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Functionalized O_6–Corona[6]arenes: Synthesis, Structure, and Fullerene Complexation Property

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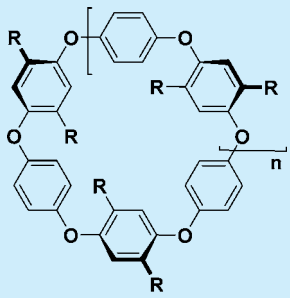
Supporting Information

ABSTRACT: The synthesis, structure, and fullerene complexation property of novel and functionalized O_n–corona[n]arenes were reported. Based on the fragment coupling strategy, ester-containing O_n–corona[n]arenes (n = 6, 8) were obtained readily starting from 1,4-hydroquinone and diethyl 2,5-difluoroterephthalate. Reduction of esters with $LiAlH_4$ produced almost quantitatively hydroxymethylated O_n–corona[n]arenes, which underwent etherification with MeI to afford methoxymethyl-substituted O_n–corona[n]arenes (n = 6, 8) in good yields. The macrocycles adopt unique corona-type conformation with a large cylindroid cavity. They are strong macrocyclic host molecules to form 1:1 complexes with fullerenes C_{60} and C_{70} in toluene with an associate constant up to $(1.59 \pm 0.04) \times 10^5$ M^{-1}.



n = 1, 2, 4
R = CO_2Et, CH_2OH, CH_2OMe

Synthetic macrocyclic receptors play an important role in supramolecular chemistry.[1] This has been manifested by the classic macrocyclic molecules such as crown ethers,[2] cryptands,[3] spherands,[4] cyclodextrin derivatives,[5] and calixarenes.[6] Since the beginning of new millennium, we have witnessed delightfully the emergence of a few novel and fascinating macrocycles such as heteracalixaromatics,[7,8] cycloparaphenylenes,[9] and pillararenes,[10] one after another. The aesthetic and privileged macrocycles provide powerful model systems in the study of the nature of various noncovalent bond interactions, molecular recognition, and self-assembly.[1−10] In addition, the functionalized macrocycles act as platforms for the fabrication of sophisticated (supra)molecular architectures, sensing systems, optoelectronic devices, and advanced materials.[11] Furthermore, the tailor-made macrocycles serve as molecular tools enabling the mechanistic study of organic reactions that involve unstable species.[12] Admittedly, however, despite a myriad of synthetic receptors, there are no universal ones in terms of application, as the function of a molecule is destined by its intrinsic structure.

We recently proposed a new class of macrocycles, namely, coronarenes.[13,14] They are composed of *para*-(het)arylenes and heteroatoms in an alternative fashion. It is envisioned that the combination of different heteroatoms with various (heterocyclic) aromatic rings would generate diverse corona[n](het)arenes of designed cylindroid cavities. Furthermore, the use of electron-rich and -deficient (het)arenes would result in corona[n](het)arenes featuring varied electronic properties. Most significantly, the heteroatoms would be unique variables, enabling the fine-regulation of macrocyclic conformation and cavity. For example, heteroatoms can adopt different electronic configuration and form various degrees of conjugation with their adjacent aromatic rings, giving rise to the variation of bond lengths and angles. We have successfully synthesized O_6–corona[3]arene[3]-tetrazines[13] and demonstrated their utility as electron-deficient macrocyclic receptors for anions based on anion–π interactions.[15] As a continuation of our endeavors, we report herein the facile construction and structure of unprecedented functionalized O_n–corona[n]arenes. The acquired electron-rich O_n–corona[n]arenes are powerful macrocyclic hosts to complex fullerenes C_{60} and C_{70} in 1:1 stoichiometry with an associate constant up to $(1.59 \pm 0.04) \times 10^5$ M^{-1}.

