Article

Stimuli-Responsive Internally Ion-Paired Supramolecular Polymer Based on a Bis-pillar[5]arene Dicarboxylic Acid Monomer

Anna Notti, Ilenia Pisagatti,* Francesco Nastasi, Salvatore Patanè, Melchiorre F. Parisi, and Giuseppe Gattuso*

Read Online

ACCESS | Metrics & More | Article Recommendations | SI Supporting Information

ABSTRACT: A novel bis-pillar[5]arene dicarboxylic acid self-assembles in the presence of 1,12-diaminododecane to yield overall neutral, internally ion-paired supramolecular polymers. Their aggregation, binding mode, and morphology can be tuned by external stimuli such as solvent polarity, concentration, and base treatment.

overall-neutral
internally ion-paired
Pillararene-based **S**upramolecular **P**olymers
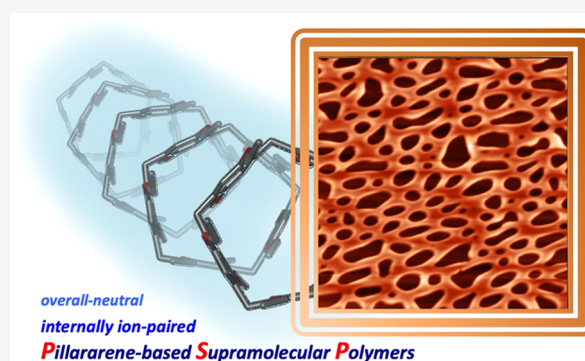
INTRODUCTION

Over the past few years, supramolecular polymers[1] have grown from promising candidates to technological reality for the construction of smart devices and functional materials. Owing to the dynamic and reversible nature of noncovalent interactions, not only do they retain traditional polymer properties, but they also display additional features including stimuli responsiveness, adaptability, self-healing, and degradability. The properties of these materials rely on the dynamic nature of their reversible bonding, which takes advantage of noncovalent interactions such as hydrogen bonding, $\pi-\pi$ stacking, metal−ligand coordination, hydrophobic interactions, and host−guest complexation. By combining multiple "weak" interactions, host−guest complexation, i.e., macrocycle recognition of complementary guest moieties, has been proven to be one of the most reliable strategies to fabricate supramolecular polymers.

The appearance of each new host macrocycle has fueled advancements in supramolecular polymer science, and in this context, the surfacing in the literature of pillar[n]arenes,[2] a new type of calixarene analogue, has already led to the successful preparation of a new generation of supramolecular functional materials.[3] Because of their highly symmetrical structure, pillararenes possess a marked affinity for both cationic and neutral molecules bearing electron-withdrawing groups.[4] In fact, compared with the calix[n]arene cone-like cavitiy, the more cylindrical one of pillar[n]arenes contributes to enhance the π-electron density of the cavity, allowing multiple favorable cation−π and CH−π interactions to take place with included guests.

The proclivity shown by pillararenes to form inclusion complexes and give rise to a variety of complex self-assembled architectures[5] has made the synthesis of a wide range of pillararene-based supramolecular polymers (PSPs) with a wide range of topological features possible.[6] Typically, they are categorized into two broad groups: linear and branched PSPs. The linear ones are mostly built from the classical AB- or AA/BB-type monomer−monomer recognition motifs, with the AB-type consisting of a self-complementary heteroditopic unimer incorporating, at the same time, a pillararene macrocycle and a suitable guest counterpart, which allows an iterative head-to-tail infinite complexation to be achieved. Conversely, the AA/BB-type polymers rely on the pairing of complementary homoditopic monomers, composed of a bis-pillararene (AA) component and a corresponding two-headed guest (BB) partner. The branched ones, on the other hand, are mainly assembled from the AB_n- and A_n/B_m-type monomer design, which rely on heteropolytopic or complementary homopolytopic building blocks, respectively. However, supramolecular hyperbranched polymers have recently been reviewed, and they will not be discussed further here.[7]

As for the linear PSPs, there are several examples of successful preparation of stimuli-responsive species.[8] AB-type

monomers spontaneously assemble giving rise to concentration-dependent aggregates[9] that, when equipped with a suitable bistable unit such as a photoisomerizable stilbene[8a] or an azobenzene,[10] can be disassembled, reassembled, or rearranged at will. Water-soluble AB-type PSPs can easily be obtained by decorating the two rims of the pillararene monomer with positively[11] or negatively[12] charged moieties. However, attachment of a suitable guest component to a pillararene macrocycle does not always deliver PSPs but occasionally results in the competitive formation of [c2]daisy chain dimers[13] or [1]rotaxanes[14] (as a result of self-inclusion). Very recently, an unusual linear AA-type PSP composed of a repeating decamethoxy-pillar[5]arene/1,4-dibromobutane pseudorotaxane held together by guest Br−Br interactions has been described.[15]

Few examples of AA/BB-type PSPs have been reported so far, based on covalently linked bis-pillar[5]arenes.[16] This approach offers some advantages, as the connecting moiety can bear groups that may endow the final PSP with additional stimuli responsiveness or specific functions. For instance, the presence of an azobenzene bridge allowed photocontrol to be exerted on the degree of polymerization (DP) of the polymer,[17] whereas the insertion of diselenide[18] bridges in a bis-pillararene dimer allowed the polymers to be disassembled by simple reductive (dithiothreitol) or γ-ray treatment. In a similar fashion, the reversible [4 + 4] photocycloaddition of anthracene[19] or the formation of dynamic covalent bonds (imines)[20] readily generated double dynamic PSPs. In some cases, the units connecting the macrocycles were even used to reversibly cross-link the bis-pillar[5]arene-containing polymers.[21] AA/BB-type PSPs based on a bis-pillararene monomer held together by orthogonal metal ion coordination have also been described.[22]

As a part of our on-going investigations into supramolecular polymers[23] and ionizable macrocycles,[24] we have recently described the formation of an AA/BB-type supramolecular polymer composed of a bis-calix[5]arene and 1,12-diaminododecane, where the connecting chain between the two calixarene units of the host-acting monomer incorporates two carboxyl groups.[25] These building blocks allowed us to produce internally ion-paired, overall neutral supramolecular polymers by means of host-to-guest double proton transfer. More specifically, protonation of diaminododecane triggered the inclusion of the resulting diammonium ions into the host cavities, following a well-known linear primary alkylammonium/calix[5]arene recognition motif.[26] Calix[5]arene/ammonium polymers were also disassembled upon treatment with a competitive chain stopper.[25,27]

As a follow up to our work, to verify the robustness of the design of this AA/BB monomer pair, we decided to swap calix[5]arene units with structurally related pillar[5]arenes[28] while keeping the rest of the design unaltered (i.e., the dicarboxylic acid spacer connecting the two macrocycles and the α,ω-diaminoalkane monomer). We hereby present a novel bis-pillar[5]arene dicarboxylic acid H capable of self-assembling in the presence of 1,12-diaminododecane (henceforth referred to as G) to yield multistimuli-responsive polymeric aggregates sensitive to base treatment, concentration, or solvents.

RESULTS AND DISCUSSION

Bis-pillar[5]arene H was synthesized in two steps starting from the known nonamethoxy-pillar[5]arene[29] 1 and *meso*-dibro-

modiester[30] 2 (Scheme S1). The two were reacted in refluxing acetonitrile in the presence of K_2CO_3 as the base to give bis-pillar[5]arene dimethyl diester 3 in a 46% yield. Compound 3 was then hydrolyzed with aqueous LiOH to provide H in a quantitative yield.

