Pillar[n]arene-Based Supramolecular Switches in Solution and on Surfaces

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The design and synthesis of new synthetic macrocycles has driven the rapid development of supramolecular chemistry and materials. Pillar[n]arenes, as a new type of macrocyclic compounds, are used as a promising type of building blocks for switchable supramolecular systems due to their versatile functionalization and the ability of binding toward various guest molecules. A number of guests can form inclusion complexes with pillar[n]arenes and their derivatives in solution, which are sensitive to different external triggers. Interestingly, the pursuit of complex stimuli-responsive functional materials and devices has largely motivated the shift of pillar[n]arene-based switches from solution media to surfaces for controllable macroscopic motions on solid platforms. Facilitated by the facile modification of pillar[n]arenes on various solid supports and the dynamic binding of host–guest complexes, numerous functional hybrid materials with adjustable physical or chemical properties and integrated functionalities have been reported in the last decade. Here, the advance of supramolecular switches in solution and on surfaces based on pillar[n]arenes and derivatives with an emphasis on the efforts and the latest contributions from the field is discussed.

1. Introduction

Inspired by the dynamic and highly self-regulating functional systems in living organisms, researchers in chemistry, biology, and materials science have devoted to the design and synthesis of sophisticated and controllable multicomponent molecular ensembles using a bottom-up approach. Supramolecular chemistry and host–guest chemistry have proven to be powerful tools for researchers to construct artificially switchable assemblies on a molecular level, known as “molecular machines,”[1] and further build smart material systems capable of generating responsive actuations at the nanoscopic or macroscopic scale.[2]

Supramolecular switches as an important member in molecular machinery are defined as molecular ensembles consisting of two or more entities held together by noncovalent interactions. They can be operated dynamically and reversibly in response to specific physical or chemical stimuli including, but not limited to, pH, light, redox, competitive agents, and temperature. In particular, pseudorotaxanes, comprising of a rod component without bulky end groups encircled by a wheel entity via noncovalent bonds, can be employed as a superior class of candidates for supramolecular switches.[3] Therefore, the study of macrocyclic receptors as the wheel entity of pseudorotaxanes has become one of the research hotspots in the field and received great attention.[4]

Following the advance of macrocyclic chemistry based on crown ethers, cyclo­dextrins, calixarenes, and cucurbit[n]urils, pillar[n]arenes (n = 5–15), first reported by Ogoshi et al. in 2008, have emerged as a rising star among synthesized macrocycles.[5] Pillar[n]arenes, composed of n hydroquinone units linked by methylene bridges at the 2- and 5-positions, possess rigid pillar-like molecular structures and π-electron rich hydrophobic cavities that are favorable for the binding of electron-deficient guests.[6] Owing to the highly modifiable rims of pillar[n]arenes, numerous pillar[n]arene derivatives with diverse functionalities can be facilely obtained either via the cyclization of pretailored 1,4-dialkoxybenzene monomers or by postsynthetic modification.[7] The versatile functionalization of pillar[n]arenes beneficially affords their possible usages in both organic and aqueous phases, making the host–guest interactions with a large variety of ionic or neutral guests possible.[8] Thus far, pillar[n]arenes and their derivatives have served as a prominent family of building blocks for the rational creation of supramolecular switches on the basis of the formation of various pseudorotaxanes upon their responsive complexation with guest entities.[3]

Although the dynamic activities of supramolecular switches are generally and fundamentally investigated in solution, growing interest has been focused on the transfer of supramolecular switches from solution phase to more condensed phases, that is, solid surfaces and interfaces. Through the incorporation on rigid solid supports of metal or other inorganic surfaces, the installed switches are able to produce amplified collective switching motions, concurrently modulating the surface properties and endowing the inherent substrates with valid responses to specific triggers.[8a,9] Hence, the shifting of supramolecular switches from solution to solid surfaces denotes a significant step toward the realization of artificial nanosystems with operationally controllable properties, stimuli-responsive features, and multifunctionalities.
In this review article, we will provide a comprehensive illustration on supramolecular switches based on pillar[n]arene derivatives, followed by the notable shift of these switchable assemblies from solution to surfaces/interfaces. Switching mechanisms of the host–guest complexes formed by pillar[n]arene derivatives and their guest molecules of different types are explained. Stimuli-responsive materials constructed by the rational hybridization of supramolecular switches with various solid surfaces, such as porous nanomaterials, metal nanoparticles (NPs), and 2D nanosurfaces, are overviewed with an emphasis on our own efforts and the latest contributions from the experts in the field.

