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Fei Wang, Christophe Bucher, Qing He, Atanu Jana, Jonathan L Sessler. Oligopyrrolic Cages: From Classic Molecular Constructs to Chemically Responsive Polytopic Receptors. *Accounts of Chemical Research*, 2022, 55 (12), pp.1646-1658. 10.1021/acs.accounts.2c00120 . hal-03870564

HAL Id: hal-03870564

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

Fei Wang, Christophe Bucher, Qing He,* Atanu Jana,* and Jonathan L. Sessler*



Cite This: <https://doi.org/10.1021/acs.accounts.2c00120>

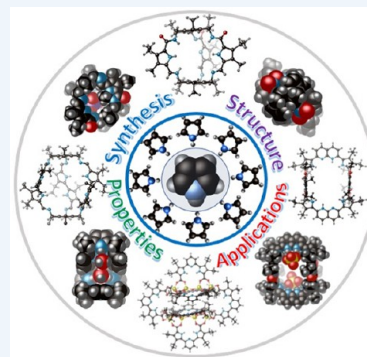


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4 CONCEPTUS: “Functional molecular systems”, discrete and self-assembled constructs
 5 where control over molecular recognition, structure, bonding, transport, release, catalytic
 6 activity, etc., is readily achieved, are a topic of current interest.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

KEY REFERENCES

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 35 [3,3,3]nonapyrrole. *J. Am. Chem. Soc.* **2001**, *123*, 9716–
 36 9717.¹ This paper is significant because it demonstrated
 37 that it is possible to prepare macrobicyclic “cryptand-like”
 38 systems based on pyrrolic building blocks. It also details
 39 an example of a structurally characterized exoreceptor,
 40 compounds that have received renewed attention of late.
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Received: March 6, 2022

Scheme 1. Synthesis of the Oligopyrrolic Calix–Cryptand 1

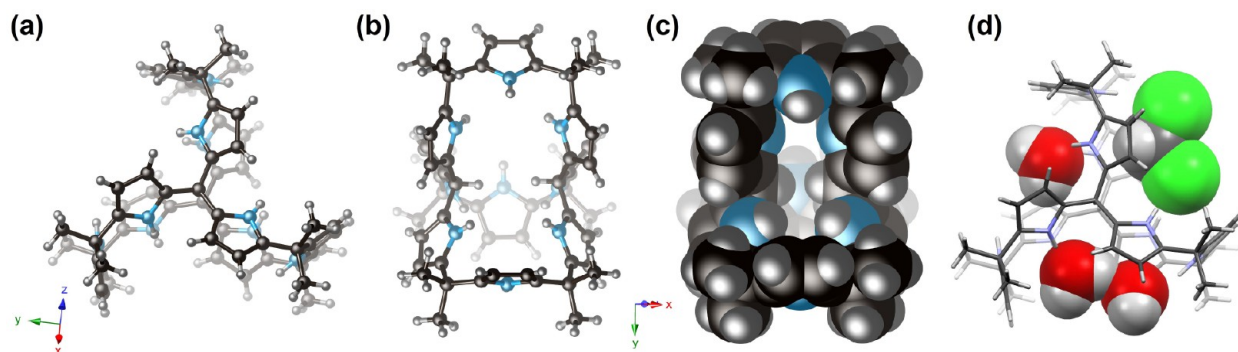
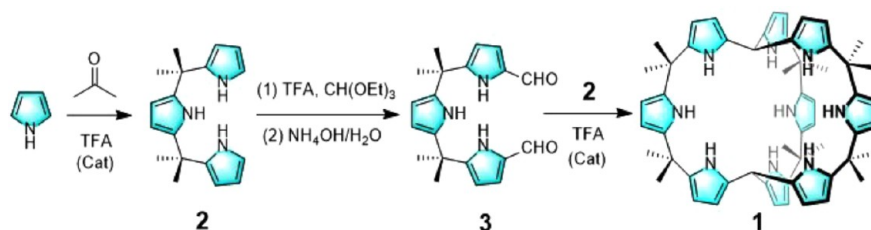


Figure 1. (a–c) Different views of cage **1** as deduced from single-crystal X-ray crystallographic analyses, showing the clefts (a) and the inner cavity (b and c). (d) X-ray crystal structure of the exo complex formed between receptor **1** and the neutral guest molecules H₂O and CH₂Cl₂. Data from ref 1.

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

- 60 • Wang, F.; Sen, S.; Chen, C.; Bähring, S.; Lei, C.; Duan, Z.;
61 Zhang, Z.; Sessler, J. L.; Jana, A. Self-Assembled Cage-
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63 ylic Acids via Proton-Coupled Anion Recognition. *J. Am.*
64 *Chem. Soc.* **2020**, *142*, 1987–1994.⁴ This report is
65 significant because it demonstrated the reversible
66 “capture” and “release” of dicarboxylic acid guests using
67 a fully organic self-assembled cage-like pyrrolic receptor.
68 Both the supramolecular recognition and the correspond-
69 ing assembly and disassembly processes were reflected in
70 visible color changes.

71 ■ INTRODUCTION

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

guests, including protons (H⁺) and ammonium (NH₄⁺, R₂NH₂⁺, 89
etc.), alkali, alkaline earth, transition metal, and actinide cations, 90
along with various negatively charged anionic species. The 91
specifics of binding depend, not surprisingly, on the structural 92
features, geometries, functionalities, and electronic environ- 93
ments (e.g., neutral or charged) provided by the cryptand host 94
with guest binding being seen within the internal cavities or 95
outside clefts or both. 96

Incorporation of pyrroles into bicyclic frameworks creates 97
cryptand-like frameworks that can act as potential functional 98
materials. This functionality can be augmented by including 99
other heterocycles, such as pyridine or naphthyridine, within the 100
superstructures.^{3,9} Incorporation of chelating units can provide 101
for metal-based self-assembly, while the use of β -substituted 102
oligopyrroles can support the formation of complex supra- 103
molecular architectures. As a class, oligopyrrolic macrocyclic 104
cages have been explored for a wide variety of functions, 105
including use as potential receptors, sensors, and gas storage 106
systems. The goal of this Account is to review our contributions 107
to this area within the framework of the field as a whole. 108
Excluded from this Account will be double-walled and 109
multiwalled bis-calix[4]pyrroles since they have been the subject 110
of recent reviews.^{10,11} 111

112 2. COVALENT OLIGOPYRROLIC CAGES

In 2001, Sessler et al. reported a cryptand-like bicyclic[3,3,3]- 112
nonapyrrole¹ (**1**, see Scheme 1) and investigated its anion- 113 s1
binding property. In the solid state, cage **1** adopts a wind 114
turbine-shaped conformation with *D*_{3h} symmetry in which both 115
of the apical CH hydrogen atoms are pointed in toward the inner 116
cavity (endo–endo orientation). The presence of pyrrolic NH 117
protons in the architecture endows cage **1** with an ability to bind 118
either anions or neutral molecules, such as solvents or water 119
(Figure 1a–c). Cage **1** interacts with these species as an exo 120 f1
receptor rather than accommodating them internally as seen in 121
the case of most classic cryptate complexes. For instance, as 122

