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Urea-Functionalized Self-Assembled Molecular Prism for Heterogeneous Catalysis in Water

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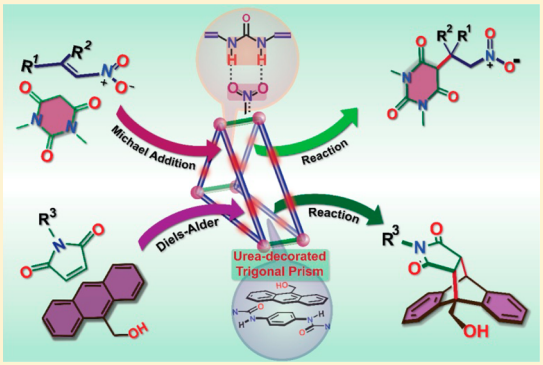
Supporting Information

ABSTRACT: Reaction of a ditopic urea "strut" ($\mathbf{L_1}$) with *cis*-(tmen)Pd(NO_3)$_2$ yielded a [3+3] self-assembled molecular triangle (**T**) [$\mathbf{L_1}$ = 1,4-di(4-pyridylureido)benzene; tmen = *N,N,N′,N′*-tetramethylethane-1,2-diamine]. Replacing *cis*-(tmen)Pd(NO_3)$_2$ in the above reaction with an equimolar mixture of Pd(NO_3)$_2$ and a clip-type donor ($\mathbf{L_2}$) yielded a template-free multicomponent 3D trigonal prism (**P**) decorated with multiple urea moieties [$\mathbf{L_2}$ = 3,3′-(1*H*-1,2,4-triazole-3,5-diyl)dipyridine]. This prism (**P**) was characterized by NMR spectroscopy, and the structure was confirmed by X-ray crystallography. The **P** was employed as an effective hydrogen-bond-donor catalyst for Michael reactions of a series of water-insoluble nitro-olefins in an aqueous medium. The **P** showed better catalytic activity compared to the urea-based ligand $\mathbf{L_1}$ and the triangle **T**. Moreover, the confined nanospace of **P** in addition to large product outlet windows makes this 3D architecture a perfect molecular vessel to catalyze Diels–Alder reactions of 9-hydroxymethylanthracene with N-substituted maleimide in the aqueous medium. The present results demonstrate new observations on catalytic aqueous Diels–Alder and Michael reactions in heterogeneous fashion employing a discrete 3D architecture of Pd(II). The prism was recycled by simple filtration and reused several times without significant loss of activity.



INTRODUCTION

Inspired by the competence, elegance, and selectivity of enzymatic catalysis[1] originating from steric confinement and precise functional group interactions,[2] chemists have long sought to design molecular reactors using abiotic platforms. This is due to the potential for developing synthetically valuable and structurally sophisticated catalysts that emulate or even exceed the capabilities of reactive cavities in biological machinery.[3] In this regard, supramolecular cages have emerged as potential candidates due to their ability to stabilize reactive intermediates/transition states, as well as their potential in stereoselective product formation.[4] Moreover, the ability to incorporate guest-accessible chemical functionalities via the organic struts makes them excellent candidates for use as catalysts.[5] Discrete nanoscopic metallacages having predetermined structures and functions can be achieved via one-pot self-assembly employing complementary organic linkers with inorganic metal nodes encoded with definite chemical and structural information.[4,6] Non-covalent cages have received more attention than their covalent analogues because of their more eloquent guest-exchange and circumvention of tedious multistep synthesis, which is obligatory for the formation of covalent cages.[7,8] Although supramolecular chemists are fascinated by the functions in biological multicomponent systems, building abiological counterparts with intricate structures from multiple precursors is sporadic. In this context, Stang, Nitschke, Schmittel, Fujita, and others have reported a few template-free multicomponent assemblies giving access to novel structures.[9] Therefore, a more accurate understanding of multicomponent self-assembly has the potential to lead to the development of functionally integrated smart architectures from multiple subunits, toward ideal candidates for catalysis along the lines of "artificial enzyme".

Considering the pivotal role of H-bonding in a myriad of natural processes, hydrogen-bond-donating (HBD) organocatalysis has emerged as a biomimetic alternative to enzyme catalysis over the past decade.[10] Among the many eligible HBD catalysts reported to mimic the biological machinery, urea and thiourea derivatives dominate the field.[11] Again, greater thermal stability of urea analogues over thiourea derivatives makes them a gold mine for catalyst discovery.[12] In the recent past, homogeneous HBD catalysts have been utilized in many reactions that gave excellent yield with high selectivity.[13] Conversely, in many cases, urea-based catalysts undergo self-association by intermolecular H-bonding, which deters substrate–catalyst recognition, leading to quenching of the catalytic efficacy (Scheme 1a).[14] Consequently, a new strategy to overcome this detrimental self-association to promote substrate recognition for "turned-on" catalytic activity is always appealing. On the other hand, discrete nanoscale

