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Periphery-modified crown ethers. Synthesis of bis-5,8-dimethoxy-1,4-methanonaphthalene-fused crown ethers

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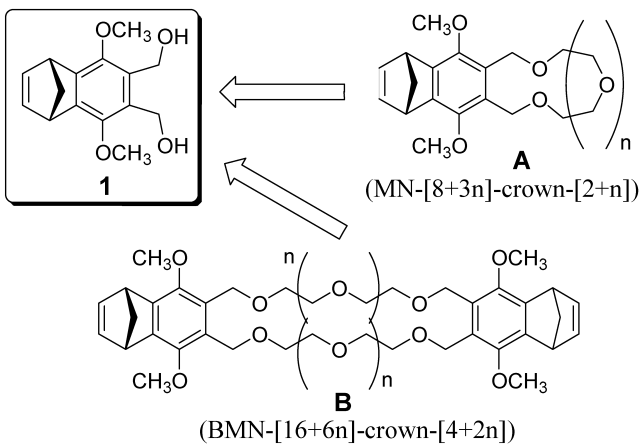
Abstract—The easily accessible and multi-functionalized 5,8-dimethoxy-6,7-dihydroxy methyl-1,4-dihydro-1,4-methanonaphthalene (**1**) has been utilized as the basic building material to synthesize the symmetric bis-methanonaphthalene-fused crown ethers **14a**–**d** (BMN-16-crown-4, BMN-22-crown-6, BMN-28-crown-8, and BMN-34-crown-10), that are constructed based on the connection between the α,β-bis-benzylic carbon atoms of diol **1** and oligoethylene glycols (**9a**–**d**) via two synthetic routes keyed upon the method of Williamson ether synthesis.

1. Introduction

Ever since Pedersen[1] foresaw the potential applications of macrocyclic polyethylene glycol ethers with the ability to form complexes with metal ions, 'crown ethers,' as the name he coined, have received a great deal of continuous attention. During the last two decades extended development in this research field by Cram's and Lehn's research groups, that emerged the discipline on macrocyclic host–guest chemistry,[2,3] has motivated extensive synthetic endeavor on the molecular designs and modification aiming at exploration of basic knowledge and implementation of the conceptual imagination of applications in various areas of chemistry and material science.[4] In general, design and modification have focused on three elements of crown-ether molecules: (1) the loop with regard to its size, interior donor atoms (O, S, and N), and quantity (multiplicity), such as the renowned cryptands;[3,5] (2) the attachments at periphery, such as lariat,[6] carbocage,[7] cyclophanes,[8] porphyrin,[9] and fullerene[10] that interfuse or link the crown-ether loop; and (3) the guest that interplays with the crown-ether loop (host), such as rotaxanes[11] and catenanes.[12]

5,8-Dimethoxy-6,7-dihydroxymethyl-1,4-dihydro-1,4-methanonaphthalene (**1**), readily made available from 2,3-dicyano-1,4-benzoquinone,[13] is multi-functionalized that contains, besides the hydroxyl groups at α,β-bis-benzylic carbon atoms, a 1,4-dimethoxybenzene ring and a double bond in the norbornadiene moiety at the periphery. The 1,4-dimethoxybenzene ring is a synthetic equivalent to 1,4-benzoquinone by oxidation and has a pair of masked phenolic hydroxyl groups that could be made to connect polyethylene glycolates to form additional crown-ether loops or to attach photochromic moieties that make the molecule to serve as a sensor. The strained double bond in the norbornadiene ring would be amendable to incorporate moieties with desirable functions or to undergo polymerization via modes of vinylic[14] or ROMP[15] by transition metal catalysts. With the intention to take advantage of these intrinsic structural features in **1**, we launched a program aiming at the synthesis of macrocyclic polyethers and their periphery-modified derivatives utilizing **1** as the basic building material. The syntheses of mono-looped crown ethers shown by the generic structures **A** (MN-[8+3*n*]-crown-[2+*n*]) and **B** (BMN-[16+6*n*]-crown-[4+2*n*]) based on the α,β-bis-benzylic carbon atoms of diol **1** were first undertaken (Scheme 1). The crown-ether rings were



Scheme 1.

Keywords: crown ethers; synthesis.
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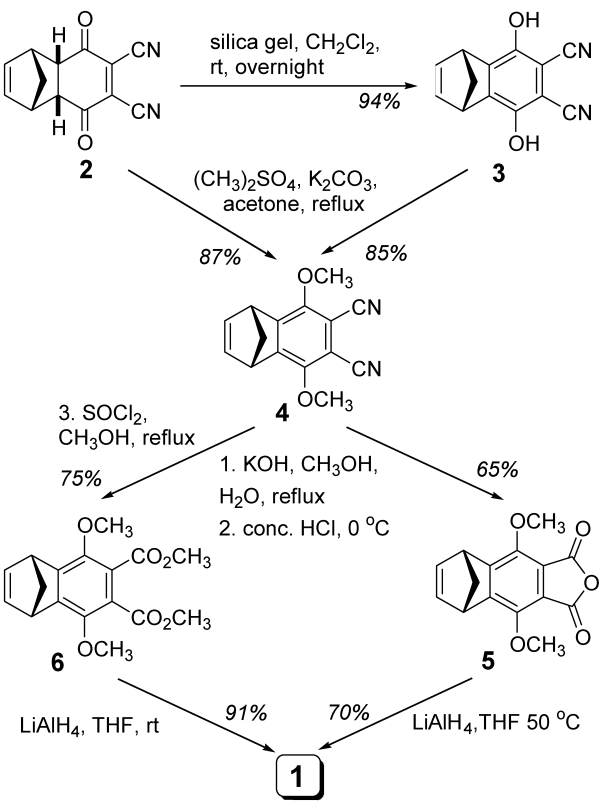
constructed by the methodology of Williamson ether synthesis,[16] in which an alkoxide (as a nucleophile) undergoes a S_N2 reaction with a halide or a tosylate. Recently, we have accomplished the syntheses of four methanonaphthaleno-crown ethers (**A**: n=1, 2, 3, 4) and four bismethanonaphthaleno-crown ethers (**B**: n=0, 1, 2, 3). The results of the synthesis of crown ethers **A**s and their complexes with metal ions will be reported separately elsewhere, and herein in this paper we described in detail the synthetic results of crown ethers **B**s.

2. Results and discussion

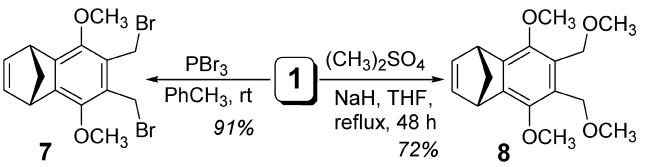
2.1. Preparation of methanonaphthalene diol 1

The preparation of diol **1**, the nucleophilic building unit for the synthesis of crown ethers of both types **A** and **B**, was accomplished in overall yields of 30–40% following the reaction sequence illustrated in Scheme 2. The synthesis was composed of three major operations starting from 1,4-methanonaphthalene-6,7-dicarbonitrile **2**, which was made available from the Diels–Alder reaction of 2,3-dicyano-1,4-benzoquinone[13] and freshly distilled cyclopentadiene under thermodynamically controlled condition.[17] When a solution of **2** in dichloromethane was stirred with silica gel overnight, the reaction generated the corresponding hydroquinone derivative **3** which, without further purification, was subsequently subjected to bis-*O*-methylation in refluxing acetone with dimethyl sulfate containing K_2CO_3 to furnish the corresponding derivative **4** in an overall yield of 80%. Alternatively, dicarbonitrile **4** could also be obtained in 87% yield from **2** by one-pot operation, in which a solution of **2** in refluxing acetone was treated with dimethyl sulfate in the presence of K_2CO_3. Following the general standard procedure, dicarbonitrile **4** was hydrolyzed with KOH in hot methanol to afford, upon careful neutralization of the reaction mixture with conc. HCl at 0°C, directly the carboxylic anhydride **5** in 65% yield. The above neutralized reaction product could also be converted to the corresponding diester **6** in 76% yield by the successive reaction with thionyl chloride in refluxing methanol. Reduction of anhydride **5** and diester **6** with lithium aluminum hydride provided diol **1** in 70 and 91% yields, respectively.