2. Supramolecular Switches Based on Pillar[n]arene Derivatives in Solution

The most commonly used pillar[n]arenes are pillar[5]arene (P5) of five-membered ring and pillar[6]arene (P6) of six-membered ring due to their facile synthesis, relatively high synthetic yields, regulated pillar structures, and the well-studied host–guest chemistry. With a cavity size of 4.7 and 6.7 Å, respectively (Scheme 1), both P5 and P6 could form 1:1 inclusion complexes with appropriate guest molecules depending on the “size-fit” principle and the matching of charges. Therefore, P5 and P6 have been intensively applied as receptors for particular guests in responsive switchable systems. Remarkably, a new analog of P6 was reported by our research group in 2018, namely, leaning pillar[6]arene (LP6), which possesses a cavity size of 6.6 Å and a macrocyclic skeleton identical to P6 but in a tilted version with four hydroxyl or alkoxy functional groups removed on the opposite phenyl rings (Scheme 1). The exploitation of LP6 as a building block of supramolecular switches has also been performed owing to the comparable structural properties and identical functionalization manner with P5 and P6. Since the investigation on the host–guest properties of LP6 is still in its infancy, fundamental studies on suitable guest species and the guest binding selectivity are expected to be conducted for further promising applications not only in switchable systems but also for many other possibilities.

Thanking to the versatility of functionalization on pillar[n]arene rings, the category of guest entities suitable for host–guest inclusion complexation includes a wide variety of candidates (Scheme 1). Cationic guests that are extensively used in the fabrication of supramolecular ensembles of pillar[n]arenes mainly comprise of methyl viologen (MV) and/or its derivatives (G1), pyridinium salts (G2), and quaternary ammonium salts (G3, G4), because of their strong electrostatic attractions with the electron-rich cavities and/or the negatively charged portal groups of pillar[n]arenes. Interestingly, anionic molecules such as aliphatic (G5) and aromatic sulphonate compounds (G6, G7) can also serve as suitable guests for pillar[n]arene derivatives when the rims of pillar[n]arenes are functionalized with cationic groups. In organic solvents, alkyl chains containing electron-withdrawing groups (halogens, cyano, imidazole, and triazole) are considered as favorable choices for host–guest complexation with hydrophilic pillar[n]arenes (G8, G9). Besides, as a unique type of neutral guests, ferrocene and its derivatives (G10) could interact with P6 cavity in aqueous media mostly driven by hydrophobic forces, while the binding affinities between their neutral states and P6 are severely dwindled in organic solvents. Especially, cation-modified azobenzene groups can also be included in pillar[n]arene cavities as photo-responsive guests (G11, G12).

On the basis of these fundamental studies, supramolecular switches that can be actuated by different triggers have been obtained by integrating the above guests with different pillar[n]arene derivatives. External stimuli including pH, light, redox processes, temperature variation, and competitive binding have been universally used for the operation of the simplest switchable complexes (Scheme 2). Uniquely, comparing to the supramolecular switches composed of other macrocycles, an important dissimilarity of pillar[n]arene-based switches is that external stimuli not only function via adjusting the chemical properties of guest entities or thermally elevating the instability of the complexes but also exert impact on the macrocyclic rings of pillar[n]arenes with modifiable rims, allowing for the expanded possibility of stimulus types. Among the triggers in the operation of pillar[n]arene-based switches, a typical example of stimulus that modulates the macrocycles...

is the pH-responsiveness of host–guest complexes formed by carboxylatopillar\[n\]arene (n = 5 or 6, in this paper, CPn is used to represent the sodium or ammonium salts form unless otherwise noted) and cationic guests (Scheme 2A,a). The protonation of the carboxylate anions on the both rims of CPn upon acidification largely moderates the electrostatic forces with the guest molecules, thus causing the decomplexation.[13a] Regarding other stimuli such as light and redox, the switching motions are mostly accomplished through the regulation of the guest molecules configurationally or electronically. Azobenzene-containing cationic guests in the trans-form could bind with pillar[6]arene derivatives via hydrogen bonds and π–π interactions, and the association could be reversibly tuned by photochemical triggers, i.e., the radiation of UV and visual light, because the larger molecular size of the azobenzene groups in the cis-form upon photoisomerization fails to match the P6 cavity (Scheme 2B,b).[17b] Different from the photoinduced structural modulation, supramolecular switches that are responsive to redox process can be operated by adjusting the electrochemical properties of guest molecules (Scheme 2C). Typically, stable host–guest complexes can form between ferrocenium cations (Fc\(^{+}\)) and per-butylated pillar[6]arene with a strong binding affinity in organic media, whereas the reduction of Fc\(^{+}\) into ferrocene can minimize the host–guest interaction and lead to the dissociation of the two components (Scheme 2c).[16a] Another model of redox-responsive switches is composed of MV groups and the pillar[n]arene hosts. Bicationic MV entities can establish multiple electrostatic interactions with anionic CPn rings, thus forming host–guest complexes with high binding strength (CP5: \(K_a = (8.20 \pm 1.70) \times 10^4\) M\(^{-1}\); CP6: \(K_a = (1.02 \pm 0.10) \times 10^8\) M\(^{-1}\)).[13] which can be dwindled as MV groups could be reduced to radical monocations in a reversible manner (Scheme 2d).[13a] On the other hand, temperature variation and competitive binding as another two types of external stimuli could trigger the dynamic motions of supramolecular switches via affecting the binding affinity of host and guest entities, which are universally applicable to almost all types of pillar[n]arene- or synthetic macrocycle-based supramolecular switches (Scheme 2D,E).