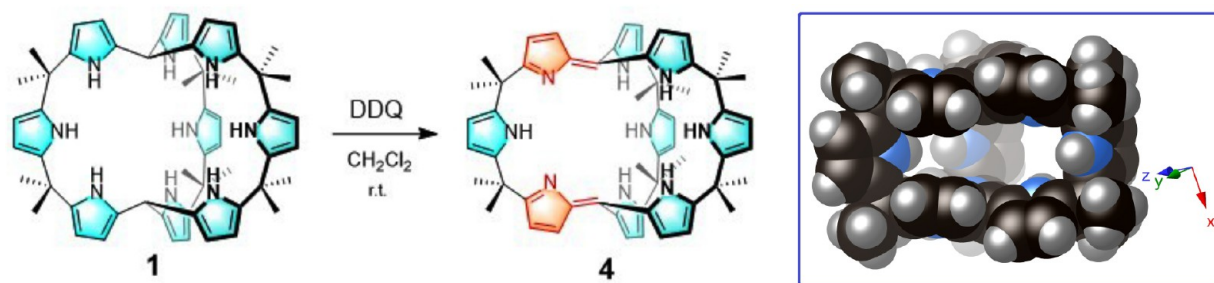


Figure 2. Synthesis of cage **4** via the partial oxidation of **1** by DDQ. (Inset) Space-filling view of the structure of cage **4** deduced from single-crystal X-ray crystallographic analysis. Neutral guest molecules, specifically H₂O, EtOH, and EtOAc, are omitted for clarity. Data from ref 12.

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

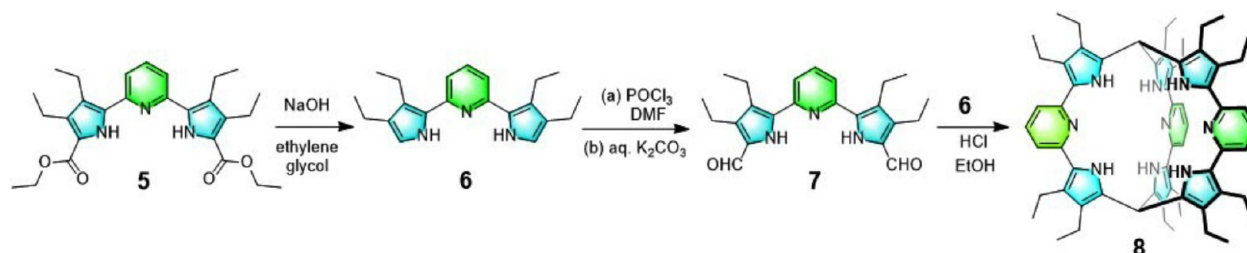
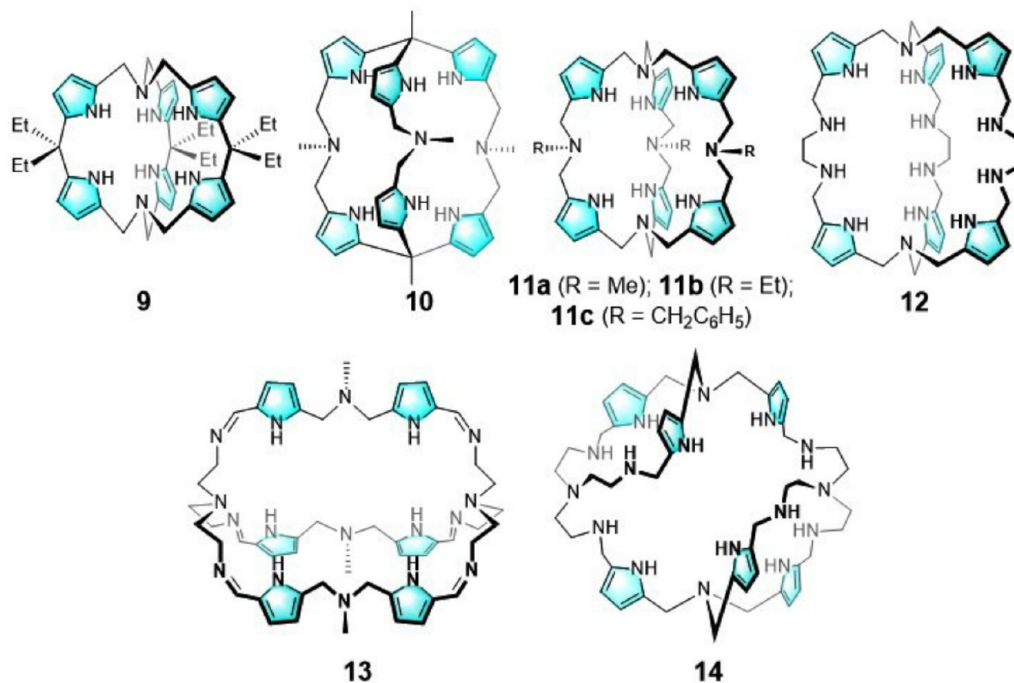


Chart 1. Chemical Structures of Various Oligopyrrolic Cryptand Cages 9–14



123 inferred from X-ray crystallographic analyses, one CH₂Cl₂
 124 solvent and three water molecules are located within the three
 125 external clefts of **1** via cooperative hydrogen-bonding, halogen-
 126 bonding, and CH $\cdots\pi$ interactions (Figure 1d). In an effort to test
 127 the ability of cage **1** to act as an anion receptor, its interactions
 128 with a range of anions, e.g., F⁻, Cl⁻, Br⁻, NO₃⁻, H₂PO₄⁻, and
 129 SCN⁻, were screened. A significant downfield chemical shift was
 130 seen in the pyrrolic NH protons when cage **1** in CD₂Cl₂ was
 131 subject to ¹H NMR spectroscopic titrations with various tetra-*n*-
 132 butylammonium (TBA) anion salts. In the representative case of
 133 NO₃⁻, 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 NO₃⁻, 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
 CD₂Cl₂ was recorded at 298 K. Very slow exchange was seen in
 the cases of H₂PO₄⁻ and SCN⁻ (as their TBA salts) under
 otherwise identical experimental conditions. Overall, these

