ACS OMEGA

http://pubs.acs.org/journal/acsodf

Article

Spatially Designed Supramolecular Anion Receptors Based on Pillar[5]arene Scaffolds: Synthesis and Halide Anion Binding Properties

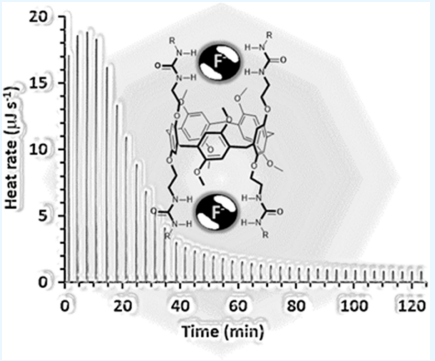
Mickey Vinodh, Fatemeh H. Alipour, and Talal F. Al-Azemi*

Cite This: *ACS Omega* 2023, 8, 1466−1475

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Urea-functionalized anion receptors based on brominated functionalized pillar[5]arenes were prepared. The binding affinity toward halide anions was investigated and probed using ^{1}H NMR titration and isothermal titration calorimetry (ITC). The complexation behavior was affected by the structure of the receptor and the nature of the anionic guest. The synthesized receptors are highly selective toward fluoride resulting in the formation of a 1:2 host-to-guest complex. The anion receptor based on the 1,3-alternate pillar[5]arene regioisomer shows the highest affinity toward fluorine anions. No significant interactions were observed with larger bromine anions. The formation of a self-assembled supramolecular polymer driven by hydrogen bonds in solution was demonstrated by diffusion-ordered spectroscopy (DOSY), ITC, and dynamic light scattering (DLS) measurements. From ITC dilution experiments, we found that the supramolecular polymer self-assembly at higher concentrations is a spontaneous process as indicated by the positive value of Gibbs free energy (ΔG = 12.04 kJ mol^{-1}).



INTRODUCTION

For many years supramolecular chemistry was related mainly to the recognition and selective binding of cations.[1,2] On the other hand, the field of anion recognition by synthetic receptors was accompanied with several difficulties because of the peculiar characteristics of anions.[3] The relatively large size of anions compared to cations requires a much larger receptor. For example, the size of the smallest ionic radius of anions, fluoride ion (1.33 Å), is comparable to the radius of the cation of the potassium ion (1.38 Å). The chloride ion (1.81 Å) is larger than the cation of cesium (1.70 Å). Another, aspect of the design of anion receptors is the different geometries of anions ranging from simple spherical (F^-, Cl^-, Br^-, I^-), linear (N_3^-, CN^-, SCN^-, OH^-), trigonal planar (CO_3^{2-}, NO_3^-), and tetrahedral (BF_4^-, ClO_4^-, SO_4^{2-}, PO_4^{3}) to octahedral (PF_6^-, $Fe(CN)_6^{3-}$) and often show multiple coordination geometries, in addition to higher values of the solvation free energy compared to similar sized cations and their higher sensitivity to pH.

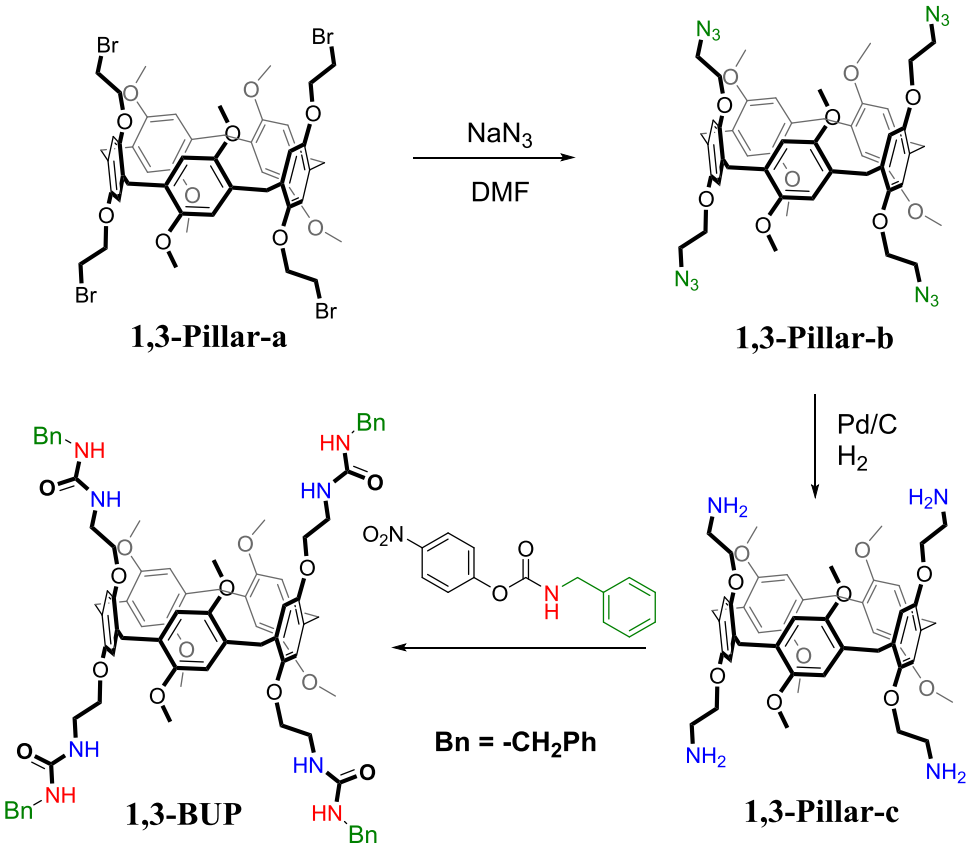
The design of anion receptors goes back to 1968, when Simmons and Park synthesized the first polyammonium-based anion receptors.[4] In spite of the difficulties, in recent years great attention has been focused on the design and construction of anion receptors.[1−19] Many neutral and/or positively charged host molecules have been developed for anion complexation through hydrogen bonding and/or electrostatic interactions. Neutral chemically designed receptors bearing multiple polarized N−H groups such as amide, (thio)urea, and pyrrole are known to achieve a strong guest−host interaction and are widely used for anion recognition.[20]

Subsequent to the report in the literature by Wilcox[21] and Hamilton[22] that demonstrated the ability of urea moieties to act as an appropriate binding site for anions, many urea and thiourea-based receptors have been developed for anion complexation.[20] The topology of host molecules also plays an essential aspect in selective recognition of the anionic species. Thus, many supramolecular compounds have been employed as a platform to enhance the selective ability of the receptor by pointing the binding entities toward a common area creating a precise binding site for a given anion with multipoint recognition capability. In practice, combination of structural modification strategies has been utilized concurrently. Cholapod,[23] polynorbornene,[24] and calixarene/resorcinarene[25−27]-based receptors have been reported.

The architecture of a molecular receptor is an important aspect to enhance binding and selectivity to the guest molecule. The unique structure of pillararenes provide an interesting platform for the synthesis of receptors with exceptional selectivity and binding abilities. There are few

Received: October 26, 2022
Accepted: December 14, 2022
Published: December 27, 2022

Scheme 1. Representative Example of the Synthesis of Urea-Functionalized Pillar[5]arenes



