

Tribenzotriquinacene-Based Crown Ethers: Synthesis and Selective Complexation with Ammonium Salts

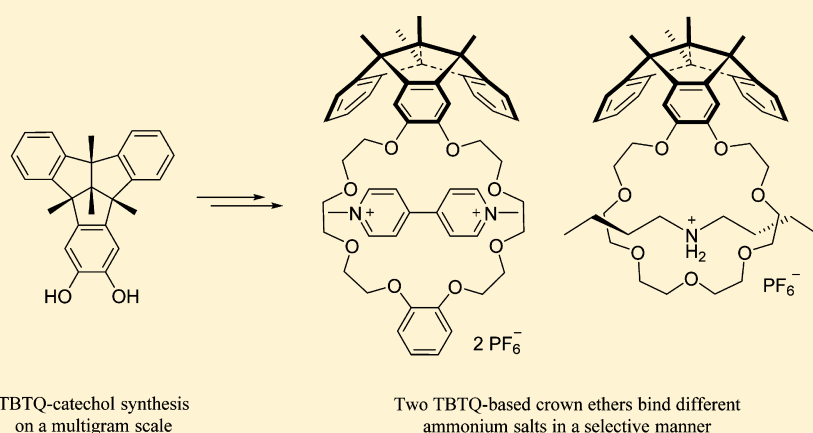
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S Supporting Information



ABSTRACT: Two tribenzotriquinacene-based crown ethers, TBTQ-dibenzo-24-crown-8 **5** and TBTQ-benzo-21-crown-7 **6**, were prepared from the key TBTQ intermediate, 2,3-dihydroxy-4b,8b,12b,12d-tetramethyltribenzotriquinacene (**13**), which in turn was synthesized in six steps using two variants of our cyclodehydration method on a multigram scale. The host–guest complexation properties of the TBTQ-based crown ethers **5** and **6** with a paraquat derivative, **16**, and two secondary ammonium salts, **17** and **18**, were studied by ¹H NMR spectroscopy and mass spectrometry. It was found that host **5** binds to the paraquat derivative **16** as a 1:1 complex in CDCl₃/CD₃CN solution with an association constant of $K_a = (9.2 \pm 1.8) \times 10^2 \text{ M}^{-1}$, whereas no complexation was found for **17** and **18**. In contrast, the TBTQ-crown ether **6** assembles selectively with dibutylammonium hexafluorophosphate **18** as a 1:1 complex in CDCl₃/CD₃COCD₃ [$K_a = (5.0 \pm 1.4) \times 10^2 \text{ M}^{-1}$], for which a threaded [2]pseudorotaxane structure is assumed.

INTRODUCTION

Bowl-shaped molecules or cavitands that can selectively bind guest molecules through specific noncovalent interactions are of great current interest in the field of supramolecular chemistry.^{1–5} Crown ethers, in particular, have a long pedigree in supramolecular chemistry⁶ and still offer new applications in host–guest complexation chemistry. Recent research for new host motifs have focused on structurally rigid systems, such as cyclodextrins,⁷ pentyptycene **1**,⁸ calixarenes **2**,⁹ and pillararenes **3**,¹⁰ to recognize various guest molecules (Figure 1). We have been working on the chemistry of tribenzotriquinacenes (TBTQs) over the last two decades because of their unique structural and reactivity properties. The molecular framework of TBTQ forms a conformationally rigid, C_{3v}-symmetrical, bowl-shaped structural motif consisting of three mutually fused indane units.^{11,12} The concave molecular surface was found to exert a strongly negative

electrostatic potential which makes it a promising core skeleton for receptors of C₆₀.^{13–15} However, TBTQ-based crown ethers in host–guest recognition have not been explored yet. Combinations of the crown ether and the TBTQ motifs with their individual electron-rich cavities may conceivably offer new opportunities to construct interesting structures that may lead to applications for the selective binding of guest molecules. *N,N'*-Dialkyl-4,4'-bipyridinium salts have been widely used as guests to generate various complexes with crown ethers and secondary dialkylammonium ions were found to form 1:1 threaded structures with dibenzo-24-crown-8 (DB24C8) or benzo-21-crown-7 (B21C7).^{16–21} Therefore, we expected that the TBTQ-based hosts **5** and **6** could also assemble with suitable ammonium guest ions.

