

Oligopyrrolic Cages: From Classic Molecular Constructs to Chemically Responsive Polytopic Receptors

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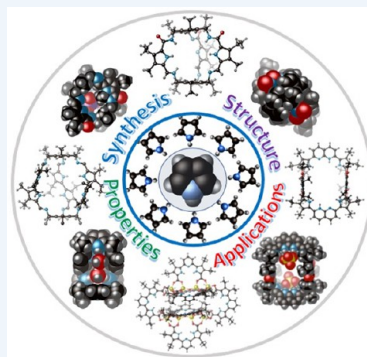
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CONSPECTUS: “Functional molecular systems”, discrete and self-assembled constructs where control over molecular recognition, structure, bonding, transport, release, catalytic activity, etc., is readily achieved, are a topic of current interest. Within this broad paradigm, oligopyrrolic cages have garnered attention due to their responsive recognition features. Due to the presence of slightly polar pyrrole subunits which can also behave as hydrogen-bonding donors, these oligopyrrolic cages are potential receptors for various polarized species. In this Account, we summarize recent advances involving the syntheses and study of (1) covalent oligopyrrolic macrobicyclic cages, (2) oligopyrrolic metallocages, and (3) oligopyrrolic noncovalently linked cages. Considered in concert, these molecular constructs have allowed advances in applied supramolecular chemistry; to date, they have been exploited for selective guest encapsulation studies, anion binding and ion-channel formation, and gas absorption, among other applications. While key findings from others will be noted, in this Account will focus on our own contributions to the chemistry of discrete oligopyrrolic macrocycles and their use in supramolecular host–guest chemistry and sensing applications. In terms of specifics, we will detail how oligopyrrole cages with well-defined molecular geometries permit reversible guest binding under ambient conditions and how the incorporation of pyrrole subunits within larger superstructures allows effective control over anion/conjugate acid binding activity under ambient conditions. We will also provide examples that show how derivatization of these rudimentary macrocyclic cores with various sterically congested β -substituted oligopyrroles can provide entry into more complex supramolecular architectures. In addition, we will detail how hybrid systems that include heterocycles other than pyrrole, such as pyridine and naphthyridine, can be used to create self-assembled materials that show promise as gas-absorbing materials and colorimetric reversible sensors. Studies involving oligopyrrolic polymetallic cages and oligopyrrolic supramolecular cages will also be reviewed. First, we will discuss all-carbon-linked oligopyrrolic bicycles and continue on to present systems linked via amines and imines linkages. Finally, we will summarize recent work on pyrrolic cages created through the use of metal centers or various noncovalent interactions. We hope that this Account will provide researchers with an initial foundation for understanding oligopyrrolic cage chemistry, thereby allowing for further advances in the area. It is expected that the fundamental design and recognition principles made in the area of oligopyrrole cages, as exemplified by our contributions, will be of general use to researchers targeting the design of functional molecular systems. As such, we have structured this Account so as to summarize the past while setting the stage for the future.



KEY REFERENCES

- Bucher, C.; Zimmerman, R. S.; Lynch, V.; Sessler, J. L. First Cryptand-Like Calixpyrrole: Synthesis, X-ray Structure, and Anion Binding Properties of a Bicyclic-[3,3,3]nonapyrrole. *J. Am. Chem. Soc.* **2001**, 123, 9716–9717.¹ This paper is significant because it demonstrated that it is possible to prepare macrobicyclic “cryptand-like” systems based on pyrrolic building blocks. It also details an example of a structurally characterized exoreceptor, compounds that have received renewed attention of late.
- Zhang, H.; Lee, J.; Lammer, A. D.; Chi, X.; Brewster, J. T.; Lynch, V. M.; Li, H.; Zhang, Z.; Sessler, J. L. Self-Assembled Pyridine-Dipyrrolic Cages. *J. Am. Chem. Soc.* **2016**, 138, 4573–4579.² This paper is noteworthy because it demonstrated the self-assembly of an angular

chelate ligand and showed how the process could be controlled via the judicious choice of a specific metal salt that resulted in the formation of pyridine–dipyrrolic polymetallic cages.

- Wang, F.; Sikma, E.; Duan, Z.; Sarma, T.; Lei, C.; Zhang, Z.; Humphrey, S. M.; Sessler, J. L. Shape-Persistent Pyrrole-Based Covalent Organic Cages: Synthesis, Structure and Selective Gas Adsorption Properties.

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Scheme 1. Synthesis of the Oligopyrrolic Calix–Cryptand 1

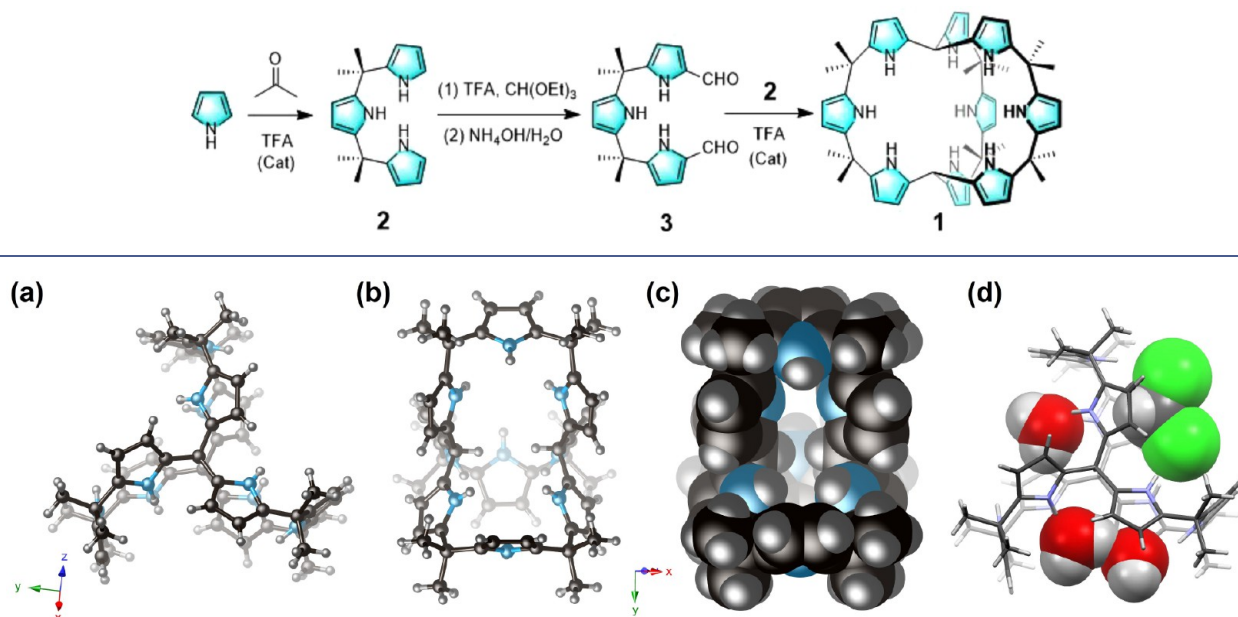


Figure 1. (a–c) Different views of cage **1** as deduced from single-crystal X-ray crystallographic analyses, showing the clefts (a) and the inner cavity (b and c). (d) X-ray crystal structure of the exo complex formed between receptor **1** and the neutral guest molecules H_2O and CH_2Cl_2 . Data from ref 1.

Chem. Commun. **2019**, 55, 6185–6188.³ This paper showcases the use of dynamic covalent chemistry (DCC) to produce symmetric three-dimensional (3D) oligopyrrolic cryptands for potential applications in the area of gas adsorption. This latter application had not previously been explored with pyrrolic cage systems.

- Wang, F.; Sen, S.; Chen, C.; Bähring, S.; Lei, C.; Duan, Z.; Zhang, Z.; Sessler, J. L.; Jana, A. Self-Assembled Cage-Like Receptor that Binds Biologically Relevant Dicarboxylic Acids via Proton-Coupled Anion Recognition. *J. Am. Chem. Soc.* **2020**, 142, 1987–1994.⁴ This report is significant because it demonstrated the reversible “capture” and “release” of dicarboxylic acid guests using a fully organic self-assembled cage-like pyrrolic receptor. Both the supramolecular recognition and the corresponding assembly and disassembly processes were reflected in visible color changes.

