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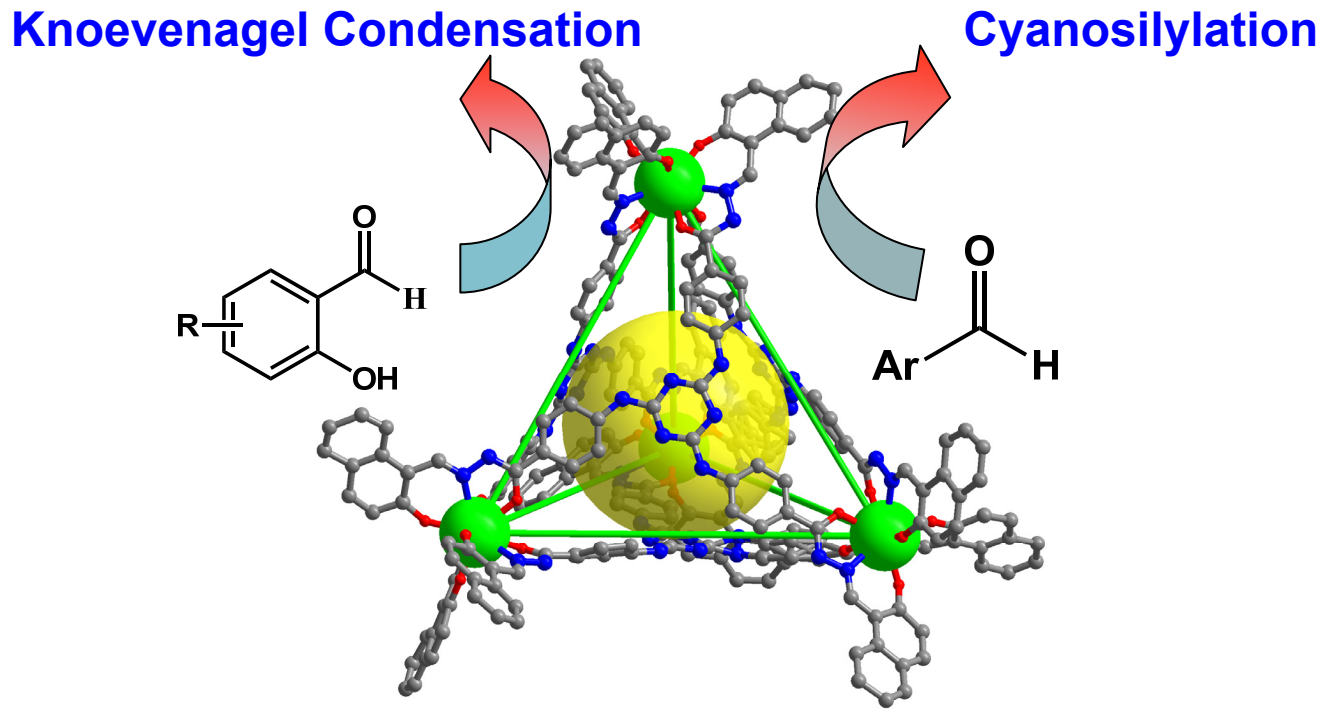

metal-organic tetarhedrons containing fruitful hydrogen bond groups work as “molecular flask” to prompt Knoevenagel condensation and Cyanosilylation reactions.

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ARTICLE

Cerium–Based M_4L_4 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 precipitated a surge of interest in the reactivity and property 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 size and shape, as well as competitive experiments using the nonreactive guests as inhibitions demonstrated that the tetrahedrons exhibited enzymatically catalytic behvior and the catalytic reactions were occurred in the "molecular flasks". Control experiments with the ligand H_6**TMBN** or H_6**TBAS** themselves as the catalyst on the Knoevenagel condensation were carried out in the same condition. For the smaller substrates, their conversions catalyzed by the ligands were obviously 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 homogeneous state.