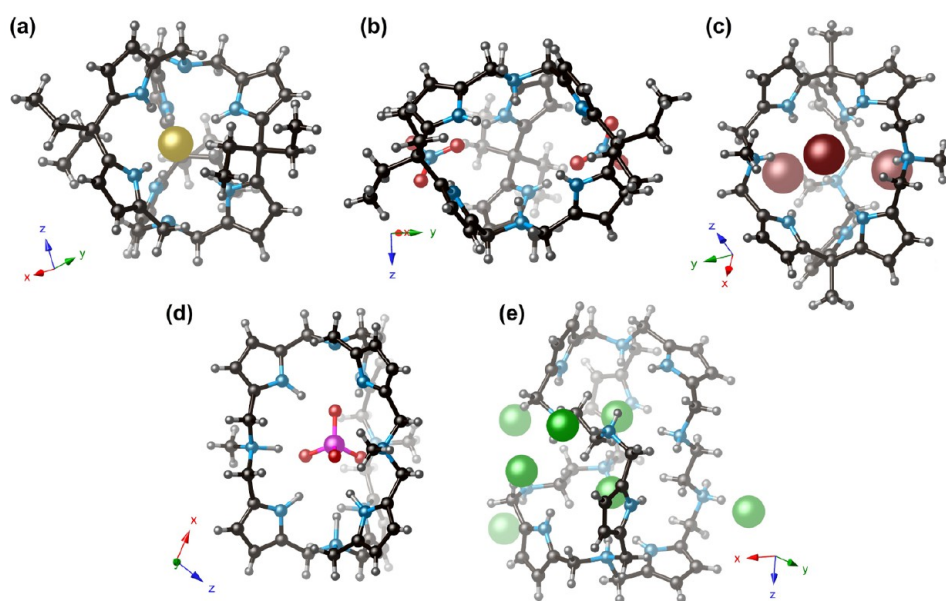
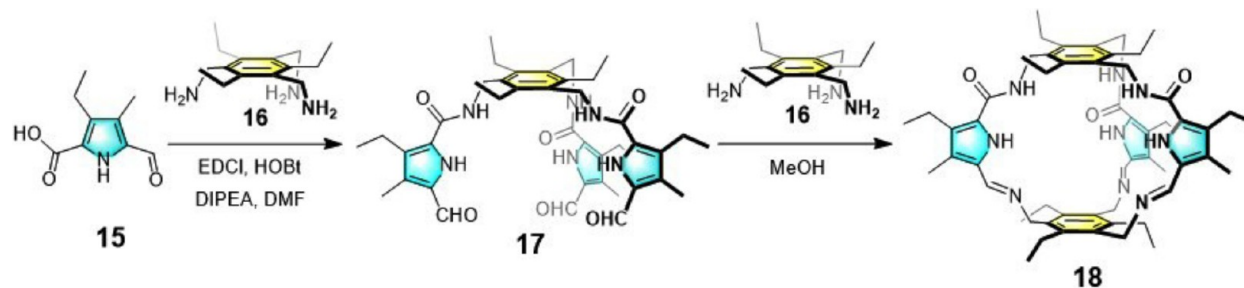


Figure 3. Single-crystal X-ray structures of representative anion-bound cryptates. (a) Fluoride complex of receptor **9**, and (b) corresponding nitrate complex. (c) Bromide complex of receptor **10**. (d) Phosphate complex of receptor **11a**. (e) Chloride complex of receptor **12**. Solvent molecules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

Scheme 3. Synthesis of Benzene Bridgehead Oligopyrrolic Cage **18**



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

146 Chemical oxidation of cage **1** by 5,6-dichloro-2,3-dicyano-*p*-
147 benzoquinone (DDQ) was found to produce an unprecedented
148 sp^2 -hybridized carbon bridgehead calixpyrrolic (**4**) (Figure 2).¹²

149 Compound **4**, as a prototypical three-dimensional (3D)
150 calixpyrrolic, belongs to a class of hybrid molecular systems that
151 bear structural and chemical analogy to both calixpyrroles and
152 porphyrins owing to the presence of both sp^2 - and sp^3 -
153 hybridized meso-like bridging carbon atoms. Distinctive broad
154 absorption maxima (λ_{\max}) at 421 and 474 nm were taken as
155 evidence for the generation of partially oxidized species in
156 solution where the characteristic “porphyrin-like” features (e.g.,
157 an absorption spectrum containing both a sharp Soret band and
158 weaker “Q” bands) are absent. In contrast to what was observed
159 in the X-ray structure of **1** where the two bridging apical –CH
160 hydrogen atoms were seen to point inward (endo–endo
161 orientation), the sp^2 -hybridized bridging carbon atom produces
162 a degree of local planarity. The net result is that cage **4** possesses
163 a more open cavity (cf. Figure 2, inset) that was expected to
164 facilitate the “inside binding” of guests.

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

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

174 Starting in 2011, Mani et al. reported a series of cages,
175 compounds **9**–**14** given in Chart 1,^{13–17} which were seen
176 capable of binding a number of representative anions (e.g., F^- ,
177 Cl^- , Br^- , NO_3^- , $H_2PO_4^-$, and HSO_4^-) in organic media such as
178 $CDCl_3$, $DMSO-d_6$, and $(CD_3)_2CO$ under ambient conditions. A
179 few representative X-ray structures of the resulting anion-bound
180 cryptates are shown in Figure 3. In the case of cages **9** and **11a**,
181 the F^- and PO_4^{3-} anions were found to be bound within the
182 cryptand cavity (cf. Figure 3a and 3d); however, most of the
183 other anions give rise to exo complexes (cf. Figure 3b, 3c, and
184 3e).

185 Dynamic covalent chemistry (DCC) has emerged as an
186 attractive and efficient means for preparing intricate molecular
187 constructs, including macrocycles,¹⁸ cages,^{19–22} and covalent
188 organic frameworks (COFs),^{23,24} and has yielded a number of
189 systems with potential applications.^{25–28} Not surprisingly, DCC
190 has been exploited to access discrete oligopyrrolic cages. Taking
191 advantage of this approach, we designed and synthesized the
192 Schiff-base macrobicyclic cage **18**²⁹ starting from a suitably
193 functionalized pyrrolic precursor (**15**) as shown in Scheme 3.

194 This phenyl-bridgehead oligopyrrolic cryptand cage contains
 195 both imine (hydrogen-bonding acceptor) and amide (hydro-
 196 gen-bonding donor) functionalities within its side arms. The
 197 latter receptor and its analogues were explored as potential
 198 supramolecular hosts for specific anions. It was found that cage
 199 **18** exhibits specificity toward tetrahedral oxyanions, e.g.,
 200 H_2PO_4^- , $\text{HP}_2\text{O}_7^{3-}$, SO_4^{2-} , and HSO_4^- , in the noncompetitive
 201 solvent chloroform at 298 K. This selectivity is reflected in the
 202 calculated K_a values of $1.56 \times 10^4 \text{ M}^{-1}$ for TBAH_2PO_4 , $1.76 \times$
 203 10^6 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
 204 $4.53 \times 10^6 \text{ M}^{-1}$ for TBAHSO_4 , respectively.

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

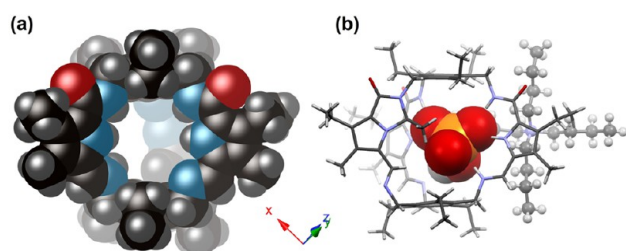


Figure 4. X-ray diffraction structure of the dihydrogen phosphate complex of receptor **18** obtained using single crystals grown by allowing hexanes to diffuse slowly into a chloroform solution of cage **18** in the presence of excess TBAH_2PO_4 . (a) Space-filling representation of receptor **18** 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.