Scheme 2.

For the synthetic purpose and making the synthetic utility of diol **1** more flexible, the corresponding α,β-bis-benzylic dibromide **7**, which could be used as an electrophilic building unit in the Williamson ether synthesis, was prepared by treatment of diol **1** with PBr_3 (Scheme 3). The bis(methoxymethyl)-substituted methanonaphthalene **8** was also prepared as a reference compound by the reaction of diol **1** with dimethyl sulfate in THF in the presence of NaH.

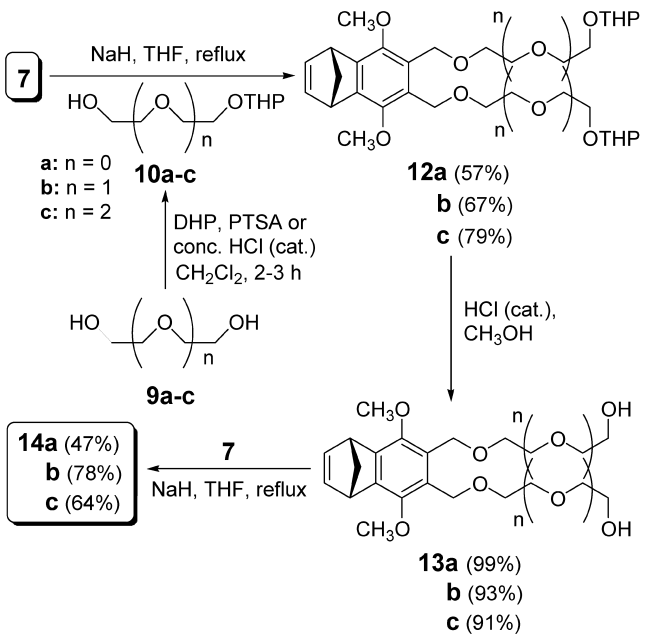


Scheme 3.

The structure of bis(dihydroxymethyl)-substituted methanonaphthalene **1**, shown by elemental analysis to have molecular formula $C_{15}H_{18}O_4$, was secured by spectral analysis. The observation of eight lines in the broadband-decoupled ^{13}C NMR spectrum for 15 carbon atoms is consistent with the presence of a mirror-plane symmetry element in diol **1**. The existence of α,β-bis-hydroxymethyl groups in **1** is indicated by (i) a strong absorption band at 3295 cm^{-1} in the infrared spectrum, (ii) a signal at 56.8 ppm in the ^{13}C NMR spectrum assignable to the carbon bearing a hydroxyl group and two hydrogens, and (iii) a broad signal at 2.86 ppm (–OH) and a four-proton singlet at 4.72 ppm in the ^1H NMR spectrum. Presumably, the conformation of diol **1** was relatively unconstrained, rendering the chemical-shift equivalence to the diastereotopic hydrogens on the benzylic carbons, and thus resulting in the observation of only seven signals in the ^1H NMR spectrum for eight groups of nonequivalent hydrogens.

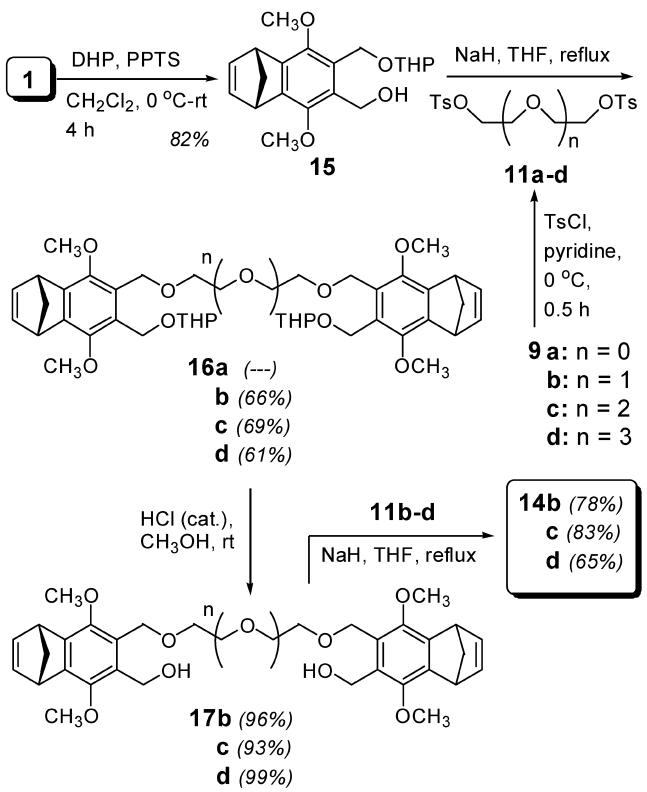
2.2. Synthesis of bis-methanonaphthalene-fused crown ethers of type B (14a–d)

Attempts to prepare bis-methanonaphthalene-fused macrocyclic ethers represented by generic structure **B** (**14a–d**) in one-step by the NaH-promoted reactions using diol **1** and bis-tosylates **11b** or polyethylene glycols **9b–d** and dibromide **7** were not successful. The reactions usually gave a complex mixture of products, including crown ethers of type **A**, which rendered tedious and difficult separation. Decision was thus made to employ stepwise methods, namely protection–deprotection technique, for the construction of macrocyclic ethers **14a–d** (Schemes 4 and 5). At the outset, effort was directed to the synthetic route

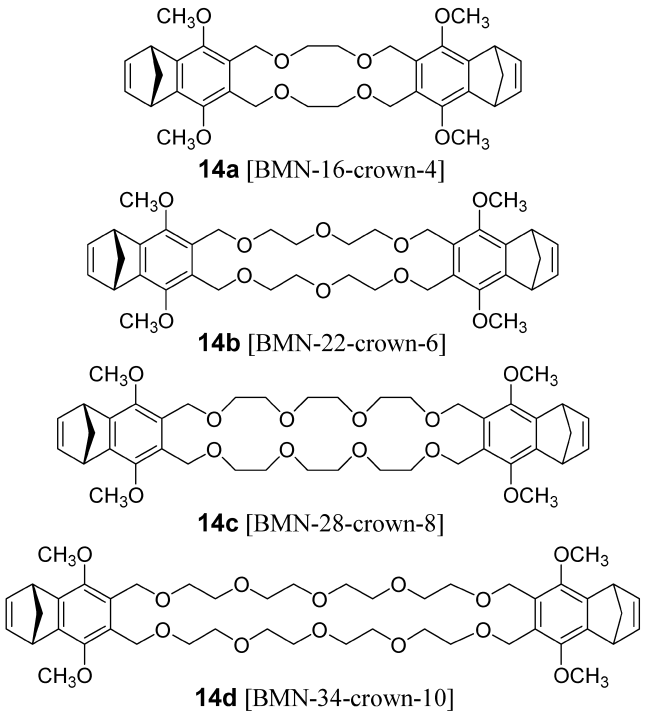


Scheme 4.

shown in Scheme 4. Dibromide **7** was first subjected to the reactions with the sodium salts of ω-tetrahydropyranyl polyethylene glycols **10a–c**[18] in THF under reflux to give bis-ω-tetrahydropyranyl polyethers **12a–c** in yields of 55–80%. Deprotection of ethers **12a–c** under acidic condition afforded diols **13a–c**, which were converted to the sodium salts in THF by NaH followed by treatment with dibromide **7** to provide bis-methanonaphthalene-fused crown ethers **14a–c** in yields of 45–80%. The overall yields of three-step synthesis of crown ethers **14a**, **14b**, and **14c** from dibromide **7** were 26, 48, and 46%, respectively.



Scheme 5.



All intermediates **12a–c** and **13a–c** were characterized by their spectral analyses (^{1}H and ^{13}C NMR, IR, and MS). In the ^{13}C NMR spectra of ethers **12a–c**, the appearance of a distinct absorption line at ~99 ppm and three lines in the region of 19–30 ppm, ascribed respectively to the acetal and propylene carbons, manifested the presence of tetrahydropyranyl groups. Strictly speaking, bis-ω-tetrahydropyranyl polyethers **12a–c** could be formed as a mixture of diastereomers from the reactions of dibromide **7** with the sodium salts derived from the racemic mixture of ω-tetrahydropyranyl polyethylene glycols **10a–c**. However, in the broadband-decoupled ^{13}C NMR spectra, only $(n+1)/2$ absorption lines were observed, where n is the number of carbon atoms in the molecule, suggesting that in solution polyethers **12a–c** could behave as having preserved the intrinsic mirror-plane symmetry element despite the fact that additional chiral centers were introduced by the tetrahydropyranyl groups.

