

審査の結果の要旨

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The elaborate substrate specificity in the binding pocket of enzymes is often governed by the subtle variation in amino acid residues that exist, not at the interior, but at the exterior of the pocket. Even a single amino acid difference at the exterior of the pocket makes a big difference. In this way, a small difference at a given remote site is transmitted and amplified over the entire cavity through space, resulting in fine-tuning of the characters and functionality of enzymes.

Synthetic coordination cages have nanometer-sized, large hydrophobic cavities where organic molecules are bound and reacted. Typically, the cage framework determines the guest-binding ability, and the outer ancillary groups locating hardly change the property of the cavity. In this study, the remote substituents on ancillary groups located outside cage cavity but significantly modified the inner cavity in size and shape, thus tuning the functionality of the cavity.

This thesis contains below 7 chapters:

Chapter 1. The introduction of “Remote Control” in natural enzyme and the purpose and design of this research.

Chapter 2. Synthesis of M_6L_4 cages with different remote pendant groups and cavity comparison of these cages. A variety of self-assembled coordination cages with *cis*-chelating phenanthroline ancillary ligands. Different substituents were introduced at 2,9-position of phenanthroline. Since the remote pendant substituents on ancillary groups of the ligand hang over the cage cavity, specific interactions can be introduced. Computational study was done for investigating how cavity volumes were affected by remote substituents. Bulky mesityl groups were proved to dramatically reduce the cavity volume of cage by 20%, comparing to the non-substituent cage. Since a variety of *cis*-chelating ligands can be employed as ancillary groups, our approach provides the most efficient and straightforward way to subtly control the binding properties of the cages.

Chapter 3. Guest binding properties of M_6L_4 cages were tuned by remote pendant groups on ancillary ligands. The binding properties of a self-assembled coordination cage were compared by encapsulation of various guest molecules. Because the different remote pendant groups have modified cavities in shape and size, guest-binding properties were found totally different from unmodified cages. Different cavities prefer different species of guest in size, shape and rigidity. The cavities of the cage were proved to be very sensitive for guest species and size. Typically, cage with shrunken cavity efficiently bound small rigid tetrahedral shape guests, whereas unmodified cage cannot. Even a single methyl difference in ancillary ligand results in big difference in guest binding. Moreover, a minor difference in size of rigid guest also results in difference in inclusion yield.

Chapter 4. Guest motion behaviors of M_6L_4 cages were tuned by remote pendant groups on ancillary ligands. Similar like guest-binding, guest mobility largely depends on the cavity volumes

of synthetic hosts. Low symmetrical guest molecules were employed to investigate guest motion with the cavities with or without modification. With increasing the bulkiness of the pendant groups, the restraint of guest motion was gradually enhanced, due to the step-wisely increasing of host-guest tightly packing. Although not involved in the framework of the cage and not touch the guest, the *para*-methyl groups on the mesityl pendant groups dictate guest motion and sufficiently freeze the guest motion at high temperature during NMR time scale.

Chapter 5. Diels-Alder reactions were dramatically accelerated by M_6L_4 cages with shrunken cavity. The shrunken cavity brings the dienes and dienophiles into close proximity and significantly low the entropy costs of Diels-Alder reaction between them, thus Diels-Alder reactions were dramatically promoted inside the shrunken cavity. Small dienes, such as phenanthrene and fluoranthene, were activated for Diels-Alder reactions only within the shrunken cavity. Furthermore, shrunken cavity serves as a discriminating cavity environment to efficiently release the Diels-Alder product, thus furnishing the reaction in a catalytic fashion. No catalytic reaction was observed for unmodified cavity due to product inhibition.

Chapter 6. Artificial structure also can be changed by remote substituents. Pyridyl groups locate far from the major metal-binding site (Schiff base units) of the chiral linear ligand but govern the formation from helicate to coordination networks. Due to the different priorities in coordinating with metal, Schiff base units firstly bind metal ions to form helicate then the network was construct by connecting the remote pyridine moieties. Such bottom-up assembly approach provide the insight of self-assembly as well as modulation of sophisticated functional materials.

Chapter 7. Summary of this thesis and outlook.

以上、本論文では、酵素に特異の高効率・高選択的な分子認識と触媒反応の遠隔制御に着目し、自己組織化中空錯体の内部空間を精密に遠隔制御することにより中空錯体に特異的な分子認識、分子運動の制御と二分子高効率Diels-Alder反応触媒化の研究を行った。遠隔置換基と中空錯体の間で相互作用が働くため、自己組織化中空錯体の内部空孔が収縮されていることが分かった。また、遠隔置換基により、自己組織化中空錯体の分子認識能と分子の運動の制御を実現した。さらに、自己組織化中空錯体の収縮された内部空孔において、Diels-Alder反応の高効率化と触媒化を実現した。最後に、ピリジン遠隔置換基により、自己組織化螺旋体からネットワーク錯体まで構造の制御を実現した。以上の知見を組み合わせることで、既存の反応開発の設計指針では達成できない新たな化学反応の開拓が可能となる。

よって本論文は博士（工学）の学位請求論文として合格と認められる。