The affinity between bis-pillar[5]arene dicarboxylic acid H and 1,12-diaminododecane was preliminarily evaluated by means of ^1H NMR spectroscopy. Upon addition of 1 equiv of diamine to a 13 mM solution ($CDCl_3/CF_3CD_2OD$, 9:1, v/v)[31] of H, the methylene groups of the guest alkyl chain underwent substantial upfield complexation-induced shifts (up to $\Delta\delta = -2.20$ ppm) as a consequence of the magnetic shielding operated by the host aromatic units, and a set of six new resonances appeared in the $\delta = 1.5$ to -2.0 ppm range (α to ζ, Figure 1). Concomitantly, a distinctive broadening as well as
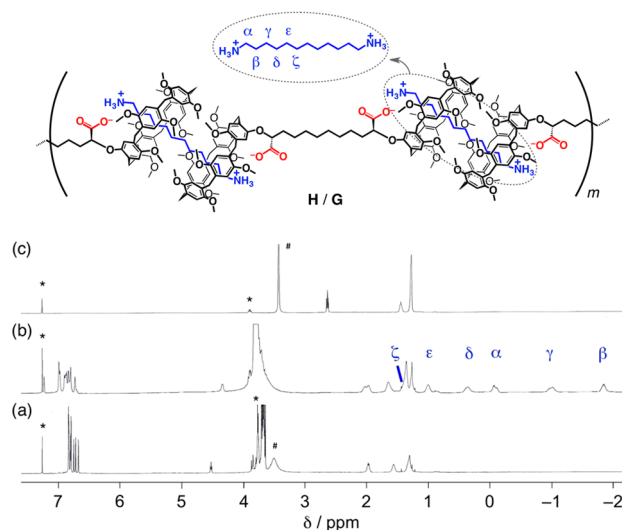

Figure 1. Top: structure of the assembled internally ion-paired H/G PSP. Bottom: ^1H NMR spectra (500 MHz, 25 °C, $CDCl_3/CF_3CD_2OD$, 9:1, v/v) of: (a) [H] = 13 mM; (b) [H] = [G] = 13 mM; and (c) [G] = 13 mM. Asterisks and hashtags indicate the residual solvent and HOD peaks, respectively.

less pronounced shifts were observed on a number of resonances of the host (e.g., downfield for ArH and upfield for the oxomethine hydrogen atom of the spacer chain at $\delta = 4.52$ ppm). Similar spectral features were also seen upon dilution of the original 1:1 H/G solution to 6 or 0.6 mM (Figure S1, see the Supporting Information). Unlike for many pillararenes,[32] the complexation in this case was found to be on a slow exchange regime on the NMR timescale.

A combined 2D correlation spectroscopy (COSY) and nuclear Overhauser effect spectroscopy (NOESY) NMR analysis shed light on the topological features of such a host−guest interaction (Figure 2, full spectra shown in Figures S2 and S3). The peaks assigned to the guest methylene groups display several intermolecular correlations with the aromatic resonances of the host, as well as with the $ArCH_2Ar$ and OCH_3 hydrogen atoms of H, indicating that the dodecanediyl moiety of G is encircled at both ends.

To verify how successful the monomer design was in terms of polymerization efficiency, a series of diffusion ordered spectroscopy (DOSY) NMR spectra were recorded on equimolar H/G samples at different concentrations. The self-diffusion coefficients (D), extracted from the peaks belonging
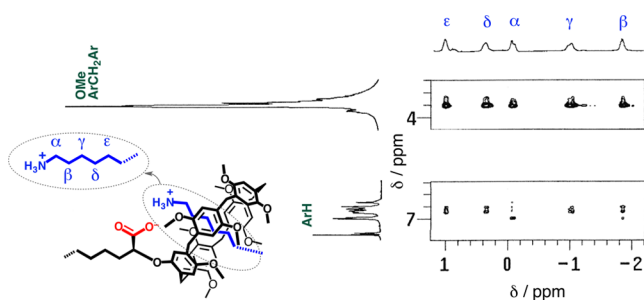
Figure 2. Sections of the 2D NOESY spectrum (500 MHz, 25 °C, CDCl$_3$/CF$_3$CD$_2$OD, 9:1, v/v) of a [**H**] = [**G**] = 13 mM solution.

to the aromatic hydrogen atoms of the pillar[5]arene moiety, decreased with respect to that measured for the free **H**, indicating the formation of larger aggregates (Table 1 and

Table 1. Self-Diffusion Coefficient and Average Molecular Mass of H and H/G Aggregates Measured at 25 °C in CDCl$_3$/CF$_3$CD$_2$OD (9:1, v/v) in the 0.6−13 mM Concentration Range[a]

[**H**] (mM)	[**G**] (mM)	D (×10^{-10} m^2/s)	$M_{aggregate}$[b] (amu)
13	13	1.23 ± 0.07	46 600[b]
6.0	6.0	1.77 ± 0.08	16 000[b]
0.6	0.6	2.82 ± 0.08	4000[b]
13	0	3.74 ± 0.08	1700

[a]The self-diffusion coefficient of **H** was found to be concentration-independent in this range. [b]Estimated by means of eq 1.

Figure 3). The self-diffusion coefficient extracted from the decay of the resonances assigned to the cavity-included **G** confirmed that both **H** and **G** are part of the same PSP aggregate.

Assuming that the polymeric species adopt a random coil spherical shape in solution, their average molecular mass at different concentrations was estimated by means of eq 1,[33] which inversely correlates the diffusion coefficients of the monomers and the aggregates to their molecular masses

$$D_{aggregate}/D_{monomer} = (M_{monomer}/M_{aggregate})^{1/3} \qquad (1)$$

At [**H**] = [**G**] = 13 mM, the aggregates displayed an estimated average M = 46 600 amu, which corresponds to ca. 24−25 **H**/**G** monomer pairs. The estimated M values follow the expected trend upon dilution, decreasing to 16 000 amu at 6 mM (ca. eight **H**/**G** pairs) and ultimately to 4000 amu at 0.6 mM (two **H**/**G** pairs), where the polymer had practically disassembled.

Further experiments were carried out to clarify whether the host-to-guest proton transfer had actually taken place under the conditions employed. Protic solvents are well known to stabilize charge-separated species and, in line with this, we have previously demonstrated, for a similar bis-calix[5]arene dicarboxylic acid/1,12-diaminododecane monomer pair, that trifluoroethanol[31] plays a pivotal role in assisting the host-to-guest proton transfer,[23f,25,34] thus increasing the natural tendency of the pillar[5]arene cavity to include amino-terminated alkyl chains by providing additional electrostatic interactions.[35] Therefore, to understand whether the proton had actually transferred from the carboxylic acid moiety of the host to the guest amino groups, we decided to carry out ^{1}H and DOSY NMR experiments on **H** and on the **H**/**G** aggregate in neat CDCl$_3$,[36] to test the behavior of the polymer under less favorable (i.e., aprotic) conditions. Addition of 1 equiv of **G** to a 10 mM solution of **H** in CDCl$_3$ provided a remarkably different picture than that previously seen for the CDCl$_3$/CF$_3$CD$_2$OD experiments (Figure 4). In this case, the peaks for the included methylene groups of the guest broadened considerably, as a result of an association process that relies exclusively on cation−π and CH−π interactions without the additional electrostatic (CO$_2$$^-$···H$_3N^+$) stabilization. Furthermore, a new broad resonance at δ = 2.75 ppm, consistent with the presence in solution of the α-CH$_2$ of an uncomplexed guest moiety, provided evidence for a less efficient complexation/polymerization process. A DOSY spectrum confirmed that the size of the aggregate had dramatically decreased (Figure S4). The self-diffusion coefficient derived from the resonances of the aromatic hydrogen atoms of the host (2.72 ± 0.03 × 10^{-10} m^2/s) allowed an average molecular mass of 8000 amu to be estimated for the new PSP,[37] significantly lower in comparison
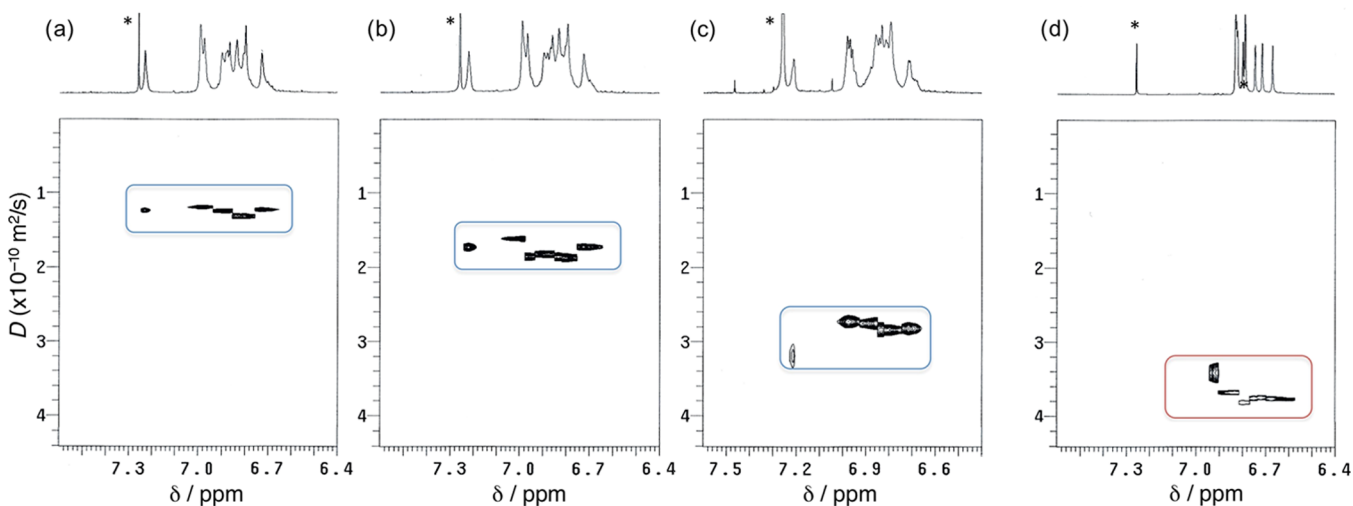