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 mimetism, their applications in reactivity modulation of bound guest, molecular recognition, and catalysis are rife with allusions and direct comparisons to the natural enzymes.[3,4] The MOPs have shown excellent advantage in rational building microenvironment isolating from bulk solution, size and shape-selective recognition of the substrate.[5] Although the construct strategy of MOPs with controllable configuration has been well established,[6] a few of "artificial enzymes" have achieved the magnificent catalysis of natural enzymes. Challenge in this field remains in the introducing 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]

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 hydrogen bonding of catalyst molecules to each other.[10] Consequently, if these catalytically active sites were incorporated into a defined environment with lager cavity, the self-quenching might be avoided.[11]

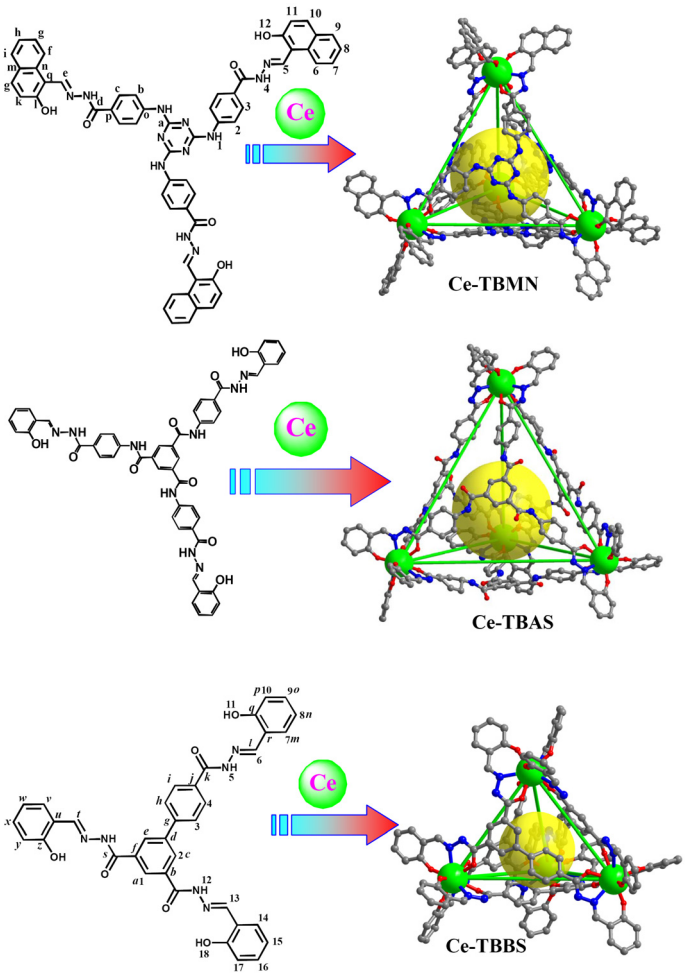
We have reported the assembly of Werner-type capsules containing amide groups as multiple hydrogen bonding trigger sites for the selective recognition of biomolecules.[12] The incorporating of amide groups as guest-accessible sites within the metal-organic cages is a powerful approach to achieve functional flasks for prompting several important reactions, because amide group is able to possess two types of hydrogen bonding sites[13] and can act as base-type catalytic driving force.[14] However, in homogeneous state, the simple molecule catalyst containing amide groups might 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 cavity 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 well

established, here we introduced a functional group, triamine-triazine(melamine), which has been showed interesting multi-hydrogen bonding formation property[16] into the Ce-based molecular tetrahedron Ce-**TBMN** containing amide groups. And the catalytic behavior of the molecular tetrahedron Ce-**TBAS** containing two types of amide groups with different size was also investigated. The catalytic behaviors of the two molecular tetrahedrons containing many hydrogen bond groups were carried out with several aldehyde substrates with various size and shape. The tetrahedrons showed interesting enzymatically catalytic behavior corresponding to the chemical transformations of the Knoevenagel condensation reaction of salicylaldehyde derivatives and Cyanosilylation reactions of aromatic aldehydes.

