ABSTRACT: A series of 22-membered unclosed cryptands end-capped with intra-annular methyl (1), phenyl (2), p-tert-butylphenyl (3), and p-nitrophenyl (4) amide substituents (lariat arm) were synthesized to elucidate the effect of steric and electronic factors on their anion recognition behavior. The $^1$H NMR titrations in DMSO-$d_6$ with 0.5% water reveal enhanced selectivity for H$_2$PO$_4^-$ vs Cl$^-$ and PhCO$_2^-$, Theth para-attachment of the electron-withdrawing nitro group (−NO$_2$ vs −H and −t-Bu) was found to increase anion-binding affinity, whereas the steric bulkiness of lariat arm (methyl vs aryl) has a marginal effect. DFT calculations reveal that binding of H$_2$PO$_4^-$ is associated with minimal conformational change in the lariat arm moiety and involve four hydrogen bond acceptor and one donor sites of host.

INTRODUCTION

Macrocyclic host compounds with well-defined structural features such as molecular weight, size and geometry of internal cavity, rigidity, and precisely arranged number of binding sites have attracted a considerable attention of the scientific community.$^1$ These special attributes of macrocycles render them particularly attractive to be successfully explored in the domain of medicine,$^2$ molecular electronics,$^3$ nanotechnology,$^4$ and supramolecular chemistry.$^5$ In the latter case, of particular interest is the development of neutral molecular receptors for anions,$^6$ especially for biologically active chloride, carboxylates, and phosphates that are pivotal in human physiology. To date, only a few general classes of macrocyclic host systems permitting selective encapsulation of a specific anionic guest were reported.$^7$ Noteworthy, attempts to modify their guest selectivity by structural modification of macrocyclic skeleton have often proven challenging. Therefore, there is a demand for the development of novel versatile macrocyclic hosts that are easily accessible from simple components and in parallel allow changing their anion-binding properties by using the same synthetic methodology.

Facing this problem, we have recently focused our attention on the new class of the macrocyclic host molecules equipped with auxiliary recognition motif in a form of flexible tether substituent (lariat arm), called unclosed cryptands (UCs).$^8$ Potential advantages of these robust macrocycles originate from their practical and cost-effective synthesis, allowing preparation of members varying in size of the macrocyclic cavity and type of the lariat arm. Noteworthy, for 26-membered tetra-admidic UCs, the lariat arm could be easily installed at the sterically demanding intra-annular position using an efficient postmacrocyclization synthetic proto-col.$^8b,8c,8e$ This approach allows preparation of a family of benzoate-selective hosts (R$_2$, Figure 1)$^8c$ as well as PTC catalysts.$^8b$ Moreover, pentamidic UCs having the 24-membered macrocyclic cavity have been found (depending on the lariat function) to selectively bind Y-shaped acetate (R$_1$, Figure 1)$^8f$ or spherical chloride (R$_3$, Figure 1)$^8a$.

As the selectivity toward these anions was modulated by varying the size of the binding pocket and careful selection of auxiliary motif, our thinking was to diminish the binding

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RESULTS AND DISCUSSION

Accordingly, in this paper, we present the synthesis and analysis of binding properties of a set of smaller 22-membered pentaamidic UCs \((n = 0, \text{Figure 1})\) varying in the type of substituent attached to the intra-annular amide function. The structures of all hosts 1–4 were unambiguously confirmed by spectroscopic methods (\(^1H\) NMR and \(^{13}C\) NMR), high-resolution mass spectroscopy (HRMS), and also single-crystal X-ray analysis. The anion-binding properties were determined using \(^1H\) NMR titration experiments in DMSO–d6. X-ray analysis. The anion-binding properties were determined using \(^1H\) NMR titration experiments in DMSO–d6 solvent mixture using tetrabutylammonium (TBA+) salts of Cl\(^–\), PhCO\(_2\)O\(^–\), and H\(_2\)PO\(_4\)\(^–\) anions. The solid-state structural changes of the conformation of hosts 2 and 4 upon chloride binding are studied and discussed. Furthermore, a relation between the binding affinity and selectivity of hosts 1–4 with respect to the type and bulkiness of the substituent mounted at sterically hindered intra-annular position is discussed (stere vs electronic factors). The demonstrated strategy let us, for the first time, find an appropriate UC structure capable of selective trapping of dihydrogen phosphate guest.