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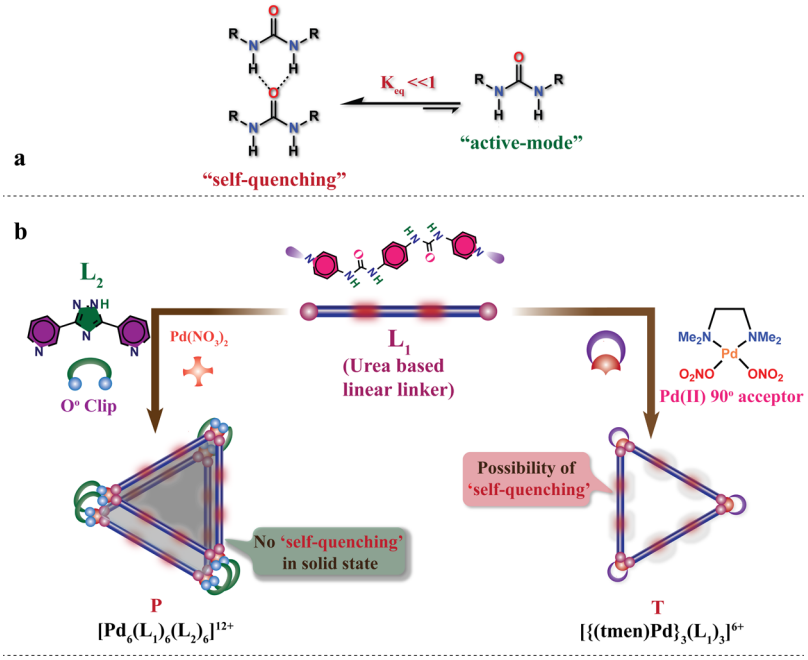
Scheme 1. (a) Idealized "Chainlike" Self-Association Pattern of Urea Derivatives and (b) Schematic Representation of the Formation of 3D Prism P and Pd(II) Triangle T



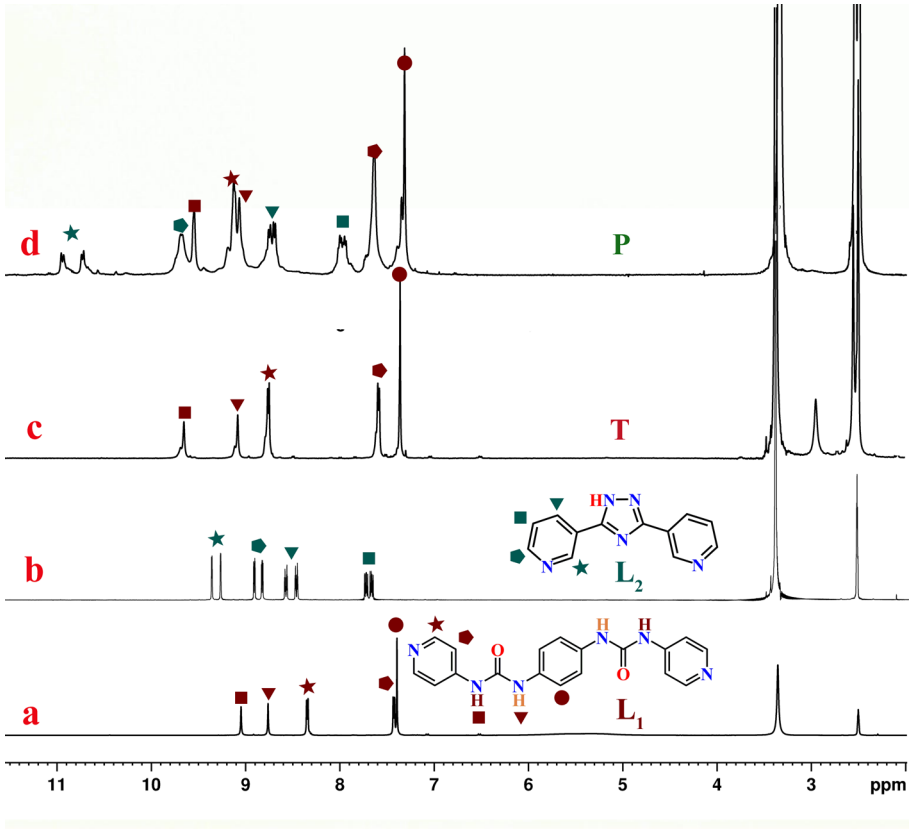


Figure 1. ^{1}H NMR spectra of **P**, **T**, L_1, and L_2 in d_6-DMSO.

molecular flasks with desired functionality have attracted special attention because they provide an excellent environment for cavity control catalysis, detection and amplification of organic analytes, stabilization of reactive species, etc.[15−17] Therefore, we envisioned that coexistence of "HBD catalytic sites and nanopockets" in a single system would be a promising approach for building enzyme-reminiscent efficient heterogeneous catalysts.

Although many interesting results have been reported in the field of cavity-induced organic transformations, in our view the area of self-assembled coordination nanocages for heterogeneous catalysis[18a] is still in an immature stage.

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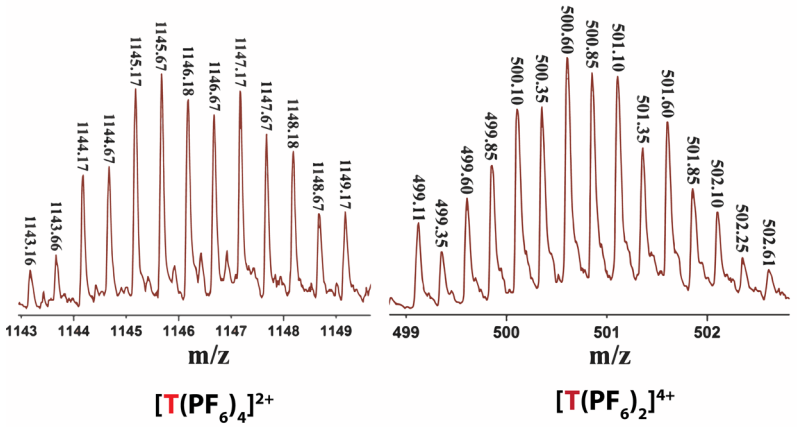

Figure 2. Experimental isotopic patterns of the fragments $[T(PF_6)_2]^{4+}$ and $[T(PF_6)_4]^{2+}$.

