Semi-Rigid Molecular-Clip-Based Molecular Crystal Gearshift

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ABSTRACT: A new version of molecular clip, with a semi-rigid symmetrical crab-type architecture and flexible cavity size, has been successfully designed and synthesized via a one-pot Friedel–Crafts alkylation reaction. The X-ray single-crystal diffraction data provide a simple and intuitive explanation, not only for its well-preorganized and regulated conformation but also for its selective and tunable guest-binding capability. For the first time, the newly designed molecular clip was demonstrated to be not only a controllable variable-speed nonporous adsorption material in solution iodine capture, but also capable of on–off switching in volatile iodine capture. The presented new concept of molecular crystal gearshift directly from the molecular clip crystals represents an important advance in the development of synthetic receptor chemistry, which will exert a significant influence on small-molecule crystallography.

KEYWORDS: molecular clip, crystalline materials, X-ray diffraction, host–guest chemistry, molecular crystal gearshift

A supramolecular toolbox containing multiple types of synthetic receptors with tailored structures and excellent host–guest properties contributes significantly to different areas of research, including host–guest chemistry, gas storage and adsorption, targeted drug delivery, molecular machinery, and energy materials. Therefore, the design and synthesis of supramolecular synthetic receptors with tunable binding affinities and responsive properties has been one of the cutting-edge research topics along with the rapid development of supramolecular chemistry.1–26 Among them, molecular tweezers and clips, a wide class of acyclic-type molecular receptors with cavities of flexible size, are the most persuasive examples.18–26 Accordingly, their syntheses, binding properties, supramolecular functions, and stimuli responsiveness have been intensively studied.19–21,24 However, some key issues of the aforementioned acyclic receptor systems remain to be solved. For example, in the syntheses of molecular tweezers and clip derivatives, repetitive Diels–Alder reactions followed by further oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone are usually needed,20 limiting their wide use and further development. Besides tedious synthetic steps, overflexible and unregulated/uncontrollable belt-shaped conformations also limited their cavity adaptability and application.17 Enlightened by the synthetic chemistry of certain macrocyclic ligands, such as cucurbit[n]urils and pillar[n]arenes that possess a stable pumpkin- or pillar-shaped cavity architecture with good rigidity by connecting their monomers with methylene bridges,3,8 we come up with an idea of designing a methylene-bridged open-shell molecular clip (MC) with regulated conformations of certain rigidity via a facile and concise synthetic approach.

Here, we report a wholly original form of a methylene-bridged, self-rigid molecular clip (MC) system, namely, 1,4-bis(2,4,6-trimethoxybenzyl)naphthalene (Figure 1 a), which has three features: (i) two pincers of 1,3,5-trimethoxybenzene are covalently connected to a naphthalene by methylene bridges at the 1- and 4'-substitution positions, (ii) two sidewalls form an extended cavity, endowing it with guest-binding capability, (iii) the naphthalene backbone together with the switching units of methylene linkers guarantees its tunable binding affinity and responsive property. Benefiting from these structural characteristics, molecular clips are expected, and also have been found, to have extraordinary conformation-variable structures, selective guest-binding capability, and more importantly, efficient application as molecular crystal gearshifts.

The synthetic strategy for MC was highly efficient and extremely straightforward, where a facile one-pot Lewis-acid-catalyzed method was employed. Briefly, 1,4-bis(chloromethyl)naphthalene was reacted with an excess amount of 1,3,5-trimethoxybenzene catalyzed by AlCl₃ in a Friedel–Crafts alkylation reaction, leading to the formation of the MC host in a good yield of 70% (Scheme S1, Figures S1–S3). Significantly, a series of high-quality single crystals of MC and...
its host–guest complexes with different targets, referred to as MCα, I$_2$⊂2(MC), 2(H$_2$O)⊂MC, DCM⊂MC, and mX⊂MC (mX represents m-xylene, Figure 1b–g, Tables S1, S2, and Figures S7–S13), have been obtained. To our surprise, inorganic and organic targets (iodine, water, dichloromethane, and m-xylene), with different shapes, sizes, and stoichiometries, can be stably hosted in the MC, and multiple intermolecular interactions enhance these sandwich type of host–guest complexes (C–H···π distance, 2.851 Å; O–H···O distance, 2.494 Å; Cl···π distance, 3.590 Å; and I···π distance, 3.123 Å), which demonstrates that the MC is highly effective for cargo capture owing to the expanded π-electron-rich cavity. The MC receptor does not have an absolutely rigid structure, and the dihedral angle values of the two pincers rendered a sharp increase in the order MCα (44.42°) < DCM⊂MC (49.76°) < 2(H$_2$O)⊂MC (51.66°) < I$_2$⊂2(MC) (54.15°) < mX⊂MC (57.15°), giving an approximate 13° angle change due to the well-known size-fit effect and guest-induced fit theory in host–guest chemistry. In addition, the diameter of the inner circle of MCα is about 7.4 Å (Figure 1b, the value of 7.4 Å was obtained by subtracting two van der Waals radii of oxygen atoms from the distance between two farthest methoxy groups). Furthermore, a molecular configuration with two pincers inverted and distorted was also simultaneously obtained (referred to as MCβ, Figure 1g), which reflects the conformational diversity and controllability of MC molecular crystals in the solid state.