A literature survey reveals only two reports on oxygen-linked corona[n]arenes, then known as cyclic oligo(*p*-phenylene oxide)s. In 1984, Franke and Vögtle[16] observed the formation of a mixture of inseparable O_n–corona[n]arenes (n = 5–9) in about 2% yield from the reaction of *p*-bromophenol. The hitherto known examples of structurally well-defined O_n–corona[n]arenes (n = 6–10) were synthesized in very low overall yields by Osakada[17] in 2006 by means of stepwise preparation of linear oligo(*p*-phenylene oxide)s followed by cyclization through the CuI-catalyzed Ullmann coupling reaction. No application of products was investigated.

We commenced our study with the synthesis of the ester-substituted O_6–corona[6]arenes based on a fragment coupling strategy. Taking the advantage of reactivity of diethyl 2,5-difluoroterephthalate **2**, two directional nucleophilic aromatic substitution reactions of **2** with 1,4-hydroquinone **1** in 3:1 and 1:3 molar ratios led readily to the formation of trimers **3** and **4** in 60% and 44% yields, respectively (Figure 1). Having had linear trimers **3** and **4** in hand, we tried [3 + 3] (method A) macrocyclic condensation reactions. As we expected, the formation of O_6–corona[6]arenes was not trivial. After screening of the conditions

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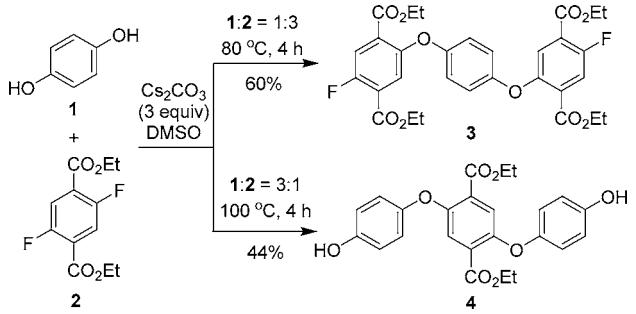
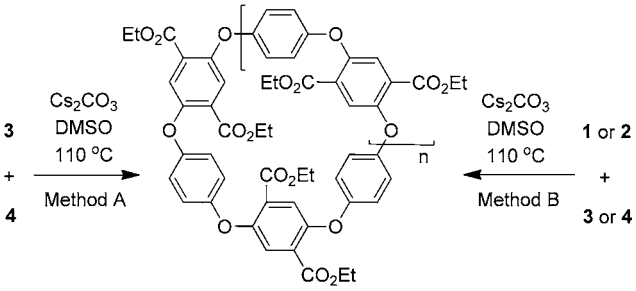


Figure 1. Preparation of fragments **3** and **4**.

Table 1. Synthesis of Ester-Containing O_n–corona[*n*]arenes 5–7



5, n = 1; **6**, n = 2; **7**, n = 4

entry	method	reactant	time (h)	**5** (%)	**6** (%)	**7** (%)
1	A	**3** + **4**	2	14		8
2	A	**3** + **4**	6	9	3	9
3	A	**3** + **4**	12		35	
4	B	**1** + **3**	3.5		28	
5	B	**2** + **4**	3.5		10	

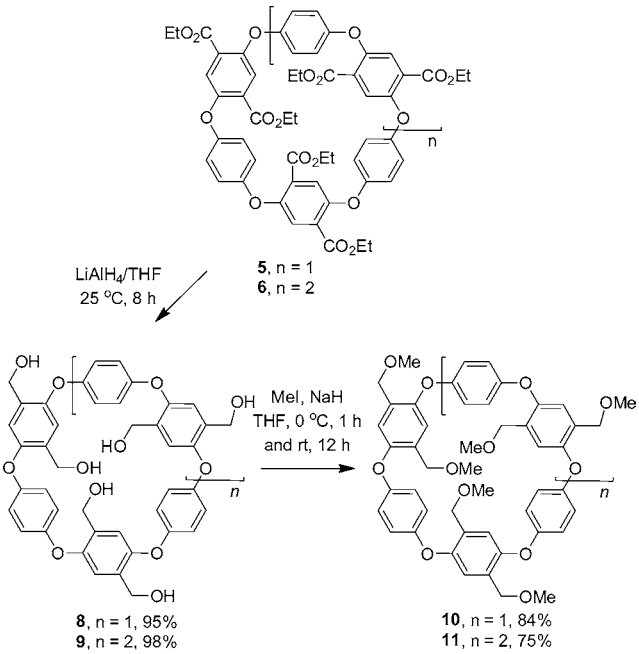


Figure 2. Synthesis of functionalized O_n–corona[*n*]arenes **8**–**11**.