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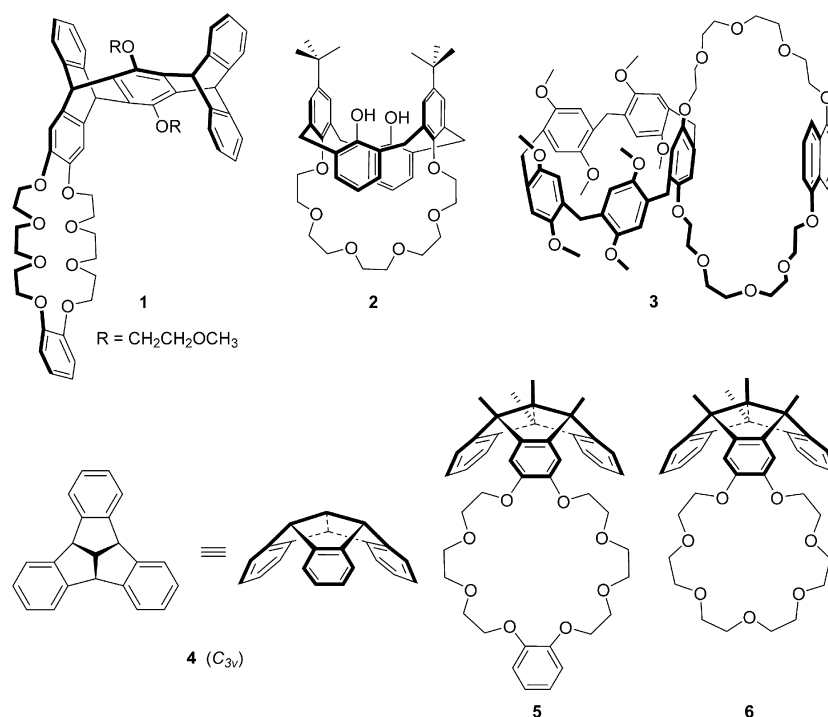
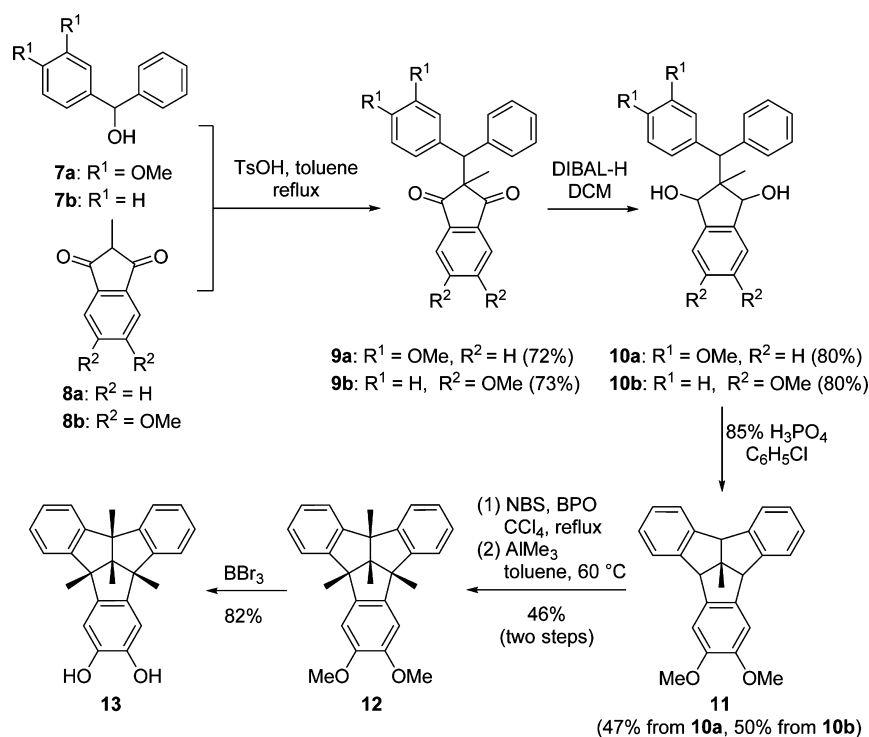


Figure 1. Structures of structurally rigid crown ether hosts: pentiptycene-derived crown ether **1**,⁸ calix[4]arene-derived crown ether **2**,⁹ pillar[5]arene-derived crown ether **3**,¹⁰ and the new crown ethers **5** and **6** based on a tribenzotriquinacene (TBTQ, **4**) core described in this work.

Scheme 1. Synthesis of TBTQ-catechol **13** by Two Complementary Variants of the Classical Two-Fold Cyclodehydration Route



Recently, we demonstrated that TBTQ-based *ortho*-benzoquinones undergo a number of useful conversions, including the facile reduction to the corresponding TBTQ-catechol **13** in various ways.²² In the present study, we disclose the synthesis of TBTQ-catechol **13** by starting from synthons that carry methoxyl substituents at the outer

peripheral positions of one of the aromatic rings. In this way, we show that the TBTQ bowl can be merged with the crown ether units of dibenzo-24-crown-8 (DB24C8) and benzo-21-crown-7 (B21C7). On this basis, we performed an investigation on the binding behavior of the TBTQ-based host species **5** and **6** and found that they underwent selective

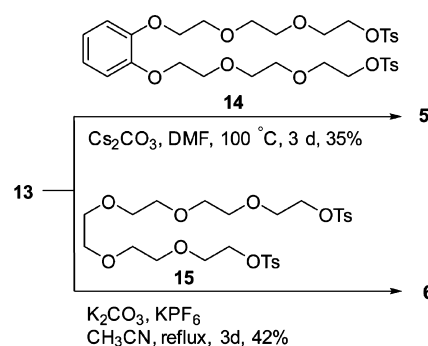
complexation with different kinds of ammonium cations as guests.

RESULTS AND DISCUSSION

Our original strategy²³ to synthesize hexamethoxy-TBTQ derivatives had been employed by McKeown et al. to generate hexa- and tetrahydroxy-TBTQ-based polymers.²⁴ Here we applied the same strategy to the synthesis of the corresponding 2,3-difunctionalized TBTQ congeners **11** and **13** (Scheme 1). Diketones **9a** and **9b** were obtained in virtually the same yields (72–73%) by reaction of 3,4-dimethoxybenzhydrol (**7a**) with 2-methyl-1,3-indanedione (**8a**),²⁵ or of diphenylmethanol (**7b**) with 5,6-dimethoxy-2-methyl-1,3-indanedione (**8b**)²⁴ in refluxing toluene, respectively, in the presence of *para*-toluenesulfonic acid. The diketones **9** were then reduced with diisobutylaluminum hydride (DIBAL-H) in dichloromethane (DCM) to yield the indane-1,3-diols **10** in high yield (80%). Whereas reduction of diketone **9a** afforded diol **10a** as a mixture of the diastereomers, reduction of diketone **9b** furnished only one single, *C_s*-symmetrical diastereomer, which was determined to be the all-*cis*-indane-1,3-diol **10b**, as revealed by ¹H and ¹³C NMR spectroscopy and X-ray diffraction analysis [Supporting Information (SI), Figure S13]. Orthophosphoric acid (85%) was employed as a catalyst for the 2-fold cyclodehydration of the benzhydrylindanedioles **10**, carried out in refluxing chlorobenzene. Tribenzotriquinacene **11** was obtained in satisfactory yield (47% from **10a** and 50% from **10b**) on a six-gram scale. The remarkably high yield in the 2-fold cyclodehydration step parallels the increased yields found with other veratrole-type TBTQ derivatives^{23,24} and may be traced to the higher reactivity and/or higher stability of the electron-rich intermediates of the intramolecular Friedel–Crafts reaction.²³ The structure of compound **11** was unambiguously confirmed by X-ray diffraction analysis of a crystal obtained from ethyl acetate/petroleum ether (SI, Figure S14). The cyclodehydration product **11** was converted to the corresponding bridgehead-tetramethyl derivative **12** by use of *N*-bromosuccinimide (NBS, 4.0 equiv),^{23,26} followed by quenching of the crude bridgehead tribromo intermediate with trimethylaluminum in toluene, which furnished **12** in 46% yield over two steps. Finally, compound **12** was readily demethylated by use of boron tribromide to give the target TBTQ-catechol **13** in 82% yield. All synthesized compounds were fully characterized by ¹H and ¹³C NMR spectroscopy and mass spectrometry. The main advantage of this route, as compared to the recently published one,²² is the reduced number of synthetic steps, enabling a facile synthesis of TBTQ-catechol **13** on a multigram scale.