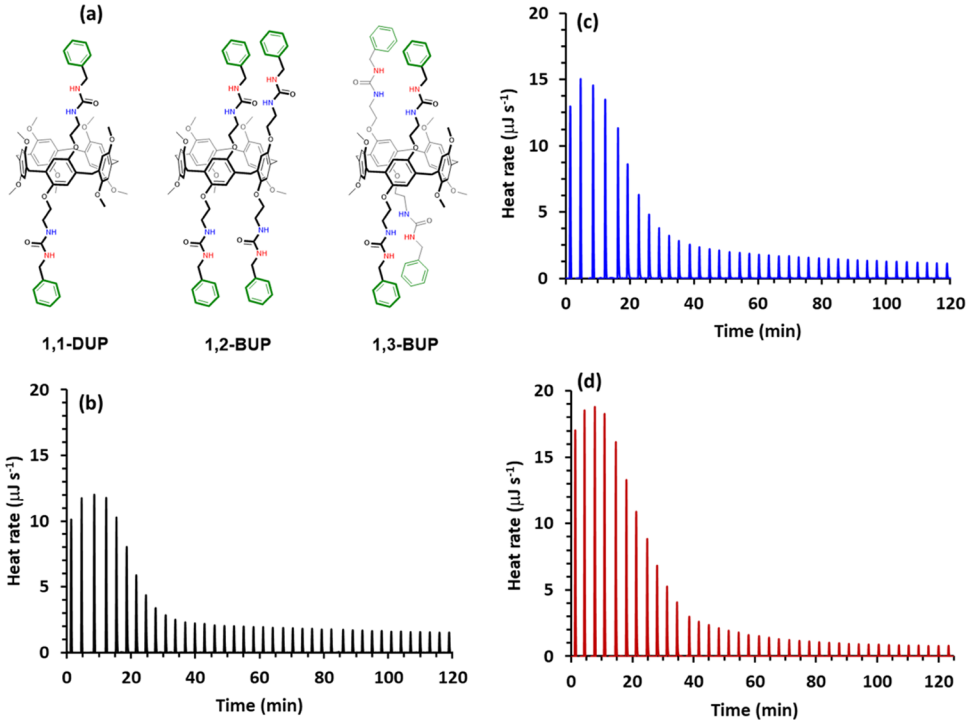


Figure 1. (a) Chemical structures of the synthesized urea-based anion receptors. Host−guest complexation ITC experiment raw heats for sequential injections in chloroform for **1,1-DUP** (b), **1,2-BUP** (c), and **1,3-BUP** (d) anion receptors with tetrabutylammonium fluoride (TBAF) guest at 25 °C.

examples in the literature of pillararenes bearing urea functional groups,[28−30] yet structural isomeric urea-functionalized pillar[5]arenes have not been reported. Recently, we have successfully synthesized functionalized regioisomers of

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

Table 1. ITC Thermodynamic Parameters Associated with the Complexation between Various Anion Receptor Hosts and Tetrabutylammonium Fluoride (TBAF) Guest[a]

entry	guest	$\Delta H°$ (KJ mol^{-1})[b]	$-T\Delta S°$ (KJ mol^{-1})[b]	K_a (M^{-1})[b]	n[c]	K_a (M^{-1})[d]
1	**1,1-DUP**	−34.92	10.41	$5.16 \pm 0.02 \times 10^3$	1.89	$5.35 \pm 0.03 \times 10^3$
2	**1,2-BUP**	−35.74	13.78	$7.01 \pm 0.02 \times 10^3$	2.31	$8.21 \pm 0.27 \times 10^3$
3	**1,3-BUP**	−56.74	30.72	$3.61 \pm 0.02 \times 10^4$	2.17	$4.65 \pm 0.16 \times 10^4$

[a]Fixed concentration of anion receptor hosts (5 mM) and varying guest concentrations in chloroform at 25 °C. [b]Calculated from the ITC measurement. [c]Experimental binding molar ratio. [d]Calculated for ^{1}H NMR titration.

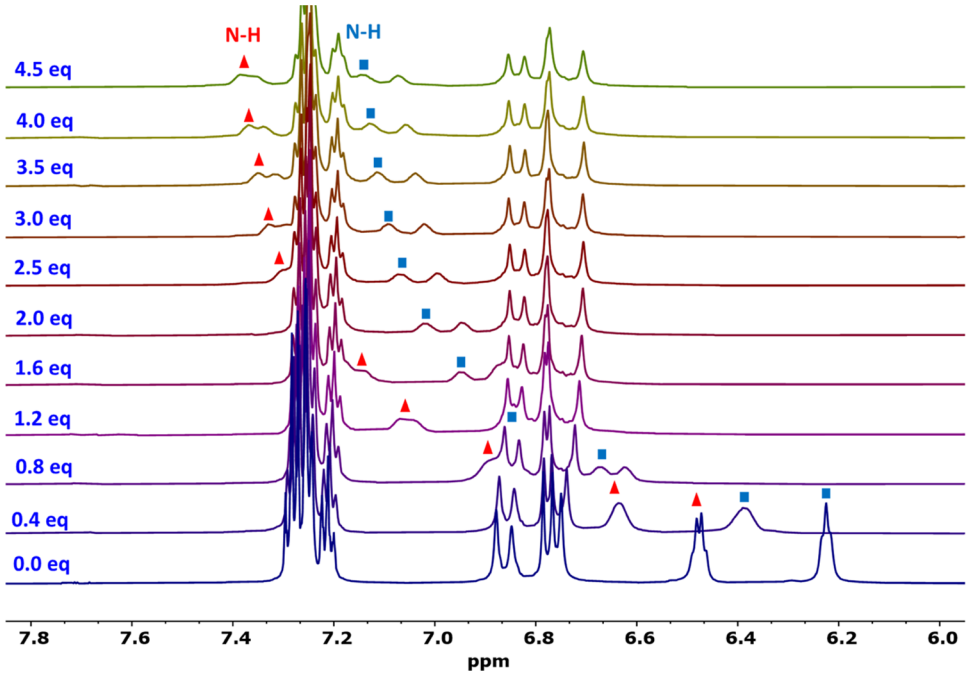


Figure 2. Expanded ^{1}H NMR (600 MHz, DMSO-d_6, 298 K) spectra of the urea region of **1,3-BUP** (5.0 mM) with increasing equimolar quantities (0 → 4.5 eq) of tetrabutylammonium fluoride (TBAF).

pillar[5]arenes by the cocyclization reaction of 1,4-bis(2-bromoethoxy)benzene with 1,4-dimethoxybenzene. The success of the separation depends on the nature of the reacting monomers. The isolated regioisomers were fully characterized by NMR and MS analyses. The structures of the isomers were assigned when their crystal structures were obtained from X-ray signal crystal diffraction analysis, which showed their different substitutional group distributions.[31] The yield of regioisomers could be controlled through manipulation of the feed ratio of hydroquinone derivatives.

In this present work, we report the synthesis of urea-functionalized receptors based on constitutional isomers of tetra-bromo-functionalized pillar[5]arenes. The influence of the receptor structure on the selectivity and binding ability toward halide anions is investigated by ^{1}H NMR titration, diffusion-order spectroscopy (DOSY), and isothermal titration calorimetry (ITC) experiments. In addition, the supramolecular self-assembly mediated by hydrogen-bond interactions of urea-functionalized substituents on the pillararene frame in solution was also characterized.

RESULTS AND DISCUSSION

Synthesis. One of the fundamental aspects of receptor design is to achieve selectivity toward a certain target or guest molecule by chemically modifying the receptor structure. Utilizing spatially well-defined pillar[5]arene scaffolds in the synthesis of urea-functionalized anion receptors is expected to tailor the receptor selectively and binding ability. On the basis of such systems, constitutional isomers of urea-functionalized pillar[5]arenes were synthesized following the strategy outlined in Scheme 1. The first step in the synthesis of a urea-based anion receptor is the use of suitable functionalized pillar[5]arenes, namely, 1A/2A-dibromoethoxy-pillar[5]arene (**1,1-Pillar-a**), 1,2-tetrabromoethoxy-pillar[5]arene (**1,2-Pillar-a**), and 1,3-tetrabromoethoxy-pillar[5]arene (**1,3-Pillar-a**).[31] The bromo-functionalized pillar[5]arenes were converted to amino derivatives by the reaction with sodium azide (NaN_3), followed by catalytic hydrogenation. The target urea-functionalized pillar[5]arenes were obtained upon the reaction with *p*-nitrophenyl benzylcarbamate (Figure 1a).[32] Suitable crystals for X-ray single crystal diffraction analysis were grown successfully by the slow evaporation method for all azido-functionalized pillar[5]arenes. Unfortunately, no suitable crystals of the amino-and urea pillar[5]arene derivatives could be obtained for X-ray analysis.