(see Supporting Information), we found that, in the presence of Cs_2CO_3, the macrocyclic [3 + 3] fragment coupling reaction between **3** and **4** in hot DMSO in 2 h gave the desired O_6–corona[6]arene **5** in 14% yield (Table 1). A giant macrocyclic

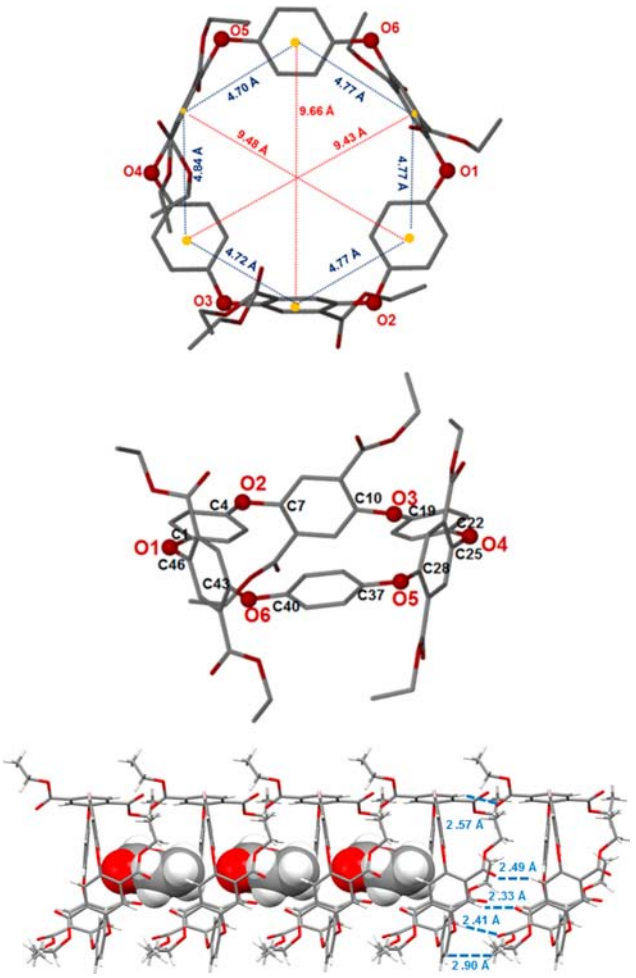


Figure 3. X-ray molecular structure of **5** with top (top) and side (middle) views. Hydrogen atoms and ethyl acetate solvent molecules are omitted for the clarity. Self-assembly of **5** forms a tubular structure (in a stick style) that complexes ethyl acetate molecules (in a space-filled style) in the solid state (bottom).

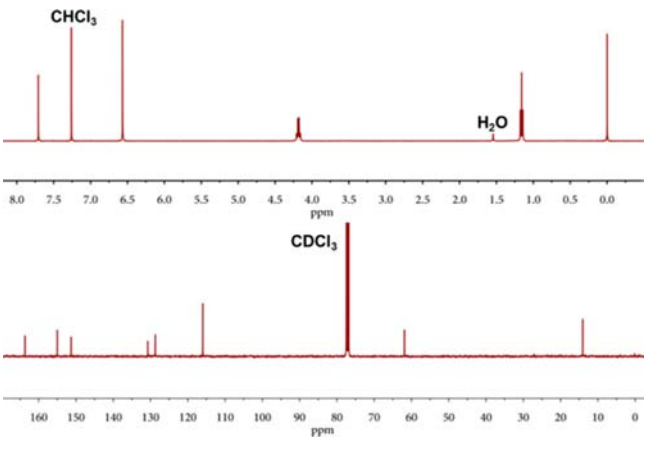


Figure 4. ^{1}H and ^{3}C NMR spectra of O_6–corona[6]arene **5**.