Considerable effort has been devoted to the exploitation of the guest species and complexation manners of pillar[n]arene derivatives, and the understanding of the switching mechanisms was strived for and obtained with extensive investigations. Based on the abovementioned modulation patterns, switchable intermolecular ensembles with more sophisticated structures and multiple responsiveness have been developed in solution using pillar[n]arene derivatives as building blocks. For example, stimuli-responsive supramolecular polymers have been fabricated in both aqueous and organic media, functioning as drug delivery systems,[19] fluorescent gels or inks,[20] and light harvesting materials.[21] The polymerization driven by host–guest binding showed excellent reversible switching activities and responses to triggers, which can be demonstrated by macroscopic processes, including morphology changes, cargo release induced by breakage of the assemblies, visible sol-gel transition, fluorescence peak shifts, and changes in fluorescent intensity. This represents an important trend of the switching systems from simple host–guest complexes to larger assemblies or bulkier materials that can function and generate responsive motions at macroscopic scale.

3. Supramolecular Switches Based on Pillar[n]arene Derivatives on Surfaces

For the fabrication of more complicated functional systems, an ensuing and essential step to afford stimuli-responsive materials or devices is to yield collective macroscopic motions via incorporation with other functionalities and effective manipulation of the switching activities.[20] On the basis of the host–guest researches that dominate the function of pillar[n]arene-based supramolecular switches in solution, the...
transfer of the switchable host–guest systems from solution phases to solid surfaces has been emphasized in the field of supramolecular chemistry and materials sciences, due to the accumulative yearning for the intelligent nanoscale artificial devices.\cite{23,24} Significantly, the versatility of functionalization of pillar[n]arene and the diversity of their guest compounds allow many possibilities for the immobilization of pillar[n]arene-based switches onto the surfaces of solid materials. Being provided a robust platform to give collective and amplified motions, supramolecular switches could offer the modified substrate with unique dynamic and controllable characteristics and stimuli-responsive properties.

### 3.1. Supramolecular Switches Based on Pillar[n]arene Derivatives on Porous Nanomaterials

With the main members comprising mesoporous silica nanoparticles (MSNs), metal–organic frameworks (MOFs), and zeolites, porous nanomaterials with stable physical and chemical properties, well-defined structures, and inherent porosities have been utilized for the accommodation and protection of cargo molecules. Owing to the significance of targeted delivery and controlled release of particular chemical compounds for diverse applications such as the therapeutic process of cancer, the exploitation of the above “vehicles” and their further functionalization have received much attention in the past decade.\cite{25} One important method of functionalization is to install gatekeepers (or nanovalves) on the surfaces of solid carriers to prevent cargo leakage and realize on-command release.\cite{26} To guarantee the desired operation of nanovalves, the selected components functionalized on surfaces are required to switch to their “open” state when activated by a variety of external stimuli that exist around the targeted sites, thus making supramolecular switches to be among most promising choices of drug-delivery strategies. Therefore, on account of their well-studied host–guest properties and functionalizing approaches, pillar[n]arene-based supramolecular switches have served as a promising type of gatekeepers for the solid cargo carriers.

#### 3.1.1. MSNs

MSNs are a major attractive type of inorganic nanomaterials, and also regarded as the first generation of solid supports that were installed with gatekeepers for controlled release of drugs and cargos.\cite{23,24} As mentioned previously, a seminal prerequisite for supramolecular switches to operate as gatekeepers for targeted release is their ability to be activated by different stimuli after being delivered to the specific sites. For instance, tumor cells are known to be relatively more acidic compared with normal cells, rendering pH-responsive nanovalves preferable in the drug delivery systems for cancer therapy. The first pillar[n]arene-based supramolecular switch functionalized on MSN surface was reported by our research group in collaboration with Stoddart in 2013, taking advantage of the pH-responsive host–guest complexation of CP5 rings and pyridinium stalk components (Figure 1A).\cite{25}

Due to the alterable binding affinity, the complex could undergo disassociation in acidic conditions where the carboxylate anions on CP5 rims are turned into its acid form, thus leading to gate opening and cargo release. On the other hand, since the dynamic nature of supramolecular switches allows multiple actuations to function simultaneously, the realization of multi-stimuli responsiveness would undoubtedly improve the release efficiency and the versatility of adjustment. Accordingly, besides the stimulus of pH changes, the pillar[n]arene-based switch is also operable by competitive binding upon the addition of MV with a larger host–guest binding affinity with CP5. Similarly, the competitive binding strategy was applied in the treatment of central nervous system diseases, where the supramolecular switch that can be activated by the complexation of CP5 and a neurotransmitter in cholinergic synapses, acetylcholine, was anchored on MSN surfaces for site-specific drug release.\cite{26}

Metal ions, especially Ca$^{2+}$ and Zn$^{2+}$, exist at various concentrations in different parts of living organisms and depend highly on the health conditions of the local tissues. Apart from pH variation and competitors, metal coordination is also a powerful stimulus to activate pillar[n]arene-based supramolecular switches. Because pillar[n]arene rings used in the gate-keeping systems are generally water-soluble and equipped with functional groups such as carboxylate and phosphonate groups that could act as coordination sites, the electrostatic forces with the guest would decrease when the negatively charged groups are coordinated (Figure 1B). CP5, CP6, and phosphonated/phosphoryl pillar[5]arene (PP5) have been used in the construction of switches that are responsive to the coordination of a variety of metal ions.\cite{27,28} Importantly, specific ion-responsiveness of the switches could also add to the targeting ability of drug carriers and further guarantee the accuracy of delivery.

