Development of Artificial Receptors Based on Assembly of Metal Complex Units and Desymmetrization of Molecular Components

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Natural receptor proteins can bind substrates selectively at the pocket surrounded by multiple amino acid residues. Relatively weak intermolecular interactions, such as hydrogen bonds, are synergistically exerted during the recognition events. Meanwhile, it was difficult for synthetic receptors to achieve precise molecular binding by arranging various interaction moieties in an unsymmetrical manner. In this presentation, novel macrocyclic receptors developed based on two concepts, that is, (1) assembly of metal coordination sites (**Fig. 1a**), and (2) desymmetrization of homooligomers (**Fig. 1b**), are reported.

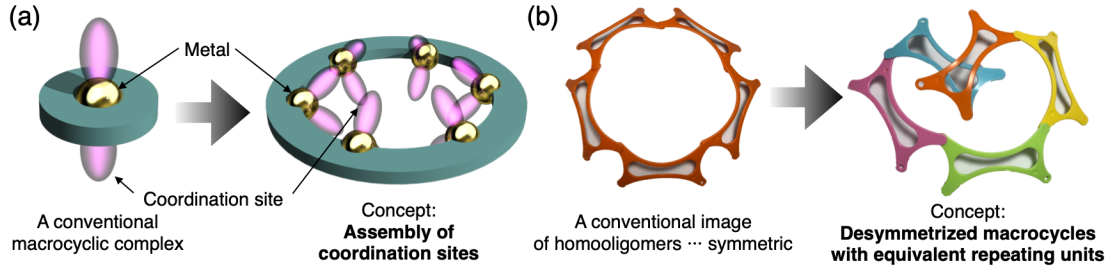

Figure 1. Approaches for macrocyclic receptors with precise molecular recognition. (a) Assembly of metal coordination sites. (b) Desymmetrization of homooligomers.

1. Hexapap[1]: Receptors that capture molecules via multipoint coordination (Fig. 2a)

A macrocyclic ligand with six pap moieties (N_2O tridentate chelate), hexapap, was designed and synthesized. Its hexanuclear zinc complex inwardly arranges multiple labile coordination sites for external molecules. The zinc complex captured two dicarboxylic acid molecules of a specific length in its cavity, and formed a unique wavy-stacked dimeric complex. The saddle-shaped deformation and dimerization realize the desymmetrization, and there are three different Zn-pap units in the dimeric complex. Utilizing this structural feature, the regulation of the guest-binding modes at specific metal coordination sites among the many present has been achieved utilizing acid/base as an external stimuli.

2. Bpytrisalen[2]: Spatial arrangement of different coordination sites (Fig. 2b)

A triangular macrocyclic ligand possessing three units each of the bpy (N_2 bidentate chelate) and salen (N_2O_2 tetradentate chelate), bpytrisalen, has been synthesized. The coordination sites of metals at the bpy are directed inward, while the ones at the salen are vertically pointing out of the macrocyclic plane. Selective anion binding onto the heteronuclear complex has been achieved utilizing the difference in coordination. Furthermore, the orthogonality in coordination has been utilized for the construction of double-decker complex.

3. Saloph-belt[3]: Belt-shaped macrocycles generated from a bis-armed bifunctional monomer (Fig. 2c)

A bis-armed bifunctional monomer bearing two salicylaldehyde units and one *o*-phenylenediamine unit has been designed. Oligomerization of the monomer resulted in the belt-shaped macrocyclic tetramer of saloph (N_2O_2 tetradentate chelate). Its zinc complex exhibited a remarkable selectivity regarding the encapsulation of fullerenes ($K_a(C_{70})/K_a(C_{60}) > 100$). The molecular recognition to distinguish the small difference in size has been realized utilizing the rigid belt-shaped scaffold.

4. Amide-cyclodextrin[4]: Multipoint hydrogen bond utilizing desymmetrized structure (Fig. 2d)

Cyclodextrin derivatives with amide groups directly attached to each pyranose ring were synthesized. The amide cyclodextrins show unique anion recognition properties by multipoint hydrogen bond. Especially, an amide-cyclodextrin derivative possessing seven bipyridyl (bpy) groups forms mononuclear complexes whose specific three bpy groups are linked in the *fac*-Λ configuration, and chiral recognition of amino acid anions has been achieved utilizing the distinctive amide groups arranged on the unsymmetrically fixed scaffold.

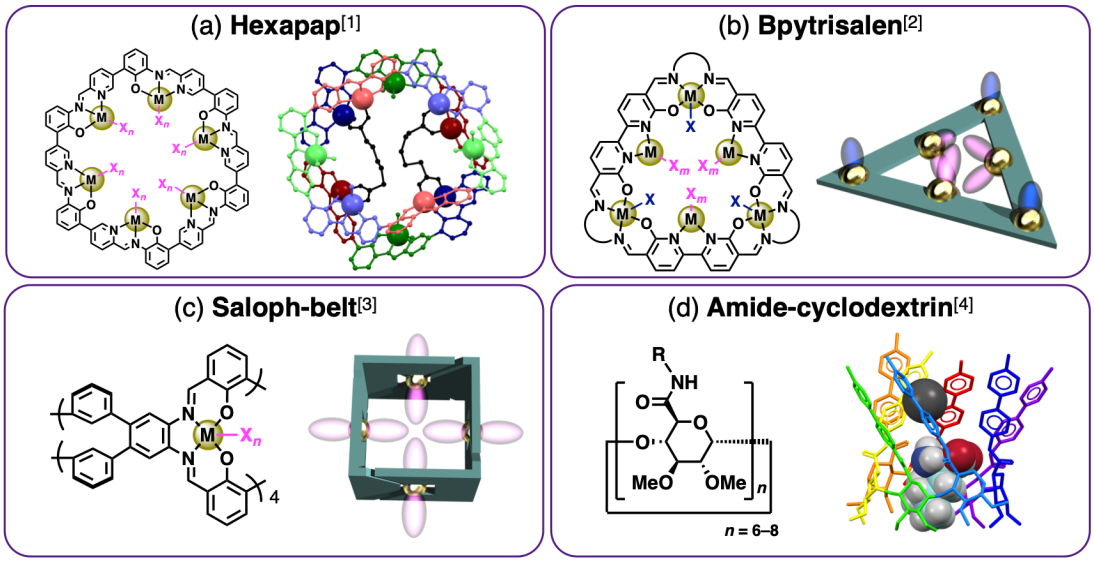

Figure 2. Macrocycles with unique molecular recognition properties developed based on the assembly of metal complex units and the desymmetrization of homooligomers.

References

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