



Synthesis and Host–Guest Properties of Acyclic Pillar[*n*]naphthalenes

Yuanyin Jia^{1†}, Ming Dong^{2†}, Bin Wang^{2*} and Chunju Li^{1,2,3*}

¹ School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai, China, ² Key Laboratory of Inorganic–Organic Hybrid Functional Material Chemistry, Ministry of Education, Tianjin Key Laboratory of Structure and Performance for Functional Molecules, College of Chemistry, Tianjin Normal University, Tianjin, China, ³ Department of Chemistry, Center for Supramolecular Chemistry and Catalysis, Shanghai University, Shanghai, China

OPEN ACCESS

Edited by:

De-Xian Wang,
Institute of Chemistry (CAS), China

Reviewed by:

Lyle Isaacs,
University of Maryland, College Park,
United States
Liu-Pan Yang,
Southern University of Science and
Technology, China

*Correspondence:

Bin Wang
hxxywangb@mail.tjnu.edu.cn
Chunju Li
cjl@shu.edu.cn

[†]These authors have contributed
equally to this work

Specialty section:

This article was submitted to
Supramolecular Chemistry,
a section of the journal
Frontiers in Chemistry

Received: 15 August 2019

Accepted: 14 November 2019

Published: 03 December 2019

Citation:

Jia Y, Dong M, Wang B and Li C
(2019) Synthesis and Host–Guest
Properties of Acyclic
Pillar[*n*]naphthalenes.
Front. Chem. 7:828.
doi: 10.3389/fchem.2019.00828

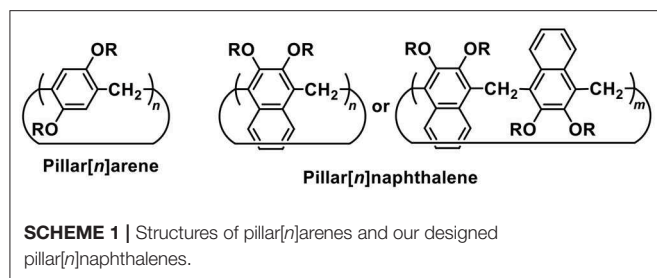
Here we report a new class of synthetic receptors, acyclic pillar[*n*]naphthalene (*n* = 2–4, **Dimer**, **Trimer**, and **Tetramer**) oligomers, which are made up of 2,3-diethoxynaphthalene units linked by methylene bridges at the 1- and 4-positions. They can be synthesized through a one-step condensation of 2,3-diethoxynaphthalene monomer and paraformaldehyde in the presence of BF₃•(Et)₂O catalyst. The crystal structure of **Tetramer** has an interesting pseudo-cycle shaped structure in the solid state. Their complexation behaviors toward several organic ammonium cations (**1**⁺–**15**⁺) and electron-deficient neutral guests (**16**–**17**), were examined by means of ¹H NMR spectroscopy. **Tetramer** shows good host-guest properties toward the ammonium guests, giving association constants (*K*_a) in the magnitude of 10²–10⁴ M^{–1}, which are comparable with those for some macrocyclic hosts.

Keywords: pillararenes, calixarenes, acyclic hosts, molecular recognition, host-guest chemistry

INTRODUCTION

Since the discover of crown ethers, the development of hosts for recognizing various guest species has mainly focused on macrocyclic structures (Cram, 1988; Lehn, 1988; Pedersen, 1988; Gong et al., 2010; Chun et al., 2013; Jurícek et al., 2014; Liu et al., 2019). Methylene-bridged macrocyclic arenes, for example calixarenes (Baldini et al., 2007; Guo and Liu, 2012), pillararenes (Ogoshi et al., 2008; Xue et al., 2012; Wang et al., 2016; Yang et al., 2016), coronarenes (Wang, 2018), helic[6]arene (Zhang et al., 2016), biphenarenes (Chen et al., 2015; Dai et al., 2017; Li et al., 2019; Wang et al., 2019b), and etc. (Guo et al., 2018; Luo et al., 2018; Ma et al., 2018) have been widely used in host-guest chemistry, self-assembly materials, and biomedical field (Song and Yang, 2015; Alsbaiee et al., 2016; Li et al., 2017; Jie et al., 2018; Chen et al., 2019; Yang et al., 2019). Naphthalene-based macrocyclic arenes, termed as calixnaphthalenes, have also been produced (Poh et al., 1989; Andreetti et al., 1993; Shorthill et al., 2004; AlHujran et al., 2012; Avetta et al., 2012). However, calixnaphthalenes have not become highly popular receptors because they do not have unique molecular recognition properties. Considering that pillararenes with pillar-shape topologic structures have shown nice host-guest properties, we wondered whether we can create acyclic pillarnaphthalenes (**Scheme 1**), which would have deep, pillar-shape, and π-rich cavities, and maybe better binding abilities than calixnaphthalenes. As detailed below, we did not get such macrocycles, but succeed in making acyclic pillarnaphthalene oligomers.

Acyclic hosts that contain partially enclosed cavities capable of binding guests provided alternatives with unique synthetic and functional advantages (Goodman et al., 2007; Seebach and Gardiner, 2008; Pan et al., 2017; Wang et al., 2019a). For example, foldamers may provide cavities that are adaptive in recognizing different guest molecules (Zhang et al., 2012; Yashima et al., 2016).



Molecular tweezers have made the way from a supramolecular host to a drug candidate, due to their ability to inhibit peptide and protein aggregation through the complexation toward amino acids (Sinha et al., 2011; Schrader et al., 2016).

Isaacs and his co-workers created acyclic cucurbit[n]uril-type receptors, which can function as solubilizing agents for insoluble drugs. Interestingly, the solubility of paclitaxel was increased 2,750 times through the formation of soluble container–drug complex (Ma et al., 2012). These highly soluble acyclic cucurbiturils could also solubilize individual single-walled carbon nanotubes (SWNTs) in water even at a concentration 100–1,000 times lower than typically required for surfactants (Shen et al., 2012). The groups of Schrader and Yoshizawa synthesized beautiful water-soluble clip and tweezer-shaped hosts based on norbornene and anthracene building blocks (Bier et al., 2013; Jono et al., 2017).