Temperature elevation could also lead to the decomplexation of pillar[n]arenes from the stalks. Thanksing to the elegantly practiced hybridization of MSNs and the photothermal agent gold nanorods (AuNRs), near-infrared (NIR) irradiation can serve as a prominent stimulus for supramolecular switches to effectively operate under elevated temperature. For instance, supramolecular switches consisting of PP5 and choline (Ch) were immobilized on the exterior surface of MSNs with AuNRs embedded in their cores by Du and co-workers (Figure 1B).\cite{27} The heat generated from conversion of NIR light energy by the AuNR core could weaken the host–guest interaction and cause PP5 to depart the Ch stalk, releasing the drugs from MSN pores. Considering the significance attached to photothermal treatment in tumor theranostics lately, drug delivery systems bearing temperature-responsive switches are promising to offer the synergetic therapeutic effect of photothermal therapy (PTT) and chemotherapy.

Apart from biomedical fields, pillar[n]arene-based supramolecular switches have been installed on MSNs for other applications such as anticorrosion coating for alloy materials.\cite{28,30} For example, Fu and co-workers reported the immobilization of CP5-based switches on MSNs and its response to alkaline and Mg$^{2+}$ for controlled release of corrosion inhibitor 2-hydroxy-4-methoxy-acetophenone (HMAM) and protection of magnesium alloy.\cite{28} Instead of detethering from the stalks, the CP5 ring would switch from the hexadiamine (HDA) station to the alkyl pyridine station because of the deprotonation of amine groups on the stalk upon raising the pH, loosening the switch to unblock the entrapped HMAM (Figure 1C).
Other types of porous silica materials have also been installed with pillar[n]arene-based gate-keeping systems. In 2016, hollow MSNs (HMSNs) modified with CP5-based supramolecular switches were fabricated by Huang and co-workers, which could release DOX at low pH values.[31] As another demonstration, we reported the use of LP6-based switches as gatekeepers on mesoporous silica nanobeans (MSNBs) for drug delivery in 2019.[32] MSNBs, as a novel type of MSNs, were synthesized and tethered with a disulfide-bond-containing stalk named 1,3-dimethyl-benzoimidazolium (MBM) and tetraphenylethene (TPE) groups (Figure 2). Upon forming host–guest complexes of carboxylated leaning pillar[6]arene (CLP6) and MBM, the nanovalves on MSNB were closed. Because of the carboxylate groups of CLP6 and the disulfide bonds of MBM, the switches could be effectively activated by either pH decrease or glutathione (GSH). Due to the quenching effect resulting from electron transfer between TPE and MBM, MSNBs showed a turn-on fluorescence in the departure of MBM upon GSH addition, exhibiting in situ imaging during drug release.

3.1.2. MOFs

Being highly emphasized and intensively investigated by researchers since the first report by Yaghi and co-workers,[33] MOFs represent a new class of porous hybrid materials and
have been widely used as cargo reservoirs because of their structural uniformity, desirable stability, biocompatibility, high surface area, and high porosity. Abundant researches have confirmed that MOFs could serve as favorable candidates in the construction of theranostic platforms for biomedical applications.[34] Particularly, MOFs serving as drug carriers can be endowed with optimized performances including less premature leakage and enhanced release precision upon the installation of supramolecular switches.

In 2015, CP5-based supramolecular switches were first anchored onto MOF exteriors by our group.[35] CP5 encircled the stalk Py on the monodispersed nanoMOFs (UMCM-1) after drug loading, closing the valve to seal the cargo inside. The supramolecular switches can be operated in response to pH variation or the addition of competitive agents (Figure 3A).