Product inhibition has been a serious issue resulting in the requirement of near-stoichiometric quantities of host cage.[18b−f] Moreover, at the outset of our work, only a limited number of reaction systems had been studied with discrete molecular cages, which include Knoevenagel condensation, Diels−Alder epoxidation, and the aza-Cope rearrangement.[9b,18e,19] Most such examples are stoichiometric reactions, with a limited number of examples of catalytic reactions but in homogeneous fashion.

Enticed by the above fact that the (thio)urea moieties activate the guest electrophile through non-covalent H-bonding, we chose $\mathbf{L_1}$ as a building unit to generate discrete molecular architectures. Treatment of $\mathbf{L_1}$ with an equimolar amount of *cis*-(tmen)Pd$(NO_3)_2$ resulted in a [3+3] self-assembled molecular triangle (Scheme 1b). The same reaction, replacing *cis*-(tmen)Pd$(NO_3)_2$ by a 1:1 mixture of naked Pd$(NO_3)_2$ and a clip-type donor $\mathbf{L_2}$ (Scheme 1b), yielded 3D trigonal prism $[Pd_6(\mathbf{L_1})_6(\mathbf{L_2})_6]$ (**P**), having multiple urea moieties. This prism **P** was successfully employed as a heterogeneous catalyst for Michael reactions and Diels−Alder reactions in an aqueous medium. To the best of our knowledge, the present **P** represents the first example of a discrete self-assembled molecular cage used as a HBD heterogeneous catalyst for Michael reactions in eco-benign solvent water under ambient conditions.

RESULTS AND DISCUSSION

Design Strategy, Synthesis, and Characterization. A survey of the literature shows that diaryl urea derivatives have a strong propensity to undergo intermolecular H-bonding between two proximal N−H groups of one urea moiety and the electron-rich carbonyl moiety of another molecule. Such self-association reduces substrate recognition, leading to lower catalytic activity (Scheme 1a).[20] On this basis, we hypothesized that the triazole-based pillar in cage **P** would avert the H-bonding interactions between the two urea-decorated triangular scaffolds, thus unlocking the HBD urea moiety for guest binding. With this in mind, we thought eradicating the *cis*-blocked amine at the Pd(II) center of the triangle **T** would expose two more sites on each Pd(II) center. These vacant sites on each Pd(II) could be used to tie two such triangles using appropriate "clips" into a single architecture to stop intermolecular self-association between two triangles for better catalytic efficiency.

In this vein, ligand $\mathbf{L_1}$ and triazole-functionalized pillar $\mathbf{L_2}$ were synthesized and characterized (Figure 1 and Supporting Information). The X-ray crystal structure (Figure S3) of $\mathbf{L_1}$ showed extensive intermolecular H-bonding between the urea moieties.

Two-component molecular triangle **T** was obtained by adding an aqueous yellow solution of *cis*-(tmen)Pd$(NO_3)_2$ ($\mathbf{M_2}$) into the solid ditopic donor $\mathbf{L_1}$ in a 1:1 molar ratio, followed by subsequent stirring at 50 °C for 3 h. The resulting clear solution was triturated with acetone to obtain **T** in pure form. The **T** formed was highly soluble in water. It was characterized by ^{1}H NMR spectroscopy (Figure 1c) and ESI-MS (Figure S4). ^{1}H NMR of the **T** exhibited sharp distinct peaks with noticeable downfield shift as compared to the ligand $\mathbf{L_1}$, which is expected owing to the coordination of $\mathbf{L_1}$ to Pd(II). Moreover, diffusion-ordered NMR spectroscopy (DOSY) confirmed the formation of a single species by the appearance of a clear single band at $D = 7.03 \times 10^{-11}$ m^2/s (log $D = -10.15$).

ESI-MS spectra of the **T** (after anion exchange with PF_6^-) in acetonitrile displayed two main peaks at m/z = 1145.67 and 500.60, with isotopic distribution patterns corresponding to $[T(PF_6)_2]^{4+}$ and $[T(PF_6)_4]^{2+}$ charge fragments, respectively (Figure 2). Further investigation by gas-phase DFT calculation gave the energy-optimized structure of the complex **T**, which shows a planar geometry. The urea groups are projected toward the perpendicular direction with respect to the molecular plane (Figure 3a).

The prism **P** was synthesized by adding a mixture of $\mathbf{L_1}$ and $\mathbf{L_2}$ to a reddish solution of Pd$(NO_3)_2$ ($\mathbf{M_1}$) in a specific ratio ($\mathbf{L_1}$:$\mathbf{L_2}$:$\mathbf{M_1}$ = 1:1:1), followed by stirring at room temperature for 2 h. The pure form of **P** was obtained as a white precipitate upon addition of excess ethyl acetate to the resulting light green solution. The **P** was only soluble in DMSO. Substantial downfield shift was observed in the ^{1}H NMR (d_6-DMSO) of the isolated product in comparison with the free ligands $\mathbf{L_1}$ and $\mathbf{L_2}$, which is characteristic of coordination of donors to Pd(II) (Figure 1d). In multi-component self-assembly, one can expect the formation of a mixture of unwanted parallel side products besides the self-assembled multicomponent discrete architecture. Notably, DOSY showed a clear single band at $D = 5.88 \times 10^{-11}$ m^2/s (log $D = -10.23$), with a hydrodynamic radius of ∼18.6 Å (Figure S5). Because of the poor solubility, the ^{13}C NMR could not be obtained. Finally, the single-crystal X-ray