The facile synthesis of TBTQ-catechol **13** provided us with the opportunity to prepare the target TBTQ-based crown ethers. Reaction of catechol **13** with ditosylate **14**¹⁶ under high dilution conditions in the presence of cesium carbonate in dimethylformamide (DMF) at 100 °C for 3 days afforded the macrocyclic host **5** in moderate yield (35%, Scheme 2). Reaction of catechol **13** with hexaethylene glycol ditosylate **15**¹⁷ in the presence of potassium carbonate and potassium hexafluorophosphate in acetonitrile at reflux temperature under argon for 3 days afforded the TBTQ-based macrocyclic host **6** in 42% yield. The structure of both crown ether hosts **5** and **6** were again characterized by ¹H and ¹³C NMR spectroscopy and mass spectrometry. In addition, the

Scheme 2. Synthesis of the TBTQ-dibenzo-24-crown-8 Host **5** and the TBTQ-benzo-21-crown-7 Host **6**



structure of compound **6** was further confirmed by X-ray diffraction analysis (Figure 2).

With these first TBTQ-based crown ethers in hand, complexation between host **5** and the guests **16**–**18** were studied in solution by ¹H NMR spectroscopic titrations (Scheme 3). The paraquat derivative **16** and the secondary ammonium salts **17** and **18** were synthesized according to literature procedures.^{16–21} The host **5** (2.0 mM) and the respective guest (1.0 equiv) were mixed in a CDCl₃/CD₃CN (1:1, v/v) solution and the shifts of the characteristic peaks were noted (Figure 3 and SI, Figures S1, S5, and S6). As shown in Figure 3b, the ¹H NMR spectrum of a 1:1 mixture of **5** and **16** showed only one set of signals that were different from those of the separated host and guest, suggesting that a new complex **5**·**16** was formed and that the complexation between **5** and **16** is a fast exchange process, in analogy to that found for other DB24C8-based complexes.^{8,16} The resonances of the aromatic protons H^a and H^b of guest **16** were shifted significantly upfield, which is attributed to the strong shielding effect of the aromatic rings of **5**. Electrospray ionization (ESI) mass spectra of the complex **5**·**16** corroborated the 1:1 stoichiometry of the complex (SI, Figure S2). The spectrum exhibited a peak for the fragment ion [**5**·**16** – PF₆]⁺ at *m/z* 1037.3, and that of the sodium adduct ion of the host, [**5** + Na]⁺, at *m/z* 729.2, among many other signals. The stoichiometry of the complex was also determined to be 1:1 by Job Plot (SI, Figure S4), and the association constant (*K_a*) for the complexation **5**·**16** was found to be (9.2 ± 1.8) × 10² M⁻¹ in CDCl₃/CD₃CN (1:1, v/v) at 22 °C, based on the 1:1 binding model as described by Thordarson (SI, Figure S3).^{27,28} This value slightly exceeds the association constant of the analogous triptycene-derived crown ether **1**·**16** (*K_a* = 4.5 × 10² M⁻¹).⁸ Thus, TBTQ-dibenzo-24-crown-8 host **5** proved to be a strong host for the paraquat derivative **16**. In contrast to guest **16**, the ammonium hexafluorophosphate salts **17** and **18** did not undergo complexation with **5**. The ¹H NMR spectra of mixtures of **5** with **17** or **18** in CDCl₃/CD₃CN (1:1, v/v) did not exhibit any chemical shift changes and/or signal doubling (SI, Figures S5–S6). Based on ¹H NMR spectroscopic evidence, it appears that **17** and **18** cannot thread into the cavity of the TBTQ-dibenzo-24-crown-8 host **5**. This observation is in stark contrast to earlier reports on DB24C8.²¹ Thus, host **5** selectively recognizes guest **16**, which may be attributed to spatial obstruction by the concave surface of the TBTQ bowl and to the intramolecular π–π interactions between the remote benzene ring of the polyether moiety and the TBTQ skeleton, which should increase the

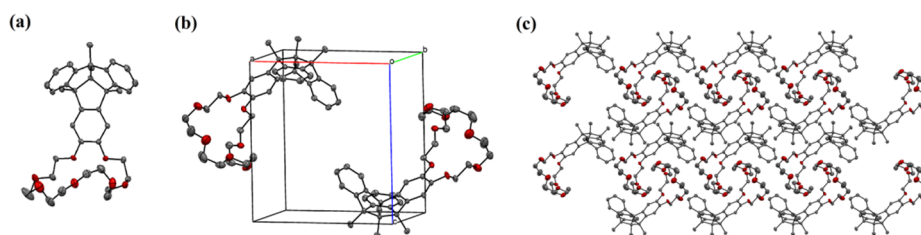
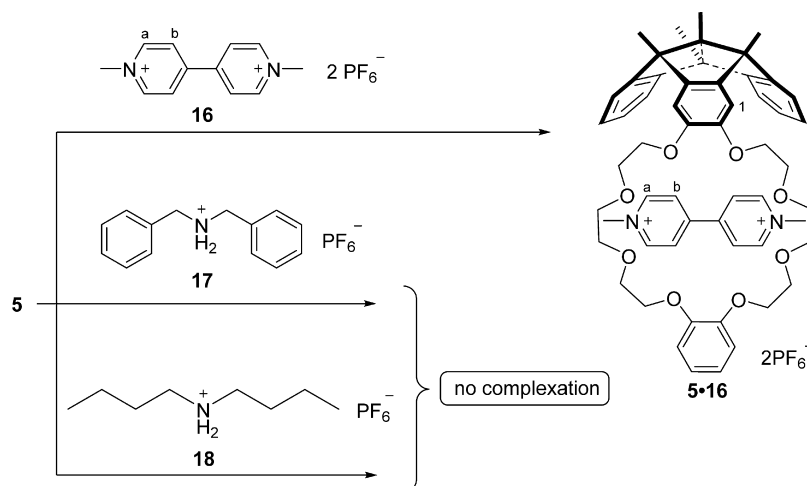