1. INTRODUCTION

This Account is concerned with the chemistry of pyrrolic cage systems. Cages of this general class have been the focus of increasing attention since the late 1990s. However, in many respects the antecedents for work in this area can be traced to the revolutionary report of laterally symmetric macrobicyclic “cryptands”⁵ and “cryptates”⁶ by Lehn et al. in 1969 as well as the 1968 report of Simmons and Park of anion binding within a bicyclic diammonium construct.⁷ A spotlight was shown on the cryptands with the awarding of a share of the 1987 Nobel Prize in Chemistry to Lehn, who codified “supramolecular chemistry” as the *chemistry beyond the molecule*.⁸ To date, more than 2000 papers have detailed the synthesis, derivatization, and application of cryptands and their supramolecular complexes to problems running the gamut from fundamental to applied. This activity reflects in large measure the fact that these macrobicyclic hosts can act as artificial synthetic organic (or metal–organic hybrid) receptors for a wide variety of ionic

guests, including protons (H^+) and ammonium (NH_4^+ , R_2NH_2^+ , etc.), alkali, alkaline earth, transition metal, and actinide cations, along with various negatively charged anionic species. The specifics of binding depend, not surprisingly, on the structural features, geometries, functionalities, and electronic environments (e.g., neutral or charged) provided by the cryptand host with guest binding being seen within the internal cavities or outside clefts or both.

Incorporation of pyrroles into bicyclic frameworks creates cryptand-like frameworks that can act as potential functional materials. This functionality can be augmented by including other heterocycles, such as pyridine or naphthyridine, within the superstructures.^{3,9} Incorporation of chelating units can provide for metal-based self-assembly, while the use of β -substituted oligopyrroles can support the formation of complex supramolecular architectures. As a class, oligopyrrolic macrobicyclic cages have been explored for a wide variety of functions, including use as potential receptors, sensors, and gas storage systems. The goal of this Account is to review our contributions to this area within the framework of the field as a whole. Excluded from this Account will be double-walled and multiwalled bis-calix[4]pyrroles since they have been the subject of recent reviews.^{10,11}

2. COVALENT OLIGOPYRROLIC MACROBICYCLIC CAGES

In 2001, Sessler et al. reported a cryptand-like bicyclic[3,3,3]-nonapyrrole¹ (**1**, see Scheme 1) and investigated its anion-binding property. In the solid state, cage **1** adopts a wind turbine-shaped conformation with D_{3h} symmetry in which both of the apical CH hydrogen atoms are pointed in toward the inner cavity (endo–endo orientation). The presence of pyrrolic NH protons in the architecture endows cage **1** with an ability to bind either anions or neutral molecules, such as solvents or water (Figure 1a–c). Cage **1** interacts with these species as an exo receptor rather than accommodating them internally as seen in

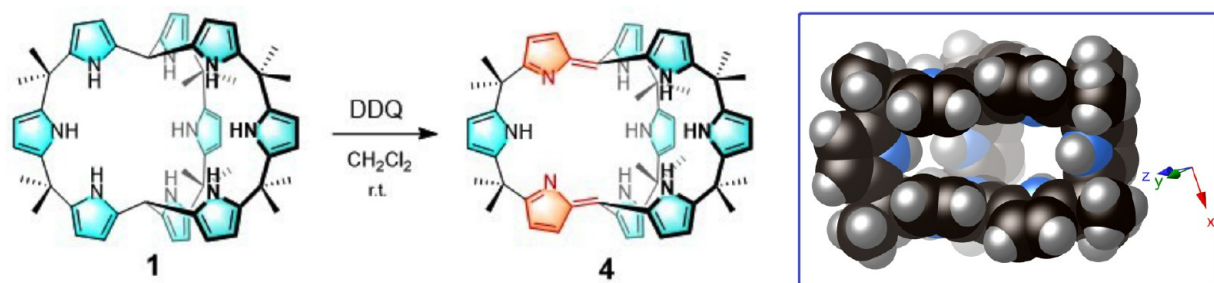


Figure 2. Synthesis of cage **4** via the partial oxidation of **1** by DDQ. (Inset) Space-filling view of the structure of cage **4** deduced from single-crystal X-ray crystallographic analysis. Neutral guest molecules, specifically H_2O , EtOH , and EtOAc , are omitted for clarity. Data from ref 12.

Scheme 2. Synthetic Scheme of Pyrrole–Pyridine–Pyrrole-Based Cryptand **8**

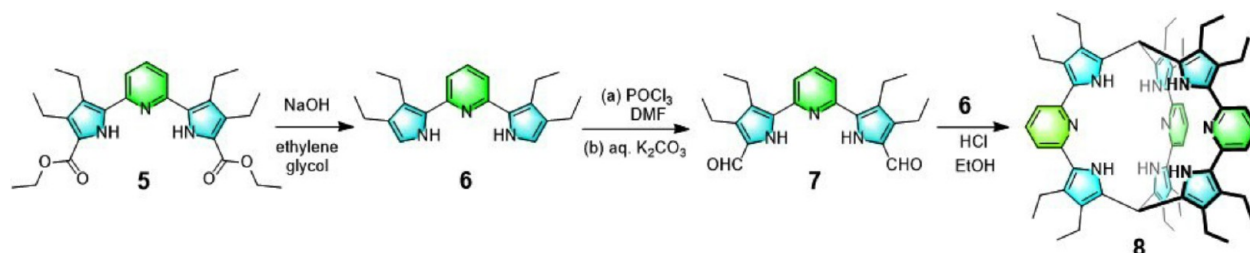
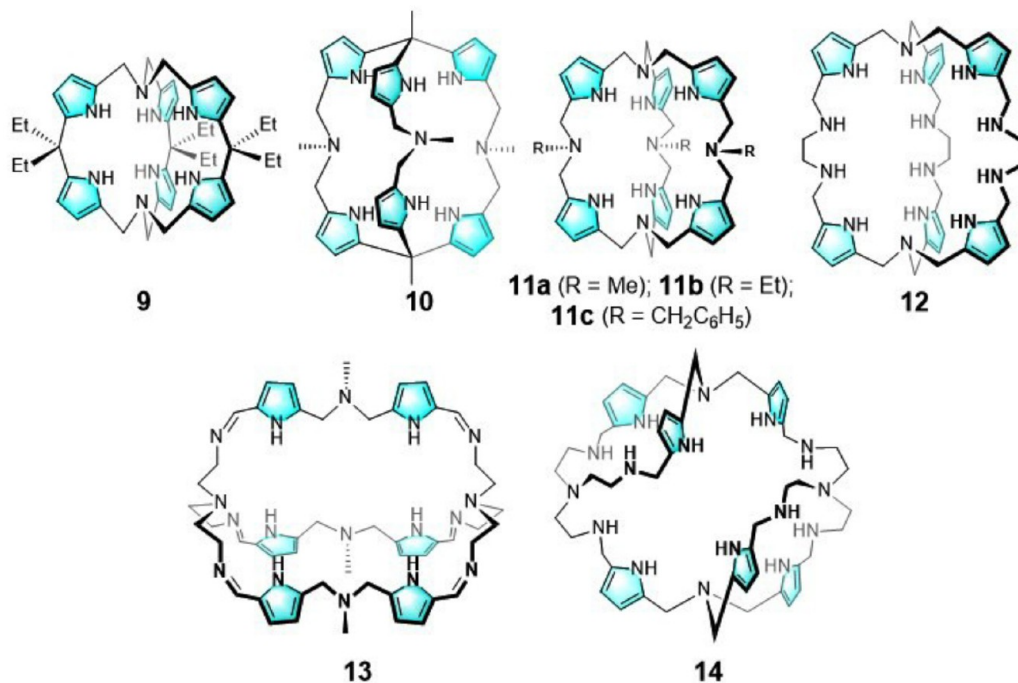


Chart 1. Chemical Structures of Various Oligopyrrolic Cryptand Cages 9–14



the case of most classic cryptate complexes. For instance, as inferred from X-ray crystallographic analyses, one CH_2Cl_2 solvent and three water molecules are located within the three external clefts of **1** via cooperative hydrogen-bonding, halogen-bonding, and $\text{CH}\cdots\pi$ interactions (Figure 1d). In an effort to test the ability of cage **1** to act as an anion receptor, its interactions with a range of anions, e.g., F^- , Cl^- , Br^- , NO_3^- , H_2PO_4^- , and SCN^- , were screened. A significant downfield chemical shift was seen in the pyrrolic NH protons when cage **1** in CD_2Cl_2 was subject to ^1H NMR spectroscopic titrations with various tetra-*n*-butylammonium (TBA) anion salts. In the representative case of