Figure 3. Selected DOSY plots (500 MHz, 25 °C, CDCl$_3$/CF$_3$CD$_2$OD, 9:1, v/v) recorded on the free **H** and upon dilution of the **H**/**G** equimolar solution: (a) [**H**] = [**G**] = 13 mM; (b) [**H**] = [**G**] = 6 mM; (c) [**H**] = [**G**] = 0.6 mM; and (d) [**H**] = 13 mM. Asterisks designate the residual solvent peak.
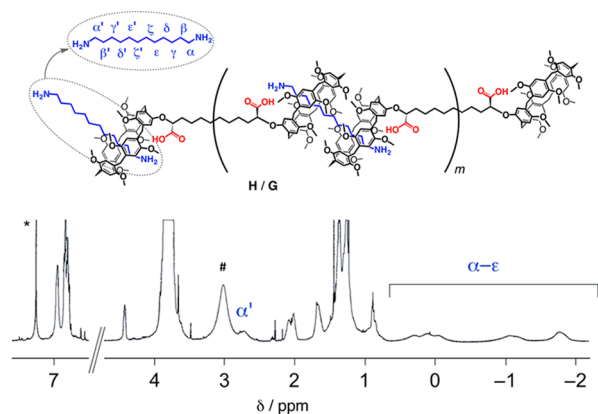
Figure 4. Top: proposed structure of the **H/G** aggregate in CDCl$_3$. Bottom: ^{1}H NMR spectrum (500 MHz, 25 °C, CDCl$_3$) of [**H**] = [**G**] = 13 mM. The asterisk and the hashtag indicate the residual solvent and H$_2$O peaks, respectively.

even than that observed at 6 mM in the CDCl$_3$/CF$_3$CD$_2$OD solvent mixture.

UV–vis titrations of **H** with **G** in the CHCl$_3$/CF$_3$CH$_2$OH (9:1, v/v) solvent mixture as well as in neat CHCl$_3$ were carried out for additional evidence on the influence of the solvent(s) on the self-assembly of PSPs (Figure 5). The absorption spectrum of **H**, in both solvents, is characterized by an intense band in the UV region at about λ_{max} = 290 nm (ε = 4.0 × 10^4 M^{-1} cm^{-1} in both solvent systems), attributed to $\pi \rightarrow$
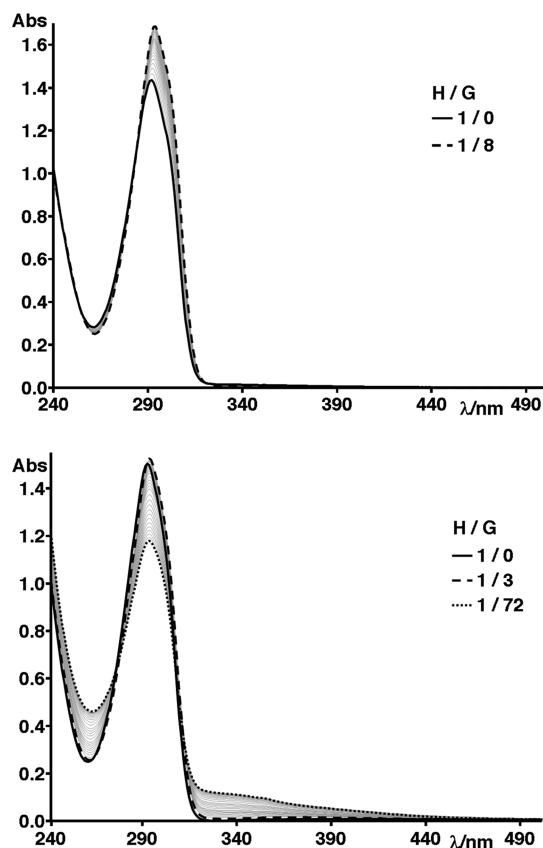
π^* transitions.[38] In analogy with what had been observed by ^{1}H NMR, depending on the medium used, the addition of **G** to a solution of **H** produced different spectral outcomes. When neat CHCl$_3$ was used, the band around 290 nm underwent a hyperchromic effect as well as a bathochromic shift (about 5 nm). Fitting of the data[39] using a 1:1 binding model (polymer formation was considered unlikely in the concentration range employed for this titration, i.e., 3.6–3.7 × 10^{-5} M) returned a K_a = 2.41 × 10^4 M^{-1} for the likely formation of a **G** ⊂ **H** complex.

In the case of the CHCl$_3$/CF$_3$CH$_2$OH mixture, on the other hand, two successive binding events were observed. Upon addition of 3 equiv of **G**, the response was similar to that observed in neat chloroform. Further addition of **G** however produced a hypochromic effect on the ~290 nm band and gave rise to a new low-intensity band between 315 and 490 nm. In this latter case, fitting of the data returned values of $K_{a(1:1)}$ = 7.16 × 10^4 M^{-1} and $K_{a(1:2)}$ = 4.52 × 10^7 M^{-2} for the 1:1 and 1:2 (**H:G**) complexes, respectively, in agreement with the formation of first a **G** ⊂ **H** and then a **G** ⊂ **H** ⊃ **G** complex.

UV–vis and ^{1}H and DOSY NMR experiments carried out in the two solvent systems, along with recent literature reports on pillararene–carboxylic acid/amine[34] and calixarene–carboxylic acid/amine[24,25] complexes, led to the conclusion that the formation of these PSPs relies heavily on the proton transfer from the carboxyl moieties of the monomer host to the amine groups of the diaminododecane monomer guest. PSPs self-assemble more efficiently in the presence of trifluoroethanol, most probably by taking advantage not only of the inclusion of the alkyl chain inside the cavity[32d] but also of the additional stabilization provided to the **H/G** pair by –CO$_2^-$···H$_3$N$^+$— electrostatic attraction. On the contrary, in neat chloroform, where proton transfer is unfavored, such an additional stabilization cannot be gained. This is further confirmed by the evidence that at the concentration used for the UV–vis titration in the CHCl$_3$/CF$_3$CH$_2$OH mixture, **H** is able to bind two **G** units (one per cavity), whereas in neat CHCl$_3$ complexation, it halts at the 1:1 stage.

Control over the self-assembly of the **H/G** PSP can be exerted using a suitable base to deprotonate the ammonium ion, thus nullifying the effects of the salt–bridge interaction. Earlier investigations on calix[5]arene/alkylammonium polymers[23d,g] had shown that base treatment led to disassembly, owing to the inability of calix[5]arenes to bind amines. It was envisaged though that the **H/G** PSP would not meet the same fate, since pillar[5]arene/alkylamine (or alkylammonium) recognition is mainly driven by CH–π interactions between the guest chain and the host cavity. Indeed, upon addition of 4 equiv of triethylamine (TEA) to a 13 mM PSP solution, the ^{1}H NMR spectrum of the **H/G** mixture dramatically changed (Figure 6). In the high-field region of the spectrum, the resonances assigned to the symmetrically complexed guest virtually disappeared, being replaced by a new set of cavity-shielded peaks and a new resonance (δ = 2.63 ppm) accounting for the presence of a cavity-unshielded α-methylene group of a primary amine (i.e., δ = 2.61 ppm for the –CH$_2$NH$_2$ of free **G**, see Figure 1c). A COSY spectrum (Figure S5) showed that all these new resonances belonged to a dodecanediamine chain with a single amino end group included in a pillar[5]arene cavity,[40] while a DOSY spectrum on the same mixture demonstrated that depolymerization of the **H/G** aggregate had taken place (Figure S6), with the self-diffusion coefficient extracted from the aromatic hydrogen