Single-crystal structure analysis on MCα and MCβ reveals a dense packing in both crystalline phases, as stabilized by multiple C–H···O and π···π interactions (Figures S7 and S8, C–H···O distance for MCα, 2.745 Å; C–H···O distance for MCβ, 2.677 Å; C–H···O distance for MCα, 3.581 Å; π···π distance for MCβ, 3.607 Å). But an average torsion angle of 20° between the 1,3,5-trimethoxybenzene units and the naphthalene ring and the stretching of two 1,3,5-trimethoxybenzene units in opposite directions were found in MCβ (Figure S8b), in sharp contrast to the 3° angle and the same direction of stretching in MCα (Figure S7b). This means that in the phase transition from MCα to MCβ, one of the claws needs a rotation of ca. 180°, followed by stretching of two pincers at a certain angle in the opposite direction along with the plane of naphthalene ring, suggesting that the symmetric and extended π-electron cavity is completely destroyed and the high-density π-electron atmosphere no longer exists in the MCβ crystal solid.

Radionuclide fission products, such as the hazardous iodine isotope ($^{129}$I and $^{131}$I), are uncontrollably spilled out and cause severe damage to human beings during nuclear waste treatment or nuclear accidents, e.g., the Fukushima nuclear disaster.27–29 According to the single-crystal structure of I$_2$⊂2(MC), as mentioned above, each iodine molecule is located in the extended cavity between two opposite but malposed MC molecules (Figure S11c), and typical charge-transfer (donor–acceptor) interactions (I···π distance, 3.123 Å) enhance the stability of the host–guest complexes. So, we anticipate that this MC receptor can serve as a new material for iodine uptake. On top of that, combined with the multiforomey and controllability of MC molecular crystals, we introduce a concept of “molecular crystal gearshift” for the first time.

To be more confirmative, MCα, MCβ, and DCM⊂MC crystals were immersed in a 1/2/n-hexane solution (0.02 mol/L). Time-dependent photographs were taken and UV–vis experiments were conducted to compare the adsorption rates, both quantitatively and qualitatively (Figures 2a,b and S18). As was expected, the reddish brown solution gradually changed to colorless at different speeds (Figure 2c). For MCα, the iodine concentration decreased to 0.003 mol/L after 140 min of successive adsorption (Figure S18c). With regard to MCβ, its adsorption rate is far less than that of the former, and a 400 min continuous solution adsorption could achieve the same effect as the 140 min adsorption of MCα (Figure S18b). Interestingly, host–guest complex crystals of DCM⊂MC, without further desolvation or activation, possess the highest adsorption capacity and efficiency among all systems. The UV–vis experiment confirmed that the iodine removal efficiency was more than 90% after only 50 min of solid–solution contact time (Figure S18a).

On the basis of the results of iodine adsorption in solution, we can easily find that the adsorption rates render a decrease in the order DCM⊂MC > MCα > MCβ, confirming a three-speed gearshift adsorption system regulated by MC. The fastest adsorption rate of DCM⊂MC indicates that the host–guest complexes of I$_2$⊂2(MC) are more stable than DCM⊂MC. Thus, straightforward guest exchange upon exposure to iodine solution resulted in the transition from DCM⊂MC to I$_2$⊂2(MC), and the powder X-ray diffraction (PXRD) patterns before and after the adsorption procedures are all in
agreement with the simulated patterns (Figure S19), further proving that the crystalline phase transition induced by guest exchange really occurred. CH$_2$Cl$_2$ molecules not only occupy the ringent cavities but also "protect" them, thus improving the available active cavity volume and reducing the interference from multiple intermolecular interactions due to all kinds of packing modes to a certain extent. As for the MC$_\beta$ crystal, the PXRD pattern after complete capture of iodine in solution is consistent with the simulated pattern from I$_2$⊂2(MC), also in step with the pattern of MC$_\alpha$ crystals after in-solution iodine loading (Figures S21 and S22), indicating that both structures change to I$_2$⊂2(MC) upon capture of iodine in solution.