NO_3^- , a fast equilibrium process and an overall $\Delta\delta = 1.1$ ppm downfield shift was seen. These spectral changes were ascribed to the formation of a 1:2 host–guest complex characterized by association constants of $K_1 = 1740 \text{ M}^{-1}$ and $K_2 = 420 \text{ M}^{-1}$, respectively. In contrast to what is seen in the case of NO_3^- , F^- was found to form a 1:1 complex with **1** as inferred from a corresponding ^1H NMR spectroscopic titration. In the case of Cl^- , an overall association constant on the order of 10^6 M^{-2} in CD_2Cl_2 was recorded at 298 K. Very slow exchange was seen in the cases of H_2PO_4^- and SCN^- (as their TBA salts) under otherwise identical experimental conditions. Overall, these

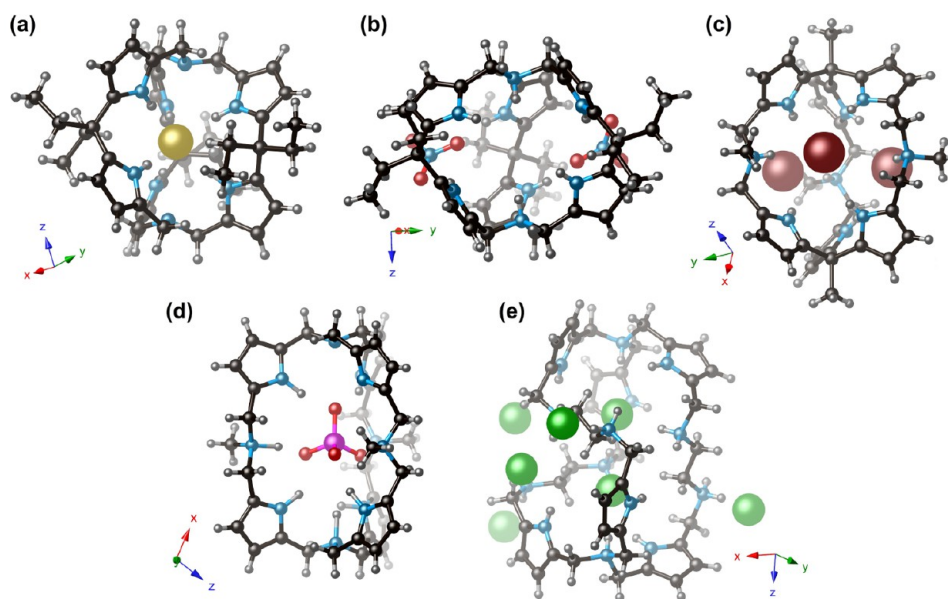
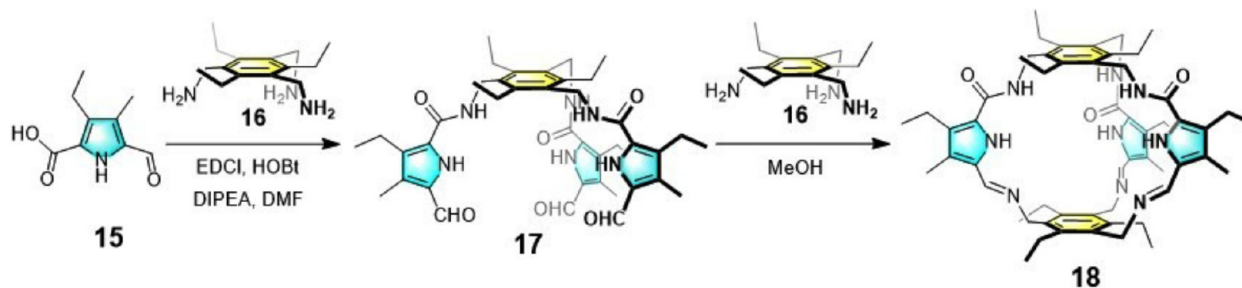


Figure 3. Single-crystal X-ray structures of representative anion-bound cryptates. (a) Fluoride complex of receptor 9, and (b) corresponding nitrate complex. (c) Bromide complex of receptor 10. (d) Phosphate complex of receptor 11a. (e) Chloride complex of receptor 12. Solvent molecules are omitted for clarity. Data from refs 13–17.

Scheme 3. Synthesis of Benzene Bridgehead Oligopyrrolic Cage 18



differences were ascribed to the combined effect of size complementary, steric, and electronic interactions.

Chemical oxidation of cage 1 by 5,6-dichloro-2,3-dicyano-*p*-benzoquinone (DDQ) was found to produce an unprecedented sp^2 -hybridized carbon bridgehead calixpyrin (4) (Figure 2).¹² Compound 4, as a prototypical three-dimensional (3D) calixpyrin, belongs to a class of hybrid molecular systems that bear structural and chemical analogy to both calixpyrroles and porphyrins owing to the presence of both sp^2 - and sp^3 -hybridized meso-like bridging carbon atoms. Distinctive broad absorption maxima (λ_{max}) at 421 and 474 nm were taken as evidence for the generation of partially oxidized species in solution where the characteristic “porphyrin-like” features (e.g., an absorption spectrum containing both a sharp Soret band and weaker “Q” bands) are absent. In contrast to what was observed in the X-ray structure of 1 where the two bridging apical $-\text{CH}$ hydrogen atoms were seen to point inward (endo–endo orientation), the sp^2 -hybridized bridging carbon atom produces a degree of local planarity. The net result is that cage 4 possesses a more open cavity (cf. Figure 2, inset) that was expected to facilitate the “inside binding” of guests.

While this Account is mainly focused on our own contributions, we would like to make clear that subsequent to our initial report of bicycle 1, many elegant oligopyrrolic cages were reported by other research groups. For instance, in 2008,

Setsune et al. reported a highly symmetric pyrrole–cryptand (8) constructed by three dipyrrolylpyridine (pyrrole–pyridine–pyrrole hybrid system) side arms.⁹ The receptor was obtained via an acid-catalyzed condensation of precursors 6 and 7 as shown in Scheme 2.

Starting in 2011, Mani et al. reported a series of cages, compounds 9–14 given in Chart 1,^{13–17} which were seen capable of binding a number of representative anions (e.g., F^- , Cl^- , Br^- , NO_3^- , H_2PO_4^- , and HSO_4^-) in organic media such as CDCl_3 , $\text{DMSO}-d_6$, and $(\text{CD}_3)_2\text{CO}$ under ambient conditions. A few representative X-ray structures of the resulting anion-bound cryptates are shown in Figure 3. In the case of cages 9 and 11a, the F^- and PO_4^{3-} anions were found to be bound within the cryptand cavity (cf. Figure 3a and 3d); however, most of the other anions give rise to exo complexes (cf. Figure 3b, 3c, and 3e).

Dynamic covalent chemistry (DCC) has emerged as an attractive and efficient means for preparing intricate molecular constructs, including macrocycles,¹⁸ cages,^{19–22} and covalent organic frameworks (COFs),^{23,24} and has yielded a number of systems with potential applications.^{25–28} Not surprisingly, DCC has been exploited to access discrete oligopyrrolic cages. Taking advantage of this approach, we designed and synthesized the Schiff-base macrobicyclic cage 18²⁹ starting from a suitably functionalized pyrrolic precursor (15) as shown in Scheme 3.

This phenyl-bridgehead oligopyrrolic cryptand cage contains both imine (hydrogen-bonding acceptor) and amide (hydrogen-bonding donor) functionalities within its side arms. The latter receptor and its analogues were explored as potential supramolecular hosts for specific anions. It was found that cage **18** exhibits specificity toward tetrahedral oxyanions, e.g., H_2PO_4^- , $\text{HP}_2\text{O}_7^{3-}$, SO_4^{2-} , and HSO_4^- , in the noncompetitive solvent chloroform at 298 K. This selectivity is reflected in the calculated K_a values of $1.56 \times 10^4 \text{ M}^{-1}$ for TBAH_2PO_4 , $1.76 \times 10^6 \text{ M}^{-1}$ for $(\text{TBA})_3\text{HP}_2\text{O}_7$, $2.66 \times 10^6 \text{ M}^{-1}$ for $(\text{TBA})_2\text{SO}_4$, and $4.53 \times 10^6 \text{ M}^{-1}$ for TBAHSO_4 , respectively.