Herein, we wish to report the synthesis of a new type of receptors, acyclic pillar[n]naphthalene ($n = 2-4$, **Dimer**, **Trimer**, and **Tetramer**) oligomers, which are made up of 2,3-diethoxynaphthalene units linked by methylene bridges at the 1- and 4-positions. **Tetramer**, bearing a pseudo-cavity, has good host-guest properties toward a series of model organic cationic guests.

MATERIALS AND METHODS

All the reagents involved in this research were commercially available and used without further purification unless otherwise noted. ^1H NMR, ^{13}C NMR, 2D NOESY, and COSY spectra (see **Supplementary Material**) were recorded with a Bruker AVANCE III 500 MHz instrument. Chemical shifts were referred to TMS. High-resolution mass spectra (HRMS) were determined on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. The single crystal X-ray data were measured by direct methods using SHELXS-971 and refined by fullmatrix least-squares procedures on F2 with SHELXL-97.2. All non-hydrogen atoms were obtained from the difference Fourier map and subjected to anisotropic refinement by full-matrix least squares on F2. Hydrogen atoms were obtained geometrically and treated as riding on the parent atoms or were constrained in the locations during refinements. Test parameters and detailed experimental data are shown in the **Supplementary Material**.

Synthesis and Characterization

To the solution of 2,3-diethoxy naphthalene (2.6 g, 12 mmol) in CHCl_3 (150 mL) was added paraformaldehyde (0.36 g, 12

mmol). Boron trifluoride diethyl etherate (2.5 mL, 20 mmol) was then added to the reaction mixture. The mixture was stirred at 25°C for 1 h. Then the reaction was quenched by addition of 50 mL water. The organic phase was separated and washed with saturated aqueous NaHCO_3 , and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (eluent: 1/1, v/v, dichloromethane: petrol ether) to afford **Dimer** (21%), **Trimer** (9%), and **Tetramer** (15%), as white solids.

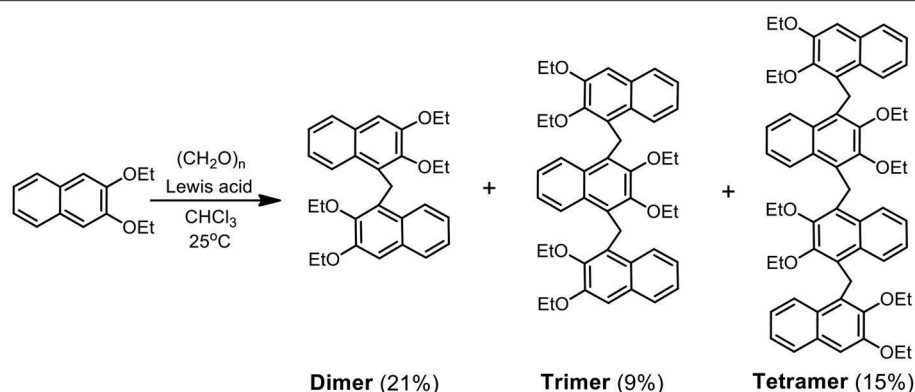
Dimer. m.p. $155-156^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3 , 298 K): δ (ppm): 8.10 (d, $J = 8.4$ Hz, 2H), 7.61 (d, $J = 7.7$ Hz, 2H), 7.28–7.24 (m, 2H), 7.23–7.20 (m, 2H), 7.07 (s, 2H), 5.00 (s, 2H), 4.22 (q, $J = 7.0$ Hz, 4H), 4.02 (q, $J = 7.0$ Hz, 4H), 1.57 (t, $J = 7.0$ Hz, 6H), 1.33 (t, $J = 7.0$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3 , 298 K): δ (ppm): 151.36, 146.37, 131.43, 129.97, 128.57, 126.80, 124.88, 124.65, 123.71, 106.85 (C of acyclic dimer), 69.11, 63.80 (C of methylene in ethoxy group), 23.55 (C of methylene bridge of acyclic dimer), 15.58, 14.86 (C of methyl in ethoxy group). HRMS (ESI): $\text{C}_{29}\text{H}_{32}\text{O}_4\text{NH}_4^+$, calcd m/z 462.2644; found m/z 462.2641.

Trimer. m.p. $171-172^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3 , 298 K): δ (ppm): 8.17 (d, $J = 8.6$ Hz, 2H), 8.04 (dd, $J = 6.5, 3.3$ Hz, 2H), 7.57 (d, $J = 7.8$ Hz, 2H), 7.23 (dd, $J = 11.0, 4.0$ Hz, 2H), 7.14–7.09 (m, 4H), 7.01 (s, 2H), 4.93 (s, 4H), 4.20–4.11 (m, 8H), 3.87 (q, $J = 7.0$ Hz, 4H), 1.51 (t, $J = 7.0$ Hz, 6H), 1.35 (t, $J = 7.0$ Hz, 6H), 1.13 (t, $J = 7.0$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3 , 298 K): δ (ppm): 151.37, 148.98, 146.30, 131.42, 130.70, 130.15, 128.93, 128.49, 126.81, 125.16, 124.90, 124.53, 124.39, 123.24, 106.78 (C of acyclic trimer), 69.21, 69.10, 63.79 (C of methylene in ethoxy group), 23.37 (C of methylene bridge of acyclic trimer), 15.77, 15.43, 14.84, 14.22 (C of methyl in ethoxy group). HRMS (ESI): $\text{C}_{44}\text{H}_{48}\text{O}_6\text{NH}_4^+$, calcd m/z 690.3795; found m/z 690.3786.