Upon acid-catalyzed removal of the tetrahydropyranyl rings from ethers **12a–c** to form diols **13a–c**, the corresponding absorption signals disappeared and a well-defined AB-quartet due to benzylic methylene hydrogens surfaced at ~4.6 ppm (4H) in their rather simple ^{1}H spectra. Diols **13a–c** exhibited ^{13}C NMR spectra that were consistent with having the molecular C_s-symmetry. The molecular constitution of each diol **13a–c** was suggested by the satisfactory molecular weight that was analyzed by HRMS for the signal of highest m/z value corresponding to the molecular ion (M^+) of diol **13a** and **13b**, and the Na-complexed ion ($M+Na^+$) of **13c**.

Although we adopted the reaction sequence shown in Scheme 4 to successfully prepare crown ethers **14a–c**, we encountered a setback: availability of the monoprotected

glycol ethers **10a–c** was limited by low yields and reproducibility. We thus explored an alternative and complementary approach that is illustrated in Scheme 5. This synthetic route demanded only one task of making diol **1** monoprotected (i.e. **15**) and utilized the bis-tosylates **11**s,[19] which could be prepared from polyethylene glycols more easily and in higher yields than the monoprotected glycol ethers **10**s. Additionally, the synthetic route shown in Scheme 5 would be more versatile, allowing one to synthesize not only crown ethers **14a–d**, but other multi-methanonaphthalene-fused crown ethers of symmetrical and unsymmetrical structures as well.

Thus, bis-benzylic diol **1** was converted into (tetrahydropyranyloxymethyl)-phenyl methanol **15** in 82% yield by reaction with dihydropyran in dichloromethane using pyridium *p*-toluenesulfonate (PPTS)[20] as the catalyst (Scheme 5). Alcohol **15** was obtained as colorless oil and exhibited a strong IR absorption band at 3487 cm^{-1}. Protection of a hydroxyl group with dihydropyran would create a stereogenic center and thus alcohol **15** was expected to consist of diastereomers. The complex ^1H and ^{13}C NMR spectra evidently suggested that the attained product was a mixture of diastereomers **15a** and **15b**. The broadband-decoupled ^{13}C NMR spectrum of **15** exhibited discernible lines more than (less than twice) the number of carbon atoms in the molecule. Two singlets at 3.86 and 3.87 ppm with total intensity equal to the three-hydrogen singlet at 3.79 ppm, designated to the hydrogens of two methyl ether groups, were observed in the ^1H NMR spectrum of **15** (Fig. 1). It is the methyl group near to the hydroxymethyl group that shows chemical shift of larger difference for diastereomers and at lower field than the other methyl group, as revealed by COSY, HMQC, and NOESY spectral analyses. The methylene hydrogens of the hydroxymethyl group exhibited a multiplet at 4.67–4.69 ppm (2H), which correlated with the broad signal at 3.17 ppm due to hydroxyl hydrogen and the carbon resonance at 56.95 ppm. However, the methylene hydrogens at benzylic carbon bearing tetrahydropyranyloxy group displayed chemical shifts of significant separation with one pair of doublets appearing at 4.92/4.90 ppm and the other pair at 4.61/4.59 ppm, each of which had J=10.7 Hz and integrated for one hydrogen atom. Both hydrogen absorption signals correlated with carbon resonance at 61.45/61.43 ppm and showed through-space correlation (NOE) with the singlet at 3.79 ppm due to the methyl ether group. The acetal methane hydrogen, which correlated with carbon resonance at 98.56/98.51 ppm, displayed a multiplet at 4.79–4.80 ppm in the ^1H NMR spectrum and interestingly the through-space interaction with only one of the methylene hydrogens at benzylic carbon bearing tetrahydropyranyloxy group (4.61/4.59 ppm). Since the tetrahydropyranyl group, and along with it the stereogenic center was to be removed in later synthesis, no effort was taken to separate these diastereomers. The alcohol **15** was used as acquired.

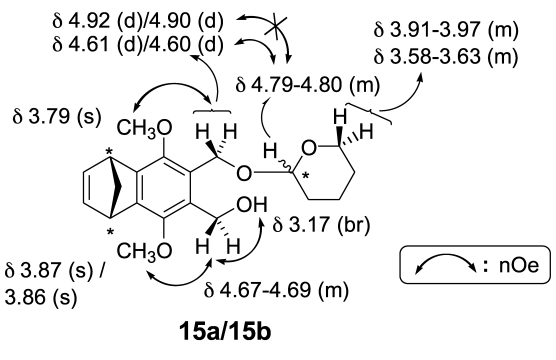


Figure 1. Partial ^1H NMR chemical shifts and the NOE experiment results for **15**.

En route for the bis-methanonaphthalene-fused crown ethers **14a–d**, the bilateral coupling of bis-tosylates **11a–d** with alcohol **15** was attempted by carrying out the reaction in refluxing THF in the presence of sodium hydride. Presumably owing to steric crowdedness, the reaction of ethylene glycol bis-tosylate (**11a**, n=0) with alcohol **15** encountered low-yield and reproducibility problems. However, the reactions of polyethylene glycol bis-tosylate (**11b–d**, n=1, 2, 3) with alcohol **15** went well without difficulty to give α,ω-dibenzyl polyethylene ethers **16b–d** in yields of ca. 70% (Scheme 5). The molecular constitution of each polyethers **16b–d** was suggested by the satisfactory molecular weight provided by HRMS. There was no hydroxyl group absorption band in the IR spectra of **16b–d**. The broadband-decoupled ^{13}C NMR spectra of **16b–d** exhibited discernible lines less than the number of carbon atoms in the molecule, but more than the number of equivalent carbon atoms expected if taking mirror-plane symmetry element into consideration. Since the stereogenic centers in **15a** and **15b** were passed onto **16b–d**, it was likely that a mixture of diastereomeric products for each α,ω-dibenzyl polyethylene ethers **16b–d** was obtained and justified the observed ^{13}C NMR spectra. It was also evident in the ^1H NMR spectra of **16b–d**, each of which was very similar to that of **15** except in region between 3.60 and 3.70 ppm where additional signals appeared by the intensity accountable for the number of ethylene hydrogen atoms inherited from bis-tosylates **11b–d**. Also, the α,ω-dibenzyl polyethylene ethers **16b–d** were used as attained in the reactions followed.

Acid-catalyzed removal of tetrahydropyranyl groups from **16b–d** was easy and the diols **17b–d** were obtained in yields of more than 90%. Their IR, MS, ^1H and ^{13}C NMR spectroscopic data were consistent with the structures. In particular, the removal of the stereogenic center in the tetrahydropyranyl rings re-established the molecular symmetry element and consequently much simpler ^1H and ^{13}C NMR spectra were observed for diols **17b–d**. All the broadband-decoupled ^{13}C NMR spectra consisted of $n/2$ lines, where n is the number of carbon atoms in the molecule of **17b–d**. In the ^1H NMR spectra of **17b–d**, the absorption signals due to α,β-benzylic hydrogens were overlapped and appeared at ~4.65 ppm as a multiplet (8H), which correlated with carbon resonances at ~56.7 ppm (HO–CH_2–Ph) and ~65.8 ppm (RO–CH_2–Ph).

With the acquisition of **17b–d**, the final step to link the two terminal hydroxy groups by a polyethylene glycolate was called for. Thus, each of diols **17b–d** in THF was treated first with sodium hydride and then with the respective bis-tosylates **11b–d**. Symmetric bis-methanonaphthalene-fused crown ethers **14b**, **14c**, and **14d** were thereby obtained in good yields (Scheme 5). The synthesis via this synthetic

route furnished crown ethers **14b**, **14c**, and **14d** in 49, 53, and 40% overall yields from **15**, respectively.