Results and discussion

Structure Study of the Tetrahedrons



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 gray, respectively. Hydrogen atoms and solvent molecules were 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, respectively.

The ligand $\mathbf{H_6TBMN}$ 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 $\mathbf{H_6TBMN}$ and $Ce(NO_3)_3{\cdot}6H_2O$ 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 a space group of C_2. The tetrahedronal 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 literatures.[18] The edge Ce···Ce separations were about 18.0 Å and the inner volume of the tetrahedron was 630 $Å^3$ with the opening size of the windows on the edge being about 18.0 × 7.6 $Å^2$, allowing the substrate molecules which have 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. Totally 12 NH groups and 12 coordinated amides groups in the tetrahedron cage could act as the hydrogen bond active sites. The complementary hydrogen bonding and the potential stacking interaction, in cooperation with the spatial affects of the tetrahedron nanocage will benefit 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 bond 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 electro spray 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, a moderate peak at m/z 1515.59, which can be assigned to the negative charged species $[(Ce–\mathbf{TBMN}\text{-}5H)+K]^{4-}$ and $[(Ce–\mathbf{TBMN}\text{-}4H)+K]^{3-}$, demonstrating 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 the 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 $Å^3$, with the opening size is about 21.0 × 11.1 $Å^2$, which were lager than those of Ce–**TBMN**. Totally 12 uncoordinated and 12 coordinated amide groups sited on the faces of the tetrahedron, also did not form any hydrogen bond 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 catalysis performances.

The ESI-MS of the Ce–**TBAS** exhibited an intense peak at *m/z* = 1057.41 which was assigned to [(Ce-**TBAS**-4H]$^{4-}$ specie, revealing the stability of the M_4L_4 tetrahedron in the solution.

The Ce–based tetrahedron analogue Ce–**TBBS** was obtained by mixing a smaller ligand **H_6TBBS** and $Ce(NO_3)_3{\cdot}6H_2O$ in DMF solution with a yield of 53 %. Compared to the former two ligands, there is only one benzene group insert into one of the three arms of the central benzene ring of ligand **H_6TBBS**. The compound was crystallized in a space group of C_2/c. In the molecular tetrahedron of the Ce–**TBBS**, the Ce…Ce distance in the long edges was 13.5 Å and in the short edges was 11.4 Å respectively, the inner volume and the opening size of the tetrahedron were quite smaller than the two cages mentioned above. The ESI-MS of the Ce–**TBAS** also showed its stability in DMF solution with the intense peak at *m/z* = 1034.22 assigned to [(Ce-**TBBS**-3H]$^{3-}$ specie.

Table 1 The crystallographic data of compounds Ce- **TBMN**, Ce- **TBAS** and Ce-**TBBS**

	Ce-**TBMN**	Ce-**TBAS***	Ce-**TBBS**
Formula	$Ce_4(C_{228}H_{156}N_{48}O_{24})\cdot 9C_3H_7NO\cdot CH_3OH\cdot 8H_2O$	$Ce_4(C_{51}H_{35}N_9O_9)_4\cdot 8C_3H_7NO\cdot 9CH_3OH\cdot 7H_2O$	$Ce_4(C_{144}H_{100}N_{24}O_{24})\cdot 9C_3H_7NO\cdot CH_3OH\cdot 2H_2O$
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 (º)	117.460(2)		112.605(2)
V/Å^3	19000.3(12)	78360(32)	20510(5)
Z	2	8	4
D_c/g cm^{-1}	0.935	0.887	1.243
μ/mm^{-1}	0.526	0.511	0.942
F(000)	5484	21504	7816
Flack parameter	0.595(13)		
No. refs measured	50323	62007	49704
No. unique refs	29828	12729	18005
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

$R_1 = \sum \| F_o \| - | F_c \| / | \sum | F_o | . wR_2 = [\sum w(F_o^2 - F_c^2)_2/\sum (F_o)^2] ½$

* The Crystal data of Ce-TBAS have been reported in previous literature[17a], the CCDC ref code is 987459.