ITC Studies. The isothermal titration calorimetry (ITC) technique has been successfully employed to study various reversible noncovalent supramolecular interactions in solution. Therefore, the complexation abilities of the urea-functionalized pillar[5]arenes with tetrabutylammonium halide salts were studied through the ITC technique. Preliminarily, ITC experiments were carried out between the synthesized anion receptors and tetrabutylammonium fluoride salts (TBAF) in

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

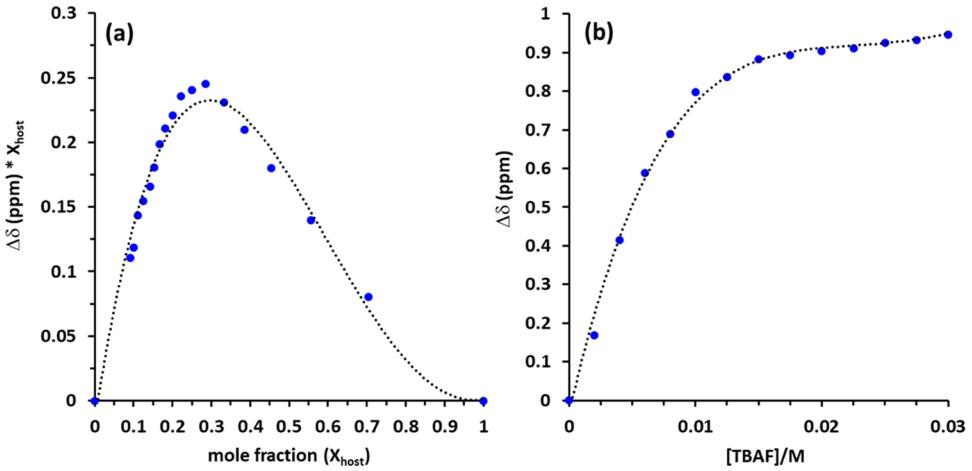


Figure 3. Job's plot for complexation of **1,3-BUP** with the **TBAF** guest (a), and plot of chemical shift (δ) changes for the host (**1,3-BUP**) NH proton urea region as a function of the guest (**TBAF**) concentration (b) determined from ^{1}H NMR titration of DMSO-d_6 at 25 °C.

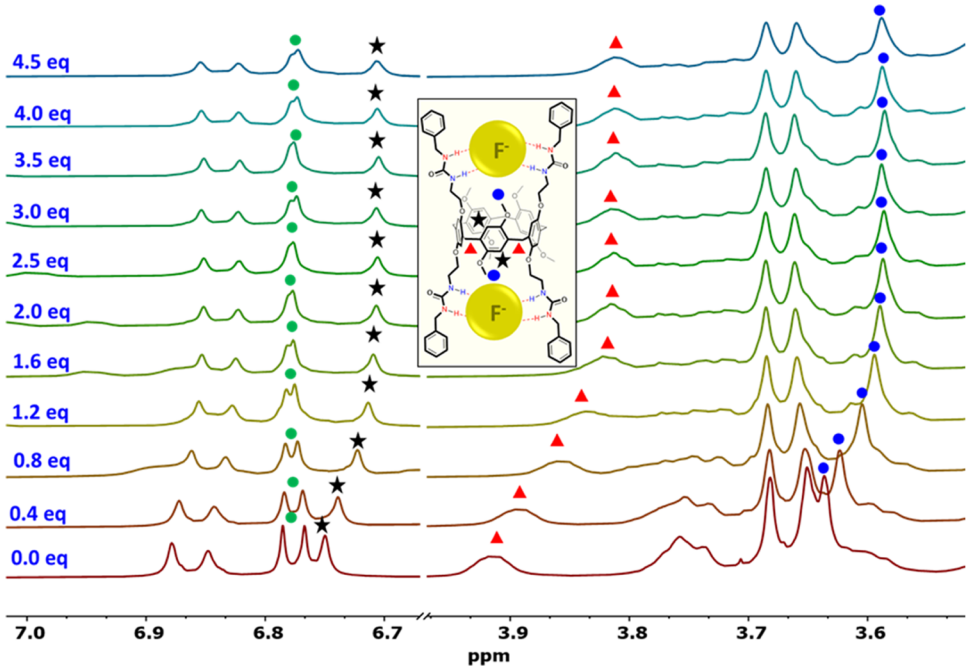


Figure 4. Expanded ^{1}H NMR (600 MHz, DMSO-d_6, 298 K) spectra for the pillar[5]arene proton resonances of **1,3-BUP** (5.0 mM) with increasing equimolar quantities (0 → 4.5 eq) of tetrabutylammonium fluoride (TBAF), and an inserted depiction of the complexation mode between **1,3-BUP** and fluorine anions (F^-).

chloroform at 25 °C. Noticeable differences were observed in the ITC thermograms among the synthesized anion receptors with fluorine anions, F^- (Figure 1). The quantitative information concerning the binding affinity and the thermodynamic parameters of the host−guest complexation obtained from ITC measurements are summarized in Table 1. All of the experimentally obtained binding molar ratios "*n*" are close to 2, which indicates a 1:2 host-to-guest stoichiometric ratio of complexation, wherein the association constant (K_a) values are dependent on the receptor structure. The association constant K_a value of the receptor based on the 1,3-alternate regioisomer **1,3-BUP** (K_a = 3.61 ± 0.02 × 10^4 M^{-1}) is 1 order of magnitude higher than the receptor based on the 1,2-alternate regioisomer, **1,2-BUP** (K_a = 7.01 ± 0.02 × 10^3 M^{-1}), which clearly demonstrates that the spatial location of the urea arms on the pillararene frame plays an important role in its binding ability. The higher affinity toward F^- was also evident from larger negative enthalpy changes of **1,3-BUP** ($\Delta H°$ = −56.74 KJ mol^{-1}) compared to **1,2-BUP** ($\Delta H°$ = −35.74 KJ mol^{-1}). Interestingly, the approximately triple the value of the negative entropy change of **1,3-BUP** ($T\Delta S°$ = −30.72 KJ mol^{-1}) relative to **1,2-BUP** ($T\Delta S°$ = −13.78 KJ mol^{-1}) indicates a substantial rise in the order of the host−guest supramolecular complex. The host−guest complexation ITC measurements for the **1,1-DUP** receptor with F^- were comparable to data obtained for **1,2-BUP**. The ITC data for **1,2-BUP** and **1,3-BUP** show the imperativeness of relative positions of the receptor groups on the pillararene rim in their binding affinity.

NMR Studies. For further insight in host−guest interactions, ^{1}H NMR titration experiments were conducted between fluoride and the synthesized pillar[5]arene-based anion receptors (**1,1-DUP**, **1,2-BUP**, and **1,3-BUP**), in

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

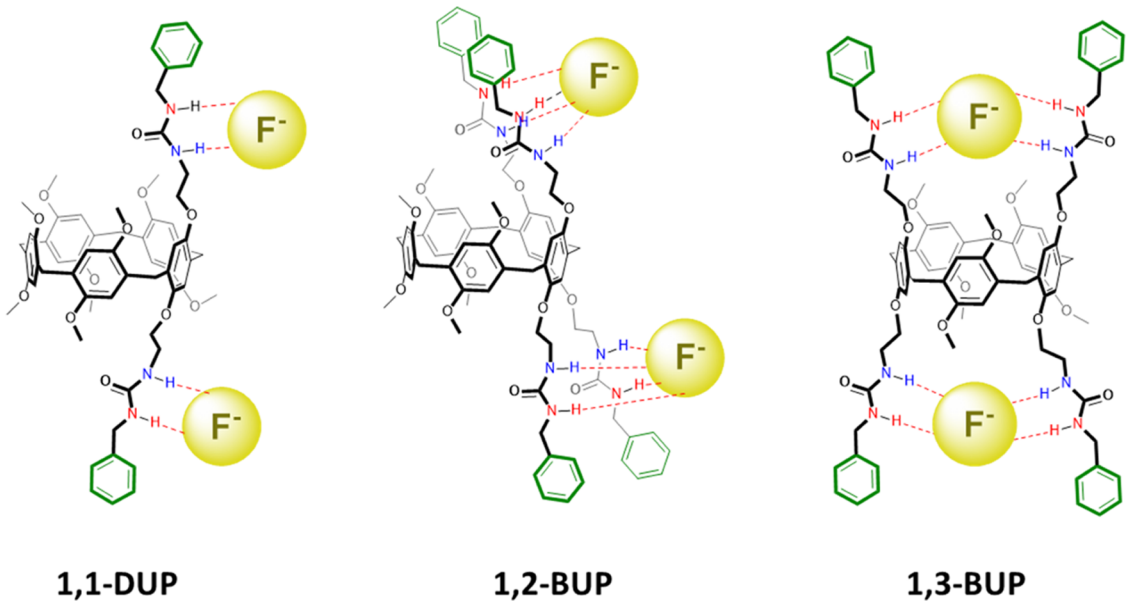


Figure 5. Depiction of the binding modes of the synthesized anion receptors toward fluorine anions (F^-).