Figure 2. Molecular and crystal structures of compound **6** (ORTEP diagrams), as obtained with crystals grown from hexane/dichloromethane. (a) View onto the concave surface of the TBTQ bowl; (b) crystallographic cell unit and (c) molecular packing viewed along the *b* axis. Ellipsoids are shown at 30% probability level; hydrogen atoms are omitted for clarity.

Scheme 3. TBTQ-dibenzo-24-crown-8 Host **5** Associates with Guest **16** but not with Secondary Ammonium Ions **17** and **18**^a



^a2.0 mM each in a solution of CDCl₃/CD₃CN (1:1, v/v).

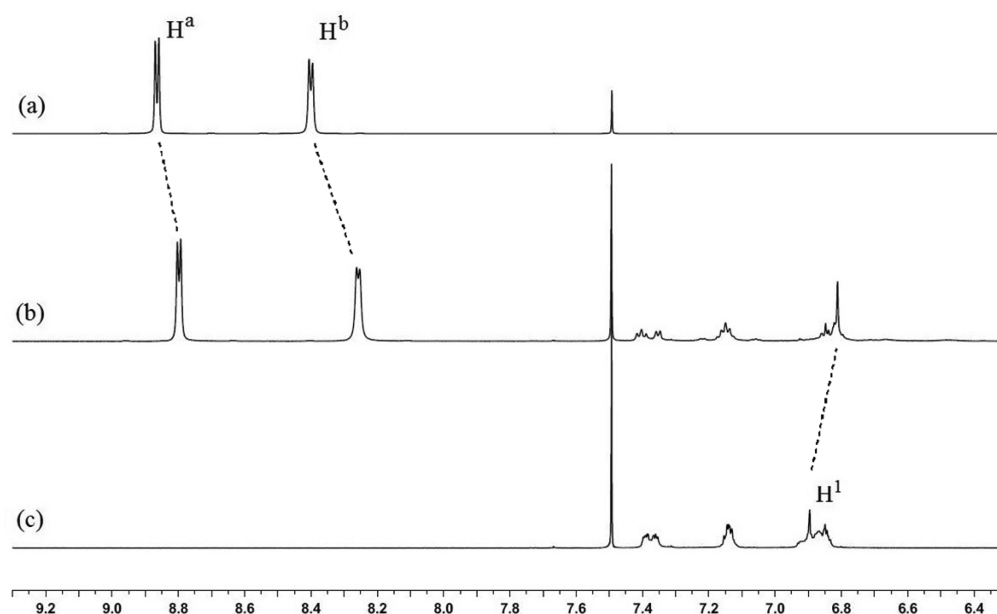
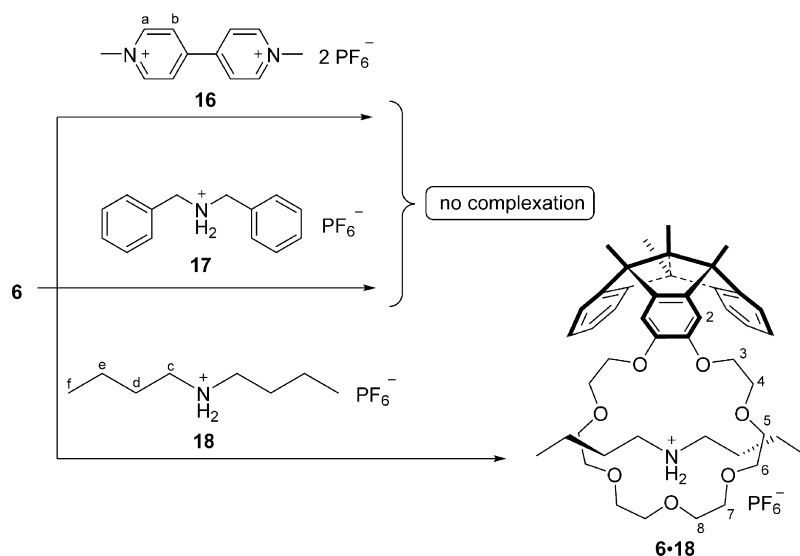


Figure 3. Partial ¹H NMR spectra [600 MHz, 22 °C, CDCl₃/CD₃CN (1:1, v/v)] of (a) guest **16** (2.0 mM), (b) a mixture of host **5**, and 1.0 equiv of **16** ($[S]_0 = 2.0$ mM), and (c) host **5** (2.0 mM).

tortuosity of the macrocyclic polyether unit and thus shrink the size of the cavity.

Complexation between host **6** and the guests **16**, **17**, and **18** were also studied by ¹H NMR spectroscopy (Scheme 4). Equimolar amounts of compounds **6** and **18** were dissolved in the solvent mixture of CDCl₃/CD₃COCD₃ (1:1, v/v). The

¹H NMR spectrum (Figure 4) showed two sets of peaks that belonged to the complexed and to the uncomplexed species, respectively, suggesting the formation of a new complex, **6**·**18**. In this case, in contrast to the complex **5**·**16**, the association between **6** and **18** is a slow-exchange process on the ¹H NMR

Scheme 4. TBTQ-benzo-21-crown-7 Host **6** Associates with the Secondary Ammonium Salt **18**, but not with Guests **16** or **17**^a

^a2.0 mM each in a solution of CDCl₃/CD₃COCD₃ (1:1, v/v).