Catalytic Study of Knoevenagel Condensation

The triamine-triazine moieties of the Ce–**TBMN** and free amide groups of the Ce–**TBAS** could act as basic catalysis sites to promote the Knoevenagel condensation reaction that requires the formation of an active methylene anion under a weak base-catalyzed mode.[19] Firstly, the recognition of the Ce-**TBMN** to the various salicylaldehyde substrates was investigated. As shown in Figure 1 (above), the emission intensity of Ce–**TBMN** exhibited about 25 times enhancement when *o*-Vanillin (5×10^{-4} M) was added into the solution. The Hill-plot profile[20] 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'-dimethyl-salicylaldehyde (**NMS**), listed in Table 2) gave the associate constant ($\log K_{ass}$) of 3.51 and 3.44 respectively.

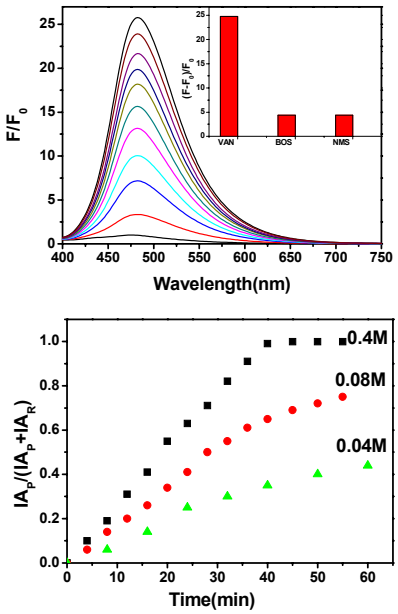


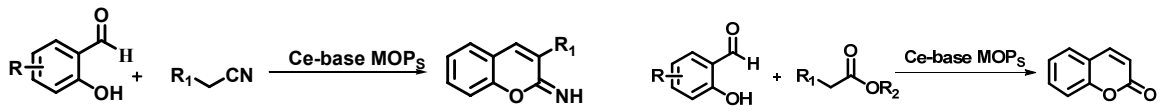
Figure 1 Above: The family of spectra of compound Ce-**TBMN** (5×10^{-6} M) in DMF solution upon the addition of a standard solution of *o*-Vanillin. The insert exhibits the respective response of Ce-**TBMN** for the other aldehydes for Knoevenagel condensation. The samples were excited at 385 nm, the emission intensities were recorded at 478 nm. Below: Time-dependence of integral area (IA) ratio variations of the reaction of *o*-Vanillin catalyzed by Ce-**TBMN** based on ^{1}H NMR detection in DMF/$CDCl_3$. IA_P and IA_R represent the NMR integral areas at 4.32 *ppm* and 9.83 *ppm* respectively.

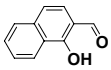
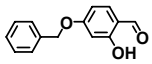
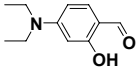
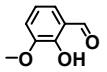
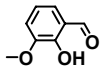
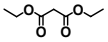
Under the condition of Ce–**TBMN** (2 mol%), *o*-Vanillin (0.08 M) and cyanoacetonitrile (0.20 M) in 2 mL DMF /benzene (v/v = 1 : 99) solution stirring at room temperature, the *o*-Vanillin almost completely reacted after 3 hours. As shown in Table 2, at the same condition, when the size of the salicylaldehyde derivatives increased, the relative conversion of the Knoevenagel condensations of malononitrile decreased obviously. The conversion of ethyl cyanoacetate and diethyl malonate with *o*-Vanillin were about 25 % and 19 %, respectively. Despite there are lots of factor influencing the conversion of the reactions, the size-selective catalytic property 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 enzymatically catalytic behavior. The reactions were monitored by ^{1}H NMR tracing process. The product

formation was pseudo-zeroth-order with the rate constant being decreased obviously. These results gave further proofs of that