Here, it was postulated that the amidic and pyrrolic protons could act as hydrogen-bond donors to the oxygen atom, whereas one or more imine nitrogen atoms could serve as hydrogen-bond acceptors for the OH protons present in H_2PO_4^- . As inferred from single-crystal X-ray diffraction analysis, the H_2PO_4^- anion was found to be nestled within the cavity of cage **18** and apparently was stabilized by such interactions (Figure 4b).

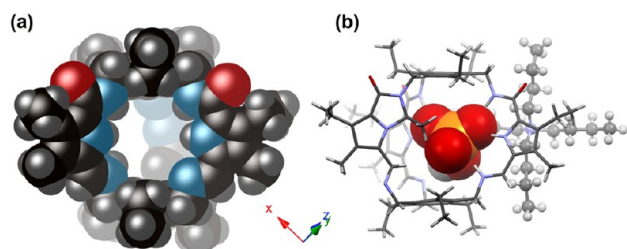


Figure 4. X-ray diffraction structure of the dihydrogen phosphate complex of receptor **18** obtained using single crystals grown by allowing hexanes to diffuse slowly into a chloroform solution of cage **18** in the presence of excess TBAH_2PO_4 . (a) Space-filling representation of receptor **18** with the bound H_2PO_4^- removed to highlight the spherical void volume of the cage that would be expected to pertain in the absence of an anionic guest. (b) Side view of the H_2PO_4^- -inclusion complex of receptor **18** showing the 1:1 host-guest binding stoichiometry. Note: tetrabutylammonium counteraction is denoted by a ball-and-stick model. Solvent molecules are omitted for clarity. Data from ref 29.

A similar [1 + 1] Schiff-base condensation reaction between the phenyl-bridgehead trialdehyde (**20**) and the triamine (**16**) allowed the macrobicyclic imine cage **21** to be synthesized (Scheme 4a).³⁰ In contrast to what was observed in the case of cage **18**, the alkyl-imine-linked system **21** was characterized by selectivity for the fluoride anion, as evidenced by K_a values of $1.01 \times 10^7 \text{ M}^{-1}$ for TBAF for cage **21** vs $1.57 \times 10^6 \text{ M}^{-1}$ for amide-imine cage **18** determined by the absorption spectroscopic titration method at 298 K. This selectivity was ascribed to the rigidity and comparatively smaller cavity size of cage **21** as compared to **18**. When cage **21** was exposed to F^- and various competing anions, e.g., Cl^- , Br^- , I^- , HCO_3^- , SO_4^{2-} , H_2PO_4^- , and $\text{HP}_2\text{O}_7^{3-}$, only F^- produced an appreciable chemical shift in the ^1H NMR spectrum in CDCl_3 at 298 K. Unexpectedly, cage **21** was able to retain the trapped fluoride anion within its cavity even after deprotonation of one or two of the receptor pyrrolic NH protons as evidenced by the ^1H and ^{19}F NMR spectroscopic analyses conducted in $\text{DMSO}-d_6$ at 298 K. The proposed fluoride-binding modes expected to pertain within the cavity of cryptand **21** upon the incremental addition, e.g., >1.66 equiv) of TBAF are shown in Scheme 4b.

Prior to our own contributions, but likewise based on the concept of dynamic imine chemistry, Roelens et al. reported^{31–33} a series of self-assembled polypyrrolic benzene-bridgehead cryptand receptors (**22–24**) (Chart 2). Among this series of receptors, cage **22** was found to recognize β -glucopyranosides with high specificity. This cryptand receptor provides six primary amino groups for complementary hydrogen-bonding interactions with this particular carbohydrate, as inferred from ^1H NMR spectroscopic analyses (CDCl_3 , 298 K). Consistent with this rationale, replacement of the pyrrole subunits in **22** by pyridines and benzenes to produce the isostructural cages **23** and **24** was found to give rise to a reduced level of guest recognition.^{32,33}

Porous organic cages (POCs) have garnered attention as examples of self-assembled architectures. They often display unique guest binding properties, such as the capture of substrates within infinite channels. This has made them of potential interest in the context of many applications, including gas storage,^{34–37} catalyses,^{38–40} and guest separation^{41–45} to name a few. In many instances, dynamic covalent chemistry has been used to access POCs. This is true in the case of pyrrole-

Scheme 4. Synthetic Route to Cage 21 and Its Proposed F^- Binding Mode

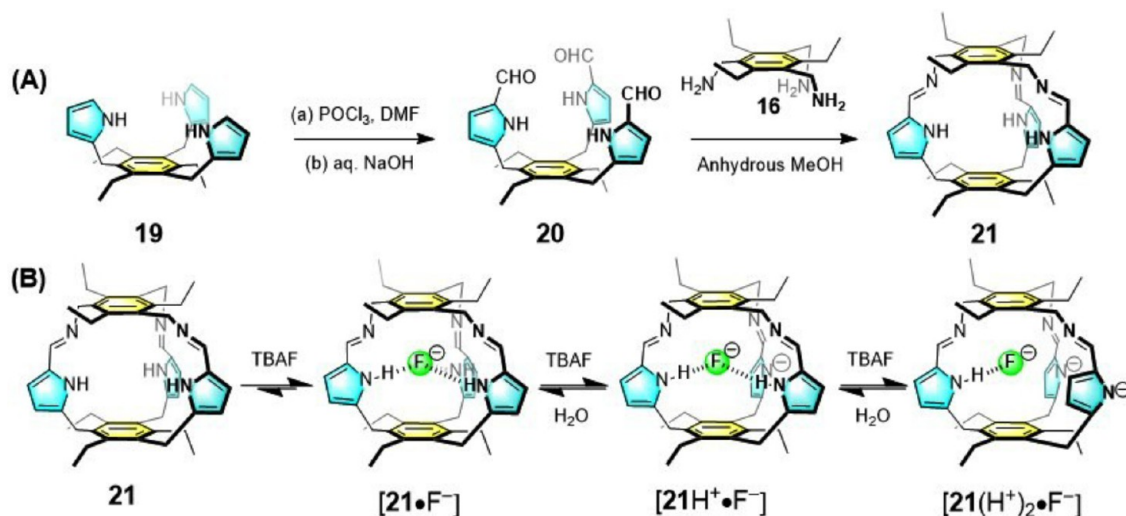
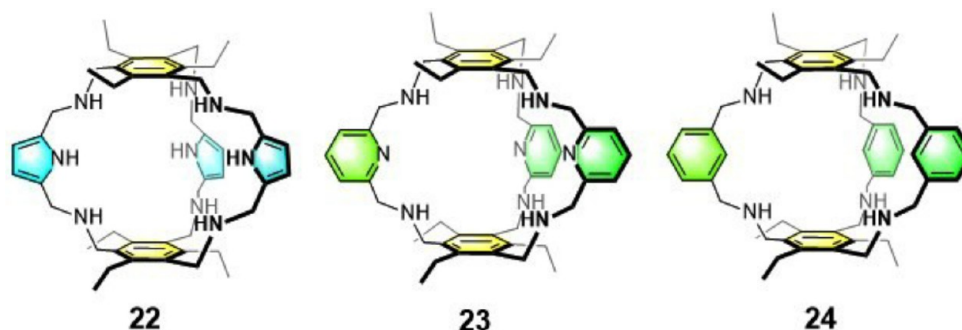
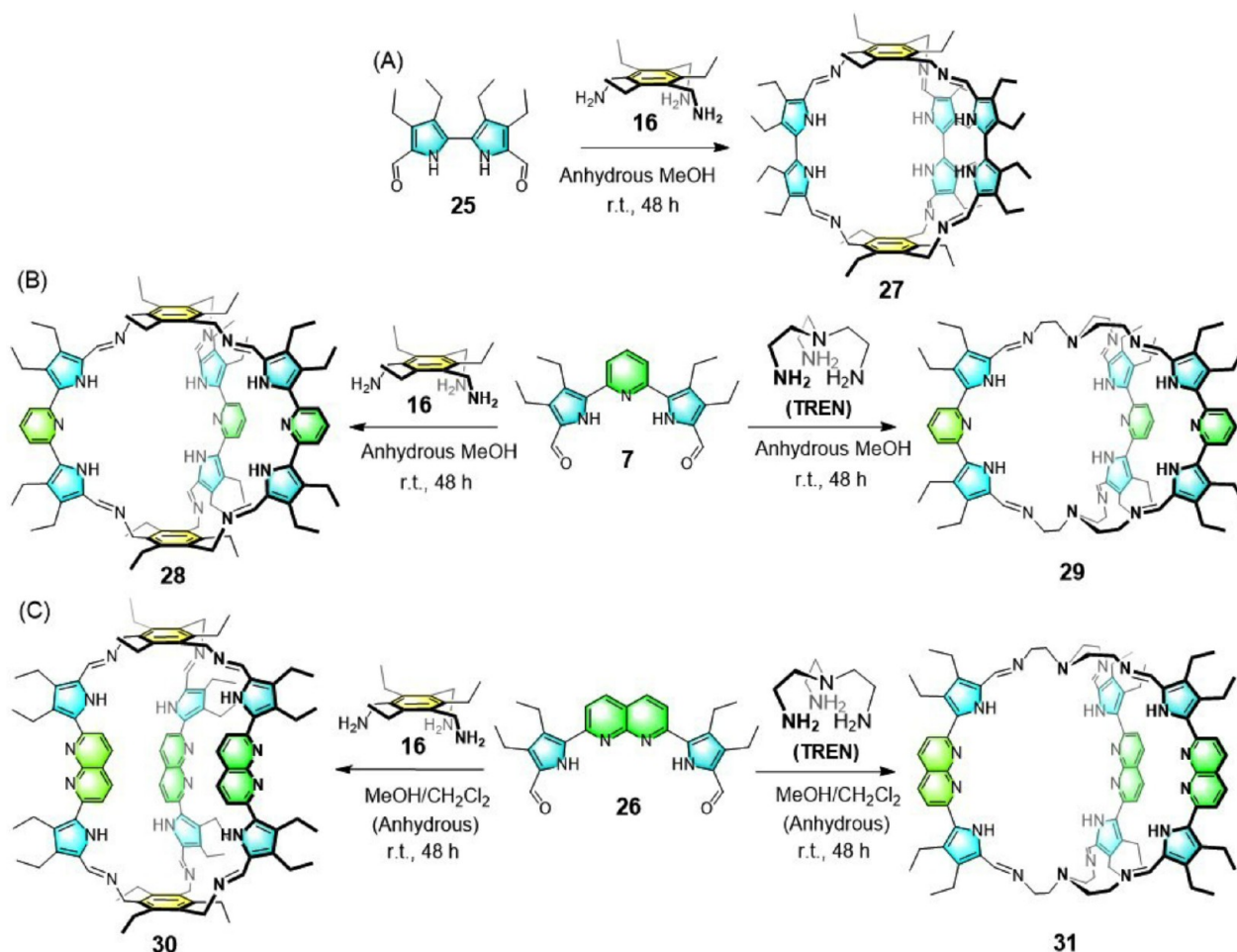