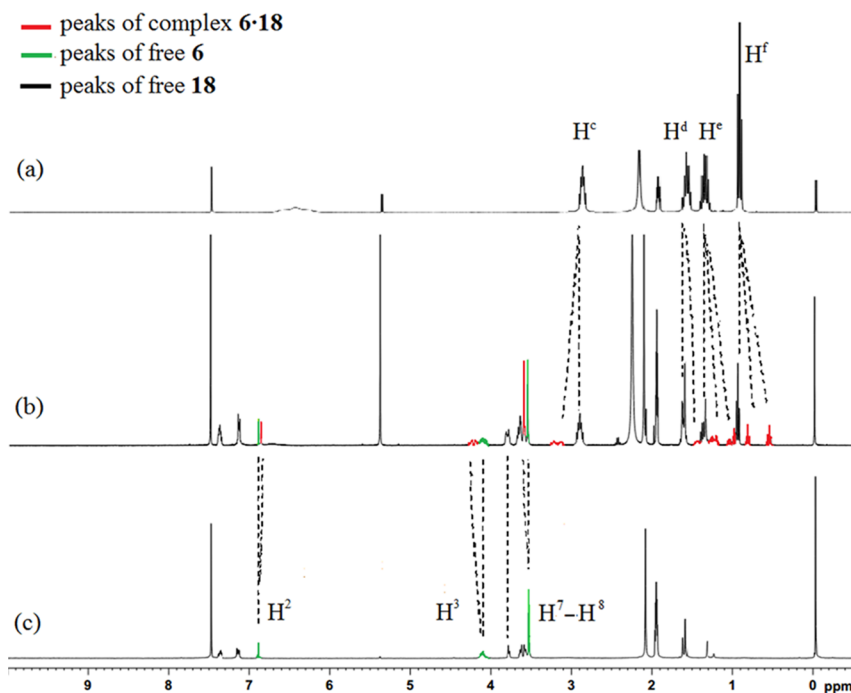


Figure 4. ¹H NMR spectra [400 MHz, 22 °C, CDCl₃/CD₃COCD₃ (1:1, v/v)] of (a) guest **18** (2.0 mM), (b) a mixture of host **6** and 1.0 equiv of **18** ([**6**]₀ = 2.0 mM), and (c) host **6** (2.0 mM).

time scale, similar to the behavior found for other B21C7-based complexes.¹⁷ This implies a threading of **18** through the cavity of **6** to form a [2]pseudorotaxane. By integration of the corresponding peaks, the stoichiometry of complexation system was determined to be 1:1 (SI, Figure S7). The association constant for the complexation of **6·18** was determined to be $K_a = (5.0 \pm 1.4) \times 10^2 \text{ M}^{-1}$ in CDCl₃/CD₃COCD₃ (1:1, v/v) at 22 °C (SI, Figure S7). ESI mass spectrometry of a solution of equimolar amounts of **6** and **18** again corroborates the 1:1 stoichiometry (SI, Figure S8). A mass fragment of [**6·18** - PF₆]⁺ (m/z 744.4) was found, together with the adduct ion [**6** + Na]⁺ (m/z 637.3). In

contrast to these results, the ¹H NMR spectra of mixtures of **6** with the paraquat **16** or the dibenzylammonium salt **17** in a solution of CDCl₃/CD₃CN (1:1, v/v) or CD₃COCD₃ showed neither chemical shift changes nor signal doubling (SI, Figures S9–S11). These findings parallel the previous study on B21C7, in which the lack of complexation was ascribed to the insufficient size of the cavity of B21C7 to accommodate the aromatic rings of the hosts.¹⁷

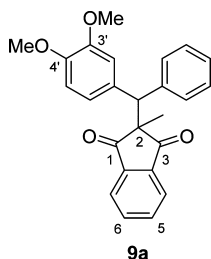
CONCLUSION

In summary, two new TBTQ-based crown ether hosts, the TBTQ-dibenzo-24-crown-8 **5** and the TBTQ-benzo-21-crown-

7 **6**, were synthesized based on the TBTQ-catechol **13**, for which two alternative synthesis approaches were developed. Furthermore, we proved that the new TBTQ hosts can undergo selective complexation with ammonium salts: The paraquat derivative **16** binds to the cavity of host **5**, whereas dibutylammonium hexafluorophosphate (**18**) can thread into the cavity of host **6**. In both cases, stable 1:1 complexes were formed in solution. The formation of these complexes was supported by ^1H NMR spectroscopy and ESI mass spectrometry. The association constants (K_a) of the complexes **5**·**16** and **6**·**18** were also determined. The development of further supramolecular systems that combine the convex-concave topography of the TBTQ bowl with other molecular host systems and the investigation of their properties is underway in our laboratories.

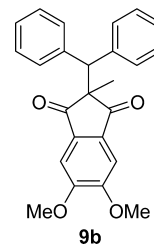
EXPERIMENTAL SECTION

General Information. All reactions that required anhydrous conditions were carried out by standard procedures under argon atmosphere. The solvents were dried by distillation over appropriate drying reagents. Petroleum ether used had a boiling range of 60–90 °C. Reactions were monitored by TLC on silica gel GF 254 plates. Column chromatography was performed through silica gel (200–300 mesh). ^1H and ^{13}C NMR spectra were recorded on either a 300, 400, or 600 MHz spectrometer, as were the DEPT 135 experiments. Chemical shift values are given in ppm and coupling constants (J) in Hz. Residual solvent signals in the ^1H and ^{13}C NMR spectra were used as an internal reference (CDCl_3 : $\delta_{\text{H}} = 7.26$, $\delta_{\text{C}} = 77.0$ ppm, $[\text{D}_6]\text{acetone}$: $\delta_{\text{H}} = 2.05$ ppm, CD_3CN : $\delta_{\text{H}} = 1.94$ ppm). Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet). Melting points were determined by use of a microscope apparatus and are uncorrected. Mass spectra were obtained using electrospray ionization (ESI) on a 4G or a microTOF mass spectrometer. Single crystal X-ray diffraction measurements were performed with a diffractometer working with graphite monochromated Mo $K\alpha$ or Cu $K\alpha$ radiation. All reagents and solvents were used as supplied. Compounds **7a**,²⁴ **8a**,²⁵ **8b**,²⁴ **14**,⁸ **15**,¹⁷ **16**,⁸ **17**,²¹ and **18**^{17,21} were synthesized as previously reported.