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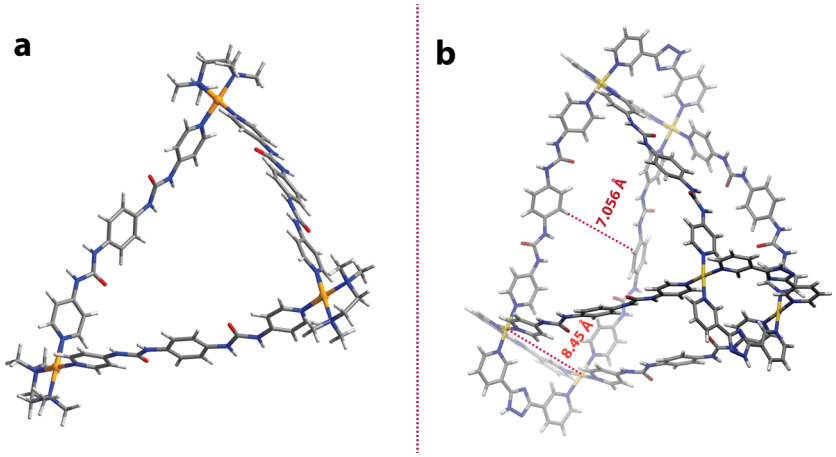

Figure 3. (a) Energy-optimized structure of **T**. (b) Single-crystal XRD structure of the cage **P**. Color codes: yellow, Pd; blue, N; dark gray, C; light gray, H.

diffraction (XRD) study unambiguously affirmed that the solid-state structure of **P** was consistent with the anticipated structure (Figure 3b). Single crystals of **P** suitable for XRD analysis were grown by the slow vapor diffusion of acetone into the concentrated DMSO solution of **P**.

Structural refinements of **P** revealed that the average length of the arms of a triangle, i.e., the nearest Pd---Pd distance within one triangle, is about 20.8 Å, while the average Pd---Pd distance between two adjacent triangles is 8.45 Å. Moreover, the closest distance between the two centroids of the adjoining triangles is measured to be about 7.056 Å, further strengthening our hypothesis that immobilization of triazole-based pillar framework between the two triangular scaffolds should preclude the commonly observed H-bonding interactions between the urea moieties of the neighboring triangles. From the average N($\mathbf{L_1}$Py)−Pd−N($\mathbf{L_1}$Py) bond angle being 90.0°, one can envisage a molecular square, but the innate flexibility of the $\mathbf{L_1}$ ligand led to the formation of an otherwise unusual trigonal prism. From the structural analysis, $\pi-\pi$ interaction between ligand $\mathbf{L_2}$ in **P** and $\mathbf{L_1}$ of the neighboring molecule was observed (Figure S7b). Neither intramolecular nor intermolecular H-bonding among the urea moieties was present in the solid-state structure. Only a nitrate ion was found to form H-bonding with one of the urea groups of $\mathbf{L_1}$. Crystal packing showed the formation of intermolecular voids (Figure S7a) in the structure. Important crystallographic data and refinement parameters of **P** are provided in Table S3.

Substrate Binding Studies. In order to examine the ability of **P** to promote substrate recognition over self-association, we recorded the IR spectra of **P** and **1l**⊂**P** [where **1l** = 1-(2-nitrovinyl)naphthalene]. IR spectra of the crystalline **1l**⊂**P** (where ⊂ denotes encapsulation) exhibited a characteristically broad band around 3061−3330 cm^{-1}, attributed to the stretching of N−H bonds participating in H-bonding. The red-shift of the N−H vibration compared to that in the cage **P** (3363 cm^{-1}) suggested a potential interaction between the urea and the nitro group (Figure S8). The recognition of **1l** by **P** was further investigated by UV−vis spectroscopy in 9:1 H_2O/EtOH (Supporting Information). A 0.1 mM solution of **1l** in 9:1 H_2O/EtOH exhibited two strong absorption bands centered at 263 and 374 nm. Solid **P** (15 mg, ~0.0031 mmol) was added to the solution of **1l**, and absorbance was measured over a time span of 2 h at an interval of 5 min without stirring. As shown in Figure 4, the intensities of the peaks at 263 and 374 nm gradually decreased ca. 1.73- and 5.0-fold,

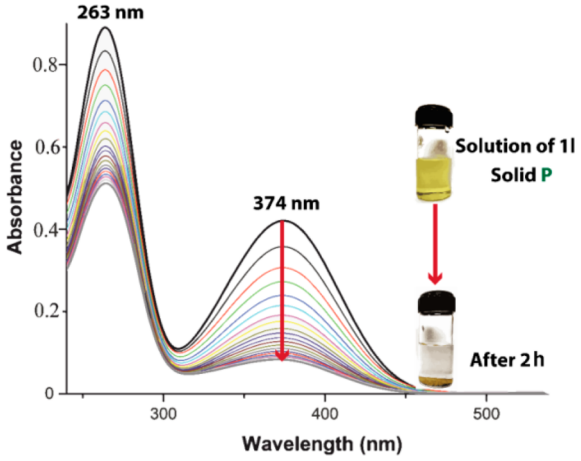

Figure 4. Absorption spectra of **1l** (0.1 mM) in the presence of **P** (0.0031 mmol) in H_2O/EtOH (9:1). Inset: Color change of the solution of **1l** 2 h after addition of **P**.

respectively. The quenching of the bands may be attributed to the interaction of **1l** with the urea N−H bonds of the **P** through non-covalent H-bonding. The decrease (with respect to the guest **1l**) in relative absorbance at ~263 nm with time clearly signifies the binding of guest to the **P** (Figures 4 and S9). The prism−analyte binding stoichiometry in **1l**⊂**P** was calculated to be 1:4.5 on the basis of UV−vis studies (Supporting Information). The formation of the inclusion complex **1l**⊂**P** was evidenced by a sharp color change (Figure 4) of the solid **P** from light yellow to dark brown upon treating with **1l** solution. Thus, the N−H protons of the **P** can activate the nitro-olefins (**1**) by H-bonding for the facile conjugate addition of the nucleophiles.