Tetramer. m.p. $212-213^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3 , 298 K): δ (ppm): 8.19 (d, $J = 8.2$ Hz, 2H), 8.13 (d, $J = 8.5$ Hz, 2H), 8.02 (d, $J = 8.2$ Hz, 2H), 7.58 (d, $J = 8.0$ Hz, 2H), 7.23 (t, $J = 7.6$ Hz, 2H), 7.16–7.04 (m, 6H), 7.02 (s, 2H), 4.92 (s, 4H), 4.89 (s, 2H), 4.17 (q, $J = 7.0$ Hz, 4H), 4.13 (q, $J = 7.0$ Hz, 4H), 3.95 (q, $J = 7.0$ Hz, 4H), 3.88 (q, $J = 7.0$ Hz, 4H), 1.52 (t, $J = 6.9$ Hz, 6H), 1.33 (t, $J = 7.0$ Hz, 3H), 1.16 (t, $J = 7.0$ Hz, 6H), 1.05 (t, $J = 7.0$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3 , 298 K): δ (ppm): 151.36, 149.00, 148.89, 146.25, 131.42, 130.71, 130.66, 130.17, 129.29, 128.78, 128.46, 126.80, 125.21, 125.19, 124.91, 124.56, 124.29, 123.92, 123.18, 106.72 (C of acyclic tetramer), 69.25, 69.13, 69.08, 63.77 (C of methylene in ethoxy group), 23.34 (C of methylene bridge of acyclic tetramer), 15.78, 15.48, 15.46, 14.85 (C of methyl in ethoxy group). HRMS (ESI): $\text{C}_{59}\text{H}_{64}\text{O}_8\text{NH}_4^+$, calcd m/z 918.4945; found m/z 918.4922.

RESULTS AND DISCUSSION

2,3-Diethoxy naphthalene was selected as the building block to condense with paraformaldehyde. Due to the electron-donating ethoxy groups, great regioselectivity can be rationalized, and the reactive sites should be 1- and 4-positions in Friedel–Crafts reaction. It was expected to produce pillar-shape macrocycles, pillar[n]naphthalenes. However, no cyclic oligomers have been obtained after many attempts; a possible reason is that big



SCHEME 2 | Synthesis of acyclic pillar[n]naphthalenes **Dimer**, **Trimer**, and **Tetramer**.

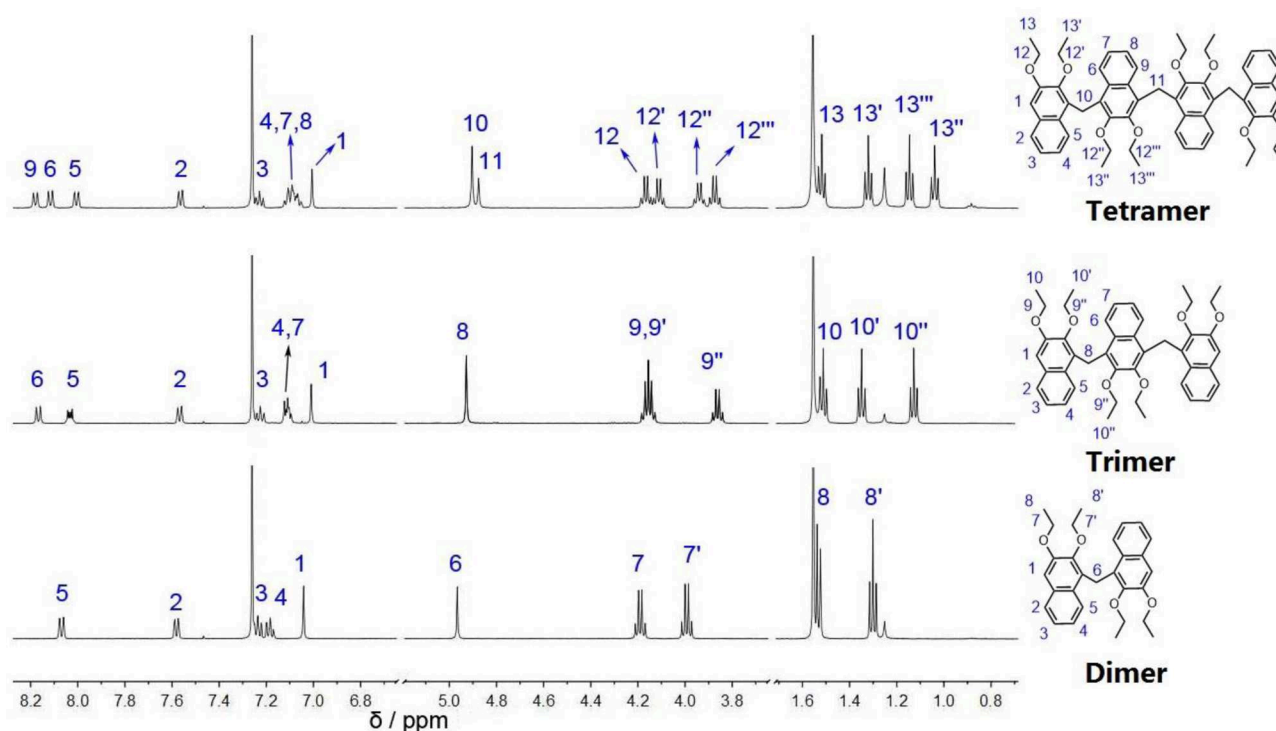


FIGURE 1 | ^1H NMR spectra (500 MHz, 2.0 mM, CDCl_3) of **Dimer**, **Trimer**, and **Tetramer**.

naphthalene units make the final cyclization quite difficult due to the steric hindrance. Fortunately, we got acyclic pillar[n]naphthalenes ($n = 2-4$).

Using $\text{BF}_3 \cdot (\text{Et})_2\text{O}$ as the catalyst, the condensation reaction of 2,3-diethoxy naphthalene and paraformaldehyde in CHCl_3 at room temperature (Scheme 2) produced oligomers **Dimer**, **Trimer**, and **Tetramer** with yields of 21, 9, and 15%, respectively. Other Lewis acid catalysts, for example TfOH , FeCl_3 , and AlCl_3 , could also work, but the reaction yields were lower than that for $\text{BF}_3 \cdot (\text{Et})_2\text{O}$. The synthesis was considerably easy since it just involved a one-step reaction of commercial starting materials

and the isolation was also convenient by column chromatography on silica gel.