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



Entry	Substrates		Conversion$_s$					
			Ce-**TBMN**	Ce-**TBMN**+ G[a]	H_6**TBMN**	Ce-**TBAS**	Ce-**TBAS**+Suc[b]	H_6**TBAS**
1			>95 %	55 %	28 %	> 95 %	39 %	24 %
2			43 %	24 %	26 %	54 %	31 %	19 %
3			15 %	11 %	22 %	17 %	13 %	18 %
4			13 %	9.4 %	20 %	14 %	10 %	15 %
5			25 %	15 %	26 %	34 %	18 %	23 %
6			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.

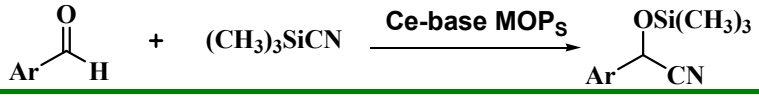
0.6 M·h^{-1}(Fig. 1 below, black line), in case of the reaction of o-Vanillin with high concentration (0.40 M). With the concentration decreased to 0.04 M, the dependence of the rate on substrate concentration tended to the first order (Fig. 1 below, green line), and the combined kinetic date followed the overall rate law: kinetic rate = k_2[guest⊂Ce–**TBMN**]. The kinetic rate of reaction depends on the concentration of host-guest complexation specie rather than the total concentration of substrate suggested that the substrate and "enzyme" participated in a reversible equilibrium with an enzyme/complex.[21] And the catalysis behavior is described in Michaelis-Menten mechanism in which substrate binding is the first equilibrium prior to the rate-limiting step of the reaction.[22]

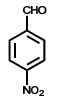
Although it could not be proven beyond a shadow of a doubt that the catalyzed reactions were displayed within the cavities of the tetrahedron Ce–**TBMN**, the size-selective catalytic property and the kinetic study of the catalytic reactions all supported this hypothesis. To further validate whether 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 specie. In this case, a biomolecule guanosine with the associate constant (logK_{ass}) being 5.78 was chosen as the inhibitor for this enzymatic system. As can be expected, in the presence of 0.16 M of guanosine, catalytic actions by the Ce–**TBMN** were all Ce–**TBMN** was an interesting molecular flasks, within which, the salicylaldehyde substrates were activated.

The size selective effect of the Knoevenagel condensation reaction was also exhibited by Ce–**TBAS**. The associate constants (logK_{ass}) of salicylaldehyde derivates calculated from fluorescence titration were 4.77, 3.59 and 3.45 for *o*-Vanillin, BOS and NMS respectively. Under the same condition of Ce–**TBMN**, *o*-Vanillin and cyanoacetonitrile almost completely reacted in 3 hours. As shown in Table 2, the conversion of the lager salicylaldehyde derivatives with malononitrile catalyzed by Ce–**TBAS** also decreased obviously. The conversion of corresponding entry were higher than that catalyzed by Ce–**TBMN** suggesting the better size-suitable of Ce–**TBAS** with lager windows and inner space toward the lager substrates. And the conversion of 4-(benzyloxy)-salicylaldehyde in two case are both low, indicating 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 the 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, catalytic actions by the Ce–**TBAS** were all decreased obviously.

Interestingly, control experiments with the ligand H_6**TMBN** or H_6**TBAS** itself as the catalyst were carried out in the same condition respectively. For the small substrates *o*-Vanillin and

Table 3 Results for the Cyanosilylation reaction catalyzed by various catalysts



Entry	Substrates	Conversion				
		Ce-**TBMN**((log K_{ass})	Ce-**TBMN**+ G[a]	Ce-**TBAS**(log K_{ass})	Ce-**TBAS**+Suc[b]	Ce-**TBBS**
1		> 97 % (4.17 ± 0.24)	66 %	89 % (3.99 ± 0.22)	53 %	72 %
2		>97 % (3.95 ± 0.16)	63 %	> 97 % (4.13 ± 0.18)	59 %	67 %
3		89 % (3.68 ± 0.17)	54 %	> 97 % (4.36 ± 0.19)	57 %	74 %
4		63 %	28 %	65 %	31 %	52 %
5		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 /$CHCl_3$ (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.