As shown in Scheme 1, the preparation of target 22-membered UCs 1–4 is started from the synthesis of the suitable \(\alpha,\omega\)-diesters \(7a–7d\) and \(\alpha,\omega\)-diamine 9.

Scheme 1. Synthesis of 22-Membered UCs 1–4 Using MeONa-Mediated Double Amidation Reaction

Briefly, intermediates \(7a–7d\) were synthetized in moderate overall yields (21–48%) starting from a commercially available 2-nitroresorcine \(5\) via successive Pd/C-catalyzed reduction of nitro group by H\(_2\) (1 atm) and treatment of the crude 2,6-dihydroxy aniline with a suitable acyl chloride, followed by double O-alkylation by the methyl bromoacetate. Consecutively, double amidation of the commercially available dimethyl 2,6-pyridinedicarboxylate \(8\) using an excess of ethylenediamine in neat conditions at rt readily provided \(\alpha,\omega\)-diamine 9 in almost quantitative yield. Having all the required macrocyclization partners in hand, the 22-membered UCs were then prepared in acceptable yields (7–39%) by employing an established methodology, relying on MeONa-mediated double amidation in methanol at rt without the necessity of employing high-dilution conditions (Scheme 1). Interestingly, the macrocyclization yields for host 4 are virtually the same, regardless of whether the pure diamine 9 or its dichloride salt was employed. This is in marked contrast to our previous reports on the preparation of bigger 24- and 26-membered UCs bearing the same \(p\)-nitrophenyl tether in which the macrocyclization yields were substantially higher when dichloride salts of homologous \(\alpha,\omega\)-diamines were employed.[9c] Compounds 1–4 and 6–7 \((a–d)\) were fully characterized by \(^1H\) NMR and \(^{13}C\) NMR spectroscopy, as well as high-resolution mass spectrometry (HRMS).

With hosts 1–4 in hand, we made attempts to examine structural features of these macrocyclic systems in the solid state. First of all, it was found that solid-state molecular packing of all hosts studied is quite similar despite obvious difference in the type of lariat arm and disparate crystallization conditions (Figure 2). Namely, the lariat amide C==O moiety is directed inward the macrocyclic cavity, thus preventing the putative binding of Cl\(^–\) and PhCO\(_2\)O\(^–\), but likely not H\(_2\)PO\(_4\)\(^–\), which might interact as both the hydrogen bond donor and acceptor, hence establishing a C==O(d)···HOPO\(_3\)H\(^–\) interaction (vide infra).

Nonetheless, the solid-state configuration of the lariat amide group is further stabilized by the short intermolecular hydrogen bond with the carbonyl group of another host \((d_{\text{H-O-C}} = 2.80–2.85\;\text{Å})\) or water molecule \((d_{\text{H-O-C}} = 2.92\;\text{Å})\) for \(1, 3, 4, \text{and 2}\). Another common feature of hosts 1–4 is the preorganization of four NH amide protons belonging to the macrocyclic skeleton, which are directed inward the macrocyclic cavity. This in turn forces the host molecule to adopt a chair-like conformation wherein 2,6-dimethoxymide and 2,6-pyridinedicarboxylamido units are almost parallel to each other. The structural preorganization of amide groups was already observed in crystal structures of various UCs; hence, it is a rather common feature for these kinds of macrocyclic host compounds.[9] In addition, entrapping of water molecule by the host molecule was observed for crystal structures of all hosts 1–4. This neutral guest is strongly held within the macrocyclic cavity by four or five hydrogen bonds, one originating from the lariat C==O moiety \((d_{\text{C=O-H-O}} = 2.82–2.94\;\text{Å})\), two (hosts 1 and 2) or three (hosts 3 and 4) originating from macrocyclic NH bond donors \((d_{\text{H-N-O}} = 2.90–3.35\;\text{Å})\), and remaining ones from the C==O macrocyclic moiety of adjacent host molecule \((d_{\text{H-O-C}} = 2.76–3.03\;\text{Å})\). Collectively, these results suggest that the conformation of macrocyclic skeleton has a decisive impact on the packing of such type of host molecule in the solid state.