Following the similar methodology, several CP5-based multistimuli-responsive switches have been functionalized on MOFs for targeted and on-command drug release aiming at the treatment of various diseases. Especially, Ca\(^{2+}\)-activation of the switches is potentially beneficial in bone regeneration,[36] while Zn\(^{2+}\)-responsiveness would be applicable in central nervous system recovery.[37]

Subsequently, pillar[n]arene-based supramolecular switches were further functionalized on tailored multifunctional MOFs to attain better therapeutic performance. Strategies for the hybridization of MOFs and other functional materials have been developed in the form of core–shell structures, and endowed the systems with integrated functionality. In 2018, we reported the fabrication of core–shell nanoplatform Fe\(_3\)O\(_4\)@MOF modified with CP6-based supramolecular switches (Figure 3B).[38] Incorporating superior magnetic resonance imaging (MRI) ability and multi-responsive drug release chemotherapy, the nano-platform was able to perform imaging-mediated drug delivery and the subsequent tumor suppression. Importantly, CP5 was used in this work for comparison to prove that CP6 had higher affinity with the stalk and contributed to the higher tightness of the nanovalves, which was advantageous for sustained release of drug. Another demonstration of supramolecular switches on hybridized MOFs was reported in the same year, where polypyrrole@UiO-66 core–shell nanohybrid was surface-functionalized with CP6-based switches and folic-acid-conjugated polyethyleneimine (PEI–Fa), for controlled release of drug and enhanced tumor targeting, respectively (Figure 3C).[39] The polypyrrole nanoparticles in the core, as the organic photothermal agent, generated higher temperature under NIR radiation and initiated chemo- and photothermal therapy simultaneously, while the combo of PEI–Fa layer and pH/temperature dual responsive switches could largely improve the accuracy of delivery. Such stratagem of installing supramolecular switches on integrated nanoplatforms provided a prominent approach by performing highly site-specific drug administration and synergistic treatment for theranostic purposes.

### 3.2. Metal Nanoparticles

Metal NPs have been considered as an important class of materials in the advancement of nanoscience and nanotechnology. Surface functionalization of metal NPs plays a vital part in tuning the characteristics including optical properties, catalytic capacities, and assembly–disassembly activities.[40] The immobilization of supramolecular switches is intensely performed on the surfaces of various metal nanoparticles including gold nanoparticles (AuNPs), Fe\(_3\)O\(_4\) NPs, quantum dots (QDs), CuS NPs, and upconversion nanoparticles (UCNPs), largely facilitating the potential applications in catalysis, biomedicine, sensors, and electronic nanodevices.[24,41] Particularly, a key step to install supramolecular switches on

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**Figure 2.** CLP6-based supramolecular switches on MSNBs for controlled drug release and real-time imaging. A) Mechanism of GSH-induced fluorescence enhancement. B) Transmission electron microscopy (TEM) image of the modified MSNB. C,D) GSH-dependent fluorescence enhancement of the DF-MSNB in deionized water (C) and conditions mimicking the tumor microenvironment (D). E) Drug release behavior of the modified MSNB by GSH or under acidic conditions: a) time-dependent DOX release at different concentrations of GSH (a) and in PBS solutions of different pH conditions (b); c) premature release in deionized water. A–E) Adapted with permission.[32] Copyright 2019, Royal Society of Chemistry.
metal NPs is to use macrocycles to yield stabilized surfaces of the NPs.\[41\] Because of the symmetric and versatile substitution on both rims, pillar[n]arene derivatives have been employed for surface modification, introducing new functions and effective regulation of the self-assembly of NPs via host–guest interactions.\[7,42\]

Among the studied metal NPs, AuNPs are one seminal class of nanomaterials that attract much attention owing to their unique properties such as inherent localized surface plasmon resonance (LSPR) and surface enhanced Raman scattering (SERS) capability. As aforementioned, it is essential to obtain stable and well-dispersed NPs in the modification of pillar[n]arenes on AuNPs. In this respect, AuNPs have been successfully stabilized by water-soluble or amphiphilic pillar[5]arene functionalized with imidazolium groups,\[43\] amine groups,\[44\] carboxylate groups,\[45\] and ammonium groups,\[46\] possessing favorable chemical stability and potentials in catalysis and sensing. Significantly, the preparation protocol was further advanced with CP5 serving as both the reducing agent and the stabilizer (Turkevich method), giving the modified AuNPs with larger diameters and high stability against salts and pH variations.\[47\] The selection of pillar[n]arene stabilizers and the researches on the preparation methodologies of hybridization have laid a robust foundation for the subsequent exploration on the switching characterizations.

Switchable operation of pillar[n]arene-modified AuNPs was first initiated via supramolecular self-assembly of CP5-AuNPs prepared by our group in 2013 (Figure 4A).\[45\] Upon addition of guest viologen molecules, self-assembly of CP5-AuNPs ensued and the switching activities were recorded by UV–vis absorption spectrometry and transmission electron microscopy (TEM), demonstrating its potential as optical probes for paraquat analogs. Interestingly, Huang and co-workers reported the fabrication of supramolecular hybrid nanostructures generated from CP6-based switches on AuNPs in aqueous media, showing various morphologies including micelles, onion-like disks, and vesicles that can be adjusted by simply adding different amount of hydrophobic chain functionalized paraquat derivative (Figure 4B).\[48\] AuNRs were also modified with CP6 to give switchable nanostructures in this work for loading and releasing cargo molecules upon low pH or NIR radiation, suggesting great potentials in biosensors and nanomedicine.