Chart 2. Chemical Structures of Various Benzene Bridgehead Amine Cages 22–24



Scheme 5. Preparation of Various Oligopyrrolic Schiff-Base Cryptands 27–31 via [3 + 2] Condensation Reactions



based systems where, for instance, several of the present authors reported recently a series of oligopyrrolic imine cages (27–31) that were found to act as shape-persistent porous organic materials.^{3,46} These relatively large oligopyrrolic cryptands were prepared via [3 + 2] Schiff-base condensations using various diformyl pyrrole precursors (25, 7, and 26) in conjunction with tripodal amines (viz. [tris(2-aminoethyl)amine], TREN, or 1,3,5-triethyl-2,4,6-trimethylamine, 16) in anhydrous methanol with the choice of pyrrole–dialdehyde and triamine precursors (Scheme 5) serving to dictate the size of the resulting cryptand-like systems. Note: The numbers in brackets reflect the number of components involved in the reaction.

Careful examination of the single-crystal X-ray structures of cryptands 27, 29, and 30 revealed key structural differences within what was ostensibly a closely matched set of ligands. For example, cage 27 possesses a pseudospherical inner cavity (see Figure 5a). In the case of cryptand 29, the pyridine nitrogen atoms “point” toward the inner core. This results in a compressed molecX-ray diffraction structure of the dihydrogen phosphate geometry (cf. Figure 5b). However, in case of cryptand 30, the naphthyridine nitrogen atoms face out from what is a relatively elongated molecular cage (cf. Figure 5c).

Inspired by Atwood, Cooper, and Mastalerz, who reported independently the gas adsorption features of porous amorphous noria and imine cages,^{47–51} the pyrrolic bicycles 27–31 were

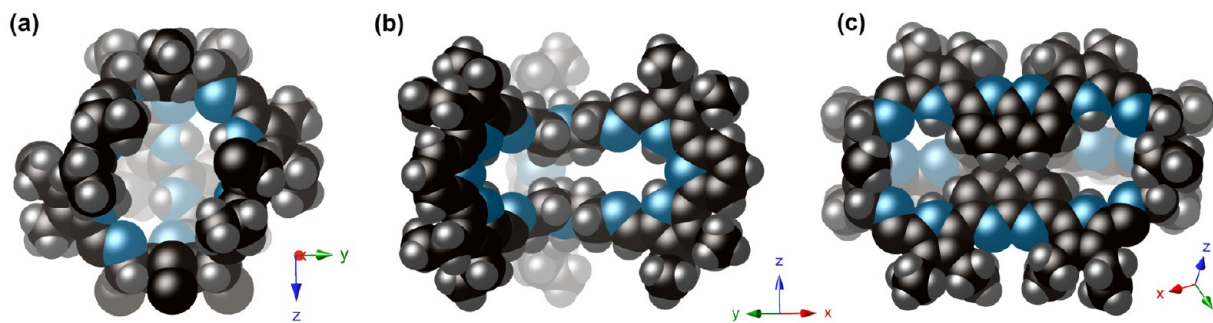


Figure 5. Single-crystal X-ray structures of various oligopyrrolic imine cages 27, 29, and 30. (a, b, and c) Space-filling representations, showing the shapes and respective sizes of the internal cavities with the solvent molecules omitted for clarity. Data from refs 3 and 46.