Dimer, **Trimer**, and **Tetramer** were well characterized by ^1H NMR, ^{13}C NMR, NOESY, and COSY spectra (Figure 1 and Supplementary Figures 1–11), and high-resolution mass spectrometry (HRMS). They have rather complex patterns of aromatic and ethoxy peaks in ^1H NMR spectra (Figure 1) because they are not highly symmetrical macrocycles, but acyclic oligomers with low symmetry.

Single crystals of **Dimer**, **Trimer**, and **Tetramer** suitable for X-ray analysis were obtained by diffusion of hexane into a solution

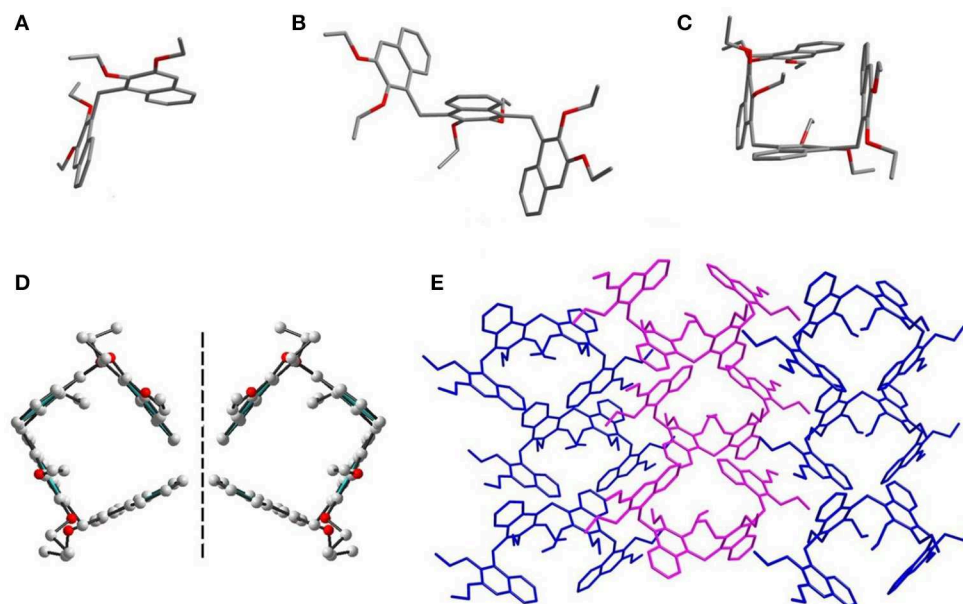


FIGURE 2 | Crystal structures of **Dimer (A)**, **Trimer (B)**, and **Tetramer (C)**. **(D)** A pair of enantiomers of **Tetramer**. **(E)** Packing mode of **Tetramer**.

of the compounds in dichloromethane at room temperature (**Figure 2**). As expected, these three acyclic oligomers had the same connecting style, i.e., 2,3-diethoxy naphthalene units were connected by methylene at 1,4-positions. As shown in **Figures 2A,B**, the acyclic **Dimer** and **Trimer**, possessing two and three naphthalene moieties, have ill-defined cavities. Particularly, the **Tetramer** exhibits a pseudocycle-shaped structure, with all the methylene bridges being orientated outwardly. There exist intramolecular sextuple C–H \cdots π interactions, with H \cdots ring center distances of 2.75–3.23 Å (**Supplementary Figure 12**), between the middle two ethoxy groups and naphthalenes, resulting in the formation of a pseudo cycle rather than a zigzag structure. More interestingly, the single crystal structures of **Tetramer** molecules exist in a pair of enantiomers in the solid state (**Figure 2D**).

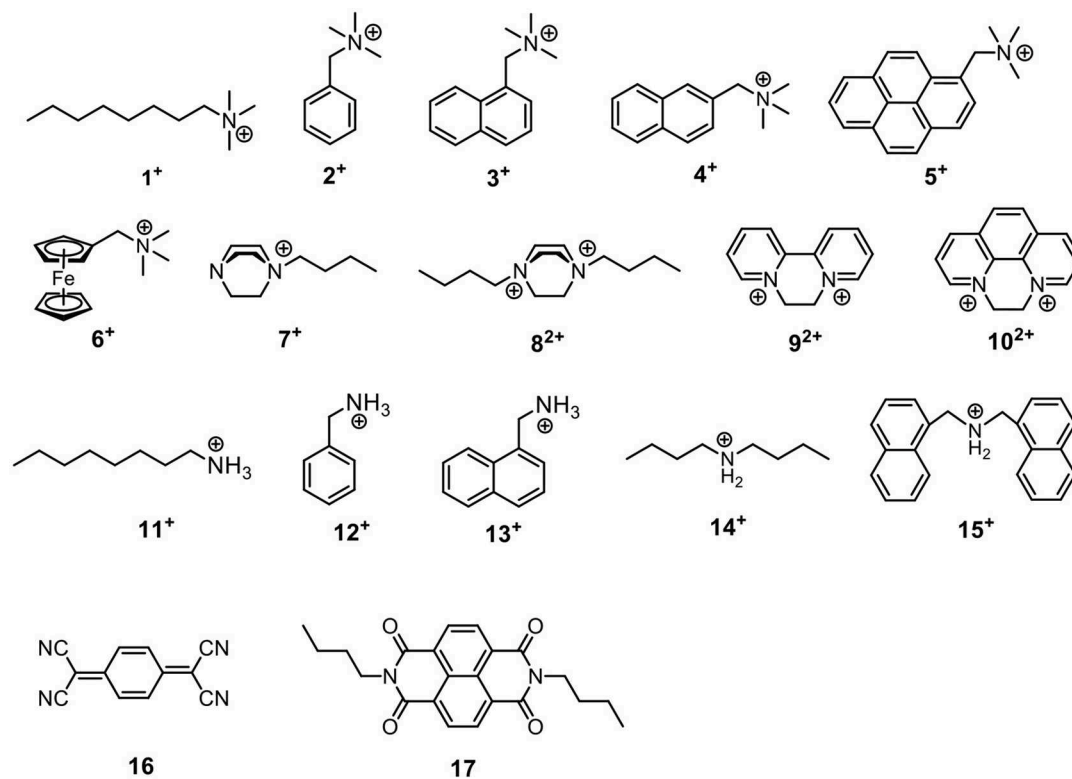
The host-guest properties of the acyclic receptors were then tested. Since they possess π -rich cavities, several cationic guests (**1**⁺–**15**⁺) and electron-deficient neutral guests (**16**–**17**) (**Scheme 3**) were chosen as model guest molecules to investigate their host-guest chemistry. In most cases, CDCl₃ was used as solvent during the ¹H NMR experiments of host-guest mixture and following NMR titrations; for guests **7**²⁺, **9**²⁺, and **10**²⁺, CD₂Cl₂ was used because of their poor solubility in CDCl₃.

