Tetrahedron 71 (2015) 503–522

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Tetrahedron report number 1063

Cryptand-based hosts for organic guests

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ARTICLE INFO

Article history:
Received 4 October 2014
Available online 7 November 2014

Keywords:
Cryptands
Organic guests
Host–guest chemistry
Self-assemblies
Molecular switches
Supramolecular polymers

Contents

1. Introduction

Cryptand-based hosts are a class of macrocyclic compounds with unique three dimensional structures, which have played important roles in constructing different kinds of complexes.[1] In

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http://dx.doi.org/10.1016/j.tet.2014.11.006

comparison with the classical synthetic macrocyclic hosts including simple crown ethers,[2] calixarenes,[3] cucurbiturils,[4] pillararenes,[5] and others,[6–8] cryptand-based compounds[9] usually exhibit much better complexation affinities for large organic guests due to their specific properties of multi-cavity structures, multi-binding sites, and multi-complexation modes.[10]

The first cryptand-based host was reported by Park and Simmons,[11a] and Lehn and his co-workers first introduced the word 'cryptand' to name bicyclic ligands in 1969.[11b] Since then, the development of novel cryptand-based hosts with the capability to bind selected substrates in specific complexation modes is always a very important and attractive topic in host–guest chemistry.[12] At the first stage, the cryptand-based hosts were designed and synthesized to bind metal ions, anions, and small organic guests.[9,13] Later on, especially during the last decade, great progress has been made in the application of cryptand-based hosts to bind large organic guest molecules.[14] To date, different kinds of interlocked assemblies,[15] such as pseudorotaxanes, rotaxanes, and catenanes, have been constructed based on cryptand-based hosts. Moreover, the complexes based on the recognition behaviors of cryptand-based hosts towards organic guests have exhibited wide potential applications in supramolecular polymers,[16] molecular machines,[17] chemical sensors,[18] drug delivery materials,[19] and so on. Thus, to design and construct new cryptand-based hosts for organic guests are not only important to the development of itself, but also very helpful and promotive to the development of materials chemistry, supramolecular chemistry, and other research areas. In this regards, Stoddart's group,[20] Gibson's group,[21] Huang's group,[14a] Chiu's group,[22] Jabin's group,[23] and our group[24] have made great achievements.

During the last two decades, there were several reviews related to cryptand-based hosts. However, most of the reviews focused on the complexation between cryptand-based hosts and anions or metal ions.[9,13] Besides, Huang's group only reviewed their own work on design and synthesis of crown ether-based macrobicyclic cryptand hosts for paraquat derivatives and the application of the cryptand/paraquat recognition motif in the fabrication of topochemical structures, molecular switches, and supramolecular polymers.[10,14a] Therefore, in this review, we will summarize recent endeavors in the synthesis of new cryptand-based hosts, including macrobicyclic-based cryptand hosts, macrotricyclic-based cryptand hosts, calixarene-based cryptand hosts, and other cryptand hosts, and further highlight the complexation between these cryptand-based hosts and organic guests. The applications of the cryptand-based hosts in the construction of mechanically interlocked molecules, such as rotaxanes and catenanes, molecular switches, and supramolecular polymers will also be discussed.

2. Macrobicyclic-based hosts for organic guests

In 1997, Gibson's group found that bis(1,3-phenylene)-32-crown-10 (BP32C10) could form the taco complexes with a series of organic guests in the solid state.[25] Inspired by this discovery, the authors further designed and synthesized the first macrobicyclic-based host **2-1** (Fig. 1) to enhance the strength of the complexation, which showed higher association constants with organic guests than those of BP32C10 as expected.[21] Since then, a series of macrobicyclic-based hosts designed for organic guests (Fig. 1) have been reported owing to their specific properties.