The molecular constitution of every crown ethers **14a–d** as being a 2:2 reaction product between diol **1** and bis-tosylates **11b–d** (or dibromide **7** and oligoethylene glycols **9a–c**) was secured by the nature of synthetic courses (Schemes 4 and 5) and by the satisfactory molecular weight via FAB-HRMS analysis for the signal of highest *m/z* value corresponding to the molecular ion (M^+ or $M+H^+$). The structures of crown ethers **14a–d** were established via analyses of their IR, MS, and ^1H and ^{13}C NMR spectroscopic data. All the broadband-decoupled ^{13}C NMR spectra of **14a–d** displayed $(n+2)/4$ lines, where n is the number of carbon atoms in the molecule (Table 1). This observation suggested that there are rotation-axis and mirror-plane symmetry elements (C_2 and σ_v or σ_h) present in the molecule of each crown ethers **14a–d**. In fact, the ^{13}C NMR spectra of **14a–c** could only be distinguished by the appearance of one, two, three, and four carbon absorption lines in the region between 70 and 73 ppm, corresponding to the number of the nonequivalent $-OCH_2-$ groups in **14a**, **14b**, **14c**, and **14d**, respectively. As the result of the presence of C_2 and σ_v (σ_h) symmetry elements, all crown ethers **14a–d** showed similar ^1H NMR spectra that could only be differentiated by in the relative intensity of absorption signals between 3.6 and 3.8 ppm, attributed to the hydrogen atoms of $-O-CH_2CH_2-O-$ and OCH_3 units (Table 1). The 12-hydrogen singlet for four $-OCH_3$ groups at aromatic rings appeared at 3.80 ppm.

One question remains to be addressed. Synthesis of the type-**B** crown ethers **14a–d** via either synthetic route shown in Schemes 4 and 5 was expected to furnish two stereoisomers, in which the two methano-bridges are either *syn* or *anti* to each other (e.g. *syn*-**14a** and *anti*-**14a**). It was the final step of synthesis (**13a–c→14a–c**) in Scheme 4 and the bilateral coupling of bis-tosylates **11b–d** with alcohol **15** (**15→16b–d**) in Scheme 5 that would determine the formation of *syn* and *anti* stereoisomeric crown ethers **14a–d**. Experimentally, however, each crude product of **14a–d** obtained by both synthetic routes was indicated to be homogeneous by the appearance of ^1H and ^{13}C NMR spectra. Attempts of separation of diastereomers by column chromatography were not successful. Crown ethers were oily material and resisted recrystallization, except **14a** that formed monocrystals suitable for X-ray crystallographic analysis. The result revealed that both *syn*-**14a** and *anti*-**14a** coexist in a unit cell (Fig. 2), and the molecule was twisted with dihedral angle of two aromatic rings being 63° for *syn*-**14a** and 66° for *anti*-**14a**.

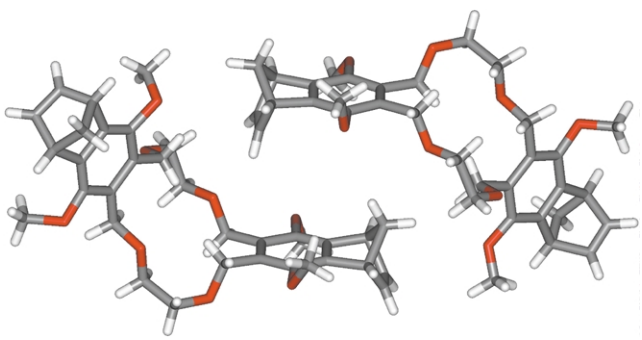
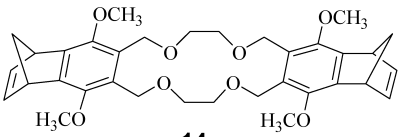
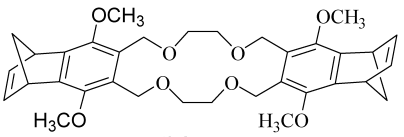


Figure 2. Crystal structures of *syn*-**14a** and *anti*-**14a** in a unit cell.



syn-**14a**



anti-**14a**

3. Conclusion

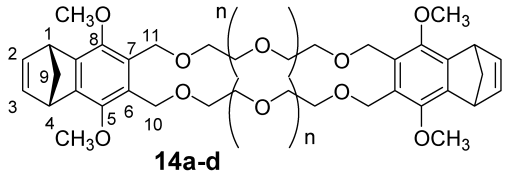
We have utilized the α,β-bis-benzylic carbon atoms of the multi-functionalized 5,8-dimethoxy-6,7-dihydroxymethyl-1,4-dihydro-1,4-methanonaphthalene (**1**) for the synthesis of bis-methanonaphthalene-fused crown ethers **14a–d** represented by generic structure **B** (BMN-[16+6*n*]-crown-[4+2*n*], *n*=0, 1, 2, 3) via two synthetic routes based on the protection–deprotection methodology (Schemes 4 and 5). The presence of both *syn*- and *anti*-stereoisomeric crown ethers **14a–d** could not be established by spectral analysis, but was expected as suggested by the X-ray crystal structural analysis of **14a**. The masked phenolic hydroxyl groups in 1,4-dimethoxybenzene rings and the strained double bonds in the norbornadiene rings would offer opportunity for synthesizing multi-looped and polymerized crown ethers. Works on investigation of the ability of crown ethers **14a–d** to form complexes with metal ions and exploitation of synthetic utilization of **1** toward other crown ethers of novel structures are under active pursuit.

4. Experimental

4.1. General remarks

Melting points were determined in capillaries on a Thomas–Hoover apparatus and are uncorrected. Infrared (IR) spectra were recorded as either a thin film pressed between two sodium chloride plates or as a solid suspended in a KBr disk. The ^1H NMR spectra were obtained at 400 MHz (^{13}C NMR at 100 MHz) using $CDCl_3$ as solvent (unless otherwise specified). All chemical shifts were expressed in δ (ppm) with reference to $CHCl_3$ (δ 7.26 for ^1H and δ 77.0 for ^{13}C). Coupling constants are reported in hertz. The number of attached hydrogen on the carbon atom was determined by the DEPT analysis. Mass (MS) and HRMS spectra were done in EI (70 eV) unless otherwise indicated. All solvents used were either reagent grade or were distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on E. Merck silica gel 60 F_{254} plate (0.20 mm). Flash chromatography was performed on E. Merck silica gel (230–400 mesh). Microanalyses were performed by the NSC Analytical Centers operated by the

Table 1. The ^{13}C and ^{1}H NMR chemical shifts (δ) of crown ethers **14a–d**, and ether **8**[a]



14a-d

n	$C_{1,4}$	$C_{2,3}$	C_9	$C_{5,8}$	$C_{6,7}$	$C_{4a,8a}$	$C_{10,11}$	$-OCH_3$	$-OCH_2-$
8	47.8	142.6	68.6	150.0	128.1	143.8	65.8	62.3	58.4 ($-OCH_3$)
0 (**14a**)	47.7	142.5	68.6	149.9	128.2	143.8	64.8	62.3	71.9
1 (**14b**)	47.7	142.6	68.6	150.0	128.4	143.8	64.7	62.4	71.1; 69.9
2 (**14c**)	47.7	142.6	68.6	150.0	128.3	143.8	64.4	62.4	70.7; 70.6; 69.8
3 (**14d**)	47.7	142.5	68.5	150.0	128.2	143.7	64.4	62.3	70.7; 70.6; 70.5; 69.8
	$H_{1,4}$	$H_{2,3}$[b]	H_9[c]	$H_{10,11}$[d]	$-OCH_3$	$-OCH_2-$			
8	4.16–4.17 (m)	6.78 (dd)	2.23 (dd)/2.16 (d) [2.19 ($\Delta\delta_{ppm}$=0.062)]	4.51 (d)/4.47 (d) [4.49 ($\Delta\delta_{ppm}$=0.037)]	3.80 (s)	3.42 (s, $-OCH_3$)			
0 (**14a**)	4.15–4.16 (m)	6.77 (dd)	2.22 (dd)/2.16 (d) [2.19 ($\Delta\delta_{ppm}$=0.057)]	4.66–4.75 (m, 8H)	3.80 (s)	3.88 (s, 8H)			
1 (**14b**)	4.14–4.15 (m)	6.77 (dd)	2.22 (dd)/2.15 (d) [2.18 ($\Delta\delta_{ppm}$=0.072)]	4.70 (d)/4.66 (d) [4.68 ($\Delta\delta_{ppm}$=0.040)]	~3.79 (s)	3.75–3.80 (m, 8H); 3.68–3.70 (m, 8H)			
2 (**14c**)	4.14–4.15 (m)	6.77 (dd)	2.22 (dd)/2.15 (d) [2.18 ($\Delta\delta_{ppm}$=0.065)]	4.66 (d)/4.62 (d) [4.64 ($\Delta\delta_{ppm}$=0.040)]	3.79 (s)	3.67–3.75 (m, 16H); 3.66 (s, 8H)			
3 (**14d**)	4.14–4.15 (m)	6.77 (dd)	2.21 (dd)/2.14 (d) [2.18 ($\Delta\delta_{ppm}$=0.070)]	4.65 (d)/4.61 (d) [4.63 ($\Delta\delta_{ppm}$=0.039)]	3.79 (s)	3.62–3.78 (m, 24H); 3.66 (s, 8H)			