Figure 3 shows the ¹H NMR spectra recorded for quarternary ammonium guest **1**⁺ in the absence and presence of **Tetramer**. As can be readily seen, upon addition of **Tetramer**, protons H_a, H_b, and H_c of **1**⁺ display substantial upfield shifts ($\Delta\delta = -0.39$, -0.29 , and -0.21 ppm) due to complexation-induced shielding effects, indicating that **1**⁺ was located inside the acyclic host's pseudo-cavity to form a host-guest inclusion complex, and the main binding site is the N⁺(Me)₃ moiety. In contrast, protons H_{n-i} undergo indistinct NMR changes, suggesting

they are located outside the cavity of **Tetramer**. [24] In the NOESY spectrum of **1**⁺ and **Tetramer**, NOE correlations were observed between methyl protons H_a of the guest and the aromatic protons H₅, H₇ and H₈ of **Tetramer**, also suggesting the host-guest encapsulation (**Supplementary Figure 13**). The formation of **1**⁺•**Tetramer** complex was further supported by ESI mass spectrometry analysis of an equimolar mixture of **1**•BArF and **Tetramer**, where an intense peak for the 1:1 complex (m/z 1072.66, calcd. for **1**⁺•**Tetramer** = 1072.67) was observed (**Supplementary Figure 14**). The encapsulation could also be rationalized by energy-minimized molecular modeling (**Figure 3D**): the oligomers wrapped around the guest to enhance the host-guest contacts driven by cation \cdots π /C–H \cdots π interactions.

The addition of **Dimer** and **Trimer** could also induce the upfield shifts of guest **1**⁺, but the $\Delta\delta$ values are smaller than those for **Tetramer** (**Supplementary Figure 15**). These results indicated relatively weak binding interactions occurred for **Dimer** and **Trimer** in comparison with **Tetramer**. These observations were consistent with the association constants (K_a) obtained from ¹H NMR titration experiments. As shown in **Table 1**, the K_a value of **1**⁺ with **Tetramer** [$(4.4 \pm 0.6) \times 10^2 \text{ M}^{-1}$] is 18 times larger than that for **Trimer**, and the affinity for **Dimer** was too small to be accurately calculated ($< 5 \text{ M}^{-1}$).

Since **Tetramer** showed interesting structure and good recognition behavior, we then examined its binding capacity toward other cationic guests (**Table 1** and **Supplementary Figures 16–29**), revealing that **Tetramer** can form host-guest complexes with them but the binding affinities are totally different. For the trimethyl ammonium guests **1**⁺–**6**⁺, **3**⁺ [$K_a = (1.2 \pm 0.2) \times 10^3 \text{ M}^{-1}$] and **4**⁺ [$K_a =$



SCHEME 3 | Structures of guest molecules. The counter anions of **1⁺**–**15⁺** are tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (BArF^-).

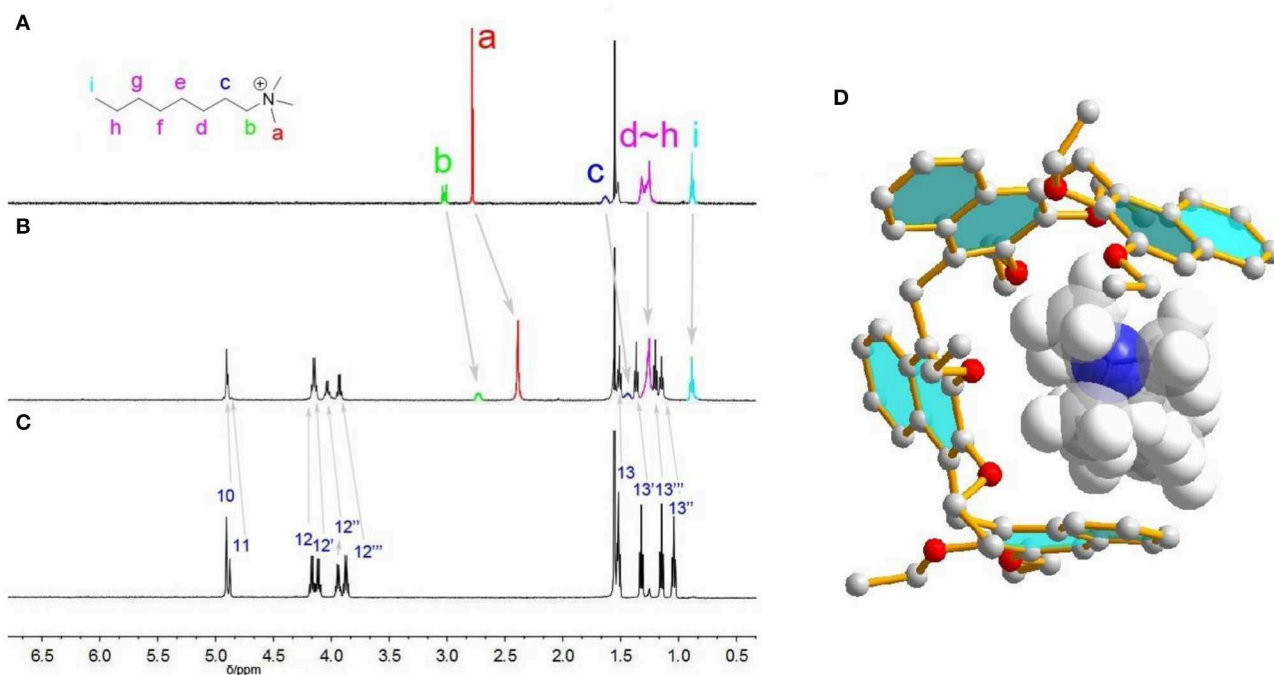


FIGURE 3 | ^1H NMR spectra (CDCl_3 , 298 K, 1.0 mmol) of (A) guest **1⁺**, (B) **1⁺** and **Tetramer** (1:1 mixture), (C) **Tetramer**. (D) Energy-minimized structures of **1⁺•Tetramer** at the semiempirical PM6 level of theory.