DMSO-d_6 at 298 K. Figure 2 shows representative expanded ^{1}H NMR spectra of a mixture of **1,3-BUP** (5 mM) and various equivalents of the tetrabutylammonium fluoride salt (TBAF). The host−guest complexation was confirmed, as evidenced from the significant upfield shift of resonances for the urea protons (N−H). From the titration experiments, the ^{1}H NMR spectra in DMSO-d_6 show only one set of peaks, indicating fast-exchange complexation on the ^{1}H NMR time scale at 25 °C.

The stoichiometry of the host−guest was established using the method of continuous variations (Job's plots) between the mole fraction of the host (X_{host}) and the chemical shift changes of urea protons (N−H) on urea-functionalized-pillar[5]arene receptors in ^{1}H NMR multiplied by the mole fraction (X_{host}). For example, Job's plots of host **1,3-BUP** with TBAF in DMSO-d_6 showed maxima at a mole fraction close to 0.33, as shown in Figure 3a. These results indicate a 1:2 host-to-guest stoichiometric ratio of complexation. Similar results were obtained for **1,1-DUP** and **1,2-BUP** anion receptors (Figures S11 and S12).

The association constants for complexation were determined from the nonlinear least-squares treatment of chemical shift changes (δ) of the urea proton (N−H) at 6.47 ppm for the receptor vs guest (TBAF) concentrations (Figure 3b). The data fitted well to a 1:2 binding isotherm and the association constants K_a were determined to be 5.35 ± 0.03 × 10^3, 8.21 ± 0.27 × 10^{31}, and 4.65 ± 0.16 × 10^4 M^{-1} for **1,1-DUP**, **1,2-BUP**, and **1,3-BUP**, respectively. The calculated association constant K_a values were affected by the number of the receptor units and the different spatial arrangement of the pillar[5]arene substituents. The anion receptor based on the 1,3-alternate regioisomer (**1,3-BUP**) shows the highest binding constant value of 4.65 ± 0.16 × 10^4 M^{-1}, which is approximately 1 order of magnitude higher than the 1,2-alternate regioisomer-based receptors (**1,2-BUP**) (8.21 ± 0.27 × 10^3 M^{-1}) and **1,1-DUP** (5.35 ± 0.03 × 10^3 M^{-1}). The data obtained from the ^{1}H NMR titrations are in good agreement with data obtained from ITC titration experiments (Table 1).

Close inspection of the host−guest ^{1}H NMR spectra revealed the different binding modes of hosts with the guest F^-. Basically, all receptors show significant chemical shift changes in the urea N−H region; however, significant differences were observed in the proton resonances of the pillar[5]arene moiety. Figure 4 displays the expanded ^{1}H NMR spectra of the macrocycle region for the receptor **1,3-BUP** at different concentrations with the guest anion (F^-). The spectra show significant upfield shifts for phenyl protons, bridging methylene protons and methyl protons sandwich between the two receptor arms; in contrast, the ^{1}H NMR spectra for **1,1-DUP** and **1,2-BUP** with fluoride (F^-) display minimum or no chemical shift changes, which indicate that the binding occurs away from the macrocycle (SI). The depictions of the different binding modes of anion receptors with fluorides (F^-) based on ^{1}H NMR titration spectral analyses are shown in Figure 5.

The anion receptor based on the 1,3-alternate constitutional isomer, **1,3-BUP**, shows the highest binding affinity toward fluoride (F^-), and thus it was evaluated for its binding ability toward larger and less basic halogen anions such as Cl^- and Br^- using ITC and ^{1}H NMR titrations. The ITC raw heat change data of the host **1,3-BUP** with the Cl^- show a substantial decrease as a result of minimum host−guest interactions (Figure S13). Upon further increase in the anion size using Br^-, no interactions were observed between the receptor **1,3-BUP** and bromine anions as evident from the relatively constant heat release. The observations from the ITC experiments were in excellent agreement with the data obtained from ^{1}H NMR titration experiments conducted between **1,3-BUP** and the halogen-based anions **TBACl** and **TBABr** (Figures S16 and S17). The data fitted to a 1:2 binding isotherm and the K_a toward chloride was determined to be 2.27 ± 0.3 × 10^2 M^{-1}, which is significantly lower than that for fluoride, 3.61 ± 0.02 × 10^4 M^{-1} (Figure S18).

Diffusion-Order Spectroscopy (DOSY) Studies. The diffusion-ordered spectroscopy (DOSY) technique has been successively employed to characterize host−guest complexation behaviors and various types of supramolecular assemblies by correlation of ^{1}H NMR signals with the diffusion coefficient (D) in solution.[33,34] Thus, the host−guest complexation behavior of compound **1,3-BUP** with fluoride (F^-) was studied by DOSY experiments. Interestingly, the DOSY

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

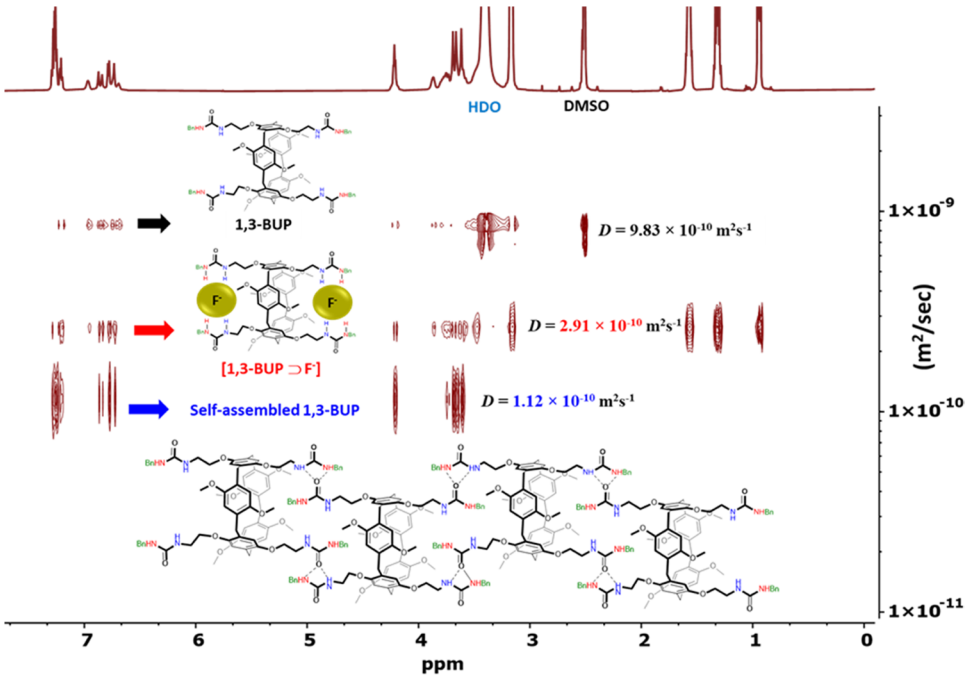


Figure 6. 2D-DOSY spectrum (600 MHz, DMSO-d_6, 298 K) of **1,3-BUP** (5.0 mM) with two equimolar quantities of tetrabutylammonium fluoride (TBAF).

spectrum in DMSO-d_6 at 5 mM of the receptor **1,3-BUP** with two equivalents of F^- revealed three sets of signals, manifesting the presence of three different aggregate sizes in solution with measured the weight-average diffusion (D) of 9.83 × 10^{-10}, 2.91 × 10^{-10}, and 1.12 × 10^{-10} m^2 s^{-1} (Figure 6).

When the DOSY spectrum was recorded for the receptor alone at 5 mM solution, the spectrum shows only two sets of signals. The absence of the sets of signals with D = 2.91 × 10^{-10} m^2 s^{-1} suggested that the set belongs to the complexation between **1,3-BUP** and F^- anions. This was confirmed when the DOSY spectrum measured for 1 mM solution of **1,3-BUP** with 8 equiv of F^- anions displayed one set of signals with the diffusion coefficient (D) corresponding to the complex formation (D = 2.91 × 10^{-10} m^2 s^{-1}).