Responses toward temperature variation and light irradiation are regarded as powerful operations for the manipulation on the assembly of nanomaterials. In 2015, Chen and co-workers demonstrated the synthesis of AuNPs modified by thermoresponsive polymers that were obtained via reversible addition-fragmentation chain transfer (RAFT) polymerization with the monomer N-isopropylacrylamide (NIPAM) and terminated by pillar[5]arene rings (Figure 4C).\[49\] The hybrid material could undergo self-assembly into micelle structures depending on ambient temperature and further transform into vesicles as the guest molecules were introduced, integrating the thermoresponsive features of polymers and host–guest properties of pillar[5]arenes. In the same year, a switchable nanosystem containing AuNPs immobilized by sulhydryl-functionalized...
pillar[n]arene (SH-P5) was constructed in organic solvents by Zhou et al., in which the assembly activity of the coated nanoparticles was efficiently regulated by the host–guest complexation and anthracene photodimerization of the guest (Figure 4D). Based on the reversible properties of the thermo- and photoresponsive switches on the AuNPs, the hybrid material SH-P5-AuNPs was testified as a promising reusable and separable catalyst in organic phases.

Novel derivatives of pillar[n]arenes have also been involved in the modification of metal NPs. For instance, in 2019, we used CLP6 to fabricate the hybrid CLP6-AuNPs via one-pot synthesis as demonstrated in previous literature, whereby self-assembly was achieved with the addition of viologen derivatives and water-soluble TPE-based guest molecules and monitored by UV–vis adsorption, solution colors, and TEM images (Figure 5A). Although abundant pillar[n]arene-modified AuNPs are fabricated via postmodification or the classic Turkewich method as conducted in the above researches, it is worth mentioning that investigations on new preparation approaches have also been carried out. In 2019, we reported the in situ syntheses of CP5- and CP6-coated AuNPs through a reversed Turkewich method, where HAuCl₄ was added dropwise into the boiled solutions of CP5 or CP6 that acted as both the reducing agent and stabilizer (Figure 5B). The as-prepared hybrid CP5-AuNPs-RT and CP6-AuNPs-RT possessed well-controlled AuNP diameters and the coverage of a nanoporous layer of the macrocycles on the particle exteriors. CP6-AuNPs-RT, selected for the further exploration of the self-assembly with MV due to the higher host–guest binding affinity between CP6 and MV, had demonstrated ultrasensitive label-free detection through UV–vis spectra and also showed superior catalytic activity for the reduction of nitrophenols.

Other types of metal nanoparticles also underwent the hybridization with pillar[n]arene-based supramolecular switches for the integration of properties and potential applications particularly in probing and sensing. For instance, AgNPs, as important building blocks for hybrid nanomaterials, have been incorporated with water-soluble pillar[n]arene derivatives by Xue and co-workers to construct switchable assemblies that were operated by host–guest interactions and monitored by TEM, SPR signals, and color changes, suggesting promising applications as optical probes for the detection of bioactive molecules including glutamic acid, paraquat analogs, and spermine. In 2013, we reported the CP5-based switches modified on Fe₃O₄ NPs, whereby the as-prepared material functioned as a magnetic extraction adsorbent in solid phase for the...
analysis of a series of pesticide residue in beverage samples. PP5 was also used to immobilize Fe$_3$O$_4$ NPs for switchable operations with imidazolium cation guest for separating and enriching cell membrane proteins from cell lysites. QDs have been installed with pillar[n]arene-based supramolecular switches in 2013 by our group, in which the assembly of the CdSe QDs can be triggered by the addition of MV bridges. Similarly, Li and co-workers also demonstrated a type of responsive liquid QD system anchored with pillar[n]arene-based switches via host–guest interactions, acting as a fluorescent film sensors for lysine. By effectively tuning the optical properties (for silver NPs) or fluorescence properties (for QDs), pillar[n]arene-based switches on these inorganic NPs could endow the inherent materials with adjustable association to the surroundings, mostly the presence of guests, thus making them promising sensors and probes for the detection of various analytes. In terms of the modified Fe$_3$O$_4$ NPs, besides analysis and separation, biomedical applications such as combined diagnosis and therapy based on MRI and drug release would also be made possible.

Remarkably, another two important inorganic nanoparticles, namely, CuS NPs and UCNPs, have been highly regarded as preferable agents in theranostic applications for their superior capacity of administrating PTT and upconversion luminescence (UCL), respectively. In 2018, Yu and co-workers reported the construction of a smart hybrid nanomaterial that integrated targeting, drug delivery, and PTT by the coating of CPS on the surface of CuS NPs (CP5@CuG) and the installation of a galactose derivative (G) for liver-cancer targeting (CP5@CuG) via host–guest binding (Figure 6A), of which the function was monitored by real-time thermal imaging and fluorescence spectroscopy. DOX was loaded onto the exterior of CP5@CuG through intermolecular electrostatic interaction with CP5, and the drug release activity can be regulated by pH and NIR irradiation, showing combined therapeutic effect. With an identical method, Gd-doped UCNPs were modified with CP5-based switches by Wang, Sun, and co-workers for pH-operated drug release capable of UCL and magnetic resonance imaging (MRI). In 2018, we reported the fabrication of PP5-based supramolecular switches on UCNPs by facile ligand exchange and the further loading of cargo molecules RhB via host–guest interactions and electrostatic forces (Figure 6B). The modified nanoparticles performed pH-responsive cargo release and ideal UCL imaging in physiological environment.