For further explanation, an important MC isomer (MC$_\alpha$), by linking 1,3,5-trimethoxybenzene at the 1'- and 5'-substitution positions (Scheme S2 and Figures S4–S6), has been designed and successfully synthesized. From the crystal structural analysis, the two claws are in parallel (3.569 Å) and in a reversed direction in the MC$_\alpha$ crystal (Figure S13), and no effective $\pi$-electron donor cavity exists in a single molecule, thus, unsurprisingly, scarcely any iodine is adsorbed (Figures 2b and S18d), which gives strong evidence for the necessity of the extended cavity of MC hosts in iodine capture. All in all, the available $\pi$-electron cavity volume indeed determines the nature of this binding speed diversity.

The three-speed direct-shift effect of MC crystals on solution iodine binding kindled our interest in finding out whether some transformation relationships exist between these "gear-shifts". Evidently, a similar crystal-to-crystal transition from MC$_\alpha$/DCM⊂MC to MC$_\beta$ is observed during heating (Scheme 1), and the PXRD profiles of these two transformed
crystals are all in good agreement with the patterns simulated from MCβ (Figures S23–S26). In other words, these crystal phase transformations are also equivalent to a shift from a high-speed gear to a low-speed gear. Meanwhile, I₂ ⊂ 2(MC) crystals laden with guests can also be transformed into MCβ upon heating, as verified by PXRD and DSC analysis (Figures S29 and S30), which means the low-speed gear is the thermodynamically favored phase, and can also be regarded as the loop start and loop end for this variable-speed adsorption cyclic process. As shown in Scheme 1 and Figure 3, the speed changing adsorption system based on the MC can be shifted down by continuous heating, and geared up by easy recrystallization in toluene (restore medium speed) or CH₂Cl₂ (restore high speed), proving to be a fully stimuli-responsive/controllable new system.

The newfangled variable speed control of MC crystals in solution iodine binding inspired us to further investigate these properties in air. Thereupon, MCα, MCβ, DCM ⊂ MC, and MC1α were placed under an I₂ vapor atmosphere for several hours to investigate their I₂ vapor sorption capacity. As depicted in Figures 2c and S32, MCα and DCM ⊂ MC crystals gradually changed from colorless to distinctive brown. But thermogravimetric measurements give a clear indication that only MCα crystals present an effective adsorption (Figures S29 and S30).
tweezer system is predominantly a receptor that occurs in solution iodine adsorption. However, as to conversion and regain the binding capability, just as liable to MAG processes. Moreover, hardly any weight loss is observed below 150 °C, which indicates the relatively high thermal stability of iodine in MCα crystalline phases (Figure S34). But, to our surprise, MCβ solids barely adsorb iodine in air, even after a longer adsorption time (Figures 2c and S32c), which means iodine vapor cannot, at any rate, easily induce the conformational conversion and regain the binding capability, just as liable to occur in solution iodine adsorption. However, as to DCM C MC, CH2Cl2 cannot stably exist, and a solid–solid transition from DCM C MC to MCβ occurs due to the relatively high temperature of the experimental process (Figures S25 and S26), which gives a good explanation for the poor adsorption in air (Figures S32b and S36).

Interestingly, the iodine vapor adsorption capability of the MC is completely on–off controllable. The molecular conformation of MCα represents the “turn-on” state, which possesses the loading/capture ability toward iodine no matter in the form of vapor or in solution. However, the MCβ crystalline phase without π-electron cavities represents the “turn-off” configuration, barely adsorbing volatile iodine. Finally, N2 adsorption experiments revealed that MCα and MCβ crystalline solids are all nonporous (Figures S44 and S45), giving much more convincing evidence that MCβ crystals are in a completely “closed” state in iodine vapor atmosphere.

**CONCLUSIONS**

In conclusion, we presented a new type of dynamic molecular clip, with synthetic ease, and multiple and absolutely controllable conformations. Taking advantage of this unique structural feature, inorganic or organic species different in shape, number, and size can be stably hosted, including but not limited to, dichloromethane, water, m-xylene, and iodine, which makes the molecular clip possess a wide array of potential applications in the capture of volatile radionuclide fission products, purification of BTEX chemicals, and water harvesting. Furthermore, the included angle changes of molecular clips also provide a simple and intuitive explanation for guest-induced fit theory and cavity adaptability in host–guest chemistry and crystal engineering, further confirming the importance of this rigid/steerable backbone in molecular recognition and cargo storage. Moreover, we have demonstrated that this molecular clip could construct a variable-speed cyclic adsorption system for iodine solution uptake, where facile switching among the high-, middle-, and low-speed gear (adsorption rate) was achieved as a result of the crystalline phase/molecular configuration-controllable manual control. Importantly, our results led to a new concept of molecular crystal gearshift, where such an organic small molecule can be employed as an adsorbent in pollutant disposal with a specified range of operating rates. However, there must be more potential gearshifts yet to be found or tested, and hopefully our current work based on this newly synthesized molecular clip will help inspire and enable further discoveries and industry applications of new molecular crystalline materials.