Comparison of the crystal structures of free hosts 1–4 and chloride complexes with hosts 2 and 4 would help us unveil similarities and relevant differences in the packing behavior and molecular environment of these structurally similar macrocyclic compounds, which differ only in terms of type of the substituent attached to the intra-annular amide function. The crystal structures of complexes of hosts 2 and 4 with TBACl demonstrate a profound conformational change of the host resulting from binding of the chloride guest (Figure 3).

Namely, in these structures, the lariat amide group turned by almost 180° in such a way that the NH proton is pointing inward the macrocyclic cavity, i.e., opposite situation as compared with the structures of free hosts 1–4. The type of \(para\)-substituent was found to dramatically affect the binding mode and topology of the host–cloride complex. Namely, host 2 bearing the phenyl group utilize three out of five NH amide protons to bind chloride, while two remaining H-bond donors serve to bind a water molecule (Figure 3a,c). In contrast, host 4 bearing the \(p\)-nitrophenyl substituent does not accommodate water in the macrocyclic cavity and utilize four

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of five NH-bond donors to bind chloride, whereas the remaining H-bond donor is not involved in any type of hydrogen bonding interaction. A closer inspection of the crystal structure reveals that host 2 and TBACl salt crystallize as a 2:2 host−salt complex possessing a diamond-shaped geometry in which two water molecules link two chloride anions (Figure 4).

Both chloride and water molecule guests are bounded by two molecules of host 2 (Figure 4a). The energy required for the stabilization of dimer is gained from the extensive net of roughly 14 hydrogen bonds, allowing overcoming the electrostatic repulsion between two negatively charged anions, Cl−···Cl−* (4.94 Å) (Figure 4b). As similar stabilization of chloride dimers by electrically neutral host−guest systems1 was previously observed for phenoxyalted oxacalix[2]arene[2]-triazine reported by Wang’s group,12a cyclic octalactam synthesized in our laboratory,12b and cyclophane reported by
Anislyn’s group. The measured Cl$^-$$^-$$^-Cl$$^- distances in the solid-state structures of these complexes are 5.53, 4.88, and 5.52 Å, respectively.

$^1$H NMR spectral titrations in a competitive DMSO-d$_6$ + 0.5% H$_2$O solvent mixture were performed in an effort to quantify binding properties of hosts 1–4 in solution. As model anionic guests, we chose tetrabutylammonium (TBA$^+$) salts of representative anions, i.e., spherical chloride (Cl$^-$), Y-shaped benzoate (PhCO$_2^-$), and tetrahedral dihydrogenphosphate (H$_2$PO$_4^-$). The corresponding association constants $K_a$’s were determined from a global shift analysis of the titration data using the Bindfit$^{13}$ program and assuming a simple 1:1 (for Cl$^-$ and PhCO$_2^-$) or full 1:1 + 1:2 host–guest (for H$_2$PO$_4^-$) binding models. The results of these experiments are collected in Table 1. Analysis of Table 1 indicates that the binding order of hosts 1–4 for anions is H$_2$PO$_4^-$ > Cl$^-$ > PhCO$_2^-$.

The slightly stronger affinity of studied hosts to the least basic chloride over benzoate could be attributed to the good size match of the binding pocket to the size of chloride as deduced from X-ray studies.