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 spectro-
 scopic 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 hydro-
 gen-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

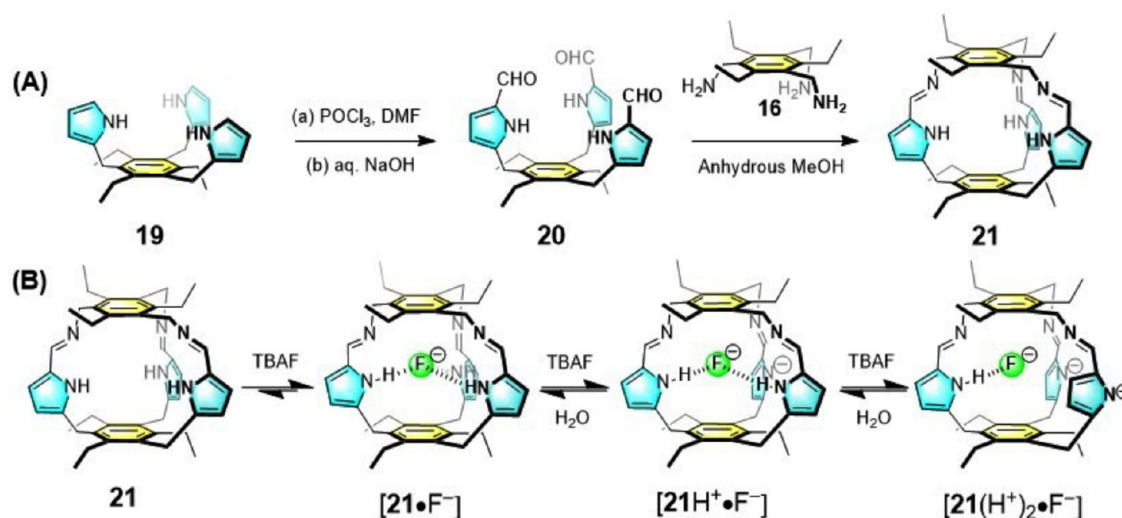
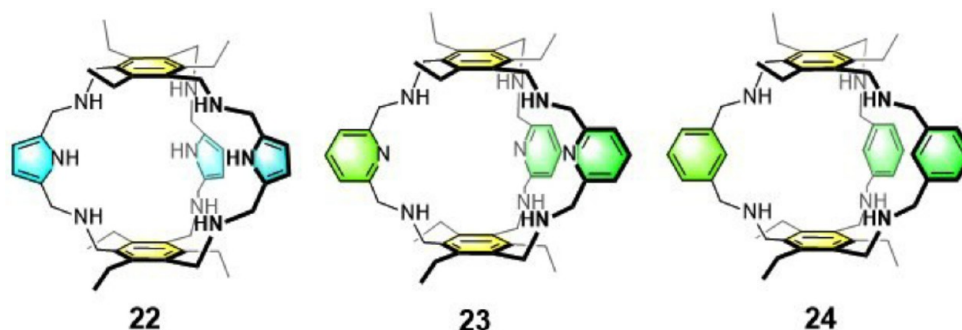
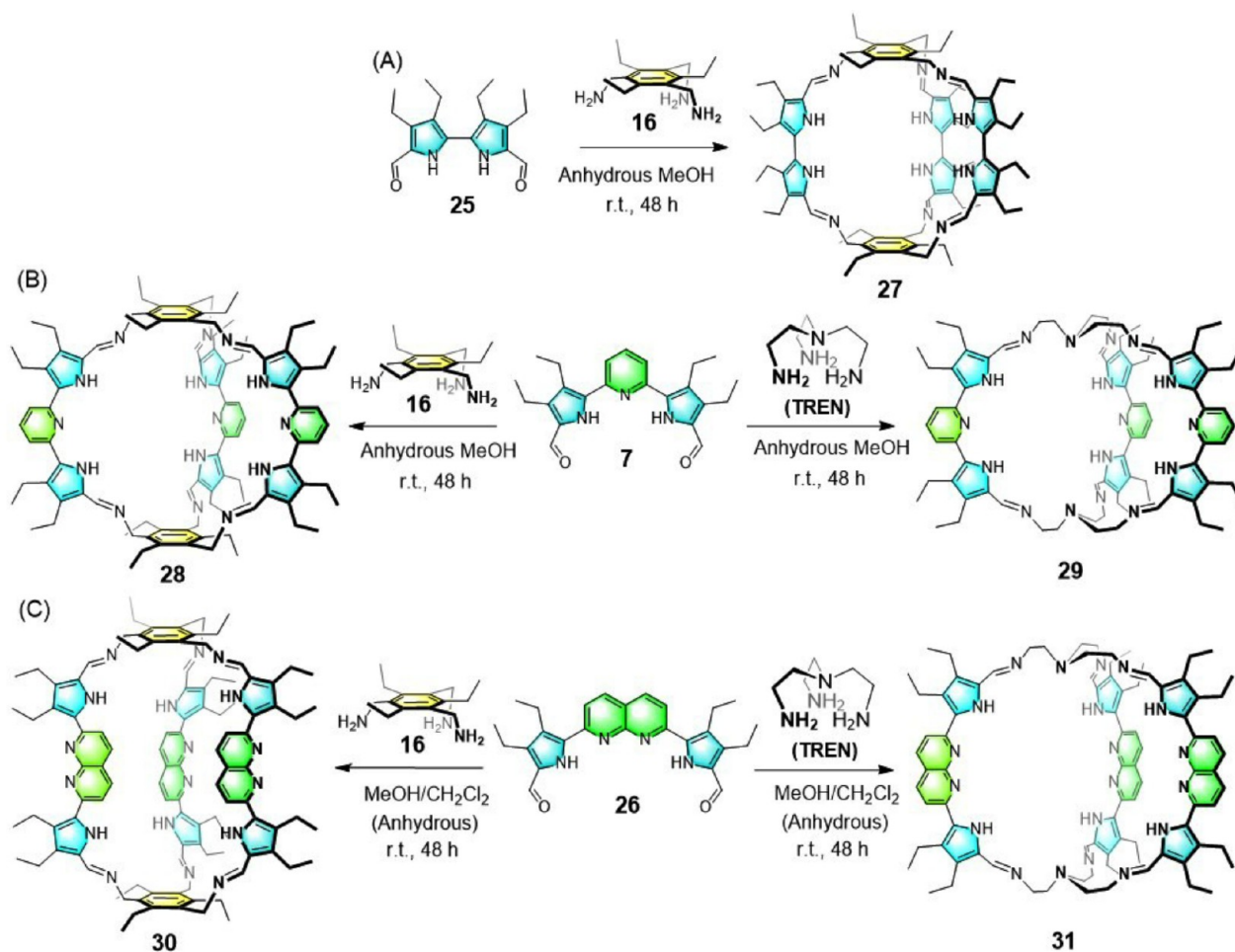