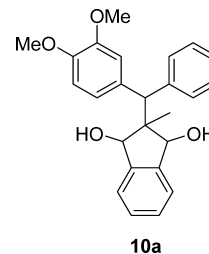


2-[(3,4-Dimethoxyphenyl)phenylmethyl]-2-methyl-1H-indene-1,3(2H)-dione (9a). A mixture of benzhydrol **7a** (7.68 g, 31.48 mmol), dione **8a** (4.99 g, 31.19 mmol), and *para*-toluenesulfonic acid monohydrate (401 mg, 2.11 mmol) in toluene (50 mL) was heated to reflux for 24 h in a flask equipped with a Dean–Stark trap. The mixture was cooled to room temperature, washed with saturated aqueous K_2CO_3 (15 mL), and extracted with dichloromethane (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 8:1, $R_f = 0.4$) afforded dione **9a** as a yellowish solid (8.70 g, 72%): mp 84–86 °C; ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ 7.80–7.78 (m, 2H), 7.69–7.64 (m, 2H), 7.46 (d, $^3J_{(\text{H,H})} = 7.2$ Hz, 2H), 7.18–7.12 (m, 3H), 7.07 (t, $^3J_{(\text{H,H})} = 7.2$ Hz, 1H), 6.94 (dd, $^4J_{(\text{H,H})} = 8.0$, 2.0 Hz, 1H), 6.65 (d, $^3J_{(\text{H,H})} = 8.4$ Hz, 1H), 4.54 (s, 1H), 3.82 (s, 3H), 3.74 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , 25 °C): δ 204.3 (C), 204.2 (C), 148.3 (C), 147.5 (C), 141.32 (C), 141.28 (C), 139.9 (C), 135.44 (CH), 135.43 (CH), 132.3 (C), 129.4 (CH), 128.2 (CH), 126.6 (CH), 122.9 (CH),

121.9 (CH), 112.8 (CH), 110.7 (CH), 58.2 (C), 57.3 (CH), 55.6 (OCH₃), 55.5 (OCH₃), 19.8 (CH₃), one Ar–CH resonance was not resolved; accurate mass (ESI-ToF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{25}\text{H}_{22}\text{O}_4\text{Na}$ 409.1410; found: 409.1421.

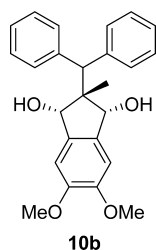


2-Benzhydryl-5,6-dimethoxy-2-methyl-1H-indene-1,3(2H)-dione (9b). The preparation procedure was the same as that used for compound **9a**. Starting from benzhydrol (**7b**, 4.21 g, 22.88 mmol), dione **8b** (4.99 g, 22.68 mmol), and *para*-toluenesulfonic acid monohydrate (401 mg, 2.11 mmol) dione **9b** was obtained as a colorless solid (6.40 g, 73%): TLC: petroleum ether/ethyl acetate 8:1 $R_f = 0.5$; mp 86–88 °C; ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ 7.47 (d, $^3J_{(\text{H,H})} = 7.2$ Hz, 4H), 7.19–7.15 (m, 6H), 7.09 (t, $^3J_{(\text{H,H})} = 7.2$ Hz, 2H), 4.56 (s, 1H), 3.96 (s, 6H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , 25 °C) δ 202.9 (C), 155.8 (C), 140.0 (C), 136.4 (C), 129.7 (CH), 128.2 (CH), 126.6 (CH), 103.0 (CH), 57.7 (CH), 56.5 (OCH₃), 20.2 (CH₃), one aliphatic C resonance was not resolved; accurate mass (ESI-ToF) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{25}\text{H}_{23}\text{O}_4$ 387.1591; found 387.1600.



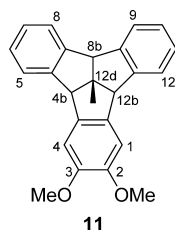
2-[(3,4-Dimethoxyphenyl)phenylmethyl]-2-methyl-2,3-dihydro-1H-indene-1,3-diol (10a, Mixture of Two Diastereomers). A solution of diisobutylaluminum hydride (65 mL, 1 M in cyclohexane, 65 mmol) was added dropwise to a stirred solution of dione **9a** (10.00 g, 25.91 mmol) in dichloromethane (175 mL) at 0 °C under argon atmosphere. The mixture was stirred at 20 °C for another 24 h. The reaction was carefully quenched with water (100 mL). The precipitated solid was collected by suction filtration and washed repeatedly with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 1:1, $R_f = 0.4$) afforded a mixture of diastereomeric diols **10a** as a colorless oil (8.08 g, 80%): ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ 7.63 (d, $^3J_{(\text{H,H})} = 7.6$ Hz, 1H), 7.57 (dd, $^3J_{(\text{H,H})} = 8.0$, 1.4 Hz, 1H), 7.44–7.42 (m, 3H), 7.35–7.06 (m, 6H), 6.90–6.83 (m, 1H), 5.46 and 5.16 (two s, total 1H), 4.82, 4.73, and 4.55 (three d, $^3J_{(\text{H,H})} = 7.6$ Hz, $^3J_{(\text{H,H})} = 15.2$ Hz, $^3J_{(\text{H,H})} = 15.6$ Hz, 2H), 3.88, 3.87, 3.863, and 3.859 (four s, total 6H), 1.88 (br, 1H), 1.42 (s, 1H), 1.09, 1.08, and 0.84 (three s, total 3H); ^{13}C NMR (100 MHz, CDCl_3 , 25 °C): δ 148.9, 148.1, 147.6, 144.8, 144.6, 144.24, 144.16, 142.6, 142.2, 142.0, 141.1, 141.0, 135.0, 134.5, 134.3, 129.9, 129.8, 129.5, 129.1, 128.5, 128.4, 128.1, 126.4, 126.2, 125.1, 125.0, 124.6, 121.83, 121.75, 121.4, 113.7, 111.4, 111.1, 82.0, 81.7, 81.0, 80.9, 55.9, 55.8, 54.8, 54.5, 53.5, 48.4, 26.9, 20.5, 15.3, 15.2; accurate mass (ESI-ToF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{25}\text{H}_{26}\text{O}_4\text{Na}^+$ 413.1723; found 413.1733.