TABLE 1 | Association constants (M^{-1}) of **Dimer**, **Trimer**, and **Tetramer** with different guests (500 MHz, 298 K).

Guest	Host	Solvent	K_a (M^{-1}) ^a
1 ⁺	Dimer	CDCl ₃	— ^b
1 ⁺	Trimer	CDCl ₃	25±7
1 ⁺	Tetramer	CDCl ₃	$(4.4 \pm 0.6) \times 10^2$
2 ⁺	Tetramer	CDCl ₃	$(2.9 \pm 0.4) \times 10^2$
3 ⁺	Tetramer	CDCl ₃	$(1.2 \pm 0.2) \times 10^3$
4 ⁺	Tetramer	CDCl ₃	$(2.1 \pm 0.4) \times 10^3$
5 ⁺	Tetramer	CDCl ₃	$(1.6 \pm 0.2) \times 10^2$
6 ⁺	Tetramer	CDCl ₃	$(1.8 \pm 0.2) \times 10^2$
7 ²⁺	Tetramer	CDCl ₃	$(2.0 \pm 0.1) \times 10^2$
8 ⁺	Tetramer	CD ₂ Cl ₂	$(1.4 \pm 0.1) \times 10^2$
9 ²⁺	Tetramer	CD ₂ Cl ₂	$(1.2 \pm 0.2) \times 10^2$
10 ²⁺	Tetramer	CD ₂ Cl ₂	$(1.7 \pm 0.3) \times 10^2$
11 ⁺	Tetramer	CDCl ₃	$(2.5 \pm 0.4) \times 10^4$
12 ⁺	Tetramer	CDCl ₃	$(4.3 \pm 0.3) \times 10^3$
13 ⁺	Tetramer	CDCl ₃	$(1.4 \pm 0.1) \times 10^4$
14 ⁺	Tetramer	CDCl ₃	$(1.4 \pm 0.2) \times 10^3$
15 ⁺	Tetramer	CDCl ₃	$(3.0 \pm 0.3) \times 10^2$
16–17	Tetramer	CDCl ₃	— ^c

^aThe K_a values were determined by NMR titrations (Supplementary Figure 30).

^bThe K_a value was too small ($<5 M^{-1}$) to be accurately calculated.

^cNo interactions were found (Supplementary Figures 28, 29).

$(2.1 \pm 0.4) \times 10^3 M^{-1}$] bearing naphthyl moieties give stronger affinities, which should be due to host-guest fitted $\pi \cdots \pi$ interactions and large contacts. The substitution of naphthyl for smaller phenyl or bigger pyrenyl in **3⁺** and **4⁺**, affording **1⁺** or **5⁺**, considerably decreases the association constants by one order of magnitude.

Binding affinities of **Tetramer** toward primary ammonium guests **11⁺**–**13⁺** were stronger than those of the corresponding quaternary ammonium guests **1⁺**–**3⁺**. For example, the K_a value of **Tetramer** and octylammonium **11⁺** [$(2.5 \pm 0.4) \times 10^4 M^{-1}$] is about 56-fold higher than that for trimethyloctylammonium **1⁺** [$(4.4 \pm 0.6) \times 10^2 M^{-1}$]. Similarly, the selectivity factors of **12⁺**/**2⁺** and **13⁺**/**2⁺** are 15 and 12, respectively. The reason for such high selectivity would be that big and spherical $N^+(Me)_3$ group is too larger compared with **Tetramer**'s size, and small NH_3^+ is a suitable one. It should be noted that the binding affinities of **Tetramer** and organic ammonium salts, with K_a values in the magnitude of 10^2 – $10^4 M^{-1}$, are

REFERENCES

- AlHujran, T. A., Dawe, L. N., and Georgiou, P. E. (2012). Synthesis of functionalized acenaphthenes and a new class of homooxacalixarenes. *Org. Lett.* 14, 3530–3533. doi: 10.1021/ol301538s
- Alsaiee, A., Smith, B. J., Xiao, L., Ling, Y., Helbling, D. E., and Dichtel, W. R. (2016). Rapid removal of organic micropollutants from water by a porous β -cyclodextrin polymer. *Nature* 529, 190–194. doi: 10.1038/nature16185
- Andreotti, G. D., Boehmer, V., Jordon, J. G., Tabatabai, M., Ugozzoli, F., Vogt, W., et al. (1993). Dissymmetric calix [4] arenes with C4- and C2-symmetry.

comparable to those for macrocyclic arenes such as pillararenes and biphenarenes.

Due to its π -electron rich cavity, the complexation of **Tetramer** and two π -deficient neutral guests, **16** and **17**, were also investigated. From Supplementary Figures 28, 29, no obvious NMR changes were detected, indicating no stable complexes can be formed.

CONCLUSIONS

In summary, acyclic pillarnaphthalenes with 2,3-diethoxynaphthalene units bridged by methylenes at 1,4-positions were synthesized through a one-pot reaction of 2,3-diethoxy naphthalene monomer and paraformaldehyde by using Lewis acid as the catalyst. Acyclic pillar[4]naphthalene **Tetramer** is able to interact organic ammonium guests cations by wrapping around them, giving association constants in the magnitude of 10^2 – $10^4 M^{-1}$. We expect that **Tetramer** bearing pseudo-cycle cavity, could have significant potential for the applications in host-guest chemistry and self-assembly.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/Supplementary Material.