[a] The spectra were recorded on a Brüker DPX-400 spectrometer using $CDCl_3$ as solvent. All chemical shifts were expressed in δ (ppm) with reference to $CHCl_3$ (^{13}C: δ 77.0; ^{1}H: δ 7.26).
[b] $J_1=J_2=1.8$ Hz.
[c] An AB-quartet, $J=7.2$ Hz. Hydrogen atom at lower field is further coupled with $J=1.4$ Hz.
[d] An AB-quartet, $J=10$ Hz.

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4.2. Materials

The adduct **2**[17] was prepared from the Diels–Alder reaction of freshly distilled cyclopentadiene and 2,3-dicyano-1,4-benzoquinone, which was made according to the reported method from commercially available 2,3-dicyano-1,4-hydroquinone by oxidation with $Pb(OAc)_4$ in ethyl acetate.[16] The ω-tetrahydropyranyl-protected polyethylene glycols **10a–c**[18] and ω,ω′-bis-tosylates **11a–d**[19] were prepared from commercially available oligoethylene glycols **9a–d** according to the reported procedure and used without further purification.

4.2.1. 5,8-Dimethoxy-1,4-dihydro-1,4-methanonaphthalene-6,7-dicarbonitrile (4). *Method A*. A solution of adduct **2** (530 mg, 2.36 mmol) in CH_2Cl_2 (10 mL) was stirring with silica gel (ca. 1 g) at room temperature overnight. The reaction mixture was filtered and the residue was thoroughly washed several times with EtOAc/*n*-Hex (1:1, 20 mL each). The filtrate was concentrated in vacuo to furnish white solids of 5,8-dihyroxyl-1,4-dihydro-1,4-methanonaphthalene-6,7-dicarbonitrile (**3**): mp 240°C (acetone), decomp., IR 3273 (br), 2238 (m), 1589 (m), 1474 (s), 1302 (s), 1271 (s), 1218 (s) (m) cm^{-1}; ^1H NMR (CD_3OD) δ 2.22 (AB system, $\Delta\delta$=0.074 ppm, J=7.5 Hz, 2H), 4.26–4.27 (m, 2H), 4.90 (bs, 2H), 6.85 (dd, J_1=J_2=1.8 Hz, 2H); ^{13}C NMR (CD_3OD) δ 49.2 (d), 71.0 (t), 101.4 (s), 115.5 (s), 143.6 (d), 148.4 (s), 149.7 (s). This material was used for the subsequent reaction without further purification.

A solution of **3** (7.50 g, 0.03 mol) in acetone (500 mL) containing K_2CO_3 (41.0 g, 0.30 mmol) was stirred under the nitrogen atmosphere for 30 min. Dimethyl sulfate (6.40 g, 0.06 mol) was added, and the reaction mixture was heated under reflux for 12 h. The reaction mixture was then filtered, and the filtrate was concentrated to leave a residue, which was taken into EtOAc (200 mL). The solution was washed with water (100 mL×3), dried, filtered, and concentrated to give dark brown oil. Flash column chromatography of residual oil afforded white solids of **4** (6.2 g, 85%).

Method B. A solution of adduct **2** (250 mg, 1.12 mmol) in acetone (30 mL) containing K_2CO_3 (3.23 g, 23.4 mmol) was stirred under the nitrogen atmosphere for 10 min. Dimethyl sulfate (220 mg, 1.78 mmol) was added, and the reaction mixture was heated under reflux in 4 h. The reaction mixture was then filtered, and the filtrate was concentrated to give a dark residue which was purified via flash column chromatography and recrystallization from EtOAc/*n*-Hex (1/3 by vol.) to afford pure **4** (800 mg, 87%) as white flakes: mp 128–129°C; IR 2228 (m), 1576 (m), 1466 (s), 1407 (s), 1306 (s), 1277 (m), 1046 cm^{-1} (s); ^1H NMR δ 6.86 (dd, J_1=J_2=1.8 Hz, 2H), 4.31–4.32 (m, 2H), 4.00 (s, 6H), 2.35 (dd, J=7.8, 1.4 Hz, 1H), 2.26 (d, J=7.8 Hz, 1H); ^{13}C NMR δ 152.3 (s), 150.6 (s), 142.6 (d), 113.6 (s), 106.8 (s), 69.3 (t), 62.1 (q), 48.5 (d); MS m/z (%) 252 (M^+, 81), 237 (100), 221 (49), 84 (80), 77 (33), 51 (86). Anal. calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.21; H, 4.86; N, 11.00.

4.2.2. 5,8-Dimethoxy-1,4-dihydro-1,4-methanonaphthalene-6,7-dicarboxylic anhydride (5). A mixture of compound **4** (340 mg, 1.35 mmol) in MeOH/H_2O (40 mL/4 mL) containing KOH (800 mg) was heated under reflux for 5 h. The reaction mixture was cooled with an ice-water bath and acidified by dropwise addition of concentrated HCl (ca. 8 mL), and then water (30 mL) was added. Most of methanol was removed by evaporation under vacuum and the aqueous residue was extracted with dichloromethane three times. The organic layers were combined, washed with brine and water, and dried ($MgSO_4$). Filtered, and the filtrate was concentrated to leave a yellow solid residue which was rinsed with a small amount of methanol to give off-white solids. Recrystallization from CH_2Cl_2/hexane (1:3 by vol.) afforded pure anhydride **5** (240 mg, 65%) as white needles: mp 143–144°C; IR 1834 (s), 1772 (s), 1569 (m), 1490 (s), 1305 (m), 1029 cm^{-1} (s); ^1H NMR δ 6.87 (dd, J_1=J_2=1.8 Hz, 2H), 4.33–4.34 (m, 2H), 4.09 (s, 6H), 2.39 (d, J=7.6 Hz, 1H), 2.31 (d, J=7.6 Hz, 1H); ^{13}C NMR δ 160.7 (s), 155.5 (s), 148.6 (s), 142.7 (d), 119.8 (s), 70.0 (t), 62.2 (q), 48.2 (d); MS m/z (%) 272 (M^+, 100), 257 (18), 227 (36), 225 (21), 213 (27), 197 (24), 185 (27), 169 (27), 138 (27), 127 (40), 113 (24). Anal. calcd for $C_{15}H_{12}O_5$: C, 66.17; H, 4.44. Found: C, 66.15; H, 4.48.