2.1. Synthesis

Starting from bisphenol **2-34** and **2-35** (Fig. 2), macrobicyclic-based cryptand hosts **2-1**, **2-7**, and **2-19** were synthesized using the pseudo-high dilution technique in 38%, 41%, and 25% yield, respectively.[21,26,27] The relatively lower yield of **2-19** might be resulted from the more rigid starting material **2-35** compared with **2-34**.[27]

Treatment of bis(5-bromomethyl-1,3-phenylene)-32-crown-10 **2-36** (Fig. 2) with hydroquinone afforded host **2-2** in 42% yield.[26] Similarly, hosts **2-3**∼**2-4**, **2-9**, and **2-10** were synthesized in reasonable yields by the reaction of **2-36** with 2-carbomethoxy- hydroquinone, 3,5-dihydroxybenzyl alcohol, 4,4′-dihydroxyazobenzene, and diethyl 2,5-dihydroxyterephthalate, respectively.[28–30] Moreover, **2-36** could also be converted into cryptand **2-8** via two steps,[31] in which the McMurry coupling reaction was utilized as the final macrocyclization step to synthesize **2-8** in the presence of $TiCl_4$–Zn in 80% yield.

Reaction of bis(5-hydroxymethyl-1,3-phenylene)-32-crown-10 **2-37** (Fig. 2) with 2,6-pyridinedicarbonyl dichloride, or 4-benzyloxypyridine-2,6-dicarbonyl dichloride in high diluted condition afforded the cryptands **2-5**[26] and **2-6**,[32] respectively. Instead of **2-37**, a series of cryptands **2-11**∼**2-18**, **2-22-2-26** were also synthesized by **2-38**∼**2-45** as the starting materials in reasonable yields, respectively.[33–37]

Cryptand **2-21** was obtained in 97% yield by an oxidative coupling method in the presence of $Cu(OAc)_2$ under O_2 at 45–50 °C.[38] With cryptand **2-21** in hands, cryptand **2-20** was then synthesized in 93% yield by Pd/C-catalyzed reduction under H_2. The yields for both two cryptands **2-20** and **2-21** are much higher than those of analogues reported in the literature previously.[38]

In addition, it has been proved that compounds **2-46**∼**2-49** were useful building blocks for the synthesis of macrobicyclic hosts **2-27**, **2-28**, and **2-31**∼**2-33**.[39–42] Biscryptands **2-29** and **2-30** could be prepared by the reactions of hydroxyl-functionalized cryptand **2-4** with terephthalic acid and 1,1′-ferrocenedicarboxylic acid, respectively.[43]

2.2. Host–guest properties

Macrobicyclic-based cryptand hosts have proven to be the powerful hosts for organic guests (Fig. 3), especially electron-deficient guests, which exhibited much higher association constants compared with analogous simple crown ethers, resulting in a series of new host–guest systems.[21]

Macrobicyclic-based cryptand host **2-1** could form a 1:1 'pseudorotaxane-like' complex with **2-50** with the association constant $K_a=6.1\times10^4$ M^{-1}, 100-fold greater than that of simple crown ether-based complexes.[21] In complex **2-1**·**2-50**, there were two H-bonding interactions between two adjacent β-protons of paraquat and the oxygen atom of water molecule besides two H-bonding interactions between two α-protons of paraquat and ether oxygen atoms, while two other H-bonding interactions between two ether oxygen atoms of the host **2-1** and the protons of this water molecule also existed. This was the first reported inclusion complex with demonstrated H-bonding of the β-protons of paraquat.

Hosts **2-3**, **2-5**, **2-6**, (*E*)-**2-8**, **2-11**, and **2-24** could also form the 1:1 complexes with paraquat **2-50**.[26,28,31,34,36] Similarly, hosts **2-1**,[21] **2-6**,[32] **2-11**,[34] **2-22**,[33] and **2-24**∼**2-26**[36,37] could form the 1:1 complexes with *N*-hydroxyethyl paraquat derivative **2-54**. In addition, host **2-10** could form 1:1 complex with guest **2-52**,[30] and **2-17** could form the 1:1 complex with **2-53**.[34] Among them, diester cryptand **2-5** with a pyridyl nitrogen atom exhibited the highest association constant $K_a=5.0\times10^6$ M^{-1} in acetone with paraquat **2-50**, 9000 times greater than that case of the simple crown ether system.[26] Moreover, X-ray crystallographic analysis of complex **2-6**·**2-50** indicated that a dimer (**2-6**·**2-50**)$_2$ was formed in solid state, which was driven by dipole–dipole and face-to-face π-stacking interactions.[32] For hosts **2-13** and **2-17**, it was found that they exhibited good binding affinities for the paraquat dichloride salt **2-51** through ion-pair recognition.[34] A chloride anion filled into the 'pocket' formed on the threading of the pyridinium dication into the cavity of cryptand **2-17** in the inclusion complex structure.[34]