homologue O_{12}–corona[12]arene **7**, which was derived from two trimer **3** and two trimer **4**, was also isolated albeit in a low yield. Surprisingly, elongating the reaction time to 6 h led to the decrease of chemical yield of **5** along with the formation of O_8–corona[8]arene **6**. Gratifyingly, the reaction terminated in 12 h furnished the compound **6** as the only macrocyclic product in

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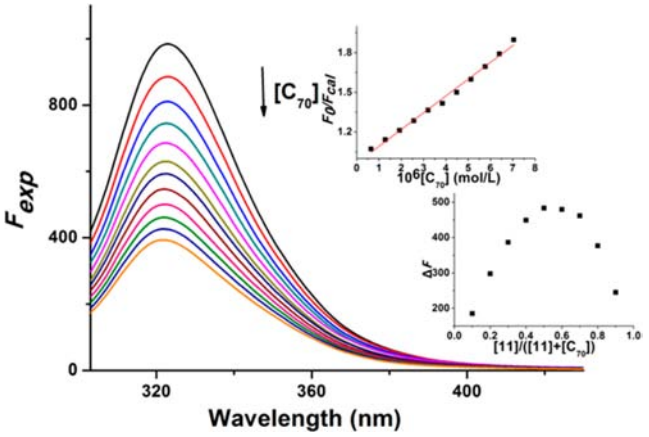

Figure 5. Fluorescence titration of **11** with C_{70} in toluene.

35%. The generation of O_8−corona[8]arene **6** from a one-pot [3 + 3] fragment coupling reaction between **3** and **4** indicates that the macrocyclic octamer is most probably a thermodynamically stable product. This was further supported by the [1 + 3] fragment coupling reactions (Method B) between **1** and **3** and between **2** and **4**, which afforded dominantly O_8−corona[8]-arene **6** in 28% and 10%, respectively. The reaction of **1** and **3** gave higher macrocyclization efficiency compared to that of **2** and **4**, suggesting the necessity to choose matched reaction partners. It may be worth addressing that the chemical yield of up to ca. 30% reflects the high efficiency of every C−O bond forming reaction as four C−O bonds were generated in the synthesis of **6** from the reaction of **1** and **3**.

The resulting O_n−corona[n]arenes are conceivably useful platforms for the construction of other functionalized macrocycles because of the versatility of an ester group in functional group transformations. To demonstrate their synthetic utility, their transformations into coroarenes, which are functionalized with hydroxy and ether groups, were conducted. As illustrated in Figure 2, treatment of **5** and **6** with $LiAlH_4$ led to the exhaustive reduction of six ester groups, producing the corresponding hydroxymethylated corona[n]arenes **8** and **9** in nearly quantitative yield. Further methylation with methyl iodide in the presence of sodium hydride furnished efficiently the production of methoxymethylated coronarenes **10** and **11**. To the best of our knowledge, all acquired ester-, hydroxy-, and ether-bearing macrocycles **5**−**11** are the first examples of functionalized oxygen-bridged coronarenes.[16,17]