To investigate the supramolecular assembly of **1,3-BUP** in solution, DOSY spectra of the receptor at 1 and 10 mM concentrations were measured in DMSO-d_6 (Figures S19 and S22). At a higher concentration of 10 mM, the spectrum shows only the slower diffusing set of signals (D = 9.83 × 10^{-10} m^2 s^{-1}), whereas at 1 mM concentration, the fast-moving set of signals were only present (D = 1.12 × 10^{-10} m^2 s^{-1}). The observed change in the diffusion coefficient (D) in the DOSY spectra is due to the fact that larger aggregates have larger hydrodynamic radii (R), and R is inversely proportional to D according to the Stokes−Einstein equation [$D = k_BT/(6\pi\eta R)$], where T denotes the temperature, k_B is the Boltzmann constant, and η is the dynamic viscosity of the solvent. As the concentration of **1,3-BUP** increased from 1 to 10 mmol L^{-1}, the value of weight-averaged diffusion coefficients (D) decreased from 9.83 × 10^{-10} to 1.12 × 10^{-10} m^2 s^{-1} (D_2/D_{10} = 8.78). The significant decrease in D indicates the formation of a high-molecular-weight aggregate. The formation of a self-assembled supramolecular polymer is attributed to hydrogen-bond interactions of urea substituents present between two adjacent pill[5]ararenes. The role of the urea functional groups in supramolecular self-assembly is evident from the absence of slower diffusing aggregates in the DOSY spectrum when access F^- anions were used. The data are supported by the ITC experiments of the host−guest complexation between the **1,3-BUP** receptor and F^- anions.

Assuming all assemblies are hydrodynamically spherical, the number-average degree of aggregation of the "supramolecular assembly" can be estimated using the diffusion coefficient obtained from DOSY measurements according to the Stokes−Einstein equation [$N \approx 1/(D/D_{ref})^3$]. The number-average degree of aggregation "N" is proportional to the reciprocal of the cubic root of the diffusion coefficient, where D and D_{ref} are the diffusion coefficients of **1,3-BUP** at 10 and 1 mM concentrations, respectively. The number-average degree of supramolecular aggregation was calculated to be 676, which corresponds to an average molecular weight of 9.5 × 10^5 at 10 mM concentration. This simple but rough calculation confirms the presence of supramolecular polymer assemblies in the solution state.

Moreover, the supramolecular assembly in solution was studied by dilution ITC experiments, which involve sequential injections of the concentrated solution of the supramolecular system into a cell containing a pure solvent following our previously reported procedure.[34] The exchanged heat is a measure of the dissociated supramolecular assemblies and is characteristic of the dissociation event. The ITC dilution data for the dissociation of self-assembled **1,3-BUP** into DMF 25 mM is shown as a plot of the heat rate (μJ s^{-1}) against time (min), which shows a series of peaks where the area under the endothermic heat peaks gives the enthalpy (ΔH) of dissociation (Figure S16). The integrated heat data fit to a dissociation model with a positive value of ΔH_{diss} = 11.26 kJ mol^{-1} and dissociation equilibrium constant of K_{diss} = 7.78 × 10^{-3} M. In addition, the positive value of Gibbs free energy (ΔG = 12.04 kJ mol^{-1}) obtained from ITC dilution experiments indicate that the formation of the self-assembled

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

supramolecular polymer at a high concentration is a spontaneous process.

Qualitative results about the self-assembled supramolecular polymer based on **1,3-BUP** were obtained from DLS experiments conducted in DMSO at 25 °C. At the three measured concentrations (2, 5, and 10 mM) of **1,3-BUP**, the DLS measurements of the hydrodynamic diameter (D_h) show pronounced scattering intensities of large-sized polymers. The measured D_h distribution for the self-assembled supramolecular polymer is proportional to the concentrations of **1,3-BUP**. In the 2 mM solution, the measured D_h distribution centered at 122 nm increased to 255 nm when the concentration was raised to 5 mM. The centered D_h distribution for the 10 mM solution further increased to 531 nm with a noticeably broader diameter distribution (Figure S23). In addition, smaller D_h values of 0.833 and 0.965 nm were also observed, which are consistent with the D_h values of the monomeric **1,3-BUP** (Figure S24). The DLS measurements clearly indicate the formation of large supramolecular entities and demonstrate that the self-assembly of **1,3-BUP** is pronouncedly concentration-dependent, which is similar to the observation reported previously for supramolecular polymer formation.[34−36]

CONCLUSIONS

Anion receptors bearing urea substituents based on A1/A2-functionalized pillar[5]arene and constitutional isomers of tetra-functionalized pillar[5]arenes, namely, 1,2-and 1,3-isomers were successfully synthesized in good yield. The synthesized receptors were screened for their binding ability toward fluoride (F^-) using tetrabutylammonium fluoride (TBAF) using isothermal titration calorimetry (ITC) and ^{1}H NMR titration. From the binding study, the noncovalent interactions between the receptors and the guest anions are affected by both the number of the urea substituents and their relative positions on the pillar[5]arene frame. It is well evident from ITC and ^{1}H NMR data that the receptors based on pillararene constitutional isomers exhibit a different affinity toward fluorides (F^-). The 1,3-alternate anion receptor association constant ($4.65 \pm 0.16 \times 10^4$ M^{-1}) is 1 order of magnitude higher than the 1,2-alternate counterpart ($8.21 \pm 0.27 \times 10^3$ M^{-1}). For other halide anions, the **1,3-BUP** receptor shows a significantly lower interaction toward Cl^- ($2.27 \pm 0.30 \times 10^2$ M^{-1}) and a no or minimum interaction for the larger Br^- anion. The formation of supramolecular polymer self-assembled entities was demonstrated in solution by ^{1}H diffusion studies and ITC dilution experiments. The concentration-dependent nature of the assembly was established by DLS studies. Further studies to develop new anion supramolecular systems to accommodate larger anionic species and the supramolecular self-assemblies are underway in our laboratories.

EXPERIMENTAL SECTION

Materials and Methods. Nuclear magnetic resonance (NMR) spectroscopy was done using a Bruker Avance II 600 MHz (Germany) spectrometer. Electron impact ionization (EI) mass spectrometry was performed using a Thermo Scientific DFS high-resolution GC/MS (Germany) mass spectrometer. Electrospray ionization in high-resolution mode was done using a Waters Xevo G2-S QToF, (Germany) LC MS/MS mass spectrometer. The single crystal data collections were made on Bruker X8 Prospector (Germany) and Rigaku Rapid II (Japan) diffractometers. ITC studies were carried out on an Affinity ITC, TA Instruments. DLS analysis was done on a Zetasizer Nano Range, Malvern PANalytical system (U.K.). Flash column chromatography was performed using silica gel (Silica gel 60, 40−60 mesh ASTM, EMD Millipore, Merck KGaA, Germany). DMF is distilled before use. All other reagents and solvents were of reagent grade purity and used without further purification. The synthesis of 1,4-bis(2-bromoethoxy)benzene, 1-(1,4-bis(2-bromoethoxy))-2,3,4,5-dimethoxy-pillar[5]arene, **1,1-Pillar-a**, 1,2-(1,4-bis(2-bromoethoxy))-3,4,5-dimethoxy-pillar[5]arene, **1,2-Pillar-a**, and 1,3-(1,4-bis(2-bromoethoxy))-2,4,5-dimethoxy-pillar[5]-arene, **1,3-Pillar-a** have been previously discussed.[31]

^{1}H NMR Titration. Briefly, 0.5 mL samples of **1-DUP**, **1,2-BUP**, and **1,3-BUP** solutions were prepared at a concentration of 5.0 mM in DMSO-d_6. A sample of the guest solution (2 mL) was prepared at a concentration of 0.1 M in DMSO-d_6. All titration experiments were carried out in NMR tubes at 298 K, and ^{1}H NMR spectra were recorded upon successive addition of aliquots of the stock solution of the appropriate guests via a microsyringe. The ^{1}H NMR spectral changes were fitted to 1:2 binding isotherms by nonlinear least-squares treatment using Microsoft Excel to determine the association constant, K_a.[35]

Preparation of Single Crystals for X-ray Diffraction. Single crystals of **1,1-Pillar-b** and **1,2-Pillar-b** were prepared by dissolving the corresponding pillararenes (10 mg) in a chloroform:1,4 dibromobutane solution mixture (9:1 v/v; 1 mL) and allowing slow evaporation of the solvent system. The single crystals of **1,3-Pillar-b** were grown by dissolving the pillararene (25 mg) in dichloromethane:DMF solution (80:20 v/v/ 1 mL), followed by slow solvent evaporation. The single crystal data collection of **1,1-Pillar-b** was made on a Bruker X8 Prospector diffractometer using Cu Kα radiation at 150 K. The reflection frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Finally, the structure was solved using the Bruker SHELXTL Software Package and refined using SHELXL-2017/1. The single crystal data collection of **1,2-Pillar-b** and **1,3-Pillar-b** was made on a Rigaku Rapid II diffractometer using Mo Kα radiation at 150 K. The data were processed using the "CrystalClear" software package. The structures were then solved by direct methods using the "CrystalStructure" crystallographic software package and the refinement was performed using SHELXL-2017/1. The crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as a supplementary publication (CCDC 2203787−2203789†).