all-cis-2-Benzhydryl-5,6-dimethoxy-2-methyl-2,3-dihydro-1H-indene-1,3-diol (10b). The preparation procedure was the same as that used for compound **10a**. Starting from dione **9b** (10.00 g, 25.91 mmol) and diisobutylaluminum hydride (65 mL, 1.0 M in cyclohexane, 65 mmol) the product **10b** was obtained as a colorless



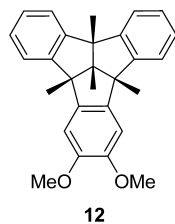
10b

solid (8.08 g, 80%): TLC: petroleum ether/ethyl acetate 1:1, $R_f = 0.5$; mp 204–206 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3 , 25 °C) δ 7.53 (d, $^3J_{(\text{H,H})} = 7.6$ Hz, 4H), 7.33 (t, $^3J_{(\text{H,H})} = 7.6$ Hz, 4H), 7.23 (t, $^3J_{(\text{H,H})} = 7.6$ Hz, 2H), 6.93 (s, 2H), 5.15 (s, 1H), 4.47 (d, $^3J_{(\text{H,H})} = 4.8$ Hz, 2H), 3.85 (s, 6H), 2.35 (d, $^3J_{(\text{H,H})} = 4.8$ Hz, 2H), 0.87 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , 25 °C): δ 149.9 (C), 141.9 (C), 136.7 (C), 129.9 (CH), 128.4 (CH), 126.3 (CH), 108.5 (CH), 81.9 (CH), 55.9 (OCH₃), 54.1 (C), 48.9 (CH), 20.8 (CH₃); accurate mass (ESI-ToF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{25}\text{H}_{26}\text{O}_4\text{Na}$ 413.1723; found: 413.1732.



11

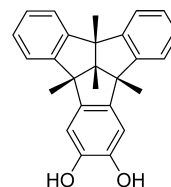
2,3-Dimethoxy-12d-methyl-4b,8b,12b,12d-tetrahydrodibenzo[2,3:4,5]pentaleno[1,6-ab]indene (11). A solution of the mixture of diols 10a (15.00 g, 38.46 mmol) or pure 10b (15.00 g, 38.46 mmol) prepared by gentle warming in chlorobenzene (200 mL) was added dropwise into a stirred solution of phosphoric acid (85%, 4 mL) in chlorobenzene (40 mL). After the addition was completed, the mixture was heated to reflux for 20 h. The reaction mixture was cooled to 25 °C and poured into water (40 mL). The organic layer was then washed with saturated aqueous NaHCO_3 and extracted with ethyl acetate (3×20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 10:1, $R_f = 0.5$) afforded the product 11 as a colorless amorphous solid (6.40 g, 47% from 10a, 6.80 g, 50% from 10b): mp 147–148 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3 , 25 °C) δ 7.43–7.37 (m, 4H), 7.19–7.12 (m, 4H), 6.89 (s, 2H), 4.42 (s, 1H), 4.37 (s, 2H), 3.84 (s, 6H), 1.64 (s, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3 , 25 °C) δ 149.2 (C), 145.5 (C), 145.3 (C), 136.9 (C), 127.3 (CH), 124.4 (CH), 124.1 (CH), 107.2 (CH), 63.4 (CH), 63.3 (CH), 61.5 (C), 56.0 (OCH₃), 27.4 (CH₃); one Ar–CH resonance was not resolved; accurate mass (ESI-ToF) m/z : $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{25}\text{H}_{22}\text{O}_2\text{Na}$ 377.1512; found: 377.1520.



12

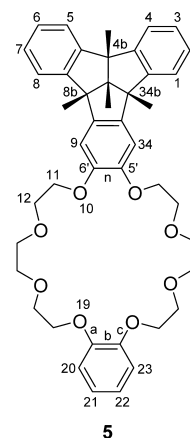
2,3-Dimethoxy-4b,8b,12b,12d-tetramethyl-4b,8b,12b,12d-tetrahydrodibenzo[2,3:4,5]pentaleno[1,6-ab]indene (12). A mixture of compound 11 (0.50 g, 1.41 mmol), *N*-bromosuccinimide (NBS, 1.00 g, 5.60 mmol) and benzoylperoxide (30 mg) was heated to reflux in CCl_4 (30 mL) under the irradiation of an infrared lamp (245 W) for 5 h. The precipitate formed was removed by suction filtration. The solution was concentrated under reduced pressure and the residue was redissolved in anhydrous benzene (50 mL). Then, a

solution of trimethylaluminum (2.80 mL, 2.0 M in toluene, 5.60 mmol) was added dropwise under argon. After the addition was complete, the mixture was heated to 50 °C for 8 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl and then extracted with dichloromethane (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 10:1, $R_f = 0.3$) afforded the product 12 as a colorless solid (257 mg, total yield from 11 to 12 was 46%): $^1\text{H NMR}$ (400 MHz, CDCl_3 , 25 °C) δ 7.39–7.37 (m, 2H), 7.33–7.31 (m, 2H), 7.17–7.15 (m, 4H), 6.82 (s, 2H), 3.86 (s, 6H), 1.66 (s, 3H), 1.64 (s, 6H), 1.35 (s, 3H). MS (ESI-ToF) m/z : $[\text{M}+\text{NH}_4]^+$ calcd for $\text{C}_{28}\text{H}_{32}\text{NO}_2$ 414.2; found: 414.2. The spectroscopy data were identical with those in the literature.²²