Figure 5. UV–vis titrations of bis-pillar[5]arene **H** with 1,12-dodecanediamine **G**. Top: in CHCl$_3$, [**H**] = 3.58 × 10^{-5} M, [**G**] = 0–7.01 × 10^{-4} M; bottom: in CHCl$_3$/CF$_3$CH$_2$OH, 9:1, v/v, [**H**] = 3.71 × 10^{-5} M, [**G**] = 0–1.26 × 10^{-3} M.
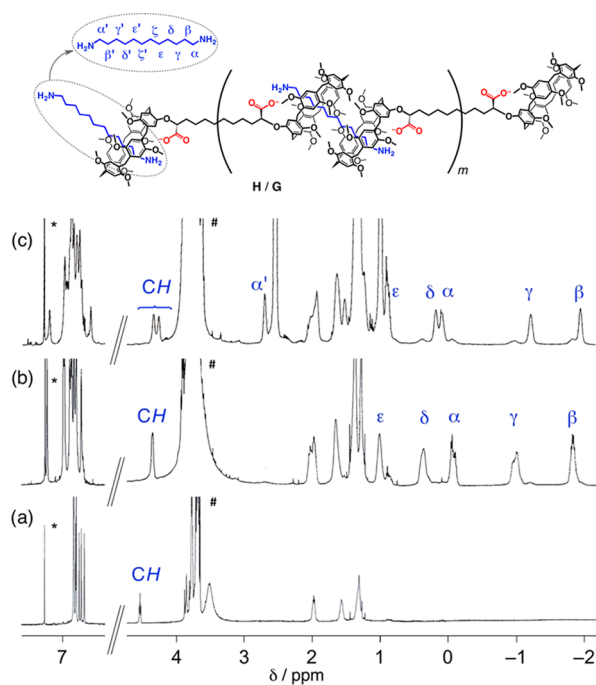
Figure 6. Top: proposed structure of the **H/G** aggregate after TEA addition. Bottom: ^1H NMR spectra (500 MHz, 25 °C, CDCl$_3$/CF$_3$CD$_2$OD, 9:1, v/v) of (a) [**H**] = 13 mM; (b) [**H**] = [**G**] = 13 mM; and (c) [**H**] = [**G**] = 13 mM, [TEA] = 52 mM. Asterisks and hashtags indicate the residual solvent and HOD peaks, respectively.

atoms (3.09 ± 0.02 × 10^{-10} m^2/s) nearing the one obtained for the free **H** (3.74 ± 0.08 × 10^{-10} m^2/s, see above).

In agreement with the data discussed so far, the assembly and disassembly of the PSP may also be deduced by observing the shifts undergone by the peaks of the methine hydrogen atom adjacent to the carboxyl moiety. Prior to **G** addition, the CHCO$_2$Hs of the free **H** resonate as a sharp triplet at δ = 4.52 ppm (Figure 6a), whereas upon host-to-guest proton transfer leading to PSP self-assembly, the newly formed CHCO$_2^-$ moieties give rise to a broad singlet at δ = 4.33 ppm (Figure 6b). Finally, after TEA treatment, the spectrum shows two distinct resonances (δ = 4.33 and 4.22 ppm of approximately the same intensity, Figure 6c) for each methine hydrogen atom (CHCO$_2^-$) adjacent to a "different" pillararene unit, fully consistent with the presence in solution of a "full" and an "empty" pillararene cavity.

Atomic force microscopy (AFM) provided interesting evidence on the morphology of the **H/G** PSP. Figure 7a shows the AFM topography of the thin film obtained from an equimolar solution of **H** and **G** spin-coated onto a silica surface. The image shows a rather regular grid-like pattern, consistent with a bundle of fibers made up of **H/G** polymers.[41] As can be seen from Figure 7b, the height of these fiber cross sections is around 140 nm.

The polymer disassembly process, caused by the base treatment of a solution of the **H/G** polymer, can be fully appreciated by AFM analysis (Figure 8). The morphology of
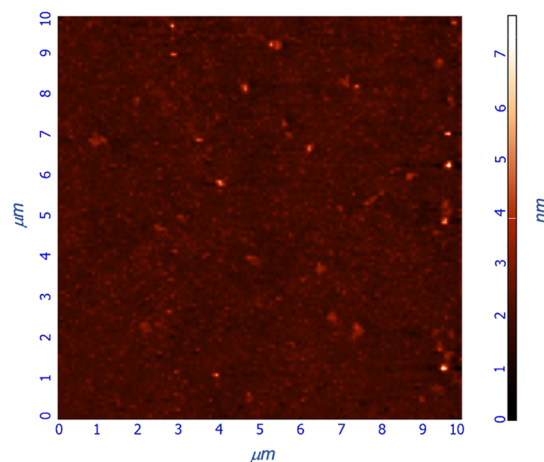

Figure 8. AFM topography image of a silica surface spin-coated with a [**H**] = [**G**] = 1 mM solution (CHCl$_3$/CF$_3$CH$_2$OH, 9:1, v/v) treated with triethylamine (4 mM).

the film obtained by spin-coating a **H/G** solution after TEA addition shows no grid structure (very similar to what is seen for a film obtained by a solution of **H**, see Figure S8), with an
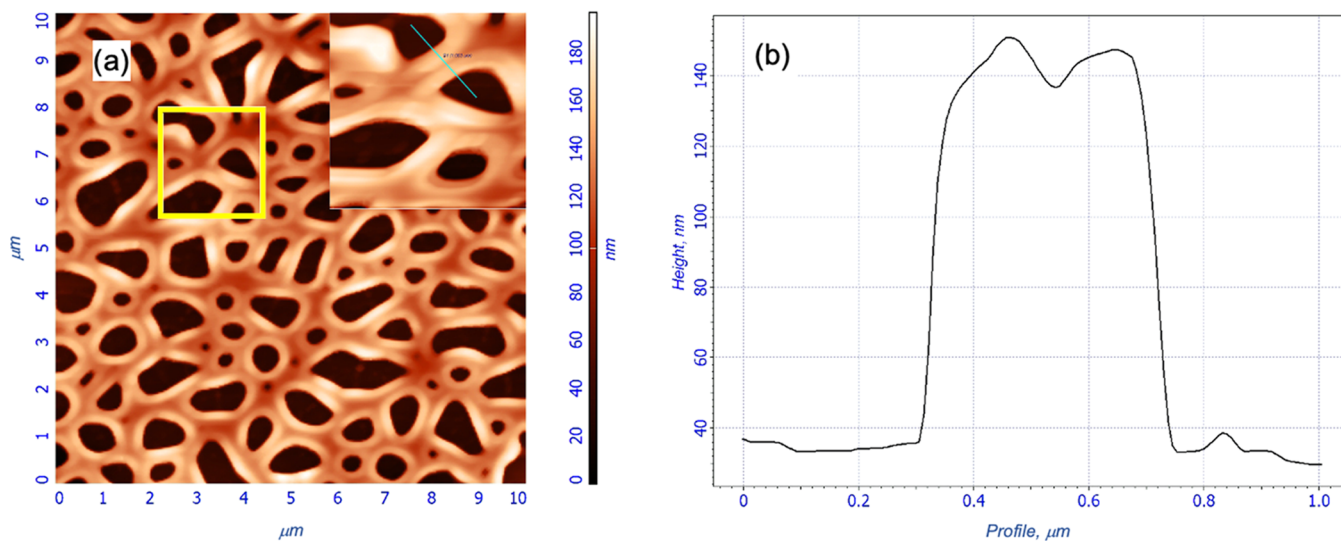
Figure 7. (a) AFM topography image of the grid obtained upon spin-coating a [**H**] = [**G**] = 1 mM solution (CHCl$_3$/CF$_3$CH$_2$OH, 9:1, v/v) onto a silica surface and (b) profile of the cross section of the fiber orthogonally cut along the blue line shown in the inset to (a).

overall landscape characterized by the presence of small discrete objects, 50−150 nm in diameter, resulting from a disorganized amorphous aggregation.

CONCLUSIONS

The self-assembly of a pillar[5]arene-based AA/BB-type supramolecular polymer has been reported. This PSP is held together by host−guest interactions between 1,12-diaminodo-decane **G** and bis-pillar[5]arene dicarboxylic acid **H**. In addition, host-to-guest double proton transfer allows for an additional electrostatic interaction between the ammonium groups of the guest monomer and the carboxylate moieties of the host monomer. We have demonstrated that it is possible to exert a high level of control over the assembly of these PSPs by changing concentration, solvent, or by addition of a base. Remarkably, each stimulus had different effects on the PSP: even though they always result in depolymerization, each of them induces a change in the recognition motif, leading to $-CO_2^-\cdots H_3N^+-$, $-CO_2H\cdots H_2N-$, or $-CO_2^-\cdots H_2N-$ inter-actions, respectively, that deeply affect the size of the PSP. These findings, taken together with our earlier contributions on internally ion-paired supramolecular assemblies, will provide new powerful means for the fine-tuning of PSP properties.

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 500 spectrometer at 25 °C, at 500 and 125 MHz respectively. Chemical shifts are reported in ppm and are referenced to the residual CDCl$_3$ solvent (δ_H 7.26 and δ_C 77.0 ppm). Structural assignments were made with additional information from gCOSY, gNOESY, and gDOSY experiments. ESI mass spectra (positive or negative ion mode) were acquired on an API-2000 AB Sciex spectrometer, using 1.0 mM CH$_3$OH stock solutions. UV−vis absorption spectra were recorded on a Jasco V-560 spectrophotometer. Nonamethoxy-pillar[5]arene[29] **1** and *meso*-dimethyl dibromododecanedioate[30] **2** were prepared according to literature procedures. Prior to use, 1,12-diaminodode-cane (>97%, purchased from Fluka) (**G**) was dissolved in CH$_2$Cl$_2$ and filtered through aluminum oxide. Anhydrous solvents were either obtained commercially or dried by standard methods prior to use, while other chemicals were of reagent grade, routinely used without any further purification. Column chromatography was performed on silica gel (Merck, 230−400 mesh).