All coronarenes obtained are colorless crystalline products. Diffusion of *n*-hexane into a solution of **5** in a mixture of chloroform and ethyl acetate afforded high quality single crystals, which permit the X-ray diffraction analysis. As shown in Figure 3, O_6−corona[6]arene **5** adopts a corona-type conformation with roughly a C_{3v} symmetry in the solid state. Notably, all bridging oxygen atoms form nearly a plane. While three *p*-phenylene rings are procumbent on the plane, three terephthalate components are nearly orthogonal to the plane, yielding a large hexagonal cavity. The average centroid distances between distal and proximal benzene rings are 9.51 and 4.76 Å, respectively. Interestingly, the multiple nonconventional hydrogen bonding and C−H/π interactions between molecules lead corona[6]-arenes to assemble into a unique hexagonal tubular structure in which ethyl acetate molecules are included. It should be noted that all functionalized corona[n]arenes (n = 6, 8, 12) gave very simple proton and carbon signals in ^{1}H and ^{13}C NMR spectra, respectively (Supporting Information). As depicted in Figure 4, for example, only one set of proton and carbon peaks corresponding to aromatic components and ester groups was observed at ambient temperature. It indicated the formation of highly symmetric structures in solution, or most likely the existence of a mixture of macrocyclic conformers, which undergo very rapid interconversions at ambient temperature relative to the NMR time scale. The conformational fluxionality of coron[n]arenes would offer great advantages in molecular recognition.

The large cylindroid-type cavities of acquired corona[n]arenes prompted us to explore their ability in fullerene recognition[18] based on the principle of complementarity. The titration of functionalized O_n−corona[n]arene hosts **5**, **6**, **10**, and **11** with a fullerene solution in toluene resulted in the gradual quench of fluorescence emission of the hosts. Evidenced by the fluorescence titration and Job's plot experiments (Figure 5 and Supporting Information), O_n−corona[n]arenes tested were able to interact with fullerenes C_{60} and C_{70} by forming 1:1 complex in toluene. Based on the titration data, the association constants for 1:1 complexation between host and guest were calculated utilizing the Stern−Volmer equation.[19] As summarized in Table 2, the association constants range from $(3.03 \pm 0.06) \times 10^4$ M^{-1} to $(1.59 \pm 0.04) \times 10^5$ M^{-1}.[20] The functionalized O_n−corona[n]arenes represent one of the strongest monomacrocyclic receptors to complex C_{60} and C_{70}.[18] It is worth noting that the MOM-substituted O_8−corona[8]arenes **10** and **11** displayed generally higher affinity toward both C_{60} and C_{70} in comparison to their ester-substituted analogues **5** and **6** owing to most probably the enhanced electron density of the macrocyclic cavity.

In conclusion, we have presented a novel type of macrocycles. Ester-functionalized O_n−corona[n]arenes were synthesized straightforwardly by nucleophilic aromatic substitution reaction from readily available starting materials. Subsequent chemical manipulations such as reduction and etherification furnished hydroxymethylated and methoxymethylated O_n−corona[n]-arenes (n = 6, 8). The macrocycles adopt unique corona-type conformation with a large cylindroid cavity, enabling strong affinity to form 1:1 complexes with fullerenes C_{60} and C_{70}. The easy availability, unique conformation, and cavity structures would engender functionalized O_n−corona[n]arenes useful macrocyclic host molecules. Their applications in supramolecular chemistry are being actively pursued in this laboratory, and results will be reported in due course.

Table 2. Association Constants (*Ka*) for the 1:1 Complexation of Functionalized O_n−Corona[n]arenes (n = 6, 8) with Fullerenes C_{60} and C_{70} at 298 K in Toluene

	5	6	10	11
C_{60}	$(3.03 \pm 0.06) \times 10^4$	$(4.39 \pm 0.07) \times 10^4$	$(1.52 \pm 0.04) \times 10^5$	$(1.28 \pm 0.06) \times 10^5$
C_{70}	$(1.59 \pm 0.04) \times 10^5$	$(1.31 \pm 0.03) \times 10^5$	$(1.59 \pm 0.03) \times 10^5$	$(1.41 \pm 0.04) \times 10^5$

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01330.

X-ray crystallographic file of **5** (CIF)

Experimental details, characterization of all products, fluorescence titration of **5**, **6**, **10**, and **11** with C_{60} and C_{70}, and ^{1}H and ^{13}C NMR spectra of products (PDF)

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Notes

The authors declare no competing financial interests.

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(20) A reviewer recommended the use of UV titration to determine association constant between fullerenes and corona[*n*]arenes, but in our hand, these proved unreliable owing to the poor solubility in toluene.

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