Catalytic Activity and Regulation. *Cage-Catalyzed Michael Addition Reactions.* The Michael addition of carbon-based nucleophiles to nitro-olefins is well known in organic synthesis not only as a C−C bond-forming reaction but also as a platform that represents a direct and most alluring approach to nitroalkanes, which are versatile synthetic precursors of a wide range of biologically and synthetically enticing molecules.[21] Taking into consideration the synthetic

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flexibility and importance of nitroalkanes, development of catalysts for such processes has been the subject of recent research efforts. Impressive progress has been made in the development of organocatalysts which potentially activate both electrophiles and nucleophiles simultaneously.[22,23] Nonetheless, in almost all the existing organocatalytic methods the catalysts are destroyed in the workup procedure and their recovery is often impossible. To evade this problem, we herein describe **P** as a heterogeneous catalyst for conjugate additions of 1,3-dimethylbarbituric acid to nitroalkenes. Moreover, the present results represent the first effort on heterogeneous 3D cage catalysis for Michael reactions in an aqueous medium.

To find the optimized reaction conditions, we initiated a catalyst screening with three different substrates in the presence of various catalysts at room temperature. The detail optimization results are reported in Table 1. Initial reaction

Table 1. Optimization of Michael Addition Reactions of 1,3-Dimethylbarbituric Acid with Nitro-olefins[a]

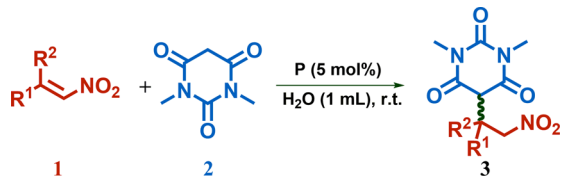
			product yield (%)[c]/time (h)		
entry	catalyst (mol%)	temp (°C)[b]	**3k**	**3l**	**3m**
1	**P** (5)	r.t.	72/1	70/1.5	75/1.5
2	**P** (1)	r.t.	50/1	48/1.5	45/1.5
3	–	r.t.	18/1	15/1.5	13/1.5
4	**L1** (30)	r.t.	25/1	20/1.5	19/1.5
5	**L2** (30)	r.t.	20/1	17/1.5	15/1.5
6	**T** (10)	r.t.	35/1	30/1.5	28/1.5
7	$\mathbf{M_1}$ (30)	r.t.	14/1	13/1.5	10/1.5
8	$\mathbf{M_2}$ (30)	r.t.	16/1	14/1.5	12/1.5
9	**P** (5)	5		9/20	
10	**P** (5)	60		16/1.5	

[a]Nitro-olefins **1** (0.2 mmol), 1,3-dimethylbarbituric acid **2** (0.2 mmol), 1 mL water, stirring. [b]Here r.t. corresponds to 25 °C. [c]Crude yields determined from ^{1}H NMR based on starting materials.

was performed in the presence of 5 mol% **P** in H_2O. In all the cases after reaction at room temperature, the reaction mixture was extracted with $CDCl_3$, and NMR showed the formation of the product. Although the ^{1}H NMR spectrum after extraction with chloroform diagnosed the formation of the product, we were able to isolate the pure product by using preparative thin layer chromatography (TLC). All the products were identified and characterized by ^{1}H and ^{13}C NMR (Supporting Information). Even 1 mol% catalyst loading also afforded the desired products, but with lesser yields. Again higher yield around 80% was obtained with 1 mol% catalyst loading in case of nitro-olefin (**1l**) when reaction was carried out for prolonged time (20 h) at room temperature. Conversely, in the absence of the catalyst, the reaction took place with much less yield under identical conditions, supporting the possible catalytic activity of **P**. The control experiments using the ligand $\mathbf{L_1}$ (30 mol%), $\mathbf{L_2}$ (30 mol%), and triangle **T** (10 mol%) were also performed. In all the cases, the yields are much less compared to that of **P**. As the $\mathbf{L_1}$ is insoluble in water, the reaction occurs in heterogeneous fashion. Therefore, the lower catalytic efficacy of $\mathbf{L_1}$ is due to detrimental self-association in the solid state. This was supported from the X-ray single-crystal structure (Supporting Information) showing extensive intermolecular H-bonding among the urea moieties. Moreover, when $Pd(NO_3)_2$ ($\mathbf{M_1}$) and *cis*-(tmen)$Pd(NO_3)_2$ ($\mathbf{M_2}$) were used independently instead of **P**, they did not significantly promote the reaction. In the hope of higher yields, further optimization efforts were performed at lower or higher temperature, but no better results were obtained.