The hybridization of metal NPs with other inorganic scaffolds is also an important and attractive area. Uniquely, pillar[n]arene-modified metal NPs have been used to act as gatekeepers for MSNs grafted with stalk entities. The NPs are immobilized onto the MSN surfaces upon the formation of supramolecular switches via host–guest complexation in order to block the cargos inside and to exert extra functionality for the system. In 2016, we reported the MSNs capped with CP5-modified AuNPs for on-command cargo release with minimized premature leakage and good responses toward higher temperature and competitive binding of ethylenediamine (EDA) (Figure 7A). Subsequently, as another demonstration of the
Fe3O4 NPs for the promotion of plant growth. The switches per­nanosystem consisting of HMSNs gated by CP5-modified with Han and co-workers, we reported a phytohormone delivery uli­responsive, and specifically selective properties.[9]

substrates and to endow the nanosurfaces with dynamic, stim­switches to function as oriented molecular machines on solid faces of substrates represents an important measure for the The implementation of supramolecular switches onto the sur­faces of 2D substrates due to the facile preparation and unique plas­matic properties. In 2015, perhydroxylated pillar[5]arene and chemical properties. In 2015, perhydroxylated pillar[5]arene were covalently attached to their readily availability and high stability regarding the physical and chemical properties. In 2015, perhydroxylated pillar[5]arene and perhydroxylated pillar[6]arene were covalently attached to a hydrophilic silica substrate to give a 2D hybrid material for effective paraquat adsorption, while the adsorption efficiency depended on the host–guest binding affinity (Figure 8C).[71] Following the same route, Li and co-workers reported the supramolecular strategy to control the adhesive binding of herbicide droplets on surfaces by immobilizing pillar[5]arene rings with alkylnyl groups on one rim onto a silica substrate (Figure 9A).[72]

3.3. 2D Nanosurfaces

The implementation of supramolecular switches onto the sur­faces of substrates represents an important measure for the switches to function as oriented molecular machines on solid substrates and to endow the nanosurfaces with dynamic, stim­uli-responsive, and specifically selective properties.[9]

Au surfaces are regarded as one of the most favorable types of 2D substrates due to the facile preparation and unique plasmonic properties. Li and co-workers reported a pillar[n]arene-based thermoresponsive switch anchored on gold surface, whereby the monofunctionalized anthracene pillar[5]arene interacted with an imidazolium-containing ionic liquid (IL) that was modified on the surface via thiol groups (Figure 8A).[66] Possessing a long alkyl chain and a positively charged “head,” the hydrophilic IL group could form inclusion complex upon interaction with the hydrophobic pillar[5]arene host. The complexation and disassociation of the switches highly depended on the temperature variations and could further modulate the surface characteristics between hydrophilicity and hydrophobicity upon heating and cooling, indicating application potential in memory storage devices and sensors.

Graphene, including its derivatives graphene oxide (GO) and reduced graphene oxide (RGO), is another emerging class of 2D nanomaterials with well-studied functionalization methods and fascinating electronic and optical properties, rendering it ideal solid substrate for the hybridization with supramolecular switches. In the preparation protocols, water-soluble pillar[n]arenes have been used for the surface modification of GO for enhanced biocompatibility and water dispersity.[67] In 2013, Diao and co-workers demonstrated the formation of a ternary nanomaterial of RGO–macrocycle–metal NPs comprising of the hybridized RGO layers modified with amine-containing amphiphilic pillar[5]arene prepared via in situ reduction and the anchoring of AuNPs in response to electrochemical switching operations.[68] Subsequently, CP5 in the protonated state was covalently modified onto RGO surfaces to yield hybrid nanosheets, which showed superior dispersity in aqueous solution and fine fluorescence quenching ability toward organic dye molecules, Rhodamine 6G (Rh6G) and neutral red (NR), owing to the fluorescence resonance energy transfer (FRET) from the dyes to RGO induced by the host–guest interaction (Figure 8B).[69] Similar work also demonstrated graphene layers functionalized with pillar[n]arene-based switches that contained fluorescent guest molecules quenched by the RGO substrate and could be activated by competitive binding upon UV ana­logs, exhibiting fluorescence turn-on imaging.[70]