Chart 2. Chemical Structures of Various Benzene Bridgehead Amine Cages 22–24



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



255 based systems where, for instance, several of the present authors
 256 reported recently a series of oligopyrrolic imine cages (27–31)
 257 that were found to act as shape-persistent porous organic
 258 materials.^{3,46} These relatively large oligopyrrolic cryptands were
 259 prepared via [3 + 2] Schiff-base condensations using various
 260 diformyl pyrrole precursors (25, 7, and 26) in conjunction with
 261 tripodal amines (viz. [tris-2-aminoethyl]amine), TREN, or
 262 1,3,5-triethyl-2,4,6-trimethylamine, 16) in anhydrous meth-
 263 anol with the choice of pyrrole–dialdehyde and triamine
 264 precursors (Scheme 5) serving to dictate the size of the resulting
 265 cryptand-like systems. Note: The numbers in brackets reflect the
 266 number of components involved in the reaction.

Careful examination of the single-crystal X-ray structures of 267
 cryptands 27, 29, and 30 revealed key structural differences 268
 within what was ostensibly a closely matched set of ligands. For 269
 example, cage 27 possesses a pseudospherical inner cavity (see 270
 Figure 5a). In the case of cryptand 29, the pyridine nitrogen 271
 atoms “point” toward the inner core. This results in a 272
 compressed molecular geometry (cf. Figure 5b). However, in 273
 case of cryptand 30, the naphthyridine nitrogen atoms face out 274
 from what is a relatively elongated molecular cage (cf. Figure 275
 5c).
 276
 Inspired by Atwood, Cooper, and Mastalerz, who reported 277
 independently the gas adsorption features of porous amorphous 278
 noria and imine cages,^{47–51} the pyrrolic bicycles 27–31 were 279

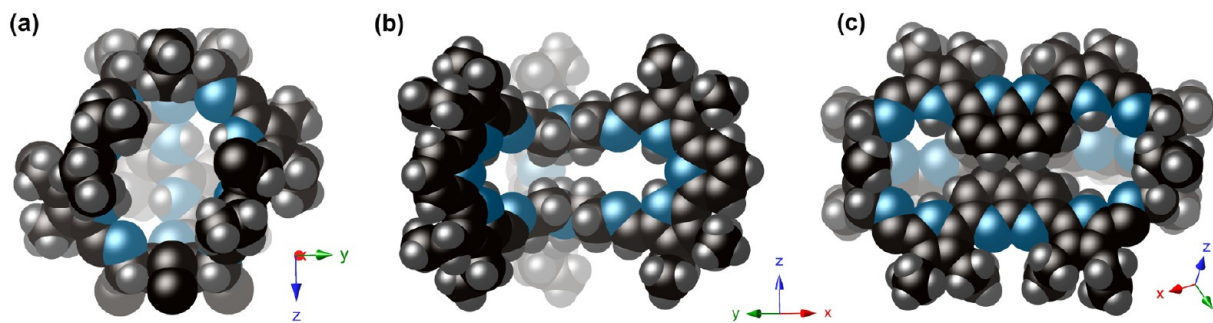


Figure 5. Single-crystal X-ray structures of various oligopyrrolic imine cages 27, 29, and 30. (a, b, and c) Ball-and-stick and (d, e, and f) space-filling representations, respectively, showing the shapes and respective sizes of the internal cavities with the solvent molecules omitted for clarity. Data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

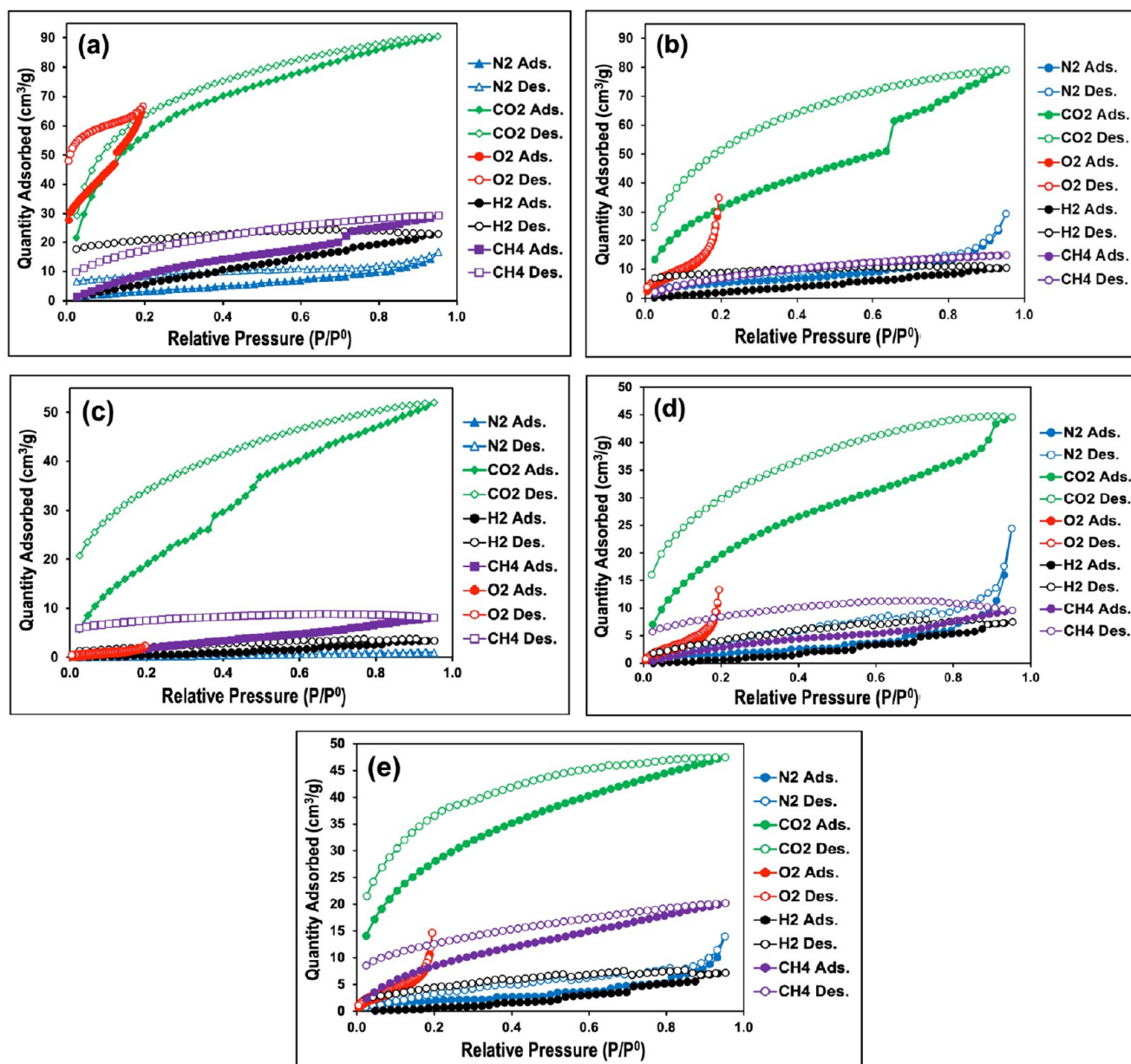


Figure 6. (a–e) Comparative sorption isotherms for the pyrrolic imine cages 27–31. Note: N₂, H₂, and O₂ isotherms were recorded at 77 K; CH₄ and CO₂ isotherms were recorded at 196 K. Reproduced with permission from refs 3 and 46. Copyright 2019 and 2020 Royal Society of Chemistry and World Scientific.