1-hydroyl-2-naphyl-aldyhede, the conversion were obviously lower than those catalyzed by Ce–**TBMN** or Ce–**TBAS** respectively. The result suggested that for the free ligand, their triamine-triazine and amid 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 the self-quenching in homogeneous state. While for the other substrates with larger size, the conversion were a little higher than that catalyzed by the tetrahedron cage. In all the case, there was no significant difference of 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 $Ce(NO_3)_2{\cdot}6H_2O$ as catalyst.

Catalytic Study of Cyanosilylation Reaction

The similar Ce-based tetrahedron reported previously in our group has shown good activity on 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 the Ce–**TBMN** and the various nitrobenzaldehyde substrates for the cyanosilylation was investigated. As shown in Figure 2 (above), the emission intensity of the Ce–**TBMN** exhibited about 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 complexation behavior with the association constant (logK_{ass}) calculated as 4.17 ± 0.24. The addition of other aldehydes (3-**NBA** and 4-**NBA**) lead to 1.35 or 1.33 times fluorescence enhancement of the solution with the associate constants (logK_{ass}) calculated as 3.95 and 3.68, respectively. Compared with the Ce-based tetrahedron Ce-**TTS** which exhibited luminescent decreasing toward the corresponding aldehydes due to the photo-induced electron transfer from its triphenylamine moiety to the guests,[13b] the different luminescent enhancement recognition occurred on Ce–**TBMN** should be attributed to the formation of hydrogen bond between the guests and the NH groups which block the PET process from the NH groups to the naphthyl moieties in the Ce–**TBMN**. The strongest association constant of the 2-NBA might be due to the formation of multi-hydrogen bond between the *o*-position nitrobenzalaldyhyde and the NH donor. The recognition between the Ce–**TBAS** and the other nitrobenzaldehyde substrates was also investigated. The associate constants (logK_{ass}) of 2, 3, and 4-NBA calculated from 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 that the free amide groups were sited in a more steric hindrance microenvironment in the cavity of Ce–**TBAS**, and were more difficult to interaction with *o*- and *m*-position nitrobenzalaldyhyde to form the hydrogen bond.

Under the condition of Ce–**TBMN** (2 mol%), 2-nitrobenzaldehyde (0.08 M) and $(CH_3)_3SiCN$ (0.20 M) in 2 mL DMF/$CHCl_3$ (v/v = 1 : 99) solution stirring 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 % conversions for various nitrobenzaldehydes. The substrate 1-

naphthyl-aldehyde and 4-hydroxy-1-naphthaldehyde with larger size gave lower conversion of about 63 % and 38 % under the same condition respectively. The product formation was pseudo-zeroth-order with the rate constant being 2.4 $M \cdot h^{-1}$(Fig. 2 below, black line), in case of the reaction of 2-NBA with high