AUTHOR CONTRIBUTIONS

CL, BW, and YJ conceived this project and designed the experiments. YJ and MD contributed to most of the experimental work. CL, MD, and BW co-wrote the paper. All authors discussed and commented on the paper and analyzed the data.

FUNDING

This work was supported by the National Natural Science Foundation of China (21772118 and 21472122), the Shanghai Pujiang Program (16PJ0024), and the Shuguang Program.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fchem.2019.00828/full#supplementary-material>

- Synthesis, X-ray structures, conformational fixation, and proton NMR spectroscopic studies. *J. Org. Chem.* 58, 4023–4032. doi: 10.1021/jo00067a040
- Avetta, C. T., Shorthill, B. J., Ren, C., and Glass, T. E. (2012). Molecular tubes for lipid sensing: tube conformations control analyte selectivity and fluorescent response. *J. Org. Chem.* 77, 851–857. doi: 10.1021/jo201791a
- Baldini, L., Casnati, A., Sansone, F., and Ungaro, R. (2007). Calixarene-based multivalent ligands. *Chem. Soc. Rev.* 36, 254–266. doi: 10.1039/B603082N
- Bier, D., Rose, R., Bravo-Rodriguez, K., Bartel, M., Ramirez-Anguila, J. M., Dutt, S., et al. (2013). Molecular tweezers modulate 14-3-3 protein–protein interactions. *Nat. Chem.* 5, 234–239. doi: 10.1038/nchem.1570