4.2.3. Dimethyl 5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene-6,7-dicarboxylate (6). A mixture of compound **4** (6.20 g, 0.03 mol) and KOH (28.1 g, 0.05 mol) in methanol (25 mL) was heated under reflux for 5 h, cooled with an ice-water bath, and then acidified with conc. HCl. The reaction mixture was filtered to remove inorganic salt and the filtrate was concentrated. The residue was dissolved in methanol (25 mL). Into the solution, cooled with an ice-water bath, was added dropwise thionylchloride (5.87 mL, 0.05 mol) in a period of 0.5 h, and the reaction mixture was then heated under reflux for 6 h. Most of methanol was removed by evaporation under vacuum and the residue was mixed with water (50 mL), extracted with EtOAc (30 mL×3). The organic layers were combined, washed subsequently with saturated $NaHCO_3$ solution, brine and water, dried ($MgSO_4$) and filtered. The filtrate was concentrated to leave a dark brown viscous oil which was purified by column chromatography on silica gel using EtOAc/*n*-Hex (1:1) as eluant (R_f=0.8) followed by recrystallization from ether to furnish pure diester **6** (5.94 g, 75%) as white crystalline: mp 74–75°C (ether); IR 1738 (s), 1444 (m), 1407 (m) 1310 (s), 1236 (s), 1036 cm^{-1} (s); ^1H NMR δ 6.81 (dd, J_1=J_2=1.8 Hz, 2H), 4.19–4.21 (m, 2H), 3.84 (s, 6H), 3.82 (s, 6H), 2.24 (AB system, $\Delta\delta$=0.056 ppm, J=7.4 Hz, 2H); ^{13}C NMR δ 47.9 (d), 52.4 (q), 62.5 (q), 68.9 (t), 124.3 (s), 142.5 (d), 147.6 (s), 148.1 (s), 166.5 (s); MS m/z (%) 319 (11), 318 (M^+, 100), 303 (15), 287 (56), 271 (37), 259 (30), 255 (38), 229 (21), 127 (34). Anal. calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 63.95; H, 5.78.

4.2.4. 6,7-Dihydroxymethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (1). *Method A*. Into a solution of anhydride **5** (200 mg, 0.78 mmol) in THF (10 mL) cooled with an ice-water bath was added portionwise $LiAlH_4$ (89 mg, 2.34 mmol) under N_2 atmosphere. After heating at 50°C for 6 h, the reaction mixture was cooled with an ice-water bath and water (10 mL) was added slowly to quench

the reaction. Most of THF was removed from the turbid reaction mixture under vacuum, followed by addition of 10% aqueous HCl (20 mL). Extraction with $CHCl_3$ (20 mL×3) and the combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. The filtrate was concentrated to leave viscous residue, which was purified via flash column chromatography to give pure diol **1** (140 mg, 70%) as white crystallines.

Method B. Into a solution of diester **6** (2.50 g, 7.86 mmol) in THF (80 mL) cooled with an ice-water bath and stirred under N_2 atmosphere was added in portions $LiAlH_4$ (0.89 g, 23.6 mmol). After stirring at room temperature for 3 h, the reaction mixture was cooled with an ice-water bath and was slowly added 10% aqueous NaOH (20 mL) to quench the reaction, followed by addition of 10% aqueous HCl (20 mL). Organic layer was separated and aqueous layer was extracted with EtOAc (50 mL×3). The organic layers were combined, washed with saturated sodium bicarbonate solution and brine, and dried ($MgSO_4$), and filtered. The filtrate was concentrated to leave an off-white solid. Recrystallization from CH_2Cl_2 afforded pure diol **1** (87 mg, 91%) as white crystallines: mp 145–146°C; IR 3295 (s), 2939 (w), 1458 (s), 1308 (s), 1266 (s), 1067 cm^{-1} (s); ^1H NMR δ 6.81 (dd, $J_1=J_2=1.8$ Hz, 2H), 4.72 (s, 4H), 4.18–4.19 (m, 2H), 3.81 (s, 6H), 2.86 (br, 2H), 2.25 (dd, $J=7.2$, 1.4 Hz, 1H), 2.18 (d, $J=7.2$ Hz, 1H); ^{13}C NMR δ 149.2 (s), 143.4 (s), 142.6 (d), 130.6 (s), 68.6 (t), 62.4 (q), 56.8 (t), 47.8 (d); MS *m/z* (%) 262 (M^+, 100), 244 (78), 229 (48), 215 (39), 185 (44), 128 (47), 127 (63), 115 (34), 114 (41). Anal. calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.92; H, 7.34.

4.2.5. 6,7-Dibromomethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (7). Into a solution of diol **1** (0.5 g, 1.91 mmol) in toluene (20 mL) cooled with an ice-water bath was slowly added PBr_3 (0.12 mL, 1.27 mmol). After addition was complete, the mixture was stirred at room temperature for 2 h, and was added water. Organic layer was separated and aqueous layer was extracted with EtOAc (20 mL×3). The organic layers were combined, washed with brine, and dried ($MgSO_4$). After filtration, the filtrate was concentrated to leave a pale yellow viscous residue, which was purified via flash column chromatography to give dibromide **7** (0.68 g, 92%) as white solids: mp 98–99°C (pentane); R_f=0.66 (EtOAc/*n*-Hex, 1:3); IR 1465 (m), 1412 (m), 1302 (m), 1271 (s), 1036 (s), 732 (w), 583 cm^{-1} (w); ^1H NMR δ 6.82 (dd, $J_1=J_2=1.8$ Hz, 2H), 4.71 (AB quartet, $\Delta\delta$=0.054 ppm, J=10 Hz, 4H), 4.20–4.21 (m, 2H), 3.92 (s, 6H), 2.23 (AB quartet, $\Delta\delta$=0.065 ppm, J=7.4 Hz, 2H); ^{13}C NMR δ 149.2 (s), 144.3 (s), 142.5 (d), 127.4 (s), 68.3 (t), 61.8 (q), 47.9 (d), 24.8 (t); MS *m/z* (%) 390 (M+4, 8), 388 (M+2, 19), 386 (M^+, 8), 309 (100), 307 (91), 228 (72), 213 (40), 152 (36), 141 (35), 127 (30), 114 (29). Anal. calcd for $C_{15}H_{16}Br_2O_2$: C, 46.42; H, 4.16; O, 8.25. Found: C, 46.35; H, 4.25; O, 8.24.

4.2.6. 6,7-Dimethoxymethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (8). Under N_2 atmosphere, sodium hydride (260 mg, 19.2 mmol) was added into a stirring solution of diol **1** (560 mg, 2.14 mmol) in THF (100 mL), and the mixture was heated under reflux for 0.5 h. Dimethyl sulfate (540 mg, 4.27 mmol) was added, and the reaction mixture was heated under reflux in 48 h. The reaction mixture was then cooled with an ice-water bath and water (25 mL) was added to quench the reaction. Most of the solvent was removed under reduced pressure and the aqueous residue was extracted with CH_2Cl_2 (50 mL×3). The combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. The filtrate was concentrated to leave a residue which was purified via flash column chromatography to afford pure **8** (450 mg, 72%) as a colorless oil: IR ($CHCl_3$) 1597 (w), 1452 (w), 1420 (w), 1220 (s), 1213 cm^{-1} (s); ^1H NMR δ 6.78 (dd, $J_1=J_2=1.8$ Hz, 2H), 4.50 (d, J=10 Hz, 2H), 4.46 (d, J=10 Hz, 2H), 4.16–4.17 (m, 2H), 3.8 (s, 6H), 3.42 (s, 6H), 2.22 (d, J=7 Hz, 1H), 2.16 (d, J=7 Hz, 1H); ^{13}C NMR δ 150.0 (s), 143.8 (s), 142.6 (d), 128.1 (s), 68.6 (t), 65.8 (t), 62.4 (q), 58.4 (q), 47.8 (d); MS (FAB) *m/z* (%) 291 (M^++H, 20), 290 (M^+, 34), 289 (34), 258 (65), 243 (39), 229 (100). HRMS calcd for $C_{17}H_{22}O_4$: 290.1518. Found: 290.1514.

4.3. General procedure for the preparation of bis-ω-tetrahydropyranyl ethers 12a–c

A solution of ω-tetrahydropyranyl polyethylene glycols **10a–c** (1.00 mmol) in dried THF (5 mL) was added NaH (1.00 mmol) under N_2 atmosphere and the reaction mixture was heated under gentle reflux. Dibromide **7** (0.50 mmol) in THF (5 mL) was added dropwise into the reaction mixture. After refluxing for 3 h, another portion of NaH (1.00 mmol) was added, and the reaction mixture was refluxed for additional 18 h, and cooled down to room temperature. Methanol (5 mL) was added to quench any unchanged NaH. Solvent (THF) was removed prior to the addition of water (30 mL) and the resulting solution was extracted with EtOAc (30 mL×3). The combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. Removal of solvent left a pale yellow viscous liquid, which was then subjected to column chromatography to afford pure **12a–c** as colorless oil.