Synthetic Procedures. *meso-Bis-pillar[5]arene Dimethyl Die-ster (3).* A suspension of nonamethoxy-pillar[5]arene **1** (216 mg, 0.29 mmol), dimethyl dibromododecanedioate **2** (54 mg, 0.13 mmol), and K$_2$CO$_3$ (75 mg, 0.54 mmol) in MeCN (30 mL) was heated to reflux in an oil bath for 1 day under a nitrogen atmosphere. After cooling, the solvent was evaporated under reduced pressure, and the resulting crude mixture was partitioned between CH$_2$Cl$_2$ (25 mL) and H$_2$O (10 mL). The organic layer was washed twice with H$_2$O (2 × 20 mL), dried over MgSO$_4$, filtered, and evaporated under reduced pressure to give a white solid. Column chromatography (SiO$_2$, toluene/AcOEt, 9:1, v/v) followed by preparative thin-layer chromatography (SiO$_2$, toluene/AcOEt, 9:1, v/v) afforded **3** as a white solid; yield: 102 mg, 46%. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.85, 6.84, 6.82, 6.81, 6.76, 6.75, 6.71, 6.66, 6.46 (9 × s, ratio 2:1:1:1:1:1:1:1:1, ArH, 20 H), 4.42 (t, J = 6.4 Hz, OCH, 2 H), 3.91−3.64 (m, ArCH$_2$Ar, 20 H), 3.76, 3.75, 3.72, 3.70, 3.69, 3.62, 3.60 (8×s, ratio 1:1:1:1:1:3:1:1, OCH$_3$, 30 H), 1.81 (quintuplet, J = 6.4 Hz, CHCH$_2$, 4 H), 1.62−1.44 (m, CH$_2$, 8 H), 1.38−1.28 (m, CH$_2$, 4 H) ppm. [13]C{^{1}H} (125 MHz, CDCl$_3$) NMR δ 172.5, 151.0, 150.62, 150.57, 150.54 (×2), 150.46, 150.44, 150.4, 150.3, 149.2, 128.8 (×2), 128.5, 128.4, 128.3, 128.13 (×2), 128.09, 127.9, 127.8, 114.9, 114.7, 114.1, 114.0, 113.8, 113.7, 113.5 (×2), 113.2, 56.1, 55.91, 55.88, 55.77, 55.75, 55.71, 55.60, 55.58, 55.8, 50.6,

33.0, 30.8, 29.6, 29.5 (×2), 29.42, 29.35 (×2), 28.3, 25.7 ppm. ESI(+)-MS m/z 1765 ([M + K]$^+$, 100%). Anal. calcd for C$_{102}$H$_{118}$O$_{24}$: C, 70.90; H, 6.88. Found: C, 70.55; H, 6.74.

meso-Bis-pillar[5]arene Dicarboxylic Acid (H). Aqueous LiOH (1 M, 3 mL) was added to a solution of bis-pillar[5]arene dimethyl diester **3** (66 mg, 0.04 mmol) in THF (15 mL), and the resulting mixture was stirred overnight in a thermostated oil bath at 50 °C. HCl (1 M, 9 mL) and H$_2$O (30 mL) were then added, and the resulting solution was extracted with CHCl$_3$ (3 × 20 mL). The combined organic layer was dried (MgSO$_4$), filtered, and evaporated under reduced pressure to give a white precipitate that was crystallized from MeCN/CH$_2$Cl$_2$ to yield **H** as white crystals; yield: 66 mg, quantitative. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.79, 6.76, 6.74, 6.72, 6.71, 6.70, 6.69, 6.67, 6.62 (9×s, ratio 1:1:1:1:1:1:2:1:1, ArH, 20 H), 4.53 (t, J = 5.8 Hz, OCH, 2 H), 3.87−3.68 (m, ArCH$_2$Ar, 20 H), 3.71, 3.67, 3.65, 3.64, 3.59, 3.58, 3.52 (7 × s, ratio 1:1:1:2:2:1:1, OCH$_3$, 27 H), 1.87 (quintuplet, J = 5.8 Hz, CHCH$_2$, 4 H), 1.45−1.38 (m, CH$_2$, 4 H), 1.28−1.22 (m, CH$_2$, 4 H), 1.19−1.11 (m, CH$_2$, 4 H) ppm. [13]C{^{1}H} (125 MHz, CDCl$_3$) NMR δ 173.1, 151.4, 151.2, 150.93, 150.91 (×2), 150.89, 150.8, 150.7, 150.6, 148.1, 128.95, 128.90, 128.5, 128.43 (×2), 128.41, 128.2, 128.08, 128.07, 127.8, 115.0, 114.6, 114.48, 114.46, 114.3 (×2), 114.0 (×2), 113.9, 113.8, 56.3 (×2), 56.2, 56.03, 56.02, 55.96 (×2), 55.94, 55.9, 55.7, 32.5, 30.3, 29.86, 29.82, 29.77, 29.70, 29,13, 29.05, 29.01, 25.0 ppm. ESI(−)-MS m/z 1697 ([M − H]$^-$, 100%). Anal. calcd for C$_{100}$H$_{114}$O$_{24}$: C, 70.65; H, 6.76. Found: C, 70.29; H, 6.81.

^{1}H NMR Dilution Experiments. ^{1}H NMR spectra (500 MHz) were recorded at 25 °C either in CDCl$_3$ or in CDCl$_3$/CF$_3$CD$_2$OD (9:1, v/v). Prior to use, CDCl$_3$ was filtered through neutral aluminum oxide to remove any traces of acid. Sample solutions of **H** + **G** were prepared by mixing together **H** and **G** in a 1 to 1 molar ratio to produce [**H**] = [**G**] = 13 mM, which was then diluted with the same solvent mixture down to [**H**] = [**G**] = 6 or 0.6 mM.

Diffusion-Ordered Spectroscopy Studies. DOSY experiments were carried out on a 500 MHz NMR spectrometer equipped with a z-gradient system capable of producing pulse gradients up to 50 gauss × cm^{-1}. Spectra were recorded either in CDCl$_3$ or in CDCl$_3$/CF$_3$CD$_2$OD (9:1, v/v) at 25 ± 0.1 °C, using a gradient stimulated echo with spin-lock and a convection compensation pulse sequence.

Atomic Force Microscopy. Spin-coated **H**/**G** thin films for AFM analysis were prepared at room temperature by casting a few drops of a [**H**] = [**G**] = 1 mM solution (CHCl$_3$/CF$_3$CH$_2$OH, 9:1, v/v) onto a silica surface while spinning at about 2000 rpm. The same procedure was also carried out with a [**H**] = [**G**] = 1 mM solution (CHCl$_3$/CF$_3$CH$_2$OH, 9:1, v/v) to which 4 equiv of trimethylamine (TEA) had subsequently been added. The images were acquired using an AFM SMENA (NT-MDT) apparatus equipped with a silicon probe working in semi-contact mode (NSG30, 6 nm typical curvature radius). All of the images were postprocessed by a plane removal numerical procedure.

ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02501.

Additional COSY, NOESY, and DOSY spectra of the PSPs; UV−vis titration data; and additional AFM image (PDF)

AUTHOR INFORMATION

Corresponding Authors

Ilenia Pisagatti − *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, 98166 Messina, Italy;* ⓞ orcid.org/0000-0001-9533-983X; Phone: +39 0906765178; Email: ipisagatti@unime.it

Giuseppe Gattuso − *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, 98166 Messina, Italy;* ● orcid.org/0000-0003-4276-7384; Phone: +39 0906765242; Email: ggattuso@unime.it

Authors

Anna Notti − *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, 98166 Messina, Italy;* ● orcid.org/0000-0002-6687-9631

Francesco Nastasi − *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, 98166 Messina, Italy*

Salvatore Patanè − *Dipartimento di Scienze Matematiche e Informatiche, Scienze Fisiche e Scienze della Terra, Università di Messina, 98166 Messina, Italy*

Melchiorre F. Parisi − *Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Università di Messina, 98166 Messina, Italy;* ● orcid.org/0000-0002-2277-0386

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.joc.0c02501

Notes

The authors declare no competing financial interest.

