loading of 2 mol% Ce-TBMN led to more than 80% conversion for various nitrobenzaldehydes. The substrate 1-naphthyl-aldehyde and 4-hydroxy-1-naphthaldehyde with larger size gave lower conversions of about 63% and 38% respectively under the same conditions. The product formation was pseudozeroth-order with the rate constant being 2.4 M h^{-1} (bottom of Fig. 2, black line), in the case of the reaction of 2-NBA with high concentration (0.40 M). With the concentration decreased to 0.04 M, the dependence of the rate on the substrate concentration tended to be first-order. Similarly, in the presence of 0.16 M of guanosine, the catalytic action of Ce-TBMN decreased significantly. The competitive inhibition behavior suggested that the catalytic action also occurred within the cavity of Ce-TBMN.

For the related cyanosilylations catalyzed by Ce-**TBAS**, as shown in Table 3, under the same reaction conditions as Ce-**TBMN**, the conversion of the various nitrobenzaldehydes was also high after 1 hour, but the sequence is different. In this case, the conversion rate of 2-NBA is lower than that of 3- and 4-NBA. The different sequence of the conversion rate in the related entries compared with those in the case of Ce-**TBMN**, as well as the same sequence of the reactivity and the response efficiency in both of the two systems, suggested that substrate binding is the first step in these catalytic reactions. The conversion rate of 1-naphthyl-aldehyde was about 65%, which was similar to that catalyzed by Ce-**TBMN**. Meanwhile, the conversion rate of 4-hydroxy-1-naphthaldehyde was 50%, higher than that by Ce-**TBMN**, suggesting the better size-suitability of the

Table 3 Results of the cyanosilylation reaction catalyzed by various catalysts

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		Ar H +	(CH ₃) ₃ SiCNCe-bas	Se MOP _S Ar CN		
		Conversion (%)				
Entry	Substrates	Ce- TBMN $(\log K_{ass})$	Ce - TBMN + G^a	Ce- TBAS $(\log K_{ass})$	$Ce-TBAS + Suc^b$	Ce-TBBS
1	NO ₂	> 97 (4.17 ± 0.24)	66	$89~(3.99\pm 0.22)$	53	72
2		$>$ 97 (3.95 \pm 0.16)	63	$>$ 97 (4.13 \pm 0.18)	59	67
3		$89~(3.68\pm0.17)$	54	$>$ 97 (4.36 \pm 0.19)	57	74
4	СНО	63	28	65	31	52
5	СНО	38	18	50	22	31

Reaction conditions: $(CH_3)_3SiCN$ (0.20 M), aldehyde (0.08 M), M_4L_4 tetrahedron (1.6 mM) at room temperature under N_2 for 1 hour in 2 mL DMF-CHCl₃ (v/v = 1:99) solution. ^{*a*} The value is the related conversion of the respective reaction in the presence of guanosine (0.16 M) as the inhibitor. ^{*b*} The value is the related conversion of the respective reaction in the presence of sucrose (0.16 M) as the inhibitor.

larger cavity of Ce-**TBAS** towards the larger substrate. Additionally, in the presence of 0.16 M sucrose, the cyanosilylation catalytic action of the Ce-**TBAS** system decreased significantly.

To further validate the size and shape-selectivity of the MOPs, the related catalytic actions by the reference tetrahedron Ce-**TBBS** were investigated. Compared with the Ce-**TBMN** and Ce-**TBAS**, Ce-**TBBS** has a smaller inner cavity and opening size, and no free hydrogen bond sites on the face. Under the same conditions, the loading of 2 mol% Ce-**TBBS** led to no more than an 80% conversion rate for the nitrobenzaldehydes. In this case, the 3-NBA gave the lowest conversion rate among the three nitrobenzaldehydes, possibly due to the *m*-position nitrobenzaldehyde being more difficult to pass through the small window of the Ce-**TBBS** (approximate two dimensional sizes calculated from Chem 3D: 2-NBA, 4.46 Å × 4.72 Å; 3-NBA 6.50 Å × 5.17 Å; 4-NBA, 6.67 Å × 4.32 Å). All of the experimental results strongly suggest that the catalytic reactions occurred within the inner cavities of the tetrahedral cages.

Conclusions

In summary, we reported the achievement of Ce-based molecular tetrahedrons Ce-**TBMN** and Ce-**TBAS** containing multi-hydrogen bond active sites. The tetrahedrons with different size windows and cavities could work as efficient molecular flasks to selectively prompt the Knoevenagel condensation reaction of salicylaldehyde derivatives and cyanosilylation reactions of aromatic aldehydes. The catalysts exhibited typical enzymatically catalytic behavior: the reactions took place within the molecular flasks, not in a normal homogeneous manner. Additionally, the multihydrogen bond groups could be fixed in the rigid MOPs to avoid the "self-quenching" between themselves, enhancing their catalytic ability in the homogeneous state.

Experimental

Materials

All chemicals were of reagent grade quality, obtained from commercial sources and used without further purification. The elemental analyses of C, H and N were performed on a Vario EL III elemental analyzer. ¹H NMR spectra were measured on a Bruker 400 M spectrometer. ESI mass spectra were carried out on a HPLC-Q-TOF MS spectrometer using CH₃CN as the mobile phase.