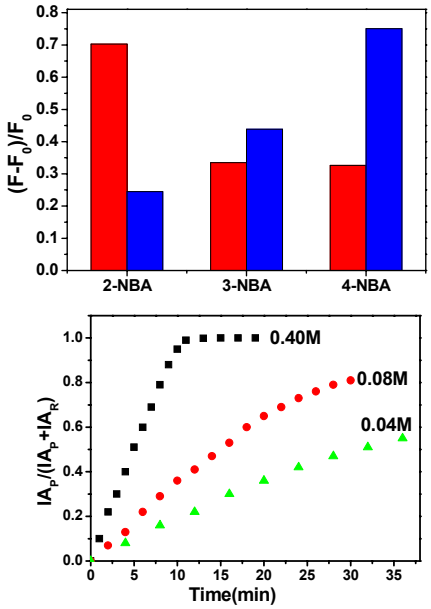


Figure 2 Above: The Luminescent response of compound Ce-**TBMN** (red column) and Ce-**TBAS** (blue column) in DMF solution upon the addition of a standard solution of various nitrobenzaldehydes. The samples were excited at 385 nm, the emission intensities were recorded at 478 nm Below: Time-dependence of integral area (IA) ratio variations of the reaction of 2-nitrobenzaldehyde catalyzed by Ce-**TBMN**, based on ^{1}H NMR detection in DMF/$CDCl_3$. IA_P and IA_R represent the NMR integral areas at 6.22 *ppm* and 10.42 *ppm*, respectively.

concentration (0.40 M). With the concentration decreased to 0.04 M, the dependence of the rate on substrate concentration tended to the first order. Similarly, in the presence of 0.16 M of guanosine, catalytic actions by the Ce–**TBMN** were all decreased obviously. 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 condition of Ce–**TBMN**, the conversion of the various nitrobenzaldehydes are 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 related entry 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**. While the conversion rate of 4-hydroxy-1-naphthaldehyde was 50 %, higher than that by Ce-**TBMN**, suggesting that better size-suitable of the lager cavity of Ce–**TBAS** toward the lager substrate. And in the presence of 0.16 M sucrose, the cyanosilylations catalyzed by the Ce–**TBAS** system were all decreased obviously.

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 smaller inner cavity and opening size, and no free hydrogen bond site on the face. Under the same condition, the loading of 2 mol% Ce–**TBBS** led to no more than 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 was more difficult to pass the small window of the Ce–**TBBS** (approximate two dimension size 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 result strongly suggested that 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 typically enzymatically catalytic behavior: the reactions were taken place within the molecular flasks, not in a normal homogeneous manner. And the multi hydrogen bond groups could be fixed in the rigid MOPs to avoid the "self-quenching" between themselves, enhancing their catalytic ability in homogeneous state.

Experimental

Materials

All chemicals were of reagent grade quality obtained from commercial source and used without further purification. The elemental analyses of C, H and N were performed on a Vario EL III elemental analyzer. ^{1}H NMR spectra were measured on a BRUKER 400M spectrometer. ESI mass spectra were carried out on a HPLC-Q-Tof MS spectrometer using CH_3CN as mobile phase.

General spectroscopic methods

Solution fluorescence titration spectra and selectivity experiments were checked using an EDINBURGH FS920 luminescence spectrometer. Stock solutions (1.0×10^{-2} 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 spectroscopic measurements, the solution was freshly prepared by diluting the high concentration stock solution to the corresponding solution. For all the titration experiments, spectra were recorded after 3 min of adding substrate to ensure the complete equilibrium. Excitation and emission slit widths were modified to adjust the luminescent intensity in 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) tri benzoate: [25] Cyanuric chloride (0.92 g, 5.0 mmol) was added in one portion to a stirred solution of the 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 %. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 9.89 (s, 3H$_{\text{-NH-}}$), 8.01 (d, J = 8.4 Hz, 6H$_{\text{Ar-H}}$), 7.93 (d, J = 8.8 Hz, 6H$_{\text{Ar-H}}$), 3.85 (s, 9H$_{\text{-CH}}$).

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 24h 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 %. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 9.64 (s, 3H$_{\text{-NH-N}}$), 9.63 (s, 3H$_{\text{-NH-}}$), 7.91 (d, J = 8.0 Hz, 6H$_{\text{Ar-H}}$), 7.81 (d, J = 8.4 Hz, 6H$_{\text{Ar-H}}$), 4.43 (s, 6H$_{\text{-NH}}$).