■ **REFERENCES**

(1) (a) Aida, T.; Meijer, E. W. Supramolecular Polymers—we've Come Full Circle. *Isr. J. Chem.* **2020**, *60*, 33−47. (b) Hakshim, P. K.; Bergueiro, J.; Meijer, E. W.; Aida, T. Supramolecular Polymerization: A Conceptual Expansion for Innovative Materials. *Progr. Polym. Sci.* **2020**, *105*, No. 101250. (c) Matern, J.; Dorca, Y.; Sánchez, L.; Fernández, G. Revising complex supramolecular polymerization under kinetic and thermodynamic control. *Angew. Chem., Int. Ed.* **2019**, *58*, 16730−16740. (d) Haino, T. Designer supramolecular polymers with specific molecular recognitions. *Polym. J.* **2019**, *51*, 303−318. (e) Yang, L.; Tan, X.; Wang, Z.; Zhang, X. Supramolecular Polymers: Historical Development, Preparation, Characterization, and Functions. *Chem. Rev.* **2015**, *115*, 7196−7239. (f) Yan, X.; Xu, D.; Chi, X.; Chen, J.; Dong, S.; Ding, X.; Yu, Y.; Huang, F. A Multiresponsive, Shape-Persistent, and Elastic Supramolecular Polymer Network Gel Constructed by Orthogonal Self-Assembly. *Adv. Mater.* **2012**, *24*, 362−369. (g) Harada, A.; Takashima, Y.; Yamaguchi, H. Cyclodextrin-based supramolecular polymers. *Chem. Soc. Rev.* **2009**, *38*, 875−882. (h) De Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. Supramolecular Polymerization. *Chem. Rev.* **2009**, *109*, 5687−5754. (i) Brunsveld, L.; Folmer, B. J. B.; Meijer, E. W.; Sijbesma, R. P. Supramolecular Polymers. *Chem. Rev.* **2001**, *101*, 4071−4097.

(2) (a) Ogoshi, T.; Yamagishi, T. A.; Nakamoto, Y. Pillar-Shaped Macrocyclic Hosts Pillar[*n*]arenes: New Key Players for Supramolecular Chemistry. *Chem. Rev.* **2016**, *116*, 7937−8002. (b) Ogoshi, T.; Kanai, S.; Fujinami, S.; Yamagishi, T.; Nakamoto, Y. *para*-Bridged Symmetrical Pillar[5]arenes: Their Lewis Acid Catalyzed Synthesis and Host−Guest Property. *J. Am. Chem. Soc.* **2008**, *130*, 5022−5023.

(3) (a) Xia, D.; Wang, P.; Ji, X.; Khashab, N. M.; Sessler, J. L.; Huang, F. Functional Supramolecular Polymeric Networks: The Marriage of Covalent Polymers and Macrocycle-Based Host−Guest Interactions. *Chem. Rev.* **2020**, *120*, 6070−6123. (b) Fang, Y.; Deng, Y.; Dehaen, W. Tailoring pillararene-based receptors for specific metal ion binding: From recognition to supramolecular assembly. *Coord. Chem Rev.* **2020**, *415*, 213−313. (c) Li, Y.; Li, Z.; Lin, Q.; Yang, Y. Functional supramolecular gels based on pillar[*n*]arene macrocycles. *Nanoscale.* **2020**, *12*, 2180−2200. (d) Zhou, Y.; Jie, K.; Zhao, R.; Huang, F. Supramolecular-Macrocycle-Based Crystalline Organic Materials. *Adv. Mater.* **2019**, No. 1904824. (e) Ogoshi, T.; Kakuta, T.; Yamagishi, T. Applications of Pillar[*n*]arene-Based Supramolecular Assemblies. *Angew. Chem., Int. Ed.* **2019**, *58*, 2197−2206. (f) Xiao, T.; Qi, L.; Zhong, W.; Lin, C.; Wang, R.; Wang, L. Stimuli-responsive nanocarriers constructed from pillar[*n*]arene-based supra-amphiphiles. *Mater. Chem. Front.* **2019**, *3*, 1973−1993. (g) Song, N.; Kakuta, T.; Yamagishi, T.; Yang, Y.-W.; Ogoshi, T. Molecular-Scale Porous Materials Based on Pillar[*n*]arenes. *Chem* **2018**, *4*, 2029−2053. (h) Sathiyajith, C.; Shaikh, R. R.; Han, Q.; Zhang, Y.; Meguellati, K.; Yang, Y.-W. Biological and related applications of pillar[*n*]arenes. *Chem. Commun.* **2017**, *53*, 677−696. (i) Xiao, T.; Xu, L.; Zhong, W.; Zhou, L.; Sun, X.-Q.; Hu, X.-Y.; Wang, L. Advanced Functional Materials Constructed from Pillar[*n*]arenes. *Isr. J. Chem.* **2018**, *58*, 1219−1229. (j) Chen, P.; Zhou, Y.; Yang, J. *In situ* supramolecular polymerization promoted by the marriage of dynamic covalent bonding and pillar[5]arene-based host−guest interaction. *Chem. Commun.* **2017**, *53*, 1144−1147.

(4) (a) Xue, M.; Yang, Y.; Chi, X.; Zhang, Z.; Huang, F. Pillararenes, A New Class of Macrocycles for Supramolecular Chemistry. *Acc. Chem. Res.* **2012**, *45*, 1294−1308. (b) Cragg, P. J.; Sharma, K. Pillar[5]arenes: fascinating cyclophanes with a bright future. *Chem. Soc. Rev.* **2012**, *41*, 597−607.

(5) Zhang, H.; Zhao, Y. Pillararene-Based Assemblies: Design Principle, Preparation and Applications. *Chem. - Eur. J.* **2013**, *19*, 16862−16879.

(6) (a) Xiao, T.; Zhou, L.; Sun, X.-Q.; Huang, F.; Lin, C.; Wang, L. Supramolecular polymers fabricated by orthogonal self-assembly based on multiple hydrogen bonding and macrocyclic host−guest interactions. *Chin. Chem. Lett.* **2020**, *31*, 1−9. (b) Li, H.; Yang, Y.; Xu, F.; Liang, T.; Wen, H.; Tian, W. Pillararene-based supramolecular polymers. *Chem. Commun.* **2019**, *55*, 271−285. (c) Kakuta, T.; Yamagishi, T. A.; Ogoshi, T. Stimuli-Responsive Supramolecular Assemblies Constructed from Pillar[*n*]arenes. *Acc. Chem. Res.* **2018**, *51*, 1656−1666. (d) Yang, L. L.; Tan, X. X.; Wang, Z. Q.; Zhang, X. Supramolecular Polymers: Historical Development, Preparation, Characterization, and Functions. *Chem. Rev.* **2015**, *115*, 7196−7239. (e) Li, C. Pillararene-based supramolecular polymers: from molecular recognition to polymeric aggregates. *Chem. Commun.* **2014**, *50*, 12420−12433.

(7) (a) Tian, W.; Li, X. X.; Wang, J. X. Supramolecular hyperbranched polymers. *Chem. Commun.* **2017**, *53*, 2531−2542. (b) Dong, S. Y.; Zheng, B.; Wang, F.; Huang, F. Supramolecular Polymers Constructed from Macrocycle-Based Host−Guest Molecular Recognition Motifs. *Acc. Chem. Res.* **2014**, *47*, 1982−1994.

(8) (a) Wang, Y.; Xu, J.-F.; Chen, Y.-Z.; Niu, L.-Y.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. Photoresponsive supramolecular self-assembly of monofunctionalized pillar[5]arene based on stiff stilbene. *Chem. Commun.* **2014**, *50*, 7001−7003. (b) Gao, L.; Zhang, Z.; Dong, S.; Xue, M. Formation of a Copillar[5]arene-Based Supramolecular Polymer in Solution and in the Solid State. *Macromol. Rapid Commun.* **2014**, *35*, 987−991. (c) Strutt, N. L.; Zhang, H.; Giesener, M. A.; Lei, J.; Stoddart, J. F. A self-complexing and self-assembling pillar[5]arene. *Chem. Commun.* **2012**, *48*, 1647−1649.

(9) Zhang, Z.; Luo, Y.; Chen, J.; Dong, S.; Yu, Y.; Ma, Z.; Huang, F. Formation of Linear Supramolecular Polymers That Is Driven by C−H⋯π Interactions in Solution and in the Solid State. *Angew. Chem., Int. Ed.* **2011**, *50*, 1397−1401.

(10) Zhang, Z.; Sun, K.; Jin, L.; Xie, C.; Li, S. Preparation of a mechanically interlocked polymer from a linear supramolecular polymer. *Org. Chem. Front.* **2020**, *7*, 1453−1462.

(11) Shi, B.; Xia, D.; Yao, Y. A water-soluble supramolecular polymer constructed by pillar[5]arene-based molecular recognition. *Chem. Commun.* **2014**, *50*, 13932−13935.

(12) Zhang, Z.; Shao, L.; Yang, J. A phosphonated copillar[5]arene: Synthesis and application in the construction of pH-responsive supramolecular polymer in water. *Tetrahedron Lett.* **2018**, *59*, 3000−3004.