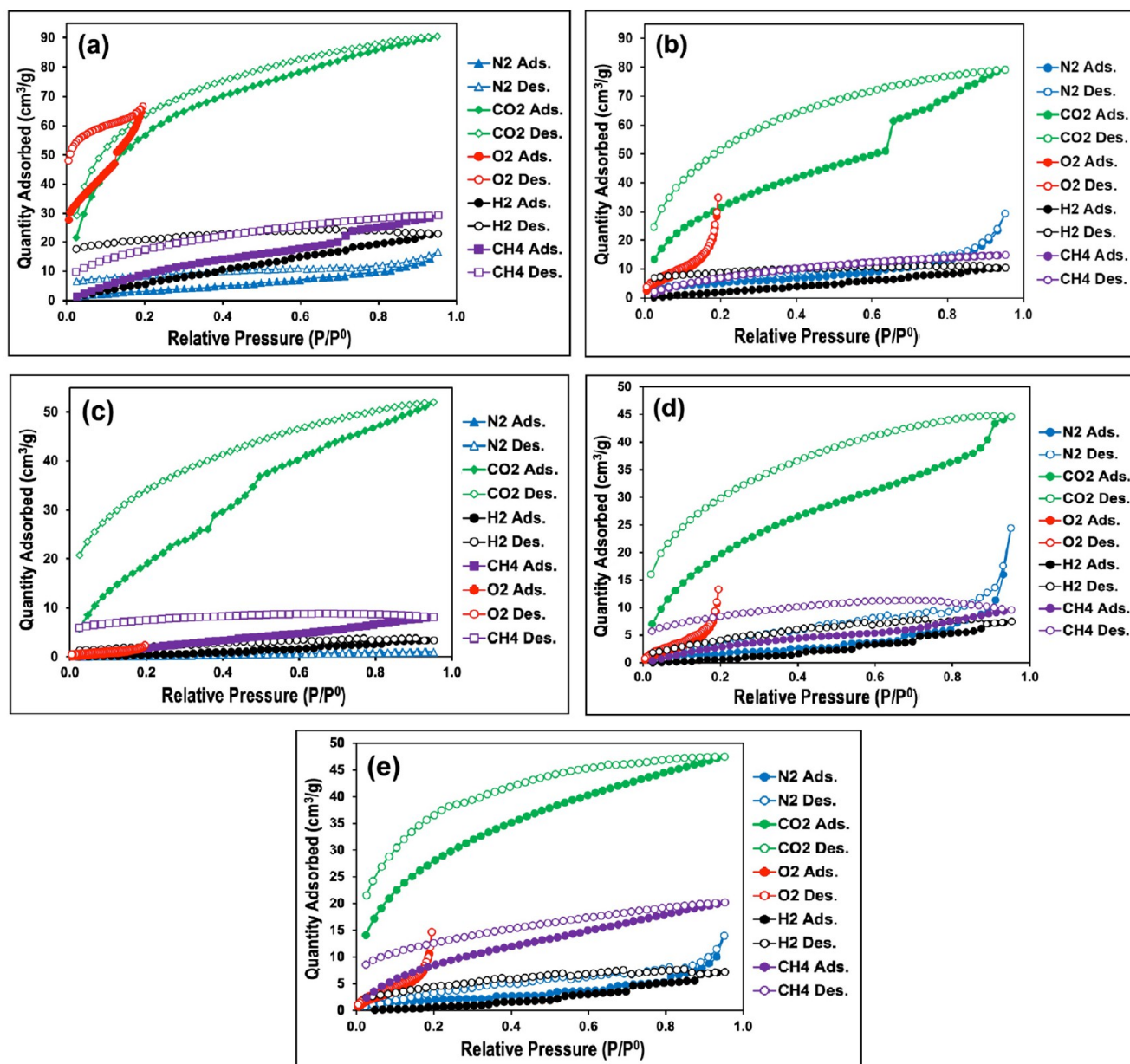


Figure 6. (a–e) Comparative sorption isotherms for the pyrrolic imine cages 27–31. Note: N₂, H₂, and O₂ isotherms were recorded at 77 K; CH₄ and CO₂ isotherms were recorded at 196 K. Reproduced with permission from refs 3 and 46. Copyright 2019 and 2020 Royal Society of Chemistry and World Scientific.

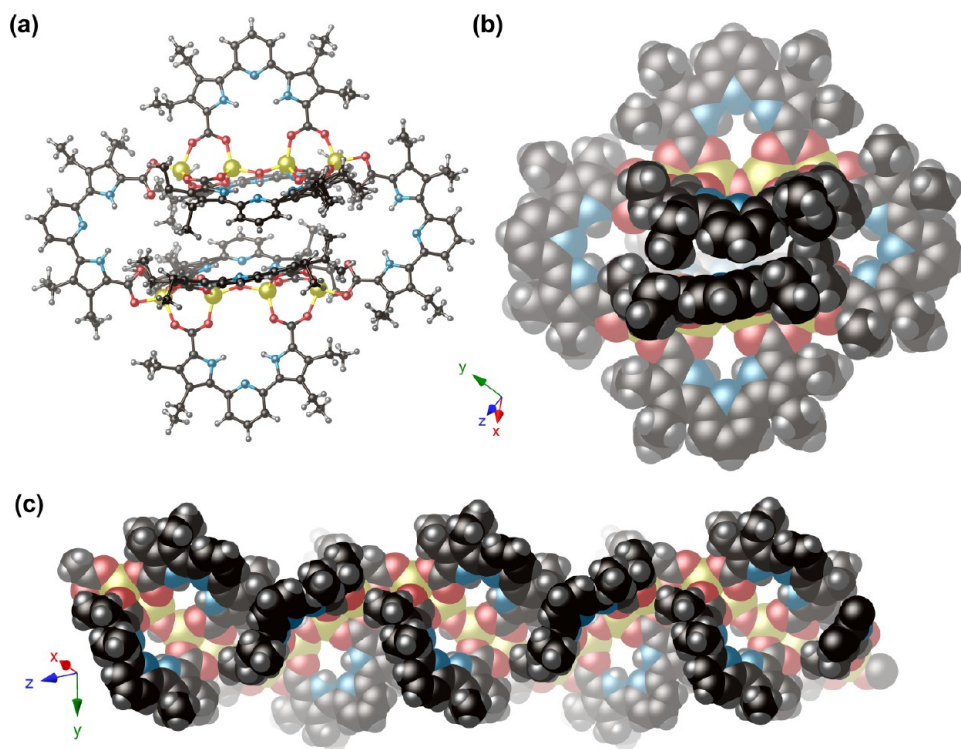
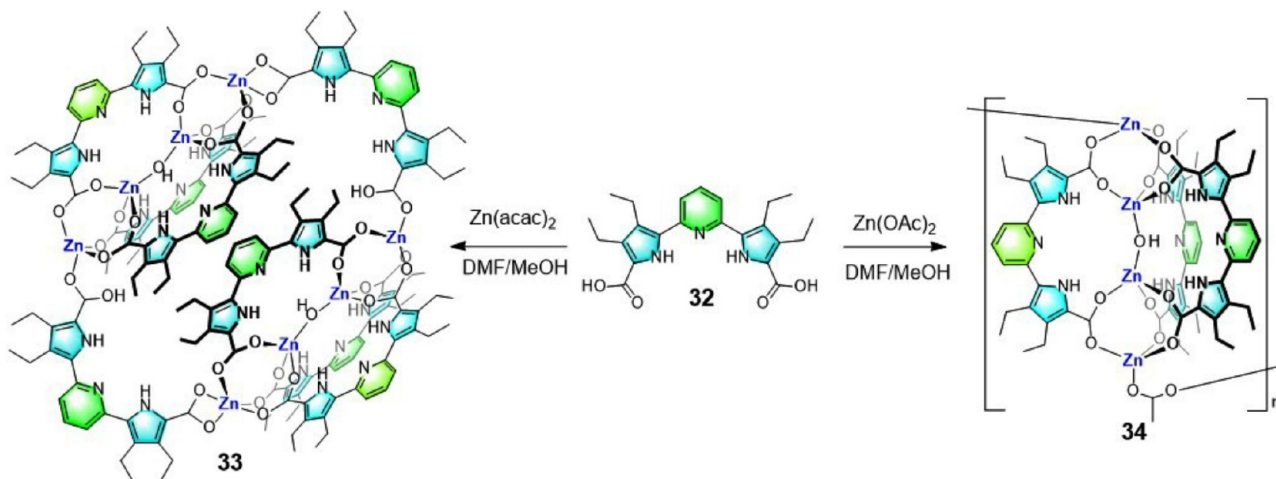


Figure 7. Single-crystal X-ray structures of the two structurally characterized products obtained when precursor **32** was allowed to react with ostensibly similar zinc(II) salts. (a and b) Different views of the discrete oligopyrrolic metallacage (**33**) obtained from the reaction of **32** with $\text{Zn}(\text{acac})_2$. (c) View of the abacus-type infinite oligopyrrolic metallacage (**34**) obtained from **32** and $\text{Zn}(\text{OAc})_2$. Data from refs 2 and 52.

Scheme 6. Synthesis of Oligopyrrolic Metallacages Controlled by Choice of Zinc Salts