13

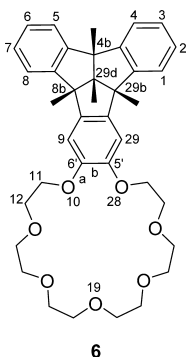
2,3-Dihydroxy-4b,8b,12b,12d-tetramethyl-4b,8b,12b,12d-tetrahydrodibenzo[2,3:4,5]pentaleno[1,6-ab]indene (13). Boron tribromide (5.90 mL, 63.70 mmol) was added dropwise to a stirred solution of 12 (5.00 g, 12.63 mmol) in dichloromethane (45 mL) at 0 °C under argon atmosphere. The reaction mixture was stirred for 10 h until the starting material was no longer detectable by TLC. The mixture was quenched with water (5 mL) and then extracted with dichloromethane (3×30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 5:1, $R_f = 0.2$) afforded 13 as a colorless amorphous solid (3.80 g, 82%): $^1\text{H NMR}$ (400 MHz, CDCl_3 , 25 °C) δ 7.37–7.35 (m, 2H), 7.27–7.23 (m, 2H), 7.15–7.13 (m, 4H), 6.77 (s, 2H), 4.98 (s, 2H), 1.63 (s, 3H), 1.57 (s, 6H), 1.31 (s, 3H); accurate mass (ESI-ToF) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{25}\text{O}_2$ 369.1849, found 369.1860. The data were identical with those in the literature.²²



5

4b,8b,34b,34d-Tetramethyl-4b,8b,11,12,14,15,17,18,25,26,28,29,31,32,34b,34d-hexadecahydrobenzo[b]dibenzo[2',3':4',5']pentaleno[1',6':1,2,3]indeno[5,6-n][1,4,7,10,13,16,19,22]octaoxacyclotetracosine (5). A suspension of cesium carbonate (195 mg, 600 μmol) in anhydrous DMF (30 mL) was stirred vigorously for 10 min and then heated to 100 °C under argon atmosphere. A solution of catechol 13 (50 mg, 136 μmol) and bistosylate 14 (93 mg, 136 μmol) in anhydrous DMF (20 mL) was added dropwise over 12 h to the mixture. The reaction mixture was stirred at 100 °C for another 3 d. After cooling down to 25 °C, the mixture was filtered and washed with dichloromethane (3×30 mL). The combined organic layers were washed several times with water and then washed

with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel ($\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ 100:1, $R_f = 0.3$) afforded the product crown ether **5** as a colorless oil (34 mg, 35%): ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ 7.37–7.36 (m, 2H), 7.36–7.28 (m, 2H), 7.15–7.13 (m, 4H), 6.90–6.83 (m, 6H), 4.11–4.10 (m, 8H), 3.90–3.55 (m, 16H), 1.64 (s, 3H), 1.60 (s, 6H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , 25 °C) δ 149.1 (C), 148.9 (C), 145.5 (C), 145.3 (C), 137.9 (C), 127.3 (CH), 124.4 (CH), 124.2 (CH), 121.3 (CH), 114.1 (CH), 110.2 (CH), 70.8 (CH_2), 70.0 (CH_2), 69.8 (CH_2), 69.7 (CH_2), 69.5 (CH_2), 69.0 (CH_2), 62.5 (C), 62.4 (C), 26.0 (CH_3), 25.7 (CH_3), 16.1 (CH_3), one Ar–CH and one aliphatic C resonances were not resolved; accurate mass (ESI-ToF) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{44}\text{H}_{50}\text{O}_8\text{Na}$ 729.3398; found 729.3400.



4b,8b,29b,29d-Tetramethyl-4b,8b,11,12,14,15,17,18,20,21,23,24-,26,27,29b,29d-hexadecahydrodibenzo[2',3':4',5']pentaleno-[1',6':1,2,3]indeno[5,6-b][1,4,7,10,13,16,19]heptaoxacycloheptacosine (6). A mixture of catechol **13** (50 mg, 136 μmol), potassium carbonate (58 mg, 420 μmol), potassium hexafluorophosphate (51 mg, 277 μmol), and bistosylate **15** (80 mg, 136 μmol) in acetonitrile (50 mL) was stirred and heated to reflux under argon atmosphere for 3 d. After cooling down to 25 °C, the mixture was filtered and washed with dichloromethane (40 mL). The filtrate was washed several times with water and then with brine, dried over Na_2SO_4 , and concentrated under reduced pressure. Flash column chromatography of the residue through silica gel (petroleum ether/ethyl acetate 1:1, $R_f = 0.2$) afforded crown ether **6** (35 mg, 42%) as a colorless solid: mp 320–322 °C; ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ 7.37–7.35 (m, 2H), 7.30–7.28 (m, 2H), 7.16–7.14 (m, 4H), 6.85 (s, 2H), 4.18–4.08 (m, 4H), 3.88–3.86 (m, 4H), 3.76–3.74 (m, 4H), 3.68–3.65 (m, 4H), 3.60 (s, 8H), 1.65 (s, 3H), 1.61 (s, 6H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , 25 °C) δ 149.3 (C), 148.9 (C), 148.8 (C), 141.4 (C), 127.5 (CH), 122.9 (CH), 122.7 (CH), 109.2 (CH), 71.03 (CH_2), 71.01 (CH_2), 70.98 (CH_2), 70.55 (CH_2), 70.0 (CH_2), 69.9 (C), 69.8 (CH_2), 62.54 (C), 62.45 (C), 26.0 (CH_3), 25.7 (CH_3), 16.1 (CH_3), one Ar–CH resonance was not resolved; accurate mass (ESI-ToF) m/z : $[\text{M} + \text{NH}_4]^+$ calcd for $\text{C}_{38}\text{H}_{50}\text{O}_7\text{N}$ 632.3582; found: 632.3587.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02326.

^1H and ^{13}C NMR spectra of all new compounds: **9a**, **9b**, **10a**, **10b**, **11**, **5**, and **6**; ^1H NMR spectroscopic titrations and ESI mass spectrum of complex **5**·**16**; and ^1H NMR spectrum and ESI mass spectrum of complex **6**·**18** (PDF)

X-ray crystallographic data for **6** (CIF)

X-ray crystallographic data for **10b** (CIF)

X-ray crystallographic data for **11** (CIF)

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Notes

The authors declare no competing financial interest.

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