General spectroscopic methods

Solution fluorescence titration spectra and selectivity experiments were checked using an EDINBURGH FS920 luminescence spectrometer. Stock solutions $(1.0 \times 10^{-2} \text{ M})$ of the substrate were prepared. High concentrations of the stock solutions of Ce-**TBMN** and Ce-**TBAS** (1.0 mM) were prepared in DMF. Before the spectroscopic measurements, the solution was freshly prepared by diluting the high concentration stock solution into the corresponding solution. For all the titration experiments, spectra were recorded 3 min after adding the substrate to ensure complete equilibrium. The excitation and emission slit widths were modified to adjust the luminescence intensity to a suitable range. All the spectroscopic measurements were performed at least in triplicate and averaged.

Trimethyl-4,4',4''-(1,3,5-triazine-2,4,6-triyl)tris(azanediyl)tribenzoate²⁵. Cyanuric chloride (0.92 g, 5.0 mmol) was added in one portion to a stirred solution of methyl 4-aminobenzoate (2.5 g, 17 mmol) in 75 mL of glacial acetic acid (AcOH), and the

mixture was heated (30 min, steam bath (100 °C)). The products precipitated from solution as white solids and were recovered by filtration. The solid products were washed with boiling water (approximately 20 mL × 3) to neutral pH and dried in vacuum. Yield: 2.4 g, 91%. ¹H NMR (400 MHz, DMSO-*d*₆, ppm): δ 9.89 (s, 3H_{-NH}-), 8.01 (d, *J* = 8.4 Hz, 6H_{Ar}-H), 7.93 (d, *J* = 8.8 Hz, 6H_{Ar}-H), 3.85 (s, 9H_{-CH}).

4,4',4"-(1,3,5-Triazine-2,4,6-triyl)tris(azanediyl)tribenzohydrazide. A mixture solution of 80% hydrazine hydrate (0.15 L) and trimethyl 4,4',4"-(1,3,5-triazine-2,4,6-triyl)tris(azanediyl)-tribenzoate (1.9 g, 3.5 mmol) was stirred for 24 h at boiling temperature. A white precipitate was formed, which was collected by filtration, washed with methanol and dried in vacuum. Yield: 1.6 g, 85%. ¹H NMR (400 MHz, DMSO-*d*₆, ppm): δ 9.64 (s, 3H_{-NH-N}), 9.63 (s, 3H_{-NH-}), 7.91 (d, *J* = 8.0 Hz, 6H_{Ar-H}), 7.81 (d, *J* = 8.4 Hz, 6H_{Ar-H}), 4.43 (s, 6H_{-NH}).

H₆**TBMN.** A mixture solution of 4,4',4''-(1,3,5-triazine-2,4,6-triyl)tris(azanediyl)tribenzohydrazide (0.81 g, 1.5 mmol) and 2-hydroxy-1-naphthaldehyde (0.87 g, 5.0 mmol) in ethanol (0.10 mL) was stirred for 24 h at boiling temperature. A brown precipitate was formed, which was collected by filtration, washed with methanol and dried in vacuum. Yield: 1.3 g, 85%. Anal calc. for C₅₇H₄₂N₁₂O₆·H₂O: H 4.40, C 67.85, N 16.66%. Found: H 4.45, C 67.79, N 16.63%. ¹H NMR (400 MHz, DMSO-*d*₆, ppm): δ 12.86 (s, 3H₁₂), 12.14 (s, 3H₄), 9.89 (s, 3H₁), 9.51 (s, 3H₅), 8.22 (d, *J* = 8.8 Hz, 3H₁₀), 8.11 (d, *J* = 8.4 Hz, 6H₃), 8.03 (d, *J* = 8.4 Hz, 6H₂), 7.94 (d, 6H₁₁), 7.91 (d, *m*, 6H₈), 7.61 (t, *J* = 7.6 Hz, 3H₇), 7.42 (t, *J* = 7.4 Hz, 3H₉), 7.25 (d, *J* = 9.2 Hz, 3H₆). ¹³C NMR (400 MHz, DMSO-*d*₆, ppm): δ 206.95 (d), 164.49 (a), 162.57 (l), 158.40 (o), 146.73 (e), 143.96 (n), 133.04 (g), 132.06 (m), 129.44 (c), 128.85 (i), 128.27 (g), 128.17 (f), 126.19 (p), 123.96 (h), 121.00 (k), 119.84 (b), 119.39 (q).

Ce-TBMN. A solution of Ce(NO₃)₃·6H₂O (44 mg, 0.10 mmol), ligand **H**₆**TBMN** (99 mg, 0.10 mmol) and NaOAc (25 mg, 0.30 mmol) in DMF (10 mL) was stirred for 2 h at room temperature. Then the solution was left for two weeks at room temperature to give X-ray-quality black block crystals. Yield: about 78% (based on the crystals washed with methanol and dried in vacuum). Anal calc. for Ce₄C₂₂₈H₁₅₆N₄₈O₂₄·4C₃H₇NO: H 3.86, C 59.99, N 15.16%. Found: H 4.10, C 58.94, N 14.92%.