We furthermore noticed that, except host 4, the binding affinity for chloride is qualitatively correlated with the bulkiness (cf. column $V_R$ in Table 1) of the R substituent; i.e., the more bulky substituent installed, the smaller interaction with chloride is clearly identified. It is also noticeable that binding affinity for H$_2$PO$_4^-$ is stronger when the R substituent is aryl (compare 1 vs 2–4), while the host 4 featured with the $p$-nitrophenyl substituent produces the most stable complex. The presence of an electron-withdrawing nitro group increases the acidity of lariat NH bond donor and reduces the electron density of aryl ring. Both these factors increase anion affinity; however, the former one additionally shortens the H-bonding between C==O(d) and N(a) moieties (compare the bond lengths in Figure 2). Such an internal hydrogen bonding has to be broken prior to binding of hydrogen bond acceptors such as Cl$^-$ and PhCO$_2^-$ to provide the proper binding conformation in which N(a) amide proton is directed inward the binding pocket (compare Figures 2 and 3). However, this is not mandatory for H$_2$PO$_4^-$, which could utilize P-OH groups to interact with the C==O(d) moiety also as a H-bond donor, thus preserving the internal C==O(d)…N(a) hydrogen bond. Noteworthy, specialized proteins employ a similar binding approach; i.e., they utilize hydrogen bond donor and acceptor sites to bind phosphates with high selectivity. However, this approach was scarcely used in the construction of artificial hosts for H$_2$PO$_4^-$.

To test the possibility of C==O(d) group actively participating in phosphate binding, we have performed a series of DFT calculations for the 4$\cdot$H$_2$PO$_4^-$ and 2$\cdot$(H$_2$PO$_4^-$·H$_2$O) complexes employing the C-PCM implicit solvation model (Figure 5). Addition of water molecule being bound by both host and anion was taken into account to improve the computational accuracy of the host–anion complex.$^{6b,16}$ In both cases, the computational calculations indicate conformations in which the NH(a) proton is directed outward the macrocyclic cavity, thus enabling binding of H$_2$PO$_4^-$ via the C==O(d) moiety to be the most stable (see the Supporting Information for details). In addition, a superposition of DFT calculation and X-ray structure of 4$\cdot$H$_2$PO$_4^-$·H$_2$O (Figure 5b; green color) and 2$\cdot$H$_2$O (Figure 5b; blue color) indicates the comparable conformation of a macrocyclic entity. Collectively, these results indicate that energetically demanding twisting of lariat arm (at least two hydrogen bonds have to be broken prior to the rotation of lariat arm) is not required to bind H$_2$PO$_4^-$, which explains the high selectivity for this anionic guest as compared with purely H-bond acceptor anions.

To further investigate if the C==O(d) moiety might participate in binding of other anions having hydrogen bond donor and acceptor groups, the host 4 was subjected to titrations with TBA salts of hydrogen sulfate (HSO$_4^-$) and pyrophosphate (HP$_2$O$_5^{3-}$). The experiments reveal, however, that host 4 exhibits lack of interaction with HSO$_4^-$ (K < 5 M$^{-1}$), whereas addition of 1 equiv of highly basic HP$_2$O$_5^{3-}$ causes deprotonation of the host, resulting in the visible color change from transparent to orange.

## CONCLUSIONS

In conclusion, 22-membered homologous unclosed cryptands end-capped with acetyl, (1), phenyl (2), tert-butylphenyl (3), and nitrophenyl (4) amide substituents (lariat arm) were prepared and characterized by the single-crystal X-ray analysis. It was found that the bulkiness of lariat arm (methyl vs aryl) has a marginal effect on crystal packing as well as on anion-binding affinity and selectivity, whereas para-attachment of the EWG nitro group (–NO$_2$ vs –H and –tert-Bu) considerably increases anion-binding affinity, in particular for H$_2$PO$_4^-$.