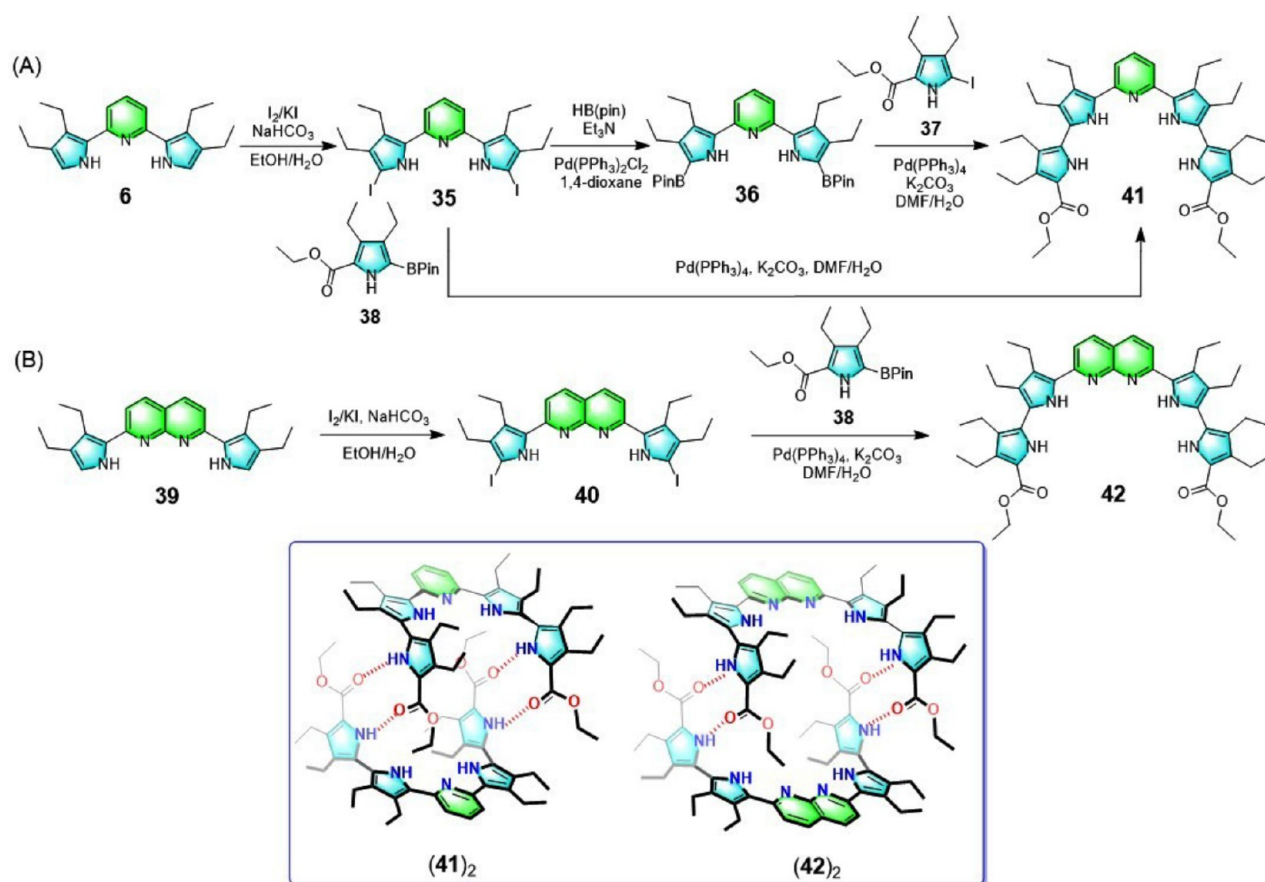
studied as possible gas capture systems. While differences among these cages were seen, in all cases, a preference for CO_2 over other tested gases (viz. N_2 , H_2 , O_2 , and CH_4) was observed. This finding was rationalized in terms of its higher polarizability relative to other gases (see Figure 6). Interestingly, at the time of the study (2019–2020), gas capture was a potential application for pyrrolic cages that apparently had yet to be explored.

3. OLIGOPYRROLIC METALLACAGES

Coordination chemistry-based approaches were also explored by Sessler et al. in an effort to construct pyrrolic nanocages.^{2,52} Here, chemically labile $\text{Zn}(\text{II})$ metal salts (i.e., $\text{Zn}(\text{acac})_2$ and $\text{Zn}(\text{OAc})_2$, respectively, where acac = acetylacetonate and OAc

= acetate) were tested in combination with an inherently nonlinear pyridine-fused oligopyrrolic dicarboxylic acid linker (**32**). Reaction of this chelate ligand **32** with $\text{Zn}(\text{acac})_2$ followed by crystallization from methanol/dimethylformamide (DMF) was found to give an octametallic cage, **33**, that consists of discrete hydroxide-bridged $\text{Zn}(\text{II})$ dimers (see Figure 7a and 7b). In contrast, when $\text{Zn}(\text{OAc})_2$ was used as the zinc(II) cation source, an abacus type of fluorescent “cage polymer” (**34**) was obtained, as inferred from single-crystal X-ray crystallographic analyses (cf. Figure 7c). The underlying chemistry is shown in Scheme 6. This work stands as a case study in how the choice of counteranion can serve to dictate the overall geometry of the

Scheme 7. Synthesis of Acyclic Pyrrolic Precursors **41** and **42** Used To Prepare the Cage-Like Supramolecular Receptors $(41)_2$ and $(42)_2$



products formed from identical pyrrolic and metal cation building blocks.

4. OLIGOPYRROLIC NONCOVALENTLY LINKED CAGES

Currently, a number of organic cages^{53–56} prepared using covalent bonds including, inter alia, dynamic covalent bonds^{18–26,57–60} are known. These impressive contributions have provided a springboard for the no less challenging task of creating cage- or capsule-like systems based on noncovalent interactions.^{61–68} Several of the authors of this Account have contributed to the development of the latter theme; they reported^{4,69} the all-organic self-assembled dimeric cage-like receptors $(41)_2$ and $(42)_2$ (cf. Scheme 7). These supramolecular systems, constructed from the acyclic pyridyl-/naphthyridyl-polypyrrolic molecular building blocks **41** and **42**, respectively, are stabilized via quadruple hydrogen-bonding interactions between individual “U”-shaped acyclic units (**41** or **42**). Notably, both $(41)_2$ and $(42)_2$ are stable in the solid state in CHCl_3 , tetrahydrofuran (THF), and dimethyl sulfoxide (DMSO) solution and even in the gas phase as evidenced from various spectroscopic analyses and single-crystal X-ray diffraction studies (Figure 8). Depending on the pK_a values of the acid guests in question as determined in aqueous solution, these self-assembled cages act as potential acid receptors. In THF solution, receptor $(41)_2$ was found to bind effectively only strong acids having pK_a values of below ca. -1.92 (e.g., methanesulfonic acid (MSA), *p*-toluenesulfonic acid (PTSA),

HNO_3 , H_2SO_4 , and HCl). In contrast, receptor $(42)_2$ proved to be an excellent receptor for biologically relevant organic dicarboxylic acids with $\text{pK}_a < 2.8$ in water (e.g., oxalic acid, maleic acid, and to a lesser extent malonic acid). It was also found to bind the same strong organic and mineral test acids that were recognized by receptor $(41)_2$.

It was speculated that the acids protonate the pyridyl or naphthyridyl moieties first, which creates a positively charged environment within the cavity of receptors $(41)_2$ and $(42)_2$ suitable for counteranion recognition. However, weaker acids (e.g., acids having $\text{pK}_a > 2.8$ in water) were deemed unlikely to induce this protonation even in the case of the more basic cage, $(42)_2$; therefore, these acids do not interact with the receptor. On this basis, the acid capture seen in organic media was termed “proton-coupled anion recognition”. Consistent with this suggestion, washing the receptor–acid complexes produced from $(41)_2$ and $(42)_2$ with water was found to regenerate the corresponding pristine cage with a visible color change. This capture and release could be repeated several times without any degradation of the constituent receptor units.

Further studies of the pyridine-containing tetrapyrrolic monomer **41** revealed subtleties associated with its self-assembly. The discrete self-assembled cage form $(41)_2$ used for the acid capture experiments was obtained by allowing precursor **41** to crystallize from the relatively noncoordinating solvent CHCl_3 . However, when this same building block was crystallized from more polar and presumably better coordinating solvents, such as tetrahydrofuran (THF) or DMF, an infinite “zig-zag” hydrogen-bonded network $(41)_n$ was obtained (cf.