ITC Measurements. All ITC studies were carried out on an Affinity ITC system (TA Instruments). The data were analyzed using NanoAnalyze, version 3.10.0. For the ITC host−guest complexation experiments, **1,1-DUP**, **1,2-BUP**, and **1,3-BUP** were dissolved in a $CHCl_3$/methanol mixture (90:10 v/v) (300 μL, 5 mM) and added to the reaction cell. The guest was then taken into a syringe and the titrations were performed in 40 injections with 2 μL per injection at a time interval of 240 s between injections. In the ITC dilution experiments, a 25 mM solution of the self-assembled **1,3-BUP** system in DMF was placed in a syringe and automatically titrated as 2 mL per injection at a time interval of 240 s into a reaction cell loaded with pure DMF (300 mL). The dissociation of the self-assembled aggregates was accompanied by nonconstant heat signals along with a constant heat of

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

dilution. A control experiment was performed using 2 mM **1,3-BUP** chloroform solution under similar experimental conditions against pure DMF. All of the titrations were conducted at 298 K.

DLS Measurements. Samples of **1,3-BUP** at different concentrations (2, 5, and 10 mM in DMSO) were analyzed on a Zetasizer Nano Range, Malvern PANalytical (U.K.) at 25 °C. All DLS measurements were performed at a scattering angle of 90°. Sample solutions were prepared by filtering each component solution through a 0.2 μm poly(tetrafluoroethylene) (PTFE) syringe filter into a clean scintillation vial.

Synthesis of Azidoethoxy-Functionalized Pillar[5]arene. *1-(1,4-Bis(2-azidoethoxy))-2,3,4,5-dimethoxy-pillar[5]arene* ***(1,1-Pillar-b).*** 1-(1,4-Bis(bromoethoxy))-2,3,4,5-dimethoxy-pillar[5]arene (0.468 g, 0.5 mmol) and sodium azide (0.26 g, 4 mmol) were dissolved in dry DMF (5 mL) and stirred at 60 °C for 12 h. After this time, the reaction mixture was poured into ice-cold water (100 mL), and the precipitate was filtered and washed with water (3 × 10 mL). The desired compound was then recrystallized from dichloromethane/methanol as a white solid (0.418 g, 97%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.42 (t, J = 5.4 Hz & 4.8 Hz, 4H), 3.65 (s, 6H), 3.70 (s, 6H), 3.72 (d, J = 1.2 Hz, 12H), 3.82 (m, 10H), 3.89 (t, J = 5.4 Hz & 4.8 Hz, 4H), 6.73 (s, 2H), 6.75 (s, 2H), 6.80 (s, 2H), 6.73 (d, J = 1.8 Hz, 4H). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 29.8, 29.9, 30.1, 50.9, 53.4, 56.0, 56.1, 56.1, 67.6, 114.1, 114.3, 114.4, 114.5, 115.7, 128.2, 128.4, 128.5, 128.8, 129.2, 150.1, 150.9, 151.0, 151.1. HRMS: (m/z): calcd for $C_{47}H_{52}O_{10}N_6$: 860.3739; found 860.3738.

1,2-(1,4-Bis(2-azidoethoxy))-3,4,5-dimethoxy-pillar[5]arene ***(1,2-Pillar-b).*** 1,2-(1,4-Bis(bromoethoxy))-3,4,5-dimethoxy-pillar[5]arene (0.112 g, 0.1 mmol) and sodium azide (0.13 g, 2 mmol) in dry DMF (4 mL) were dissolved in dry DMF (5 mL) and stirred at 60 °C for 12 h. After this time, the reaction mixture was poured into ice-cold water (100 mL), and the precipitate was filtered and washed with water (3 × 10 mL). The desired compound was then recrystallized from dichloromethane/methanol as a white solid. Yield: 93 mg (96%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.51 (m, 8H), 3.72 (m, 18H), 3.83 (m, 10H), 3.96 (m, 8H), 6.77 (s, 2H), 6.79 (m, 6H), 6.85 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 29.9, 30.0, 30.1, 51.0, 56.1, 56.1, 56.1, 56.2, 67.6, 67.7, 67.8, 114.2, 114.5, 114.6, 115.6, 115.8, 128.3, 128.5, 128.6, 129.1, 129.2, 150.0, 150.1, 151.0, 151.1, 151.1. HRMS: (m/z):calcd for $C_{49}H_{54}O_{10}N_{12}$: 970.4080; found 970.4084.

1,3-(1,4-Bis(2-azidoethoxy))-2,4,5-dimethoxy-pillar[5]arene ***(1,3-Pillar-b).*** 1,3-(1,4-Bis(bromoethoxy))-2,4,5-dimethoxy-pillar[5]arene (0.224 g, 0.2 mmol) and sodium azide (0.26 g, 4 mmol) in dry DMF (6 mL) were dissolved in dry DMF (5 mL) and stirred at 60 °C for 12 h. After this time, the reaction mixture was poured into ice-cold water (100 mL) and the precipitate was filtered and washed with water (3 × 10 mL). The desired compound was then recrystallized from dichloromethane/methanol as a white solid. Yield: 189 mg (97%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.48 (t, J = 4.8 Hz, 4H), 3.50 (t, J = 4.8 Hz, 4H), 3.68 (s, 6H), 3.70 (s, 6H), 3.72 (s, 6H), 3.80 (s, 2H), 3.82 (m, 8H), 3.92 (t, J = 4.8 Hz, 4H), 3.96 (t, J = 5.4 Hz & 4.8 Hz, 4H), 6.75 (s, 2H), 6.77 (s, 4H), 6.78 (s, 2H), 6.83 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$), δ: 29.8, 30.0, 30.0, 31.7, 51.0, 53.5, 56.1, 56.1, 56.2, 67.6, 67.7, 114.2, 114.5, 114.6, 115.6, 115.7, 128.3, 128.5, 128.6, 129.1, 129.2, 150.0, 150.1,150.9, 151.1, 151.1. HRMS: (m/z): calcd for $C_{49}H_{54}O_{10}N_{12}$: 970.4080; found 970.4093.

Synthesis of Aminoethoxy-Functionalized Pillar[5]arene. *1,1-Pillar-c.* **1,1-Pillar-b** (0.344 g, 0.4 mmol) was dissolved in a dichloromethane/methanol mixture (40 mL; 1:1 v/v) and Pd/C (100 mg) was added. The reaction mixture was stirred at room temperature under an atmosphere of hydrogen for 12 h in a hydrogenation chamber. The catalyst was filtered through Celite. The Celite pad was washed with a 1:1 dichloromethane/methanol mixture (50 mL × 2) and then with pure methanol (20 mL × 2). The combined filtrate was concentrated under reduced pressure and recrystallized from ethanol/hexane to afford the desired product as a white solid. Yield: 0.305 g (94%). ^{1}H NMR (600 MHz, DMSO-d_6), δ: 3.24 (m, 4H), 3.67 (m, 34H), 4.06 (m, 4H), 6.78 (s, 2H), 6.80 (s, 2H), 6.81 (s, 2H), 6.84 (s, 2H), 6.86 (s, 2H), 8.24 (m, 4H). ^{13}C NMR (150 MHz, DMSO-d_6), δ: 28.6, 28.8, 29.0, 43.4, 55.4, 55.5, 55.5, 64.6, 113.1, 113.2, 113.2, 113.6, 114.2, 127.5, 127.6, 127.6, 128.0, 148.8, 149.8, 149.8, 149.9, 162.3. HRMS: (m/z): calcd for $C_{47}H_{56}O_{10}N_2$: 808.3929; found 808.3931.