In addition, DFT calculations reveal that binding of H$_2$PO$_4^-$ is

Table 1. Stability Constants $K_a$’s (M$^{-1}$) for the Complexes of Hosts 1–4 with Anions$^a$

| host | R   | $V_R$ $^b$ | Cl$^-$ | PhCO$_2^-$ | H$_2$PO$_4^-$ |
|------|-----|-----------|--------|-------------|--------------|
| 1    | Me  | 32        | 85     | n.d.        | 180 (13)     |
| 2    | Ph  | 98        | 75     | 35          | 303 (18)     |
| 3    | $p$-C$_6$H$_4$+Bu | 170 | 70 | 41 | 188$^c$ |
| 4    | $p$-C$_6$H$_4$NO$_2$ | 120 | 96 | 93 | 1576 (75) |

$^a$Anions added as TBA salts, determined by $^1$H NMR titration experiments in DMSO-d$_6$/H$_2$O (99.5:0.5, v/v) at 303 K; values in parentheses are for the 1:2 complex; for error estimates, see Table S2. n.d., not determined. $^bV_R$, calculated volume of the substituent attached to intra-anular amide function (in Å$^3$). $^c$Fitted using a 1:1 binding model (see the Supporting Information).
associated with a small conformational change of the macrocyclic entity and involve four hydrogen bond acceptor and one donor sites of the host, likewise to phosphate-binding proteins. This new binding mode interaction of UCs with phosphates and this strategy are currently explored in our laboratory to construct even more H₂PO₄⁻-selective hosts.

**EXPERIMENTAL SECTION**

Materials and Methods. All the reagents were used as received. All solvents were obtained from common suppliers and used as received (including anhydrous DCM and DMF). All reactions were performed, avoiding moisture by standard procedures and under an argon atmosphere. Flash column chromatography was performed on silica gel (230–400 mesh), and thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel. The ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Mercury 400 at 400 and 100 MHz, respectively, and on a Varian 600 at 600 MHz, and used as received (including anhydrous DCM and DMF).

**N-(2,6-Hydroxyphenyl) Acetamide (6a).** The title product was obtained following general procedure A with 70% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 9.32 (s, 3H); 6.87 (t, 1H, J = 8.2); 6.35 (d, 2H, J = 8.2); 2.11 (s, 3H, COCH₃). ¹³C NMR (125 MHz), DMSO-d₆: δ = 170.3 (NHCOCH₃), 152.0, 126.6, 114.1, 107.6, 22.7 (COCH₃).

**N-(2,6-Dihydroxyphenyl)-benzamide (6b).** The title product was obtained following general procedure A with 75% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 9.32 (s, 1H); 9.26 (s, 2H); 8.02–7.97 (m, 2H); 7.64–7.46 (m, 3H); 6.96 (t, 1H, J = 8.4); 6.46 (d, 2H, J = 8.4); 13C NMR (500 MHz, DMSO-d₆): δ = 169.3 (NHCOPh), 153.7, 134.2, 131.4, 128.2, 127.9, 127.1, 113.4, 107.1.

**N-(2,6-Dihydroxyphenyl)-4-tert-butylbenzamide (6c).** The title product was obtained following general procedure A with 80% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 9.42 (bs, 3H); 8.40 (d, 2H, J = 8.4); 8.26 (d, 2H, J = 8.4); 6.99 (t, 1H, J = 8.1); 6.43 (d, 2H, J = 8.1); 13C NMR (500 MHz, DMSO-d₆): δ = 164.3 (NHCOPh), 154.4, 153.4, 131.3, 127.7, 127.0, 125.0, 113.5, 107.2, 34.6 (C(CH₃)₃), 30.9 (C(CH₃)₂).

**N-(2,6-Dihydroxyphenyl)-4-nitrobenzamide (6d).** The title product was obtained following general procedure A with 65% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 9.32 (s, 1H); 8.40 (d, 2H, J = 8.4); 8.26 (d, 2H, J = 8.4); 6.99 (t, 1H, J = 8.1); 6.43 (d, 2H, J = 8.1); 13C NMR (500 MHz, DMSO-d₆): δ = 169.2 (NHCOPh), 169.2 (CH₂CO), 154.7, 127.1, 116.4, 106.8, 65.6 (OCH₂CO), 52.1 (OCH₃).