4.3.1. 6,7-Bis-(4-tetrahydropyran-2′-yloxy-2-oxa-1-butyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (12a). Yield 57%. R_f=0.68 (EtOAc/*n*-Hex, 1:1); IR 2939 (s), 2870 (m), 1461 (m), 1267 (m), 1124 (s), 1076 (s), 1034 (s) cm^{-1}; ^1H NMR δ 6.76 (dd, $J_1=J_2=1.8$ Hz, 2H), 4.60–4.62 (m, 6H), 4.13–4.14 (m, 2H), 3.82–3.87 (m, 4H), 3.78 (s, 6H), 3.68–3.71 (m, 4H), 3.59–3.61 (m, 2H), 3.44–3.49 (m, 2H), 2.17 (AB quartet, $\Delta\delta$=0.068 ppm, J=7.1 Hz, 2H), 1.47–1.58 (m, 12H); ^{13}C NMR δ 150 (s), 143.7 (s), 142.5 (d), 128.2 (s), 98.7 (d), 69.7 (t), 68.5 (t), 66.5 (t), 64.3 (t), 62.3 (q), 62.0 (t), 47.6 (d), 30.5 (t), 25.4 (t), 19.3 (t); MS *m/z* (%) 518 (M^+, weak), 372 (16), 289 (37), 288 (40), 273 (100), 244 (39), 229 (58), 129 (29). HRMS calcd for $C_{29}H_{42}O_8$: 518.2880. Found: 518.2878.

4.3.2. 6,7-Bis-(7-tetrahydropyran-2′-yloxy-2,5-dioxa-1-heptyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (12b). Yield 67%. R_f=0.70 (EtOAc); IR 2938 (s), 2870 (s), 1460 (m), 1350 (m), 1303 (m), 1267 (m), 1125 (s), 1077 (s), 1034 (s), 1021 cm^{-1} (m); ^1H NMR δ 6.78 (dd, $J_1=J_2=1.7$ Hz, 2H), 4.60 (m, 6H), 4.15 (m, 2H), 3.47–3.85 (m, 26H), 2.21 (AB quartet, $\Delta\delta$=0.069 ppm, J=7.1 Hz, 2H), 1.49–1.61 (m, 12H); ^{13}C NMR δ 149.9 (s), 143.6 (s),

142.5 (d), 128.1 (s), 98.8 (d), 70.4 (t), 70.3 (t), 69.6 (t), 68.5 (t), 66.6 (t), 64.2 (t), 62.3 (q), 62.1 (t), 47.6 (d), 30.5 (t), 25.3 (t), 19.4 (t); MS (FAB, NBA) *m/z* (%) 606 (M^+, 1), 605 (2), 416 (15), 311 (14), 309 (11), 229 (100), 215 (14), 149 (24), 85 (92), 57 (32). HRMS calcd for $C_{33}H_{50}O_{10}$: 606.3404. Found: 606.3406.

4.3.3. 6,7-Bis-(10-tetrahydropyran-2′-yloxy-2,5,8-trioxa-1-decyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (12c). Yield 79%. R_f=0.40 (EtOAc/*n*-Hex,1:1); IR 2938 (s), 2875 (s), 1460 (m), 1267 (w), 1124 (s), 1072 (s), 1034 cm^{-1} (s); ^1H NMR δ 6.76 (dd, $J_1=J_2$=1.8 Hz, 2H), 4.57–4.62 (m, 6H), 4.13 (br, 2H), 3.82–3.85 (m, 6H), 3.78 (s, 6H), 3.58–3.68 (m, 20H), 3.45–3.51 (m, 2H), 2.17 (AB quartet, $\Delta\delta$=0.071 ppm, J=7.1 Hz, 2H), 1.47–1.69 (m, 12H); ^{13}C NMR δ 150.0 (s), 143.7 (s), 142.5 (d), 128.1 (s), 98.9 (d), 72.5 (t), 70.5 (t), 70.4 (t), 69.6 (t), 68.5 (t), 66.6 (t), 66.5 (t), 64.2 (t), 62.3 (q), 62.1 (t), 47.6 (d), 30.5 (t), 25.4 (t), 19.4 (t); MS (FAB) *m/z* (%) 694 (M^+, weak), 460 (15), 377 (12), 311 (6), 229 (100), 228 (10), 85 (73), 45 (13). HRMS calcd for $C_{37}H_{58}O_{12}$: 694.3928. Found: 694.3922.

4.4. General procedure for hydrolysis of bis-ω-tetrahydropyranyl ethers 12a–c. Formation of ω,ω′-diols 13a–c

Ether **12a–c** (0.20 mmol) was dissolved in methanol (10 mL) with addition of two drops of conc. HCl and the solution was stirred at room temperature for 2 h. Methanol was removed from the reaction mixture after it was neutralized with $NaHCO_3$, and the residue thus obtained was stirred with EtOAc (10 mL) for a few minutes, and then filtered. The filtrate was concentrated to leave a pale yellow viscous liquid, which was purified via flash column chromatography to give ω′-diol **13a–c** as a colorless oil.

4.4.1. 6,7-Bis-(4-hydroxy-2-oxa-1-butyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (13a). Yield 99%. R_f=0.32 (EtOAc/*n*-Hex, 1:1); IR 3418 (br), 2935 (s), 2875 (m), 1612 (s), 1460 (s), 1268 (s), 1096 (s), 1068 (s), 1018 cm^{-1} (s); ^1H NMR δ 6.82 (dd, $J_1=J_2$=1.8 Hz, 2H), 4.61 (AB quartet, $\Delta\delta$=0.030 ppm, J=10.5 Hz, 4H), 4.18–4.19 (m, 2H), 3.81 (s, 6H), 3.66–3.70 (m, 8H), 2.66 (br, 2H), 2.23 (AB quartet, $\Delta\delta$=0.052 ppm, J=7.1 Hz, 2H); ^{13}C NMR δ 150.0 (s), 143.9 (s), 142.6 (d), 127.9 (s), 71.8 (t), 68.6 (t), 64.6 (t), 62.3 (q), 61.6 (t), 47.9 (d); MS (FAB) *m/z* (%) 350 (M^+, 4), 311 (9), 288 (44), 243 (18), 229 (100), 215 (15), 199 (12), 141 (8), 128 (9), 115 (9), 77 (6), 45 (9). HRMS calcd for $C_{19}H_{26}O_6$: 350.1729. Found: 350.1720.

4.4.2. 6,7-Bis-(7-hydroxy-2,5-dioxa-1-heptyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (13b). Yield 93%. R_f=0.17 (EtOAc); IR 3416 (br), 2933 (s), 2875 (m), 1616 (w), 1459 (m), 1267 (m), 1127 (m), 1075 (s), 1017 (m), 891 (w), 735 cm^{-1} (w); ^1H NMR δ 6.78 (dd, $J_1=J_2$=1.7 Hz, 2H), 4.69 (AB quartet, $\Delta\delta$=0.042 ppm, J=10.3 Hz, 4H), 4.15–4.16 (m, 2H), 3.78 (s, 6H), 3.55–3.71 (m, 16H), 2.19 (AB quartet, $\Delta\delta$=0.066 ppm, J=7.2 Hz, 2H); ^{13}C NMR δ 150.0 (s), 143.8 (s), 142.6 (d), 127.9 (s), 72.6 (t), 70.7 (t), 69.2 (t), 68.6 (t), 64.1 (t), 62.3 (q), 61.7 (t), 47.8 (d); MS (EI, 70 eV) *m/z* (%) 438 (M^+, weak), 332 (100), 244 (16), 243 (26), 229 (44). HRMS calcd for $C_{23}H_{34}O_8$: 438.2254. Found: 438.2260.

4.4.3. 6,7-Bis-(10-hydroxy-2,5,8-trioxa-1-decyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (13c). Yield 91%. R_f=0.92 (EtOAc); IR 3409 (br), 2936 (m), 2873 (s), 1460 (m), 1268 (m), 1081 (s), 1018 cm^{-1} (m), 934 (w); ^1H NMR δ 6.76 (dd, $J_1=J_2$=1.5 Hz, 2H), 4.59 (AB quartet, $\Delta\delta$=0.042 ppm, J=10.1 Hz, 4H), 4.13 (br, 2H), 3.77 (s, 6H), 3.55–3.69 (m, 24H), 3.04 (br, 2H), 2.17 (AB quartet, $\Delta\delta$=0.072 ppm, J=7 Hz, 2H); ^{13}C NMR δ 150.0 (s), 143.7 (s), 142.5 (d), 128.0 (s), 72.5 (t), 70.5 (t), 70.3 (t), 69.5 (t), 68.5 (t), 64.2 (t), 62.3 (q), 61.6 (t), 61.5 (t), 47.7 (d); MS (FAB) *m/z* (%) 549 (M^++Na, 6), 515 (1), 376 (20), 375 (4), 229 (100), 199 (10), 133 (4), 89 (12). HRMS calcd for $C_{27}H_{42}O_{10}{\cdot}Na^+$: 549.2676. Found: 549.2671.