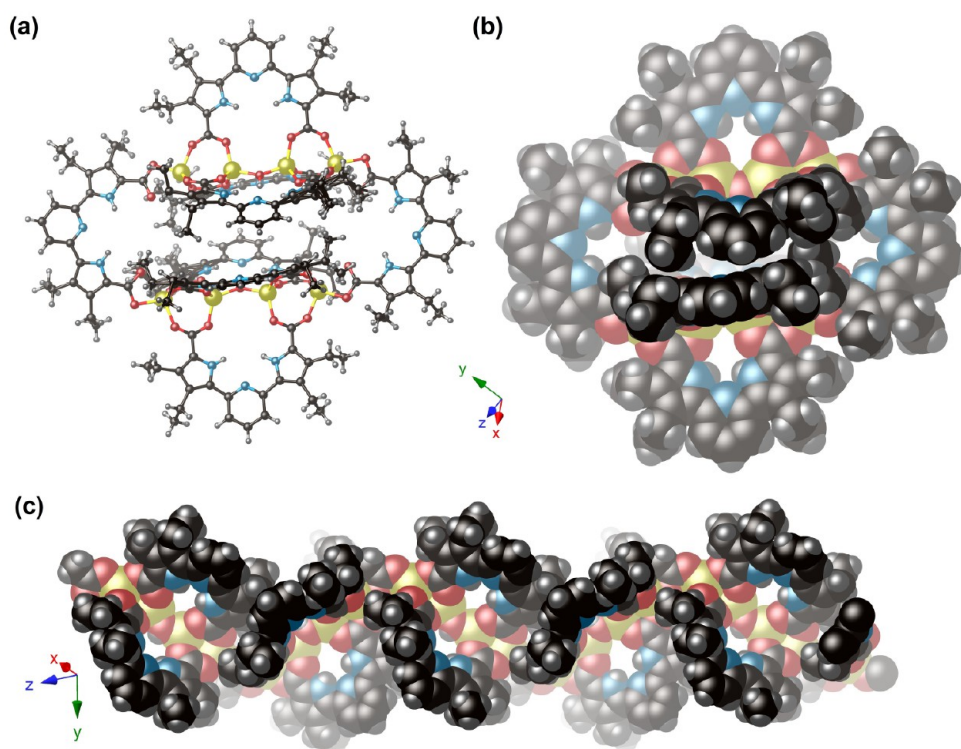
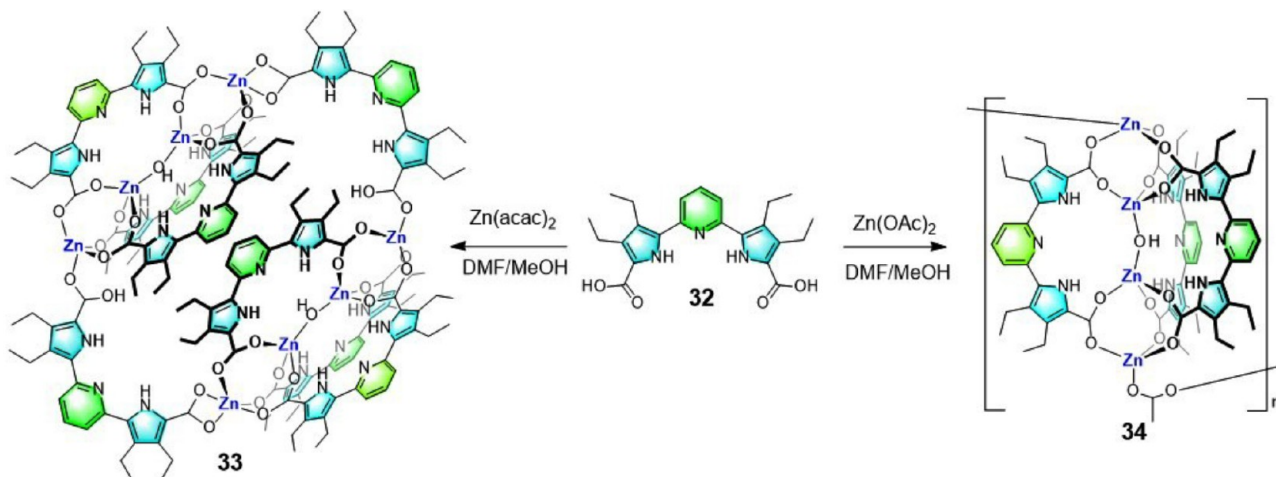


Figure 7. Single-crystal X-ray structures of the two structurally characterized products obtained when precursor **32** was allowed to react with ostensibly similar zinc(II) salts. (a and b) Different views of the discrete oligopyrrolic metallacage (**33**) obtained from the reaction of **32** with $\text{Zn}(\text{acac})_2$.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