**Dimethyl 2,2′-([(2-Acetylamino)benzene-1,3-diyl]bis(oxy))-diacetate (7a).** The title product was obtained following general procedure B with 60% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 8.92 (bs, 1H, PhNHCOCO); 6.75 (t, 1H, J = 8.3); 6.25 (d, 2H, J = 8.3); 4.58 (s, 4H, OCH₂CO); 3.73 (s, 6H, OCH₃). ¹³C NMR (125 MHz, DMSO-d₆): δ = 169.2 (NHCOPh), 169.2 (CH₂CO), 154.7, 127.1, 116.4, 106.8, 65.6 (OCH₂CO), 52.1 (OCH₃).

**Dimethyl 2,2′-[(2-((Phenylcarbamoyl)amino)benzene-1,3-diyl)bis(oxy))-diacetate (7b).** The title product was obtained following general procedure B with 30% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 8.72 (bs, 1H, PhNHCOCO); 7.99 (d, 2H, J = 7.9); 7.57 (m, 1H), 7.56 (m, 2H), 7.21 (t, 1H, J = 8.4); 6.68 (d, 2H, J = 8.4); 4.76 (s, 4H, OCH₂CO); 3.66 (s, 6H, OCH₃). ¹³C NMR (125 MHz, DMSO-d₆): δ = 169.1 (NHCOPh), 155.0 (CH₂CO), 143.5, 131.2, 128.2, 127.7, 127.5, 116.4, 106.9, 65.8 (OCH₂CO), 51.7 (OCH₃).

**Dimethyl 2,2′-[(2-((4-(tert-Butyl)phenyl)carbonyl)amino)benzene-1,3-diyl)bis(oxy))-diacetate (7c).** The title product was obtained following general procedure B with 34% yield. ¹H NMR (500 MHz), acetone-d₆: δ = 8.82 (bs, 1H, PhNHCOCO); 8.00 (d, 2H, J = 8.2); 7.55 (d, 2H, J = 8.2); 7.19 (t, 1H, J = 8.6); 6.73 (d, 2H, J = 8.6); 4.73 (s, 4H, OCH₂CO); 3.70 (s, 6H, OCH₃); 1.43 (s, 9H, C(CH₃)₃). ¹³C NMR (125 MHz, Acetone-d₆): δ = 170.3 (NHCOPh), 165.9 (CH₂CO), 153.8, 155.3, 133.3, 128.4, 127.9, 126.0, 119.3, 109.3, 10.6 (OCH₂CO), 52.2 (OCH₃), 35.4 (C(CH₃)₂), 31.5 (C(CH₃)₃); MS (ESI-HRMS, MeOH) for C₂₃H₂₇NO₇Na+: 542.1685; found, 542.1681.