Silica substrates have been widely used as solid supports for the immobilization of materials at molecular level because of their readily availability and high stability regarding the physical and chemical properties. In 2015, perhydroxylated pillar[5]arene and perhydroxylated pillar[6]arene were covalently attached to a hydrophilic silica substrate to give a 2D hybrid material for effective paraquat adsorption, while the adsorption efficiency depended on the host–guest binding affinity (Figure 8C).[71] Following the same route, Li and co-workers reported the supramolecular strategy to control the adhesive binding of herbicide droplets on surfaces by immobilizing pillar[5]arene rings with alkylnyl groups on one rim onto a silica substrate (Figure 9A).[72]
The pillar[5]arene-functionalized surface performed selective binding toward the paraquat droplets (G2) through host–guest interactions, which was verified by the sliding behaviors of the droplets (Figure 9B), providing a new approach for improving the efficiency of herbicide usage. Interestingly, another pillar[n]arene-based switch was constructed for protein adsorption by regulating the surface properties of a silicon substrate, in which the host–guest interactions between pillar[5]arene functionalized with ten butyl groups and the guest adipic acid on the substrate were operated by pH variations (Figure 9C), leading to the switchable adsorption of bovine serum albumin (BSA) through hydrophobic effect.[73]

An important and eye-catching topic in biological fields and materials science is the design and construction of biomimetic artificial channels as well as the functionalization of the inner channel walls. In 2016, Li and co-workers reported...
a biomimetic potassium-transporting nanochannel fabricated from poly(ethylene terephthalate) (PET) gated by supramolecular switches based on the host–guest complexation of mercaptoacetic acid pillar[5]arene (MAP5) and HDA for the inhibition of mercury poisoning (Figure 9D). The MAP5-based switches could be modulated from “on” to “off” via the specific binding of mercury ions and thiol groups and the dethreading of MAP5 from HDA, concurrently causing the alteration of the surface charge and wettability of the nanochannel and thus controlling the potassium ion transport. The pillar[n]arene-based supramolecular switches on the nanochannel internal surfaces endowed the material with great potential in biosensors, toxicological analysis for Hg^{2+}, and programmable electronic logic devices.

4. Summary and Outlook

Since pillar[n]arenes first sprouted in 2008 as a new branch of macrocyclic chemistry, considerable fundamental research has been concentrated on the diversified functionalization on pillar[n]arene rims and molecular recognition between the pillar[n]arene rings and guest compounds, associated with the capacity to accommodate various types of guest species and the versatile controlling approaches to adjust the binding dynamics that are investigated in solution. Accordingly, the results of these basic investigations have powerfully supported the further pursuit of more complicated switchable systems based on the host–guest chemistry of pillar[n]arene derivatives.

In this review, we have presented the creation and operation patterns of pillar[n]arene-based supramolecular switches triggered by different external stimuli, followed by the noteworthy evolution of these switches from solution phases to the surfaces of a broad variety of solid substrates and the applications of the afforded responsive materials in many fields. Among the materials modified by pillar[n]arene-based supramolecular switches, porous nanomaterials including MSNs and MOFs are principally used in the range of biomedicine as drug delivery systems. Metal nanoparticles are equipped with the switches for
the controllable assembly–disassembly activities and the efficient capture of particular guest molecules, finding applications in smart sensors and catalysis. 2D nanosurfaces, with gold, silica, or graphene as the substrates, can perform tunable physical or chemical characteristics and optimized surface properties endowed by the installment of the pillar[n]arene-containing switches. Multi-responsiveness to several triggers can also be realized in the hybridization with the solid surfaces. The successful tethering and functioning of the pillar[n]arene host–guest complexes on the surfaces or interfaces can persuasively

Figure 9. A–E) Pillar[n]arene-based supramolecular switches on silica substrates (A–C) and on inner walls of artificial nanochannels (D, E). A) Tunable surface properties on silica substrate via host–guest interaction for controllable assembly of paraquat aqueous droplets and B) the selective adhesion of the PSA-functional surface to G2 (paraquat) droplets among a series of viologen derivatives on the PSA-modified surface tilted to 45°. A, B) Reproduced with permission.© 2016, Wiley-VCH. C–a) pH-activated supramolecular switches on silicon substrate that can be turned “on” and “off” via pillar[n]arene-based host–guest binding for protein BSA adsorption, whereby the on-off switching behavior of the wettability of the substrate is shown in (b). C) Reproduced with permission.© 2016, Wiley-VCH. D) Supramolecular switches based on MAP5 for the regulation of the ion transporting of the nanochannel and the switching activities in response to Hg²⁺. c) The changes of contact angles of the modified surface. D) Reproduced under the terms of the CC-BY Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/).© 2016, Royal Society of Chemistry. E) Supramolecular switches based on CP5 on the interior nanochannel surface for temperature responses. d) The current–voltage curve and e) contact angles before and after the close of the switches. E) Reproduced with permission.© 2017, Wiley-VCH.
demonstrate the strong possibility for pillar[n]arene-based supramolecular switches to be used in the rational design and establishment of responsive functional materials. With the emergence of new pillar[n]arene derivatives and the advance of host-guest chemistry based on synthetic macrocycles, future developments of switchable systems based on pillar[n]arenes are envisaged to further enrich the application range of supramolecular switches and benefit the advance of stimuli-responsive materials and intelligent nanodevices.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

nanoparticles, pillararenes, stimuli-responsive materials, supramolecular materials
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