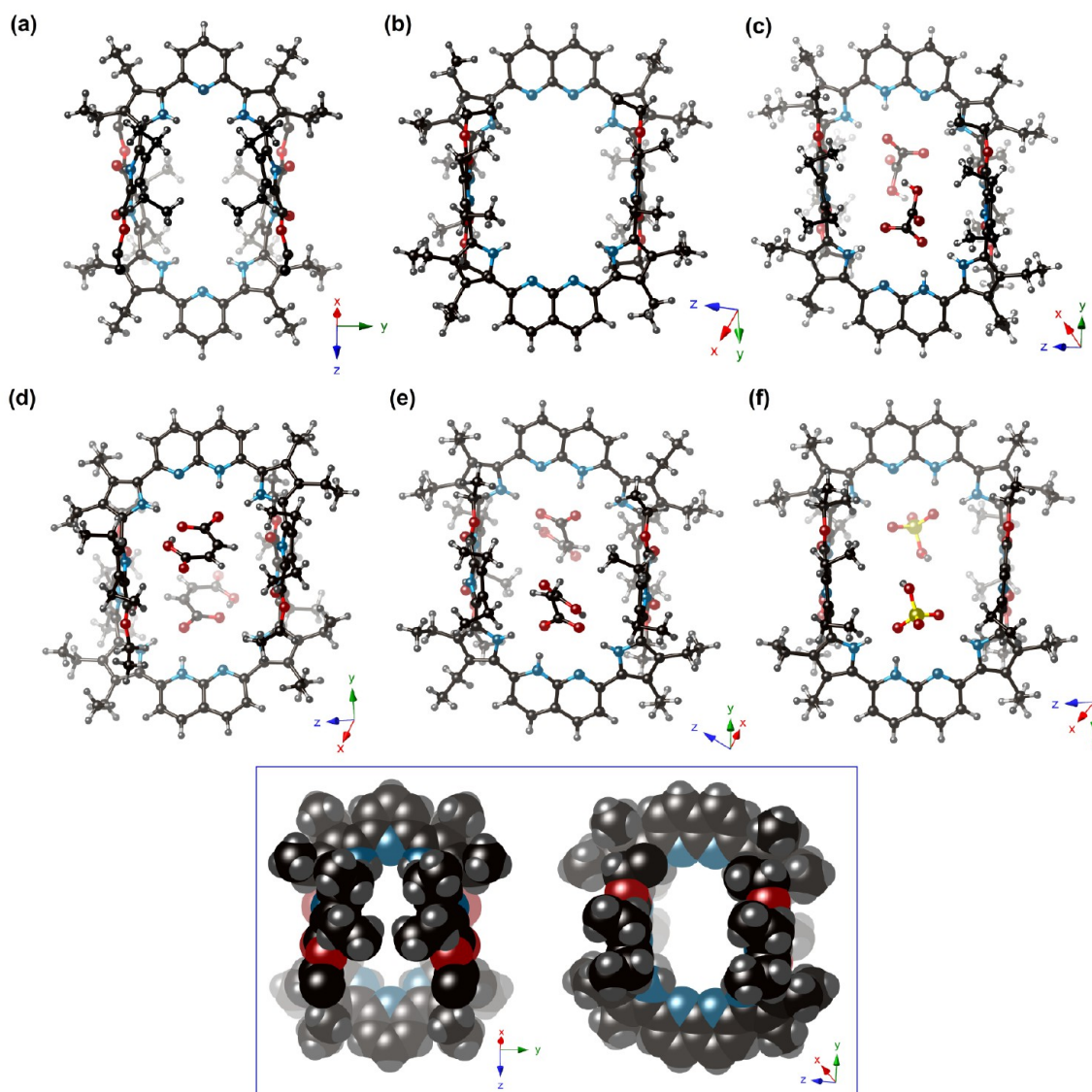
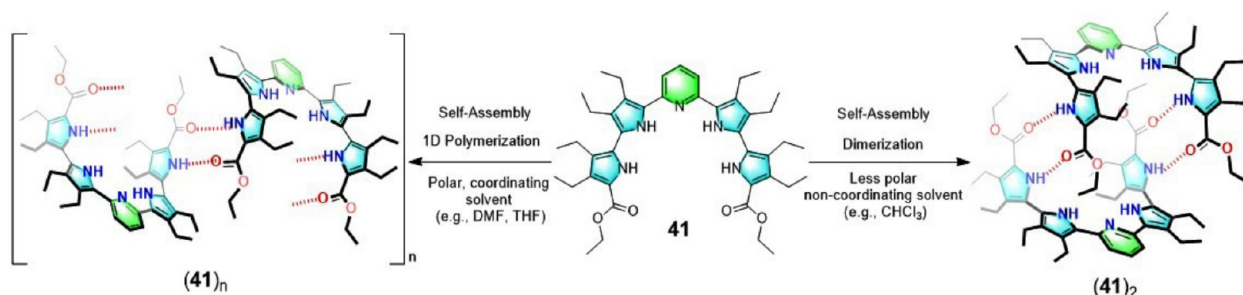


Figure 8. (a and b) Solid-state structures of receptors $(41)_2$ and $(42)_2$ as determined by single-crystal X-ray structural analyses. (c–f) Single-crystal X-ray structures of discrete supramolecular complexes with empirical chemical formula $[(42H)_2 \cdot 2^+C(\text{counteranion})^-]_2$ formed between receptor $(42)_2$ and various biologically relevant small organic dicarboxylic acids (oxalic acid, maleic acid, malonic acid) and a mineral acid (H_2SO_4). Note: Solvent molecules inside the cavity are omitted for clarity. (Inset) Comparative “space-filling” models of pyridine- and naphthyridine-based supramolecular cage-like structures formed by quadruple hydrogen bonding showing the void volumes for the guest-free forms. Data from refs 4 and 69.

Scheme 8. Schematic Representation of the Solvent-Dependent Self-Assembled Macrocyclization Process Leading to Dimer $(41)_2$ and the Corresponding Oligomeric Product $(41)_n$



Scheme 8). The factors regulating the dynamics and outcome of this supramolecular assembly and how they may be influenced

by the presence of potentially bound guests, such as acids, remain as subjects for future study.

5. CONCLUSIONS AND OUTLOOK

Macrobicyclic receptors inspired by Lehn's seminal work on cryptands and other early contributions to molecule recognition continue to attract tremendous attention within the supramolecular community. Effort is being devoted not only to exploring new synthetic strategies, such as those based on dynamic combinatorial chemistry and controlled metal coordination, but also to investigating the functional properties of the resulting systems including in the areas of selective ion recognition, carbohydrate binding and neutral guest capture, selective gas adsorption, and luminescent and electrochemical sensor development to highlight a few topical themes. Oligopyrrolic macrobicyclic systems are rather new additions to the ever-expanding cryptand-like cage firmament. There thus remains a large scope for further contributions in terms of both designing and synthesizing new classes of oligopyrrolic macrobicyclic receptors and exploring their recognition features. New members of this class with presumed new functions can likely be obtained by expanding the scope of pyrrolic building blocks used for their creation to include precursors that bear functional groups, such as free amines or carboxylate moieties, or which incorporate fluorescent subunits. The resulting putative systems might be expected to display enhanced recognition features or display optical and electronic properties that would make them of interest as sensors, redox-active or photoactive switches, or potential ion carriers. Given these opportunities for future contributions, in this Account, we have attempted to summarize recent progress in the area of oligopyrrolic cryptands with a focus on their molecular design, synthesis, self-assembly, and potential applications. Our hope is that this summary will inspire the further study of "chemistry within cages" and will accelerate specifically the development of pyrrole-based cryptand-like systems in the context of supramolecular chemistry and materials-related research.

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Notes

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Christophe Bucher obtained his Ph.D. degree in Physical Chemistry from the University of Burgundy at Dijon in 1999. He worked as a postdoctoral fellow with Professor J. L. Sessler at the University of Texas at Austin from November 1999 to September 2001 working on pyrrole-based macrocycles and cryptands for applications in sensing. He started his independent academic career in 2001 as a CNRS researcher at the University Joseph Fourier, Grenoble, France, in the Laboratory of Organic Electrosynthesis and Redox Photochemistry. In 2012, he joined the Ecole Normale Supérieure de Lyon (ENS), where he currently serves as a CNRS research director. His research interests cover different aspects of supramolecular–electrochemistry, including the design, synthesis, and applications of electron-switchable molecular and supramolecular materials with a particular emphasis on molecular hosts featuring electron-switchable recognition properties and electron-responsive self-assembled supramolecular materials.

Qing He obtained his Ph.D. degree in Chemistry in 2015 from the Institute of Chemistry, Chinese Academy of Sciences (ICCAS). He then moved to The University of Texas at Austin to work in the laboratory of Professor Jonathan L. Sessler as a postdoctoral fellow. In November of 2018, he joined the College of Chemistry and Chemical Engineering at Hunan University, where he is currently a full professor of chemistry. His research interests are focused on superphane chemistry and the development of new functional macrocycles and supercycles for molecular recognition, sensing, mass transport, extraction, assembly, catalysis, and ion manipulation as well as their application in the areas of critical material development, energy, the environment, and biology.

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Jonathan L. Sessler received his B.Sc. degree in Chemistry in 1977 from the University of California, Berkeley. He obtained his Ph.D. degree from Stanford University in 1982. After postdoctoral stays in Strasbourg and Kyoto, he accepted a position as an assistant professor of chemistry at the University of Texas at Austin, where he is currently

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