With these optimized conditions in hand, the scope of **P** as a catalyst was examined using a series of nitro-olefins (Table 2). Among the aromatic nitro-olefins, phenyl rings with

Table 2. Evaluation of Prism (P) in Catalytic Michael Addition Reactions of 1,3-Dimethylbarbituric Acid to Nitro-olefins[a]



1 2 3

					yield (%)[c]	
entry	R^1	R^2	product	time	with **P**	without **P**
1	Ph	H	**3a**	15 min	59	20
2	4-Me-Ph	H	**3b**	15 min	62	9
3	4-MeO-Ph	H	**3c**	30 min	65	14
4	4-NO_2-Ph	H	**3d**	15 min	50	10
5	4-F-Ph	H	**3e**	15 min	73	16
6	4-Cl-Ph	H	**3f**	15 min	59	10
7	2,4-$(Cl)_2$-Ph	H	**3g**	15 min	55	8
8	3-NO_2-Ph	H	**3h**	15 min	58	11
9	2-furanyl	H	**3i**	15 min	64	13
10	*tert*-butyl-1*H*-indole-1-carboxylate[d]	H	**3j**	24 h	64	9
11	Ph	Me	**3k**	1 h	72	18
12	1-naphthyl	H	**3l**	90 min	70	15
13	2-naphthyl	H	**3m**	90 min	75	13
14	1-pyrene[d]	H	**3n**	72 h	60	14

[a]Nitro-olefins **1** (0.2 mmol), 1,3-dimethylbarbituric acid **2** (0.2 mmol), catalyst **P** (5 mol%), water (1 mL), r.t. stirring. [b]Here r.t. corresponds to 25 °C. [c]Crude yields determined from ^{1}H NMR based on starting materials. [d]2 mmol of 1,3-dimethylbarbituric acid was used.

neutral (entry 1), electron-donating (entries 2 and 3), and electron-withdrawing groups (entries 4–8) at *o*-, *m*-, and *p*-positions all afforded moderate to good yields in the presence of **P**. Observable amounts of Michael products **3** were detected when nitro-olefins were used with **2** in absence of **P**. This supports the considerable acidic nature of 1,3-dimethylbarbituric acid in water,[24] thereby, it acts as an autocatalyst to promote the Michael reactions. Heterocyclic nitroalkene bearing a furan moiety was also found to be a good substrate for this reaction (entry 9). It was pleasing to find that sensitive N-Boc protected group also reacted very efficiently with no side reactions (entry 10). Remarkably, less reactive (1-methyl-2-nitrovinyl)benzene also gave product **3k** in good yield within 1 h (entry 11). Despite the mild conditions, even sterically bulky 1-naphthyl and 2-naphthyl nitro-olefins underwent efficient Michael addition (entries 12 and 13). However, when bulkier pyrene substituted nitro-olefin was employed the relative reaction rate was decreased as indicated from the reaction completion time (72 h) (entry 14). This size-selective catalytic nature provides evidence that the catalytic reactions might occur in the cavity (intra- or intermolecular) of **P**.

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The recyclability of **P** was also investigated in the model reaction of **1l** and **2**. After extraction of the reaction mixture with chloroform, the catalyst was isolated by filtration, washed thoroughly with chloroform and dried under vacuum for several hours, and stored in a desiccator for consecutive reaction runs. It was found that the catalyst has the potential of efficient recycling for at least four times without much loss of catalytic activity (Figure S11). The ^{1}H NMR spectrum of the recovered catalyst confirmed that the cage remained intact (Figure S12) after catalytic cycles. The products were extracted with $CDCl_3$, and the NMR spectra showed no trace of $\mathbf{L}_2$, which indicated that the **P** was not collapsed or decomposed during the reaction.

A plausible reaction cascade for the catalytic Michael addition reactions in the presence of **P** is shown in Figure 5.

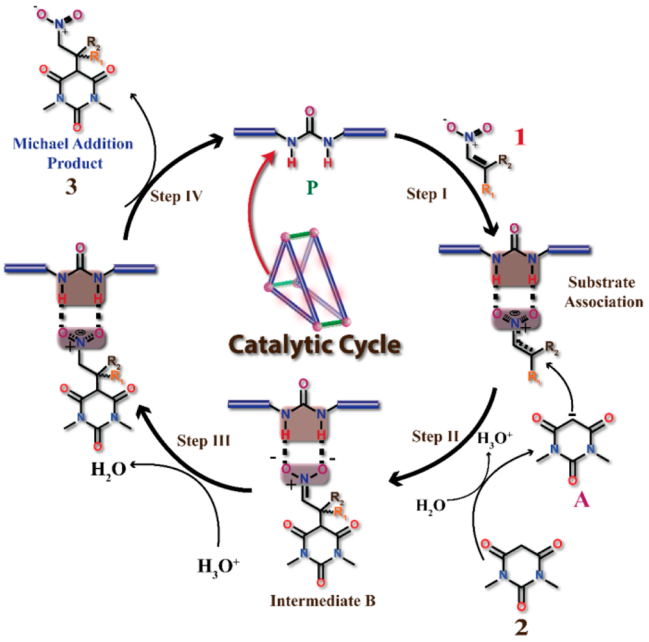


Figure 5. Probable catalytic cycle for the Michael addition reactions in the presence of **P**.

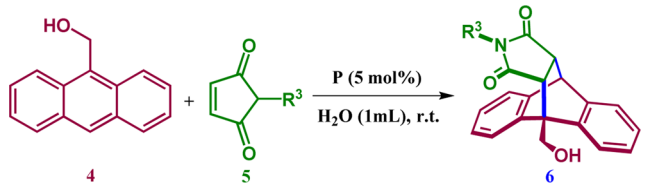
The reaction commences with the binding of nitro-olefin through H-bonding interaction with urea moieties curved within the catalyst **P** skeleton to form the complex **1l⊂P** [Step I]. 1,3-Dimethylbarbituric acid **2**, which is water-soluble, exists in equilibrium with its enolate form because of its low pK_a value (4.68).[24a] The enolate **A** attacks the bonded nitro-olefin to generate nitronate intermediate **B** [Step II]. The stability of the nitronate intermediate can be explained as follows: (a) the generated nitronate has two negatively charged oxygens on the nitrogen atom which are efficiently stabilized by the urea moiety present in the catalyst scaffold,[11b] and (b) the anionic nitronate intermediate **B** is stabilized by the cationic charge of the cage.[25] This intermediate nitronate **B** takes the proton from the water to afford the product **3** [Step III]. Finally, the product **3** being too large to be fully encapsulated in the cavity resulted in its spontaneous release [Step IV], making room for the new incoming molecule of **1**.