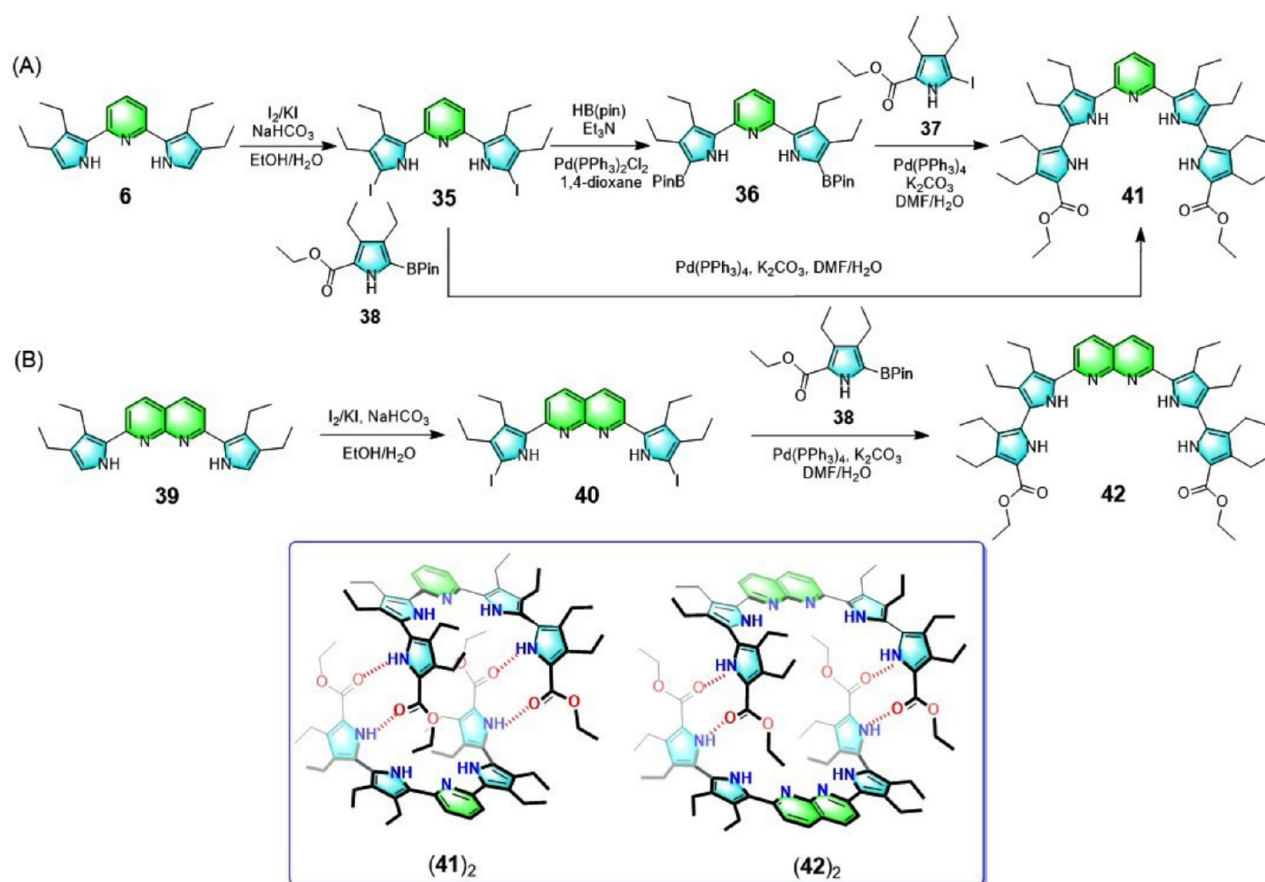


280 studied as possible gas capture systems. While differences among
 281 these cages were seen, in all cases, a preference for CO_2 over
 282 other tested gases (viz. N_2 , H_2 , O_2 , and CH_4) was observed. This
 283 finding was rationalized in terms of its higher polarizability
 284 relative to other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

3. OLIGOPYRROLIC METALLACAGES

287 Coordination chemistry-based approaches were also explored
 288 by Sessler et al. in an effort to construct pyrrolic nanocages.^{2,52}
 289 Here, chemically labile Zn(II) metal salts (i.e., $\text{Zn}(\text{acac})_2$ and
 290 $\text{Zn}(\text{OAc})_2$, respectively, where acac = acetylacetonate and OAc

= acetate) were tested in combination with an inherently
 291 nonlinear pyridine-fused oligopyrrolic dicarboxylic acid linker
 292 (**32**). Reaction of this chelate ligand **32** with $\text{Zn}(\text{acac})_2$ followed
 293 by crystallization from methanol/dimethylformamide (DMF)
 294 was found to give an octametallic cage, **33**, that consists of
 295 discrete hydroxide-bridged Zn(II) dimers (see Figure 7a and
 296 7b). In contrast, when $\text{Zn}(\text{OAc})_2$ was used as the zinc(II)
 297 cation source, an abacus type of fluorescent “cage polymer” (**34**)
 298 was obtained, as inferred from single-crystal X-ray crystallographic
 299 analyses (cf. Figure 7c). The underlying chemistry is shown in
 300 Scheme 6. This work stands as a case study in how the choice of
 301 302 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

303 products formed from identical pyrrolic and metal cation
304 building blocks.

4. OLIGOPYRROLIC NONCOVALENTLY LINKED CAGES

305
306 Currently, a number of organic cages^{53–56} prepared using
307 covalent bonds including, inter alia, dynamic covalent
308 bonds^{18–26,57–60} are known. These impressive contributions
309 have provided a springboard for the no less challenging task of
310 creating cage- or capsule-like systems based on noncovalent
311 interactions.^{61–68} Several of the authors of this Account have
312 contributed to the development of the latter theme; they
313 reported^{4,69} the all-organic self-assembled dimeric cage-like
314 receptors (**41**)₂ and (**42**)₂ (cf. Scheme 7). These supramolecular
315 systems, constructed from the acyclic pyridyl-/naphthyridyl-
316 polypyrrolic molecular building blocks **41** and **42**, respectively,
317 are stabilized via quadruple hydrogen-bonding interactions
318 between individual “U”-shaped acyclic units (**41** or **42**).
319 Notably, both (**41**)₂ and (**42**)₂ are stable in the solid state in
320 CHCl₃, tetrahydrofuran (THF), and dimethyl sulfoxide
321 (DMSO) solution and even in the gas phase as evidenced
322 from various spectroscopic analyses and single-crystal X-ray
323 diffraction studies (Figure 8). Depending on the pK_a values of
324 the acid guests in question as determined in aqueous solution,
325 these self-assembled cages act as potential acid receptors. In
326 THF solution, receptor (**41**)₂ was found to bind effectively only
327 strong acids having pK_a values of below ca. –1.92 (e.g.,
328 methanesulfonic acid (MSA), *p*-toluenesulfonic acid (PTSA),

HNO₃, H₂SO₄, and HCl). In contrast, receptor (**42**)₂ proved to
329 be an excellent receptor for biologically relevant organic
330 dicarboxylic acids with pK_a < 2.8 in water (e.g., oxalic acid,
331 maleic acid, and to a lesser extent malonic acid). It was also
332 found to bind the same strong organic and mineral test acids that
333 were recognized by receptor (**41**)₂.
334

335 It was speculated that the acids protonate the pyridyl or
336 naphthyridyl moieties first, which creates a positively charged
337 environment within the cavity of receptors (**41**)₂ and (**42**)₂
338 suitable for counteranion recognition. However, weaker acids
339 (e.g., acids having pK_a > 2.8 in water) were deemed unlikely to
340 induce this protonation even in the case of the more basic cage,
341 (**42**)₂; therefore, these acids do not interact with the receptor.
342 On this basis, the acid capture seen in organic media was termed
343 “proton-coupled anion recognition”. Consistent with this
344 suggestion, washing the receptor–acid complexes produced
345 from (**41**)₂ and (**42**)₂ with water was found to regenerate the
346 corresponding pristine cage with a visible color change. This
347 capture and release could be repeated several times without any
348 degradation of the constituent receptor units.