**Dimethyl 2,2′-[(2-((4-(tert-Butyl)phenyl)carbonyl)amino)benzene-1,3-diyl)bis(oxy))-diacetate (7d).** The title product was obtained following general procedure B with 74% yield. ¹H NMR (500 MHz), DMSO-d₆: δ = 9.82 (bs, 1H, PhNHCOCO); 8.34 (d, 2H, J = 7.9); 8.20 (d, 2H, J = 7.9); 7.21 (t, 1H, J = 8.4); 6.68 (s, 2H, J = 8.4); 4.77 (s, 4H, OCH₂CO);
N-(4,9,15,20-Tetraoxo-2,22-dioxo-5,8,16,19,28-pentaazatricyclo[21.3.1.1\(27\),10-28(11,13,23,25-hexaen-27-yl)acetamide (1). Following general procedure C, the target compound was obtained as a colorless powder; yield: 15%; m.p. 258-259 °C; for host 3 (CCDC 2016775), 1H NMR (500 MHz, DMSO-\[d_6\]): \(\delta = 9.46\) (bs, 1H, PhNHCOCO); 8.65 (bs, 2H, NHCO); 8.11 (d, 2H, J = 8.8); 7.86 (bs, 2H, CONH); 7.84 (d, 2H, J = 8.8); 6.84 (t, 1H, J = 8.4); 6.65 (d, 2H, J = 8.4); 4.63 (s, 4H, OCH\(_2\)CO); 3.43 (bs, 4H, NHCO); 3.31 (s, 4H, CONH); \^13\)C NMR (125 MHz, DMSO-\[d_6\]): \(\delta = 167.8\) (CONH); 166.6 (NHCONH); 165.8 (NHCO); 150.4, 153.5, 149.0, 139.1, 127.4, 124.2, 106.3, 67.6 (OCH\(_2\)CO); 30.8 (C(CH\(_3\))\(_3\)); MS (ESI-HRMS) (MeOH) \([M + Na^+]\): \(C_{42}H_{34}N_{16}O_{10}Na\), 821.1755; found, 821.1772. 

4-tert-Butyl-N-(4,9,15,20-tetraoxo-2,22-dioxo-5,8,16,19,28-pentaazatricyclo[21.3.1.1\(27\),10-28(11,13,23,25-hexaen-27-yl)benzamide (3). Following general procedure C, the target compound was obtained as a colorless crystalline material; yield: 12%; m.p. 169-170 °C; \(^1\)H NMR (500 MHz, DMSO-\[d_6\]): \(\delta = 10.28\) (bs, 1H, PhNHCOCO); 8.65 (bs, 2H, NHCO); 8.11 (d, 2H, J = 8.8); 7.86 (bs, 2H, CONH); 7.84 (d, 2H, J = 8.8); 6.84 (t, 1H, J = 8.4); 6.65 (d, 2H, J = 8.4); 4.63 (s, 4H, OCH\(_2\)CO); 3.43 (bs, 4H, NHCO); 3.31 (s, 4H, CONH); \^13\)C NMR (125 MHz, DMSO-\[d_6\]): \(\delta = 167.8\) (CONH); 166.6 (NHCONH); 165.8 (NHCO); 153.7, 150.0, 148.9, 139.1, 133.2, 131.8, 128.2, 127.7, 124.3, 115.5, 106.3, 67.6 (OCH\(_2\)CO); 37.8 (NCH\(_2\)CH\(_2\)OH); 30.8 (C(CH\(_3\))\(_3\)); MS (ESI-HRMS, MeOH) \([M + Na^+]\): \(C_{42}H_{34}N_{16}O_{10}Na\), 852.1959; found, 852.1978.

Titration Experiments. As the source of anions, commercially available tetrabutylammonium (TBA) salts were used. HPLC-grade water was added to the commercially available DMSO-\(d_6\) of 99.9% isotopic purity to obtain the 0.5% water concentration. The host solution was titrated in a NMR tube with the solution of the respective TBA salt in receptor aliquots. The binding constants were calculated from the changes in chemical shifts of ligand protons, which shift during titration. Nonlinear curve fitting was carried out with the Binds\(^1\) program with fitting to the appropriate global binding model (see Table S2).

X-ray Studies. Single crystals of hosts suitable for the X-ray analysis were obtained by slow diffusion of solvent into solution of host in DMSO/water mixture: 1-butanol for host 1 (CCDC 2016733), water for host 2 (CCDC 2016774), and acetonitrile for host 3 (CCDC 2016775). The X-ray crystal structure of 2-TBACl complex was growth by diffusion of CH\(_2\)Cl\(_2\) into solution of 2 and TBACl in DMSO/water (CCDC 16781). Crystal structures of hosts 4 (CCDC 1498216) and 4-TBACl complex (CCDC 1534256) were published previously.
Notes
The authors declare no competing financial interest.

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