1,2-Pillar-c. Hydrogenation of **1,2-Pillar-b** (0.085 g, 0.088 mmol) was carried out in a dichloromethane/methanol mixture (25 mL; 1:1 v/v) using Pd/C (60 mg), following the same procedure. Yield: 73 mg (96%). ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.26 (m, 8H), 3.68 (m, 28H), 4.07 (m, 4H), 4.13 (m, 4H), 6.77 (s, 2H), 6.81 (s, 2H), 6.83 (s, 2H),6.86 (s, 2H), 6.90 (s, 2H), 8.27 (m(br), 8H). ^{13}C NMR (150 MHz, DMSO-d_6), δ: 28.6, 28.7, 29.0, 31.3, 48.6, 55.5, 55.7, 55.7, 64.8, 64.8, 113.3, 113.4, 113.8, 114.4, 115.2, 127.6, 127.6, 127.7, 128.2, 128.2, 148.8, 149.0, 149.7, 149.8, 149.8, 149.9. HRMS: (m/z):calcd for $C_{49}H_{62}O_{10}N_4$: 866.4460; found 866.4461.

1,3-Pillar-c. Hydrogenation of **1,3-Pillar-b** (0.165 g, 0.17 mmol) was carried out in a dichloromethane/methanol mixture (40 mL; 1:1 v/v) using Pd/C (120 mg), following the same procedure. Yield: 0.141 mg (96%). ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.24 (s(br), 8H), 3.62 (s(br), 4H) 3.69 (m, 20H), 3.93 (s(br), 4H), 4.09 (s(br), 8H), 6.78 (s, 2H), 6.83 (s, 2H), 6.84 (m, 6H), 8.46 (s(br), 8H). ^{13}C NMR (150 MHz, DMSO-D6), δ: 28.7, 29.0, 38.6, 55.7, 55.7, 64.6, 113.3, 113.7, 113.8, 114.3, 127.5, 127.6, 128.1, 128.1, 148.8, 149.8, 149.9, 150.0. HRMS: (m/z):calcd for $C_{49}H_{62}O_{10}N_4$: 866.4460; found 866.4452.

Synthesis of Urea-Functionalized Pillar[5]arenes. *1,1-DUP.* **1,1-Pillar-c** (0.162 g, 0.2 mmol) was dissolved in DMF (5 mL) at 60 °C with stirring. Triethyl amine (112 μL; 0.8 mmol) and *p*-nitrophenyl benzylcarbamate (0.218 g; 0.8 mmol) were added to this solution, and the mixture was stirred at 60 °C for 12 h. The DMF was evaporated at reduced pressure, and the residue was extracted with a dichloromethane:methanol mixture (30 mL, 80:20 v/v) and was adsorbed on silica gel. The crude mixture was then purified by column chromatography starting with 100% dichloromethane, followed by slowly increasing the solvent polarity by the stepwise addition of methanol. The intended product was obtained when the solvent mixture was dichloromethane:methanol 96:4 v/v. The product was dried in vacuum to obtain a white solid. Yield: 146 mg (68%). ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.46 (m, 4H), 3.64 (m, 32H), 3.77 (m, 4H), 3.87 (m, 2H), 4.23 (t, J = 5.4 Hz & 4.8 Hz, 4H), 6.22 (t, J = 5.4 Hz & 6.0 Hz, 2H), 6.47 (t, J = 6.0 Hz, 2H), 6.75 (s, 2H), 6.76 (s, 2H), 6.78 (s, 4H), 6.85 (s, 2H), 7.25 (m, 10H). ^{13}C NMR (150 MHz, DMSO-d_6), δ: 29.0, 43.0, 55.1, 55.4, 55.5, 67.9, 113.3, 113.4,

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475

113.7, 114.4, 126.6, 127.0, 127.4, 127.5, 127.6, 127.6, 127.9, 128.2, 140.8, 158.2. HRMS: (m/z): calcd for $C_{63}H_{71}O_{12}N_4$: 1075.5068; found 1075.5553.

1,2-BUP. **1,2-Pillar-c** (65 mg, 0.075 mmol), triethyl amine (84 μL; 0.6 mmol), and *p*-nitrophenyl benzylcarbamate (0.159 g; 0.6 mmol) were dissolved in DMF (5 mL) at 60 °C and stirred for 12 h. The product purification was carried out following the same procedure. The intended compound was obtained as a white solid. Yield: 68 mg (65%). ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.47 (m, 8H), 3.67 (m, 28H), 3.85 (m, 8H), 4.23 (m, 8H), 6.24 (t, J = 6.0 Hz & 5.4 Hz, 2H), 6.28 (t, J = 5.4 Hz & 4.8 Hz, 2H), 6.49 (t, J = 5.4 Hz & 6.0 Hz, 2H), 6.53 (t, J = 5.4 Hz & 6.0 Hz, 2H), 6.78 (s, 2H), 6.81 (s, 4H), 6.88 (s, 2H),6.89 (s, 2H), 7.25 (m, 20H). ^{13}C NMR (150 MHz, DMSO-d_6), δ: 28.7, 28.9, 42.9, 42.9, 43.6, 55.4, 67.6, 67.88, 79.1, 113.0, 113.5, 114.2, 114.3, 126.5, 127.0, 127.4, 127.5, 127.6, 127.7, 127.9, 128.1, 140.8, 149.1, 149.7, 149.8, 158.1, 158.2. HRMS: (m/z): calcd for $C_{81}H_{91}O_{14}N_8$: 1399.6655; found 1399.7307.

1,3-BUP. **1,3-Pillar-c** (130 mg, 0.15 mmol), triethyl amine (168 μL; 1.2 mmol), and *p*-nitrophenyl benzylcarbamate (0.318 g; 1.2 mmol) were dissolved in DMF (8 mL) at 60 °C and stirred for 12 h. The product purification was carried out following the same procedure. The intended compound was obtained as a white solid. Yield: 149 mg (71%). ^{1}H NMR (600 MHz, DMSO-d_6) δ: 3.45 (m, 6H), 3.49 (m, 4H) 3.63 (m, 16H), 3.68 (m, 6H), 3.74 (m, 8H), 3.91 (m, 4H), 4.22 (m, 8H), 6.22 (m, 4H), 6.48 (m, 4H), 6.77 (m, 6H), 6.88 (m, 4H), 7.26 (m, 20H). ^{13}C NMR (150 MHz, DMSO-D6), δ: 28.6, 28.8, 29.0, 42.9, 55.4, 67.8, 113.1, 113.5, 113.6, 114.2, 114.3, 126.5, 127.0, 127.5, 127.6, 127.9, 128.0, 128.1, 140.8, 149.1, 149.1, 149.8, 149.9, 158.1. HRMS: (m/z): calcd for $C_{81}H_{91}O_{14}N_8$: 1399.6655; found 1399.7153.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c06903.

Characterization data (^{1}H and ^{13}C NMR spectra); DOSY data; DLS data; and ITC measurement data (PDF)

Accession Codes

Crystallographic data (CIF).

■ AUTHOR INFORMATION

Corresponding Author

Talal F. Al-Azemi − *Chemistry Department, Kuwait University, Safat 13060, Kuwait;* orcid.org/0000-0003-3722-7877; Email: t.alazemi@ku.edu.kw

Authors

Mickey Vinodh − *Chemistry Department, Kuwait University, Safat 13060, Kuwait*

Fatemeh H. Alipour − *Chemistry Department, Kuwait University, Safat 13060, Kuwait*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.2c06903

Author Contributions

All authors contributed equally to this work. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Funding

The support received from the Kuwait Foundation for the Advancement of Science (KFAS) made available through research Grant No. PR17-14SC-07, Graduate School at Kuwait University, and the facilities of the RSPU (Grant Nos. GS01/01, GS03/01, GS01/03, GS01/10, and GS03/08) is gratefully acknowledged.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support received from the Kuwait Foundation for the Advancement of Science (KFAS), Kuwait University and the Graduate School at Kuwait University is gratefully acknowledged.

■ ABBREVIATIONS

CCR2, CC chemokine receptor 2; CCL2, CC chemokine ligand 2; CCR5, CC chemokine receptor 5; TLC, thin-layer chromatography

■ REFERENCES

(1) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Weinheim, 1995.

(2) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry: An Introduction*; Wiley: Chichester, 2000.

(3) Sessler, J. L.; Gale, P. A.; Cho, W.-S. *Anion Receptor Chemistry*; RSC Publishing: Cambridge, U.K., 2006.