(13) (a) Zhang, Q.; Zhang, C.-H.; Yang, J.-H.; Xin, P.-Y.; Xuan, X.-P.; Wang, J.-G.; Ma, N.-N.; Guo, H.-M.; Qu, G.-R. A four-unit [*c*2]daisy chain connected by hydrogen bonds. *Chem. Commun.* **2015**, *51*, 15253−15256. (b) Wang, K.; Wang, C. Y.; Zhang, Y.; Zhang, S. X. A.; Yang, B.; Yang, Y. W. Ditopic pillar[5]arene-based fluorescence enhancement material mediated by [*c*2]daisy chain formation. *Chem. Commun.* **2014**, *50*, 9458−9461.

(14) (a) Zhao, Q.; Chen, Y.; Sun, B.; Qian, C.; Cheng, M.; Jiang, J.; Lin, C.; Wang, L. Pillar[5]arene Based Pseudo[1]rotaxane Operating as Acid/Base-Controllable Two State Molecular Shuttle. *Eur. J. Org. Chem.* **2019**, 3396−3400. (b) Chen, Y.; Cao, D.; Wang, L.; He, M.; Zhou, L.; Schollmeyer, D.; Meier, H. Monoester Copillar[5]arenes: Synthesis, Unusual Self-Inclusion Behavior, and Molecular Recognition. *Chem. - Eur. J.* **2013**, *19*, 7064−7070.

(15) 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.

(16) Wei, T.-B.; Qi, L.-H.; Zhang, Q.-P.; Zhang, W.-H.; Yao, H.; Zhang, Y.-M.; Lin, Q. Stimuli-responsive supramolecular polymer network based on bi-pillar[5]arene for efficient adsorption of multiple organic dye contaminants. *New J. Chem.* **2020**, *44*, 12531−12537.

(17) Ogoshi, T.; Yoshikoshi, K.; Aoki, T.; Yamagishi, T. Photo-reversible switching between assembly and disassembly of a supramolecular polymer involving an azobenzene-bridged pillar[5]-arene dimer. *Chem. Commun.* **2013**, *49*, 8785−8787.

(18) (a) Wang, Y.; Lv, M.-Z.; Song, N.; Liu, Z.-J.; Wang, C.; Yang, Y.-W. Dual-Stimuli-Responsive Fluorescent Supramolecular Polymer Based on a Diselenium-Bridged Pillar[5]arene Dimer and an AIE-Active Tetraphenylethylene Guest. *Macromolecules* **2017**, *50*, 5759−5766. (b) Zhou, Y.; Jie, K.; Shi, B.; Yao, Y. A γ-ray and dual redox-responsive supramolecular polymer constructed by a selenium containing pillar[5]arene dimer and a neutral guest. *Chem. Commun.* **2015**, *51*, 11112−11114.

(19) Xu, J.-F.; Chen, Y.-Z.; Wu, L.-Z.; Tung, C.-H.; Yang, Q.-Z. Dynamic Covalent Bond Based on Reversible Photo [4 + 4] Cycloaddition of Anthracene for Construction of Double-Dynamic Polymers. *Org. Lett.* **2013**, *15*, 6148−6151.

(20) Chen, P.; Zhou, Y.; Yang, J. *In situ* supramolecular polymerization promoted by the marriage of dynamic covalent bonding and pillar[5]arene-based host−guest interaction. *Chem. Commun.* **2017**, *53*, 1144−1147.

(21) (a) Ali, W.; Ning, G.; Hassan, M.; Gong, W. Construction of Pillar[5]arene Tetramer-Based Cross-Linked Supramolecular Polymers through Hierarchical Charge-Transfer and Host-Guest Interactions. *Asian J. Org. Chem.* **2019**, *8*, 74−78. (b) Shao, L.; Yang, J.; Hua, B. A dual-responsive cross-linked supramolecular polymer network gel: hierarchical supramolecular self-assembly driven by pillararene-based molecular recognition and metal−ligand interactions. *Polym. Chem.* **2018**, *9*, 1293−1297.

(22) Shi, B.; Jie, K.; Zhou, Y.; Xia, D.; Yao, Y. Formation of fluorescent supramolecular polymeric assemblies via orthogonal pillar[5]arene-based molecular recognition and metal ion coordination. *Chem. Commun.* **2015**, *51*, 4503−4506.

(23) (a) Manganaro, N.; Pisagatti, I.; Notti, A.; Parisi, M. F.; Gattuso, G. Self-sorting assembly of a calixarene/crown ether polypseudorotaxane gated by ion-pairing. *New J. Chem.* **2019**, *43*, 7936−7940. (b) Gattuso, G.; Manganaro, N.; Notti, A.; Pisagatti, I.; Pappalardo, S.; Parisi, M. F. Calix[5]arene-based supramolecular

polymers. *Curr. Org. Chem.* **2015**, *19*, 2271−2280. (c) Villari, V.; Gattuso, G.; Notti, A.; Pappalardo, A.; Micali, N. Self-assembled calixarene derivative as supramolecular polymer. *J. Phys. Chem. B* **2012**, *116*, 5537−5541. (d) Capici, C.; Cohen, Y.; D'Urso, A.; Gattuso, G.; Notti, A.; Pappalardo, A.; Pappalardo, S.; Parisi, M. F.; Purrello, R.; Slovak, S.; Villari, V. Anion-assisted Supramolecular Polymerization: from Achiral AB-type Monomers to Chiral Assemblies. *Angew. Chem., Int. Ed.* **2011**, *50*, 11956−11961. (e) Gargiulli, C.; Gattuso, G.; Notti, A.; Pappalardo, S.; Parisi, M. F. Supramolecular AA/BB-type oligomer formation from a hetero-tetratopic bis-calix[5]arene monomer and octanediyldiammonium dichloride. *Tetrahedron Lett* **2011**, *52*, 7116−7120. (f) Gattuso, G.; Notti, A.; Pappalardo, A.; Parisi, M. F.; Pisagatti, I.; Pappalardo, S.; Garozzo, D.; Messina, A.; Cohen, Y.; Slovak, S. Self-Assembly Dynamics of Modular Homoditopic Bis-calix[5]arenes and Long-Chained α,ω-Alkanediyldiammonium Components. *J. Org. Chem.* **2008**, *73*, 7280−7289. (g) Pappalardo, S.; Villari, V.; Slovak, S.; Cohen, Y.; Gattuso, G.; Notti, A.; Pappalardo, A.; Pisagatti, I.; Parisi, M. F. Counterion Dependent Proton-Driven Self-Assembly of Linear Supramolecular Oligomers Based on Amino-Calix[5]arene Building Blocks. *Chem. - Eur. J.* **2007**, *13*, 8164−8173.

(24) (a) Brancatelli, G.; Gattuso, G.; Geremia, S.; Manganaro, N.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Pisagatti, I. Encapsulation of biogenic polyamines by carboxylcalix[5]arenes: when solid-state design beats recognition in solution. *CrystEngComm* **2016**, *18*, 5012−5016. (b) Brancatelli, G.; Gattuso, G.; Geremia, S.; Manganaro, N.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Pisagatti, I. α,ω-Alkanediyldiammonium dications sealed within calix[5]arene capsules with a hydrophobic bayonet-mount fastening. *CrystEngComm* **2015**, *17*, 7915−7921. (c) Manganaro, N.; Lando, G.; Gargiulli, C.; Pisagatti, I.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Gattuso, G. Unique binding behavior of water-soluble polycationic oxacalix[4]-arene tweezers towards the paraquat dication. *Chem. Commun.* **2015**, *51*, 12657−12660. (d) Brancatelli, G.; Gattuso, G.; Geremia, S.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Pisagatti, I. Probing the Inner Space of Salt-Bridged Calix[5]arene Capsules. *Org. Lett.* **2014**, *16*, 2354−2357. (e) Gattuso, G.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Pisagatti, I.; Patanè, S. Encapsulation of monoamine neuro-transmitters and trace amines by amphiphilic anionic calix[5]arene micelles. *New J. Chem.* **2014**, *38*, 5983−5990. (f) Capici, C.; Gattuso, G.; Notti, A.; Parisi, M. F.; Pappalardo, S.; Brancatelli, G.; Geremia, S. Selective amine recognition driven by host-guest proton transfer and salt bridge formation. *J. Org. Chem.* **2012**, *77*, 9668−9675.

(25) Manganaro, N.; Pisagatti, I.; Notti, A.; Pappalardo, A.; Patanè, S.; Micali, N.; Villari, V.; Parisi, M. F.; Gattuso, G. Ring-chain morphology control in overall-neutral, internally ion-paired supra-molecular polymers. *Chem. - Eur. J.* **2018**, *24*, 1097−1103.