1,1'-**Biphenyl-3,4**',**5**-**tricarbohydrazide.** A mixture solution of 80% hydrazine hydrate (12 g, 0.18 mmol), trimethyl-1,1'biphenyl-3,4',5-tricarboxylate (0.98 g, 3.0 mmol) and methanol (0.10 L) was stirred for 12 h at boiling temperature. A white precipitate was formed, which was collected by filtration, washed with methanol and dried in vacuum. Yield: 0.86 g, 88%. ¹H NMR (400 MHz, DMSO-*d*₆, ppm): δ 9.98 (s, 2H_{-NH-N}), 9.87 (s, 1H_{-NH-N}), 8.29 (s, 1H_{Ar-H}), 8.27 (s, 2H_{Ar-H}), 7.98 (d, *J* = 8.0 Hz, 2H_{Ar-H}), 7.92 (d, *J* = 8.0 Hz, 2H_{Ar-H}), 4.59 (s, 6H_{-NH}).

H₆**TBBS.** A mixture solution of 1,1'-biphenyl-3,4',5-tricarbohydrazide (0.66 g, 2.0 mmol) and 2-hydroxybenz-1-aldehyde (0.81 g, 6.6 mmol) in methanol (0.10 mL) was stirred for 12 h at boiling temperature. A white precipitate was formed, which was collected by filtration, washed with methanol and dried in vacuum. Yield: 1.2 g, 93%. Anal calc. for C₃₆H₂₈N₆O₆·2H₂O: H 4.77, C 63.90, N 12.42%. Found: H 4.71, C 67.82, N 12.45%. ¹H NMR (400 MHz, DMSO-*d*₆, ppm): δ 12.36 (s, 2H₁₈), 12.24 (s, 1H₁₁), 11.29 (s, 1H₅), 11.19 (s, 2H₁₂), 8.73 (s, 2H₁₃), 8.71 (s, 1H₆), 8.56 (s, 1H₁), 8.52 (s, 2H₂), 8.18 (d, J = 8.0 Hz, 2H₄), 8.09 (d, J = 8.0 Hz, 2H₃), 7.60 (3H_{7,14}), 7.33 (3H_{9,16}), 6.95 (6H_{7,10,15,17}). ¹³C NMR (400 MHz, DMSO- d_6 , ppm): δ 162.82 (k,s), 162.50 (q,z), 157.98 (l,t), 149.10 (f,b), 149.00 (j), 142.44 (g), 140.16 (d), 134.59 (e,c), 132.81 (m), 132.03 (v), 131.90 (k,i), 130.02 (l,h), 129.82 (o), 129.64 (x), 128.99 (a), 127.70 (n), 127.41 (w), 119.86 (r), 119.82 (u), 119.22 (p), 119.16 (y).

Ce-TBBS. A solution of Ce(NO₃)₃·6H₂O (44 mg, 0.10 mmol), ligand H₆TBBS (64 mg, 0.10 mmol) and NaOAc (25 mg, 0.30 mmol) in DMF (10 mL) was stirred for 2 h at room temperature. Then the solution was left for two weeks at room temperature to give X-rayquality black block crystals. Yield: about 53% (based on the crystals washed with methanol and dried in vacuum). Anal calc. for Ce₄C₁₄₄H₁₀₀N₂₄O₂₄·5C₃H₇NO: H 3.91 C 54.93 N 11.68%. Found: H 4.12, C 55.36, N 11.20%.

Crystallography

The intensities of Ce-TBMN and Ce-TBBS were collected on a Bruker SMART APEX CCD diffractometer with graphite monochromated Mo-K α radiation (λ = 0.71073 Å) using the SMART and SAINT programs.²⁶ The structures were solved by direct methods and refined on F^2 by full-matrix least-squares methods with SHELXTL version 5.1.27 The SQUEEZE protocol inside PLATON was used to remove the void electron density of the two structures. In the structural refinement of Ce-TBMN, one of the central benzene rings and the nitrogen atom attached to it were disordered into two parts with their s.o.f. being refined as free values, and the C-C bond distance and the diagonal C-C distance in one disordered phenyl ring were fixed as 1.39 Å and 2.78 Å, respectively. Except for the disordered parts and partly occupied solvent molecules, the other non-hydrogen atoms were refined anisotropically. Hydrogen atoms within the ligand backbones and the solvent DMF molecules were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. To assist the stability of the refinements, several restrains were applied: several bond distances in solvent DMF molecules were restrained as idealized values. Thermal parameters on adjacent atoms in two of the naphthyl rings were restrained to be similar. In the structural refinement of Ce-TBBS, all the non-hydrogen atoms were refined anisotropically. Except for the solvent methanol and water molecules, hydrogen atoms within the ligand backbones and solvent DMF molecules were fixed geometrically at calculated distances and allowed to ride on the parent non-hydrogen atoms. Thermal parameters on adjacent atoms of several solvent DMF molecules were restrained to be similar.

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