(4) Park, C. H.; Simmons, H. E. Macrobicyclic Amines. III. Encapsulation of Halide Ions by in, in-1, (k+2)-diazabicyclo[k.l.m.] alkane Ammonium Ions. *J. Am. Chem. Soc.* **1968**, *90*, 2431−2432.

(5) Amendola, V.; Esteban-Gomez, D.; Fabbrizzi, L.; Licchelli, M. What Anions Do to N-H Containing Receptors. *Acc. Chem. Res.* **2006**, *39*, 343−353.

(6) Beer, P. D.; Schmitt, P. Molecular Recognition of Anions by Synthetic Receptors. *Curr. Opin. Chem. Biol.* **1997**, *1*, 475−482.

(7) Beer, P. D.; Gale, P. A. Anion Recognition and Sensing: The State of the Art and Future Perspectives. *Angew. Chem., Int. Ed.* **2001**, *40*, 486−516.

(8) Bojinov, V.; Georgiev, N. Molecular Sensors and Molecular Logic Gates. *J. Univ. Chem. Technol. Metall.* **2011**, *46*, 3−26.

(9) Bondy, C. R.; Loeb, S. J. Amide Based Receptors for Anion. *Coord. Chem. Rev.* **2003**, *240*, 77−99.

(10) Busschaert, N.; Kirby, I. L.; Young, S.; Coles, S. J.; Horton, P. N.; Light, M. E.; Gale, P. A. Squaramides as Potent Transmembrane Anion Transporters. *Angew. Chem., Int. Ed.* **2012**, *51*, 4426−4430.

(11) Busschaert, N.; Gale, P. A. Small-Molecule Lipid-Bilayer Anion Transporters for Biological Applications. *Angew. Chem., Int. Ed.* **2013**, *52*, 1374−1382.

(12) Crabtree, R. H.; Kavallieratos, K.; Bertao, C. M. Hydrogen Bonding in Anion Recognition. A Family of Versatile, Non-preorganized, Neutral and Acyclic Receptors. *J. Org. Chem.* **1999**, *64*, 1675−1683.

(13) Gale, P. A. Structural and Molecular Recognition Studies with Acyclic Anion Receptors. *Acc. Chem. Res.* **2006**, *39*, 465−475.

(14) Gale, P. A. Anion Receptor Chemistry. *Chem. Commun.* **2011**, *47*, 82−86.

(15) Martínez-Máñez, R.; Sancenón, F. Fluorogenic and Chromogenic Chemosensors and Reagents for Anions. *Chem. Rev.* **2003**, *103*, 4419−4476.

(16) Pomecko, R.; Asfari, Z.; Hubscher-Bruder, V.; Bochenska, M.; Arnaud-Neu, F. Anion Recognition by Phosphonium Calix[4]arenes: Synthesis and Physicochemical Studies. *Supramol. Chem.* **2010**, *22*, 275−288.

(17) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; John Wiley & Sons Ltd, 2009.

(18) Wagner-Wysiecka, E.; Chojnacki, J. Chromogenic Amides of Pyridine-2,6- Dicarboxylic Acid as Anion Receptors. *Supramol. Chem.* **2012**, *24*, 684−695.
(19) Yamnitz, C. R.; Negin, S.; Carasel, I. A.; Winterb, R. K.; Gokel, G. W. Dianilides of Dipicolinic Acid Function as Synthetic Chloride Channels. *Chem. Commun.* **2010**, *46*, 2838−2840.
(20) Li, A. -F.; Wang, J. -H.; Wang, F.; Yun-Bao Jiang, Y. -B. Anion Complexation and Sensing Using Modified Urea and Thiourea-Based Receptors. *Chem. Soc. Rev.* **2010**, *39*, 3729−3745.
(21) Smith, P. J.; Reddington, M. V.; Wilcox, C. S. Ion Pair Binding by a Urea in Chloroform Solution. *Tetrahedron Lett.* **1992**, *33*, 6085−6088.
(22) Fan, E.; Van Arman, S. A.; Kincaid, S.; Hamilton, A. D. Molecular Recognition: Hydrogen-Bonding Receptors That Function in Highly Competitive Solvents. *J. Am. Chem. Soc.* **1993**, *115*, 369−370.
(23) Ayling, A. J.; Pe′rez-Paya′n, M. N.; Davis, A. P. New "Cholapod" Anionophores; High-Affinity Halide Receptors Derived from Cholic Acid. *J. Am. Chem. Soc.* **2001**, *123*, 12716−12717.
(24) Pfeffer, F. M.; Gunnlaugsson, T.; Jensen, P.; Kruger, P. E. Anion Recognition Using Preorganized Thiourea Functionalized [3]Polynorbornane Receptors. *Org. Lett.* **2005**, *7*, 5357−5360.
(25) Sun, X. H.; Li, W.; Xia, P. F.; Luo, H. -B.; Wei, Y.; Wong, M. S.; Cheng, Y. -K.; Shuang, S. Phenyl-calix[4]arene-Based Fluorescent Sensors: Cooperative Binding for Carboxylates. *J. Org. Chem.* **2007**, *72*, 2419−2426.
(26) Beyeh, N. K.; Jo, H. H.; Kolesnichenko, I.; Pan, F.; Kalenius, E.; Anslyn, E. V.; Ras, R. H. A.; Rissanen, K. Recognition of Viologen Derivatives in Water by N-Alkyl Ammonium Resorcinarene Chlorides. *J. Org. Chem.* **2017**, *82*, 5198−5203.
(27) Dinare′s, I.; de Miguel, C. G.; Mesquida, N.; Alcalde, E. Bis(imidazolium)-Calix[4]arene Receptors for Anion Binding. *J. Org. Chem.* **2009**, *74*, 482−485.
(28) Ni, M.; Hu, X.-Y.; Jiang, J.; Wang, L. The Self-Complexation of Mono-Urea-Functionalized Pillar[5]arenes with Abnormal Urea Behaviors. *Chem. Commun.* **2014**, *50*, 1317−1319.
(29) Duan, Q.; Xia, W.; Hu, X.; Ni, M.; Jiang, J.; Lin, C.; Pan, Y.; Wang, L. Novel [2]Pseudorotaxanes Constructed by Self-assembly of Bis-Urea-Functionalized Pillar[5]arene and Linear Alkyl Dicarboxylates. *Chem. Commun.* **2012**, *48*, 8532−8534.
(30) Feng, W.-X.; Sun, Z.; Zhang, Y.; Legrand, Y.-M.; Petit, E.; Su, C.-Y.; Barboiu, M. Bis-15-Crown-5-Ether-Pillar[5]arene K^+-Responsive Channels. *Org. Lett.* **2017**, *19*, 1438−1441.
(31) Al-Azemi, T. F.; Vinodh, M.; Alipour, F. M.; Mohamod, A. A. Constitutional Isomers of Brominated Functionalized Copillar[5]-arenes: Synthesis, Characterization, and Crystal Structures. *RSC Adv.* **2019**, *9*, 13814−13819.
(32) Liu, Q.; Luedtke, N. W.; Tor, Y. A Simple Conversion of Amines into Monosubstituted Ureas in Organic and Aqueous Solvents. *Tetrahedron Lett.* **2001**, *42*, 1445−1447.
(33) Al-Azemi, T. F.; Vinodh, M. Concentration-Dependent Supramolecular Self-assembly of A1/A2-Asymmetric-Difunctionalized Pillar[5]arene. *RSC Adv.* **2021**, *11*, 2995−3002.
(34) Al-Azemi, T. F.; Vinodh, M. Pillar[5]arene-Based Self-assembled Linear Supramolecular Polymer Driven by Guest Halogen−Halogen Interactions in Solid and Solution States. *Polym. Chem.* **2020**, *11*, 3305−3312.
(35) Hong, M.; Zhang, Y. M.; Liu, C. Y.; Liu, Y. Supramolecular Polymerization of a Pillar[5]arene Induced by a Symmetric Biaryl Sulfonate with Dual Binding Sites. *Asian J. Org. Chem.* **2016**, *5*, 321−324.
(36) Thordarson, P. Determining association constants from titration experiments in supramolecular chemistry. *Chem. Soc. Rev.* **2011**, *40*, 1305−1323.

https://doi.org/10.1021/acsomega.2c06903
ACS Omega 2023, 8, 1466−1475