- Chen, H., Fan, J., Hu, X., Ma, J., Wang, S., Li, J., et al. (2015). Biphen[n]arenes. *Chem. Sci.* 6, 197–202. doi: 10.1039/C4SC02422B
- Chen, J., Ni, H., Meng, Z., Wang, J., Huang, X., Dong, Y., et al. (2019). Supramolecular trap for catching polyamines in cells as an anti-tumor strategy. *Nat. Commun.* 10:3546. doi: 10.1038/s41467-019-11553-7
- Chun, Y., Singh, N. J., Hwang, I. C., Lee, J. W., Yu, S. U., and Kim, K. S. (2013). Calix [n] imidazolium as a new class of positively charged homo-calix compounds. *Nat. Commun.* 4:1797. doi: 10.1038/ncomms2758
- Cram, D. J. (1988). The design of molecular hosts, guests, and their complexes. *Science* 240, 760–767. doi: 10.1126/science.3283937
- Dai, L., Ding, Z. J., Cui, L., Li, J., Jia, X., and Li, C. (2017). 2, 2'-Biphen[n]arenes (n = 4–8): one-step, high-yield synthesis, and host-guest properties. *Chem. Commun.* 53, 12096–12099. doi: 10.1039/C7CC06767D
- Gong, H. Y., Rambo, B. M., Karnas, E., Lynch, V. M., and Sessler, J. L. (2010). A "Texas-sized" molecular box that forms an anion-induced supramolecular necklace. *Nat. Chem.* 2, 406–409. doi: 10.1038/nchem.597
- Goodman, C. M., Choi, S., Shandler, S., and DeGrado, W. F. (2007). Foldamers as versatile frameworks for the design and evolution of function. *Nat. Chem. Biol.* 3, 252–262. doi: 10.1038/nchembio876
- Guo, D. S., and Liu, Y. (2012). Calixarene-based supramolecular polymerization in solution. *Chem. Soc. Rev.* 41, 5907–5921. doi: 10.1039/C2CS35075K
- Guo, S., Song, Y., He, Y., Hu, X. Y., and Wang, L. (2018). Highly efficient artificial light-harvesting systems constructed in aqueous solution based on supramolecular self-assembly. *Angew. Chem. Int. Ed.* 57, 3163–3167. doi: 10.1002/anie.201800175
- Jie, K., Zhou, Y., Li, E., and Huang, F. (2018). Nonporous adaptive crystals of pillararenes. *Acc. Chem. Res.* 51, 2064–2072. doi: 10.1021/acs.accounts.8b00255
- Jono, K., Suzuki, A., Akita, M., Albrecht, K., Yamamoto, K., and Yoshizawa, M. (2017). A polyaromatic molecular clip that enables the binding of planar, tubular, and dendritic compounds. *Angew. Chem. Int. Ed.* 129, 3570–3574. doi: 10.1002/anie.201612489
- Juríček, M., Strutt, N. L., Barnes, J. C., Butterfield, A. M., Dale, E. J., Baldrige, K. K., et al. (2014). Induced-fit catalysis of corannulene bowl-to-bowl inversion. *Nat. Chem.* 6, 222–228. doi: 10.1038/nchem.1842
- Lehn, J. M. (1988). Supramolecular chemistry—scope and perspectives molecules, supermolecules, and molecular devices (Nobel Lecture). *Angew. Chem. Int. Ed.* 27, 89–112. doi: 10.1002/anie.198800891
- Li, B., Meng, Z., Li, Q., Huang, X., Kang, Z., Dong, H., et al. (2017). A pH responsive complexation-based drug delivery system for oxaliplatin. *Chem. Sci.* 8, 4458–4464. doi: 10.1039/c7sc01438d
- Li, B., Wang, B., Huang, X., Dai, L., Cui, L., Li, J., et al. (2019). Terphen[n]arenes and quaterphen[n]arenes (n = 3–6): one-pot synthesis, self-assembly into supramolecular gels, and iodine capture. *Angew. Chem. Int. Ed.* 58, 3885–3889. doi: 10.1002/anie.201813972
- Liu, Y., Zhao, W., Chen, C. H., and Flood, A. H. (2019). Chloride capture using a C–H hydrogen bonding cage. *Science* 365, 159–161. doi: 10.1126/science.aaw5145
- Luo, J., Ao, Y. F., Wang, Q. Q., and Wang, D. X. (2018). Diversity-oriented construction and interconversion of multicavity supermacrocycles for cooperative anion- π binding. *Angew. Chem. Int. Ed.* 57, 15827–15831. doi: 10.1002/anie.201810836
- Ma, D., Hettiarachchi, G., Nguyen, D., Zhang, B., Wittenberg, J. B., Zavalij, P. Y., et al. (2012). Acyclic cucurbit [n] uril molecular containers enhance the solubility and bioactivity of poorly soluble pharmaceuticals. *Nat. Chem.* 4, 503–510. doi: 10.1038/nchem.1326
- Ma, Y. L., Ke, H., Valkonen, A., Rissanen, K., and Jiang, W. (2018). Achieving strong positive cooperativity through activating weak non-covalent interactions. *Angew. Chem. Int. Ed.* 57, 709–713. doi: 10.1002/anie.201711077
- Ogoshi, T., Kanai, S., Fujinami, S., Yamagishi, T. A., and Nakamoto, Y. (2008). para-Bridged symmetrical pillar [5] arenes: their Lewis acid catalyzed synthesis and host-guest property. *J. Am. Chem. Soc.* 130, 5022–5023. doi: 10.1021/ja711260m
- Pan, S. J., Ye, G., Jia, F., He, Z., Ke, H., Yao, H., et al. (2017). Regioselective synthesis of methylene-bridged naphthalene oligomers and their host-guest chemistry. *J. Org. Chem.* 82, 9570–9575. doi: 10.1021/acs.joc.7b01579
- Pedersen, C. J. (1988). The discovery of crown ethers. *Science* 241, 536–540. doi: 10.1126/science.241.4865.536
- Poh, B. L., Lim, C. S., and Khoo, K. S. (1989). A water-soluble cyclic tetramer from reacting chromotropic acid with formaldehyde. *Tetrahedron Lett.* 30, 1005–1008. doi: 10.1016/S0040-4039(00)95302-4
- Schrader, T., Bitan, G., and Klärner, F. G. (2016). Molecular tweezers for lysine and arginine—powerful inhibitors of pathologic protein aggregation. *Chem. Commun.* 52, 11318–11334. doi: 10.1039/C6CC04640A
- Seebach, D., and Gardiner, J. (2008). β -peptidic peptidomimetics. *Acc. Chem. Res.* 41, 1366–1375. doi: 10.1021/ar700263g
- Shen, C., Ma, D., Meany, B., Isaacs, L., and Wang, Y. (2012). Acyclic cucurbit [n] uril molecular containers selectively solubilize single-walled carbon nanotubes in water. *J. Am. Chem. Soc.* 134, 7254–7257. doi: 10.1021/ja301462e
- Shorthill, B. J., Avetta, C. T., and Glass, T. E. (2004). Shape-selective sensing of lipids in aqueous solution by a designed fluorescent molecular tube. *J. Am. Chem. Soc.* 126, 12732–12733. doi: 10.1021/ja047639d
- Sinha, S., Lopes, D. H., Du, Z., Pang, E. S., Shanmugam, A., Lomakin, A., et al. (2011). Lysine-specific molecular tweezers are broad-spectrum inhibitors of assembly and toxicity of amyloid proteins. *J. Am. Chem. Soc.* 133, 16958–16969. doi: 10.1021/ja206279b
- Song, N., and Yang, Y. W. (2015). Molecular and supramolecular switches on mesoporous silica nanoparticles. *Chem. Soc. Rev.* 44, 3474–3504. doi: 10.1039/C5CS00243E
- Wang, M. X. (2018). Coronarenes: recent advances and perspectives on macrocyclic and supramolecular chemistry. *Sci. China Chem.* 61, 993–1003. doi: 10.1007/s11426-018-9328-8
- Wang, Y., Liu, T., Jiang, J., Chen, Y., Cen, M., Lu, D., et al. (2019a). Syntheses of water-soluble acyclic naphthalene oligomers and their applications in water. *Dalton Trans.* 48, 6333–6336. doi: 10.1039/C9DT00709A
- Wang, Y., Ping, G., and Li, C. (2016). Efficient complexation between pillar [5] arenes and neutral guests: from host-guest chemistry to functional materials. *Chem. Commun.* 52, 9858–9872. doi: 10.1039/C6CC03999E
- Wang, Y., Xu, K., Li, B., Cui, L., Li, J., Jia, X., et al. (2019b). Efficient separation of cis- and trans-1, 2-dichloroethene isomers by adaptive biphen[3]arene crystals. *Angew. Chem. Int. Ed.* 58, 10281–10284. doi: 10.1002/anie.201905563
- Xue, M. I. N., Yang, Y., Chi, X., Zhang, Z., and Huang, F. (2012). Pillararenes, a new class of macrocycles for supramolecular chemistry. *Acc. Chem. Res.* 45, 1294–1308. doi: 10.1021/ar2003418
- Yang, B., Zhang, X. D., Li, J., Tian, J., Wu, Y. P., Yu, F. X., et al. (2019). *In situ* loading and delivery of short single- and double-stranded dna by supramolecular organic frameworks. *CCS Chem.* 1, 156–165. doi: 10.31635/ccschem.019.20180011
- Yang, K., Pei, Y., Wen, J., and Pei, Z. (2016). Recent advances in pillar [n] arenes: synthesis and applications based on host-guest interactions. *Chem. Commun.* 52, 9316–9326. doi: 10.1039/C6CC03641D
- Yashima, E., Ousaka, N., Taura, D., Shimomura, K., Ikai, T., and Maeda, K. (2016). Supramolecular helical systems: helical assemblies of small molecules, foldamers, and polymers with chiral amplification and their functions. *Chem. Rev.* 116, 13752–13990. doi: 10.1021/acs.chemrev.6b00354
- Zhang, D. W., Zhao, X., Hou, J. L., and Li, Z. T. (2012). Aromatic amide foldamers: structures, properties, and functions. *Chem. Rev.* 112, 5271–5316. doi: 10.1021/cr300116k
- Zhang, G. W., Li, P. F., Meng, Z., Wang, H. X., Han, Y., and Chen, C. F. (2016). Triptycene-based chiral macrocyclic hosts for highly enantioselective recognition of chiral guests containing a trimethylamino group. *Angew. Chem. Int. Ed.* 55, 5304–5308. doi: 10.1002/anie.201600911

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Copyright © 2019 Jia, Dong, Wang and Li. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.