349 Further studies of the pyridine-containing tetrapyrrolic
350 monomer **41** revealed subtleties associated with its self-
351 assembly. The discrete self-assembled cage form (**41**)₂ used
352 for the acid capture experiments was obtained by allowing
353 precursor **41** to crystallize from the relatively noncoordinating
354 solvent CHCl₃. However, when this same building block was
355 crystallized from more polar and presumably better coordinating
356 solvents, such as tetrahydrofuran (THF) or DMF, an infinite
357 “zig-zag” hydrogen-bonded network (**41**)_n was obtained (cf. 357 8)

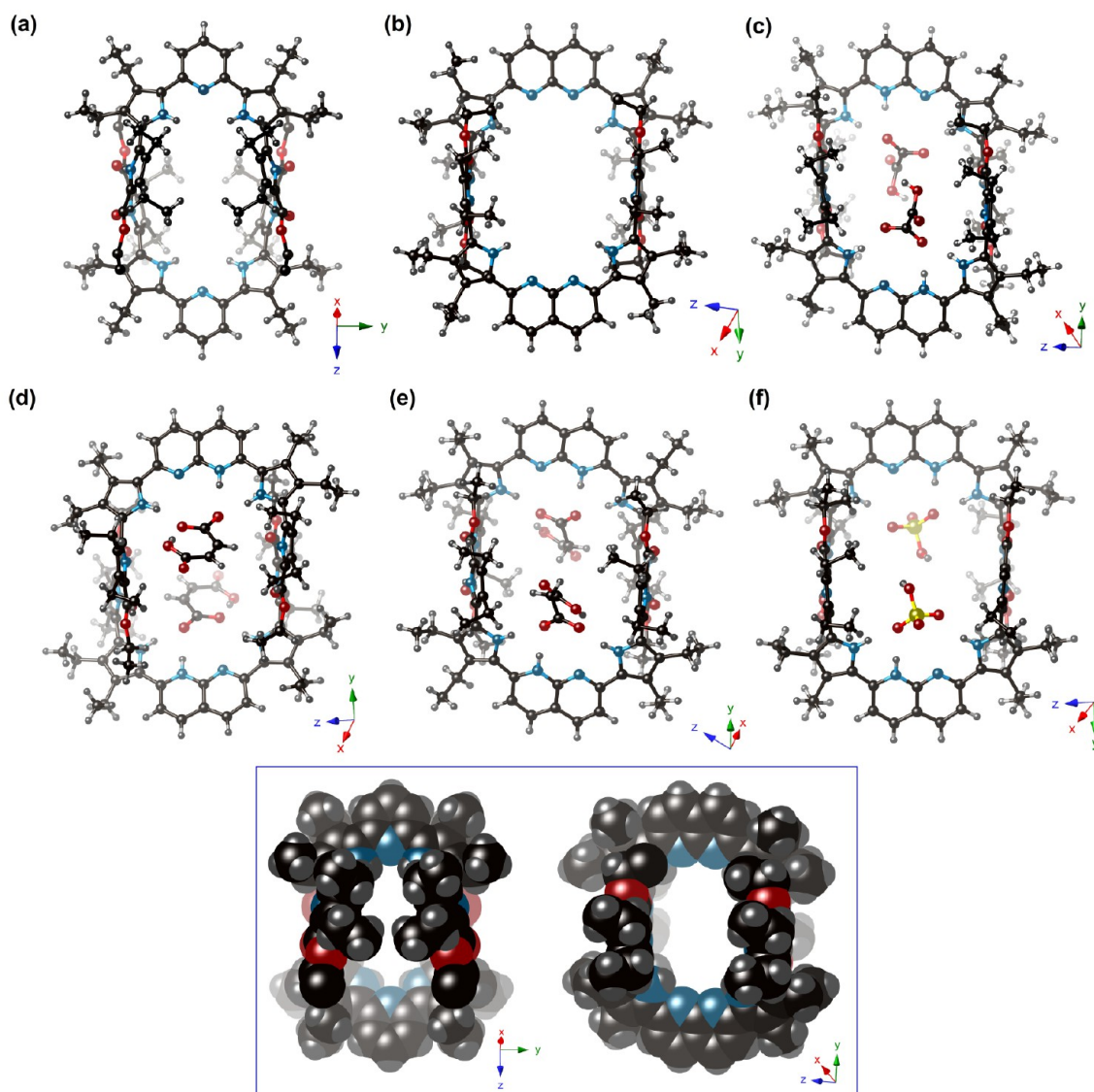
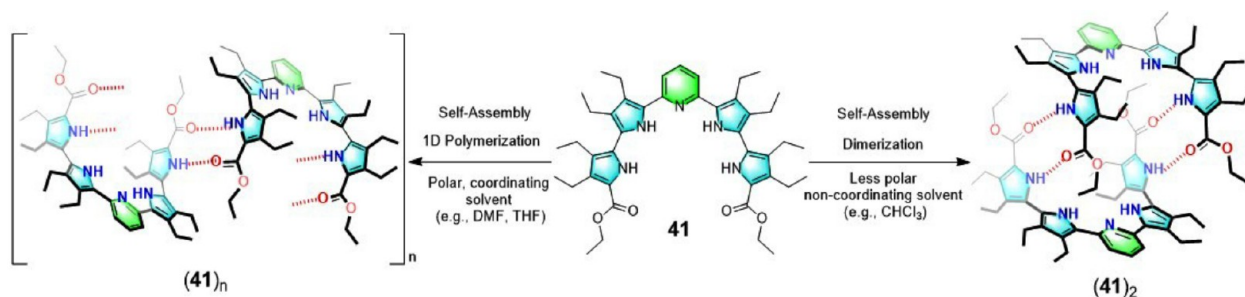


Figure 8. (a and b) Solid-state structures of receptors $(41)_2$ and $(42)_2$ as determined by single-crystal X-ray structural analyses. (c–f) Single-crystal X-ray structures of discrete supramolecular complexes with empirical chemical formula $[(42H)_2^{2+}C(\text{counteranion}^-)_2]$ formed between 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 $(41)_n$



5. CONCLUSIONS AND OUTLOOK

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

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421

Notes

422

The authors declare no competing financial interest.

423

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424

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486 ■ ACKNOWLEDGMENTS

487 The work at Hunan University was funded by the National
488 Natural Science Foundation of China (22071050 and 21901069
489 to Q.H.), the Science and Technology Plan Project of Hunan
490 Province, China (Grant No. 2019RS1018 to Q.H.), and
491 Fundamental Research Funds for the Central Universities
492 (Startup Funds to Q.H.). A.J. expresses thanks to the Science
493 and Engineering Research Board (SERB), Government of India,
494 for a core research grant (CRG/2021/000674) and the GITAM
495 Visakhapatnam campus for providing basic research facilities
496 and initial support. C.B. and J.L.S. gratefully acknowledge the
497 ENS de Lyon for financial support in the form of an Invited
498 Professorship for J.L.S. during the spring of 2022. C.B. thanks
499 the Groupements de Recherches of the Centre National de la
500 Recherche Scientifique (GDR CNRS) no. 2067 “Macrocycles
501 Pyrroliques” for research support. J.L.S. is grateful to the Robert
502 A. Welch Foundation for providing Chair support (F-0018).

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