(26) (a) Lupo, F.; Capici, C.; Gattuso, G.; Notti, A.; Parisi, M. F.; Pappalardo, A.; Pappalardo, S.; Gulino, A. Optical Recognition of *n*-Butylammonium and 1,5-Pentanediammonium Picrates by a Calix[5]-arene Monolayer Covalently Assembled on Silica Substrates. *Chem. Mater.* **2010**, *22*, 2829−2834. (b) Buscemi, S.; Pace, A.; Palumbo Piccionello, A.; Pappalardo, S.; Garozzo, D.; Pilati, T.; Gattuso, G.; Pappalardo, A.; Pisagatti, I.; Parisi, M. F. Lower Rim Arylation of Calix[*n*]arenes with Extended Perfluorinated Domains. *Tetrahedron Lett.* **2006**, *47*, 9049−9052.

(27) Gargiulli, C.; Gattuso, G.; Notti, A.; Pappalardo, S.; Parisi, M. F. Orthogonal chain length control in calix[5]arene-based AB-type supramolecular polymers. *Tetrahedron Lett.* **2011**, *52*, 6460−6464.

(28) (a) Barbera, L.; De Plano, L. M.; Franco, D.; Gattuso, G.; Guglielmino, S. P. P.; Lando, G.; Notti, A.; Parisi, M. F.; Pisagatti, I. Antiadhesive and antibacterial properties of pillar[5]arene-based multilayers. *Chem. Commun.* **2018**, *54*, 10203−10206. (b) Barbera, L.; Franco, D.; De Plano, L. M.; Gattuso, G.; Guglielmino, S. P. P.; Lentini, G.; Manganaro, N.; Marino, N.; Pappalardo, S.; Parisi, M. F.; Puntoriero, F.; Pisagatti, I.; Notti, A. A water-soluble pillar[5]arene as a new carrier for an old drug. *Org. Biomol. Chem.* **2017**, *15*, 3192−3195.

(29) Ogoshi, T.; Demachi, K.; Kitajima, K.; Yamagishi, T. Monofunctionalized pillar[5]arenes: synthesis and supramolecular structure. *Chem. Commun.* **2011**, *47*, 7164−7166.

(30) Zhang, C.; Ling, J.; Wang, Q. Radical Addition-Coupling Polymerization (RACP) toward Periodic Copolymers. *Macromolecules* **2011**, *44*, 8739−8743.

(31) (a) Culik, R. M.; Abaskharon, R. M.; Pazos, I. M.; Gai, F. Experimental Validation of the Role of Trifluoroethanol as a Nanocrowder. *J. Phys. Chem. B* **2014**, *118*, 11455−11461. (b) Povey, J. F.; Smales, C. M.; Hassard, S. J.; Howard, M. J. Comparison of the effects of 2,2,2-trifluoroethanol on peptide and protein structure and function. *J. Struct. Biol.* **2007**, *157*, 329−338. (c) Sönnichsen, F. D.; Van Eyk, J. E.; Hodges, R. S.; Sykes, B. D. Effect of Trifluoroethanol on Protein Secondary Structure: An NMR and CD Study Using a Synthetic Actin Peptide. *Biochemistry* **1992**, *31*, 8790−8798.

(32) (a) Cohen, Y.; Slovak, S. Diffusion NMR for the characterization, in solution, of supramolecular systems based on calixarenes, resorcinarenes, and other macrocyclic arenes. *Org. Chem. Front.* **2019**, *6*, 1705−1718. (b) Du, X.-S.; Wang, C.-Y.; Jia, Q.; Deng, R.; Tian, H.-S.; Zhang, H.-Y.; Meguellati, K.; Yang, Y.-W. Pillar[5]arene-based [1]rotaxane: high-yield synthesis, characterization and application in Knoevenagel reaction. *Chem. Commun.* **2017**, *53*, 5326−5329. (c) Han, Y.; Huo, G.-F.; Sun, J.; Xie, J.; Yan, C.-G.; Zhao, Y.; Wu, X.; Lin, C.; Wang, L. Formation of a series of stable pillar[5]arene-based pseudo[1]-rotaxanes and their [1]rotaxanes in the crystal state. *Sci. Rep.* **2016**, *6*, No. 28748. (d) Strutt, N. L.; Forgan, R. S.; Spruell, J. M.; Botros, Y. Y.; Stoddart, J. F. Monofunctionalized Pillar[5]arene as a Host for Alkanediamines. *J. Am. Chem. Soc.* **2011**, *133*, 5668−5671. (e) Ma, Y.; Ji, X.; Xiang, F.; Chi, X.; Han, C.; He, J.; Abliz, Z.; Chen, W.; Huang, F. A cationic water-soluble pillar[5]arene: synthesis and host−guest complexation with sodium 1-octanesulfonate. *Chem. Commun.* **2011**, *47*, 12340−12342.

(33) (a) Pisagatti, I.; Barbera, L.; Gattuso, G.; Parisi, M. F.; Geremia, S.; Hickey, N.; Notti, A. Guest-length driven high fidelity self-sorting in supramolecular capsule formation of calix[5]arenes in water. *Org. Chem. Front.* **2019**, *6*, 3804−3809. (b) Wong, A.; Ida, R.; Spinder, L.; Wu, G. Disodium Guanosine 5′-Monophosphate Self-Associates into Nanoscale Cylinders at pH 8: A Combined Diffusion NMR Spectroscopy and Dynamic Light Scattering Study. *J. Am. Chem. Soc.* **2005**, *127*, 6990−6998. (c) Waldeck, A. R.; Kuchel, P. W.; Lennon, A. J.; Chapman, B. E. NMR diffusion measurements to characterise membrane transport and solute binding. *Prog. Nucl. Magn. Reson. Spectrosc.* **1997**, *30*, 39−68.

(34) (a) Sahu, S.; Das, M.; Bharti, A. K.; Krishnamoorthy, G. Proton transfer triggered proton transfer: a self-assisted twin excited state intramolecular proton transfer. *Phys. Chem. Chem. Phys.* **2018**, *20*, 27131−27139. (b) Koeppe, B.; Pylaeva, S. A.; Allolio, C.; Sebastiani, D.; Nibbering, E. T. J.; Denisov, G. S.; Limbache, H.-H.; Tolstoy, P. M. Polar solvent fluctuations drive proton transfer in hydrogen bonded complexes of carboxylic acid with pyridines: NMR, IR and ab initio MD study. *Phys. Chem. Chem. Phys.* **2017**, *19*, 1010−1028.

(35) (a) Yu, G.; Hua, B.; Han, C. Proton Transfer in Host−Guest Complexation between a Difunctional Pillar[5]arene and Alkyldiamines. *Org. Lett.* **2014**, *16*, 2486−2489. (b) Hua, B.; Yu, G. Proton transfer-assisted host−guest complexation between a difunctional pillar[5]arene and amine-based guests. *Tetrahedron Lett.* **2014**, *55*, 6274−6276.

(36) HCl-free CHCl$_3$ and CDCl$_3$ were filtered through neutral alumina prior to use.

(37) (a) Evans, R.; Deng, Z.; Rogerson, A. K.; McLachlan, A. S.; Richards, J. J.; Nilsson, M.; Morris, G. A. Quantitative Interpretation of Diffusion-Ordered NMR Spectra: Can We Rationalize Small Molecule Diffusion Coefficients? *Angew. Chem., Int. Ed.* **2013**, *52*, 3199−3202. (b) Cohen, Y.; Avram, L.; Frish, L. Diffusion NMR Spectroscopy in Supramolecular and Combinatorial Chemistry: An Old Parameter—New Insights. *Angew. Chem., Int. Ed.* **2005**, *44*, 520−554.

(38) Bhattacharyya, P. K. Reactivity, aromaticity and absorption spectra of pillar[5]arene conformers: A DFT study. *Comput. Theor. Chem.* **2015**, *1066*, 20−27.

(39) Binding constants were obtained by curve-fitting calculations, using the ReactLab Equilibria software (Jplus Consulting Pty Ltd). See Figure S7.

(40) Interestingly, the chemical shifts of the guest methylene groups in the 1:1 **G ⊂ H** complex obtained by TEA treatment significantly differ from those of the 1:1 complex seen in neat CDCl$_3$, indicating that the dodecanediamine guest threads the pillararene cavity in a different fashion. This probably derives from the different interactions between the amino group of **G** and the carboxylate/carboxyl groups of H (i.e, $-CO_2^-\cdots H_2N-$ in the TEA experiment vs $-CO_2H\cdots H_2N-$ in neat CDCl$_3$).

(41) Haino, T.; Matsumoto, Y.; Fukazawa, Y. Supramolecular Nano Networks Formed by Molecular-Recognition-Directed Self-Assembly of Ditopic Calix[5]arene and Dumbbell [60]Fullerene. *J. Am. Chem. Soc.* **2005**, *127*, 8936−8937.