Catalytic Activities toward Diels–Alder Reactions. Host-mediated Diels–Alder reactions in homogeneous fashion have been well explored in recent past.[4f,15d,26] In those cases Diels–Alder reactions are significantly accelerated in the synthetic pockets, but strong complexation of the product within the cage compared to the reactant results in product inhibition and thereby prevents catalytic turnover. Therefore, enhancing catalyst turnover through effortless product departure has been a serious issue to researchers. On the contrary, such Diels–Alder reactions using discrete cages in heterogeneous fashion in an aqueous medium are yet to be explored well.

To find the optimized reaction conditions, we performed the preliminary reaction between 9-hydroxymethylanthracene (**4**, 0.2 mmol) and *N*-phenylmaleimide (**5a**, 0.2 mmol) in water to check the catalytic performance of **P** in a heterogeneous manner (Table S2). A 5 mol% amount of **P** sufficed to catalyze the Diels–Alder reaction of **4** and **5a** within a time span of 60 h at room temperature with the formation of about 84% product **6a** (based on NMR analysis), whereas, in the absence of the cage only 12% of the product had formed under identical conditions. After extraction of the reaction mixture with chloroform, the catalyst was filtered and the ^{1}H NMR spectrum of the recovered catalyst did not show any trace of the encapsulated product, signifying the weak interaction of the product with the cage. The control experiment using $\mathbf{L}_1$ + $\mathbf{L}_2$ (30 mol%) and triangle **T** (10 mol%) resulted 25% and 40% conversions, respectively. Moreover, the metal components $\mathbf{M}_1$ and $\mathbf{M}_2$ alone did not catalyze the reaction. The binding of **4** with the urea moieties of the cage **P** was further investigated by UV spectroscopy in 9:1 H_2O/EtOH. A 0.001 mM solution of **4** in 9:1 H_2O/EtOH exhibited strong absorption bands centered at 348, 365, and 385 nm. Solid cage **P** (30 mg, 0.006 mmol) of was added to the solution of **4**, and absorbance was observed over a time span of 12 h at an interval of 1 h (without stirring). As shown in Figure S13, the intensities of the peaks at 365 and 385 nm gradually decreased.

We performed a number of reactions with and without the presence of **P** by employing various N-substituted maleimides (**5**) (Table 3). Among the *N*-phenylmaleimides, phenyl rings with neutral (entry 1), electron-donating (entries 2 and 3), and electron-withdrawing groups (entries 4 and 5) at *p*-

Table 3. Diels–Alder Reactions in the Presence of P[a]



entry	R^3 (**5**)	product	time (h)	product yield (%)[c] with **P**	without **P**
1	Ph (**5a**)	**6a**	60	84	12
2	*p*-Me-Ph (**5b**)	**6b**	60	83	14
3	*p*-MeO-Ph (**5c**)	**6c**	60	71	10
4	*p*-Br-Ph (**5d**)	**6d**	60	70	17
5	*p*-Cl-Ph (**5e**)	**6e**	60	76	13
6	1-cyclohexyl (**5f**)	**6f**	60	74	4
7	1-naphthyl[d] (**5g**)	**6g**	96	60	15
8	1-pyrene[d] (**5h**)	**6h**	120	69	16

[a]9-Hydroxymethylanthracene **4** (0.2 mmol), N-substituted maleimide **5** (0.2 mmol), catalyst **P** (5 mol%), water (1 mL), r.t. stirring. [b]Here r.t. corresponds to 25 °C. [c]Crude yields determined from ^{1}H NMR, based on starting materials. [d]2 equiv of **5** was used.

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positions afforded good yields in the presence of the cage. Even in the absence of $\pi-\pi$ stacking interactions within the cage, in case of *N*-cyclohexylmaleimide (**5f**), a considerably good yield resulted (76%), which further indicates that H-bonding might have a definite role to play in the catalysis. The cage also efficiently catalyzed the reaction even when sterically bulky *N*-naphthylmaleimide was employed (60%). However, when bulkier pyrene-substituted maleimide was employed, the reaction yield was decreased, as indicated from the NMR analysis. These results further throw light on the fact that the cavity plays a role in the above reactions. Moreover, the final structure was confirmed by X-ray crystallographic analysis of the compound **6b** (Figure S14).