H$_6$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 24h 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 $C_{57}H_{42}N_{12}O_6 \cdot H_2O$: H 4.40, C 67.85, N 16.66 %. Found: H 4.45, C 67.79, N 16.63 %. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 12.86 (s, 3H$_{12}$), 12.14 (s, 3H$_4$), 9.89 (s, 3H$_1$), 9.51 (s, 3H$_5$), 8.22 (d, J = 8.8 Hz, 3H$_{10}$), 8.11 (d, J = 8.4 Hz, 6H$_3$), 8.03 (d, J = 8.4 Hz, 6H$_2$), 7.94 (d, 6H$_{11}$), 7.91 (d, m, 6H$_8$),7.61 (t, J = 7.6 Hz, 3H$_7$), 7.42 (t, J = 7.4 Hz, 3H$_9$), 7.25 (d, J = 9.2 Hz, 3H$_6$). ^{13}C 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 $Ce(NO_3)_3 \cdot 6H_2O$ (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 2h 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 crystal washed with methanol and dried in vacuum). Anal calc. for $Ce_4C_{228}H_{156}N_{48}O_{24} \cdot 4C_3H_7NO$: 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-tricarohydrazide: 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 12h 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 %. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 9.98 (s, 2H$_{\text{-NH-N}}$), 9.87 (s, 1H$_{\text{-NH- N}}$), 8.29 (s, 1H$_{\text{Ar-H}}$), 8.27 (s, 2H$_{\text{Ar-H}}$), 7.98 (d, J = 8.0 Hz, 2H$_{\text{Ar-H}}$), 7.92 (d, J = 8.0 Hz, 2H$_{\text{Ar-H}}$), 4.59 (s, 6H$_{\text{-NH}}$).

H$_6$TBBS: A mixture solution of 1,1'-biphenyl-3,4',5-tricarohydrazide (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 12h 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 $C_{36}H_{28}N_6O_6 \cdot 2H_2O$: H 4.77, C 63.90, N 12.42 %. Found: H 4.71, C 67.82, N 12.45 %. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): δ 12.36 (s, 2H$_{18}$), 12.24 (s, 1H$_{11}$), 11.29 (s, 1H$_5$), 11.19 (s, 2H$_{12}$), 8.73 (s, 2H$_{13}$), 8.71 (s, 1H$_6$), 8.56 (s, 1H$_1$), 8.52 (s, 2H$_2$), 8.18 (d, J = 8.0 Hz, 2H$_4$), 8.09 (d, J = 8.0 Hz, 2H$_3$), 7.60 (3H$_{7,14}$), 7.33 (3H$_{9,16}$), 6.95 (6H$_{7,10,15,17}$). ^{13}C 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 $Ce(NO_3)_3 \cdot 6H_2O$ (44 mg, 0.10 mmol), ligan d **H$_6$TBBS** (64 mg, 0.10 mmol) and NaOAc(25 mg, 0.30 mmol) in DMF (10 mL) was stirred for 2h at room temperature. Then the solution was left for two weeks at room temperature to give X-ray quality black block crystals. Yield about 53 % (based on the crystal washed with methanol and dried in vacuum). Anal calc. for $Ce_4C_{144}H_{100}N_{24}O_{24} \cdot 5C_3H_7NO$: H 3.91 C 54.93 N 11.68 %. Found: H 4.12, C 55.36, N 11.20 %.

Crystallography

Intensities of Ce–**TBMN** and Ce–**TBBS** were collected on a Bruker SMART APEX CCD diffractometer with graphite monochromated Mo-Kα (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, respectively. In the structural refinement of Ce–**TBMN**, one of the central benzene ring and the nitrogen atom attached on it were disordered into two parts with their s.o.f. being refined as free value, the C−C bond distance and the diagonal C−C distance in one disordered phenyl ring were fixed as 1.39 Å of and 2.78 Å, respectively. Except 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 refinements, several restrains were applied: Several bond distance in one 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 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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Notes and references

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