CONCLUSION

In conclusion, we report here multicomponent self-assembly of a 3D trigonal Pd(II) prism (**P**) decorated with multiple urea moieties. A [3+3] self-assembly of a ditopic urea "strut" ($\mathbf{L_1}$) with cis-blocked 90° Pd(II) acceptor resulted a molecular triangle where two adjacent sites on each Pd(II) were occupied by a chelating bidentate ligand. A similar three-component self-assembly of $Pd(NO_3)_2$, $\mathbf{L_1}$, and triazole-based $\mathbf{L_2}$ clip led to the formation of **P**, which was characterized by X-ray diffraction. The presence of many urea moieties made the prism suitable for nitro-olefins that can form strong H-bonds with urea moieties. The two triangular units in the prism were well separated (~7 Å) by the clip donor, thereby averting H-bonding interactions between the urea moieties of the neighboring triangles. The prism was successfully employed as a heterogeneous catalyst to perform several Michael addition reactions of a series of water-insoluble nitro-olefins with dimethylbarbituric acid in an aqueous medium. Moreover, the cage is found to be efficient for catalytic Diels–Alder reactions in aqueous medium. Though the majority of the previous examples of cavity-promoted reactions with abiotic metallacages are stoichiometric, the open nature of **P** (as evidenced from the crystal structure) allows easy exit[4e,25] of the products to make the presented reactions catalytic in nature. The **P** was recycled by simple filtration and reused several times without much loss in catalytic activity. To the best of our knowledge, the present results demonstrate the first report of Michael addition reactions in eco-benign water using a discrete molecular 3D prism architecture as a heterogeneous catalyst. The freshly blossomed urea-decorated prism sets the stage for the incorporation of other functional groups for the development of a new generation of heterogeneous catalysts in the future.

EXPERIMENTAL SECTION

Materials and Methods. All the reagents were purchased from different commercial sources and used without further purification. NMR spectra were recorded on Bruker 400 MHz spectrometer, and the chemical shifts (δ) in the ^{1}H NMR spectra are reported in ppm relative to tetramethylsilane (Me_4Si) as an internal standard (0.0 ppm) or proton resonance resulting from incomplete deuteration of the solvents $(CD_3)_2SO$ (2.51 ppm), $CDCl_3$ (7.26 ppm), and D_2O (4.79 ppm). Electrospray ionization mass spectrometry (ESI-MS) experiments were carried out on a Bruker Daltonics (Esquire 300 Plus ESI model) spectrometer using standard spectroscopic-grade solvents. HRMS spectra were recorded on a Q-TOF electrospray instrument. IR spectra were recorded on a Bruker ALPHA FT-IR spectrometer. Elemental analyses (C, H, N) were performed using a PerkinElmer 240C elemental analyzer.

Synthesis of T. *cis*-(tmen)$Pd(NO_3)_2$ ($\mathbf{M_2}$) (34.6 mg, 0.100 mmol) was dissolved in 3 mL of H_2O. The clear yellow solution was added to the solid ligand $\mathbf{L_1}$ (34.8 mg, 0.100) and heated at 50 °C with stirring for 3 h, resulting in a clear greenish solution. The solution was then concentrated under reduced pressure and treated with 15 mL of acetone to obtain an off-white precipitate. The precipitate was then isolated and washed with acetone, followed by drying under vacuum, to get an off-white powder of **T**. Isolated yield: 59 mg (84%). ^{1}H NMR (400 MHz, d_6-DMSO): δ = 9.65 (s, 2H), 9.08 (s, 2H), 8.77 (d, 4H), 7.60 (d, 4H), 7.36 (s, 4H), 2.95 (s, 4H), 2.55 (s, 12H). ESI-MS (m/z): 1145.67 $[\mathbf{T}(PF_6)_4]^{2+}$, 500.60 $[\mathbf{T}(PF_6)_2]^{4+}$.

Synthesis of P. Ligands $\mathbf{L_1}$ (34.8 mg, 0.100 mmol) and $\mathbf{L_2}$ (22.3 mg, 0.112 mmol) were dissolved in 2 mL of DMSO, and the clear solution was added to another 1 mL of a DMSO solution of $Pd(NO_3)_2{\cdot}H_2O$ ($\mathbf{M_1}$) (24.8 mg, 0.100 mmol). The clear solution was stirred at room temperature for 2 h and then treated with 20 mL of ethyl acetate to obtain a mustard yellow precipitate, which was collected by filtration, followed by washing with water and acetone. It was then dried under vacuum and dissolved in DMSO-d_6 to record ^{1}H NMR spectra. Isolated yield: 57 mg (70%). ^{1}H NMR (400 MHz, d_6-DMSO): δ = 10.96 (d, 1H), 10.75 (d, 1H), 9.70 (d, 2H), 9.55 (s, 2H), 9.13 (s, 4H), 9.07 (s, 2H), 8.76–8.69 (m, 2H), 8.01–7.94 (m, 2H), 7.64 (s, 4H), 7.32 (s, 4H).

General Procedure for the Synthesis of 3a–3n. Nitro-olefins **1** (0.02 mmol), 1,3-dimethylbarbituric acid (**2**) (3.12 mg, 0.0200 mmol), and 5 mol% **P** catalyst in water (1 mL) were stirred at room temperature for the respective time period (see Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with chloroform. The solvents were evaporated in a rotary evaporator, and the products were characterized by standard analytical techniques such as ^{1}H and ^{13}C NMR, elemental analysis, and ESI-MS.

General Procedure for the Synthesis of 6a–6h. 9-Hydroxymethylanthracene (**4**) (4.16 mg, 0.0200 mmol), the corresponding N-substituted maleimides **5** (0.02 mmol), and 5 mol % **P** catalyst in water (1 mL) were stirred at room temperature for respective time period (see Table 3). The progress of the reactions was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with chloroform. The solvents were evaporated in a rotary evaporator, and the products were characterized by NMR and X-ray single crystal structure.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b12237.

Synthesis of the ligands, NMR spectra, and characterization data of the products of catalytic reactions, including Figures S1–S42 and Tables S1–S4 (PDF)
X-ray crystallographic data for **6b** (CIF)
X-ray crystallographic data for $\mathbf{L_1}$ (CIF)
X-ray crystallographic data for **P** (CIF)

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Notes

The authors declare no competing financial interest.

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