4.4.4. Preparation of 6-Hydroxymethyl-7-(tetrahydropyran-2′-yloxymethyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene (15). Into a solution of diol **1** (0.50 g, 1.91 mmol) in CH_2Cl_2 (50 mL) containing a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS), cooled with an ice-water bath, was slowly added a solution of DHP (0.26 mL, 2.86 mmol) in a period of 30 min. After the addition was complete, the reaction mixture was stirring at room temperature and monitored by TLC every hour. Water (20 mL) was added immediately when the formation of bis-protected product was observed on TLC plate (4 h). Organic layer was separated and washed with brine (20 mL×3), dried ($MgSO_4$), and filtered. Concentration of the filtrate to give oily residue which was purified via flash column chromatography to give **15** (0.49 g, 74%) as a colorless viscous liquid: R_f=0.48 (EtOAc/*n*-Hex, 1:1); IR 3487 (br), 2929 (s), 2853 (m), 1459 (m), 1266 (m), 1117 (m), 1073 (m), 1021 cm^{-1} (s); ^1H NMR δ 6.82 (dd, $J_1=J_2$=1.7 Hz, 2H), 4.92/4.90 (2d, J=10.7 Hz, 1H), 4.80–4.82 (m, 1H), 4.67–4.69 (m, 2H), 4.61/4.60 (2d, J=10.7 Hz, 1H), 4.18–4.20 (m, 2H), 3.91–3.97 (m, 1H), 3.87/3.86 (2s, 3H), 3.79 (s, 3H), 3.58–3.63 (m, 1H), 3.17 (br, 2H, –OH), 2.23/2.20 (unresolved AB quartet, 2H), 1.72–1.75 (m, 2H), 1.52–1.60 (m, 4H); ^{13}C NMR δ 149.53/149.48 (2s), 143.86 (s), 143.29/143.26 (2s), 142.72/142.66 (2d), 142.61 (s), 132.09/132.07 (2s), 126.98/126.94 (2s), 98.56/98.51 (2d), 68.68 (t), 62.48 (q), 62.22 (t), 61.45/61.43 (2t), 56.95 (t), 47.78/47.75/47.72 (3d), 30.56/30.54 (2t), 25.25 (t), 19.25/19.23 (2t); MS (FAB, NBA) *m/z* (%) 346 (M^+, 66), 329 (20), 245 (100), 229 (93), 215 (34), 154 (62), 136 (44), 85 (90). HRMS calcd for $C_{20}H_{26}O_5$: 346.1780. Found: 346.1775.

4.5. General procedure for the preparation of bis-(1,4-methanonaphthalen-6-yl)ethers 16b–d

A solution of benzyl alcohol **15** (1.00 mmol) in dried THF (20 mL) was added NaH (3.00 mmol) under N_2 atmosphere and the reaction mixture was heated under gentle reflux. Bis-toluene-*p*-sulfonate **11b–d** (0.50 mmol) in THF (5 mL) was added dropwise into the reaction mixture. After refluxing for 10 h, another portion of NaH (3.00 mmol) was added, and the reaction mixture was refluxed for additional 20 h, and cooled down to room temperature. Methanol (10 mL) was added. Solvent (THF) was removed prior to the addition of water (50 mL) and the resulting solution was extracted with EtOAc (30 mL×3). The

combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. Removal of solvent left a pale yellow viscous liquid, which was subjected to purification via column chromatography to afford **16b–d** as colorless oil.

4.5.1. 1,9-Bis[7-(tetrahydropyran-2′-yloxymethyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8-trioxanonane (16b). Yield 66%. R_f=0.37 (EtOAc/*n*-Hex, 1:1); IR 2936 (m), 2867 (m), 1459 (m), 1267 (m), 1134 (m), 1116 (m), 1076 (m), 1022 cm^{-1} (s); ^1H NMR δ 6.77 (dd, J_1=J_2=1.8 Hz, 4H), 4.86/4.83 (2d, J=10.3 Hz, 2H), 4.75 (m, 2H), 4.61/4.58 (2 AB quartets, $\Delta\delta$=0.053/0.054 ppm, J=10.0/9.9 Hz, 4H), 4.50/4.48 (2d, J=10.4 Hz, 2H), 4.14–4.16 (m, 4H), 3.94–3.99 (m, 2H), 3.78–3.80 (m, 12H), 3.62–3.66 (m, 10H), 2.19 (AB quartet, $\Delta\delta$=0.060 ppm, J=7.1 Hz, 4H), 1.52–1.59 (m, 12H); ^{13}C NMR δ 150.18/150.15 (2s), 150.02/150.00 (2s), 143.74/143.72 (2s), 143.65/143.62 (2s), 142.58/142.54 (2d), 128.21/128.15/128.12 (3s), 98.64/98.59 (2d), 70.37 (t), 69.58 (t), 68.51 (t), 64.38 (t), 62.38/62.36 (2q), 62.31 (t), 62.07/62.03 (2t), 61.03/61.00 (2t), 47.72/47.66 (2d), 30.68/30.66 (2t), 25.48 (t), 19.46/19.44 (2t); MS (FAB, NBA) *m/z* (%) 762 (M^+, weak), 426 (7), 334 (3), 229 (100), 228 (19), 141 (5), 185 (5). HRMS calcd for $C_{44}H_{58}O_{11}$: 762.3979. Found: 762.3991.

4.5.2. 1,12-Bis[7-(tetrahydropyran-2′-yloxymethyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8,11-tetraoxadodecane (16c). Yield 69%. R_f=0.24 (EtOAc/*n*-Hex, 1:1); IR 2938 (s), 2875 (m), 1460 (m), 1348 (m), 1304 (m), 1267 (s), 1116 (m), 1076 (m), 1022 cm^{-1} (s); ^1H NMR δ 6.78 (dd, J_1=J_2=1.8 Hz, 4H), 4.86/4.83 (2d, J=10.3 Hz, 2H), 4.75 (m, 2H), 4.60 (dt, J_1=23.2 Hz, J_2=10 Hz, 4H), 4.50/4.47 (2d, J=10.3 Hz, 2H), 4.15–4.16 (m, 4H), 3.93–3.99 (m, 2H), 3.79–3.81 (m, 12H), 3.60–3.67 (m, 14H), 2.20 (AB quartet, $\Delta\delta$=0.060 ppm, J=7.1 Hz, 4H), 1.52–1.60 (m, 12H); ^{13}C NMR δ 150.16/150.13 (2s), 149.99/149.96 (2s), 143.74/143.72 (2s), 143.63/143.60 (2s), 142.57/142.56 (2d), 142.52/142.51 (2d), 128.19/128.11/128.08 (3s), 98.61/98.57 (2d), 70.45 (t), 69.57 (t), 68.50 (t), 64.34 (t), 62.36/62.29 (2q), 62.04/62.01 (2t), 61.02/60.98 (2t), 47.69/47.64 (2d), 30.66/30.64 (2t), 25.45 (t), 19.43/19.41 (2t); MS (FAB, NBA) *m/z* (%) 806 (M^+, 5), 705 (M^+−−OTHP), 427 (35), 377 (17), 375 (16), 245 (57), 244 (89), 243 (99), 231 (24), 230 (88), 229 (100), 215 (40), 213 (42), 85 (98), 67 (33), 57 (57). HRMS (FAB) calcd for $C_{46}H_{62}O_{12}$: 806.4241. Found: 806.4251.

4.5.3. 1,15-Bis[7-(tetrahydropyran-2′-yloxymethyl)-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8,11,14-pentaoxadodecane (16d). Yield 61%. R_f=0.66 (EtOAc); IR 2938 (s), 2869 (m), 1612 (w), 1459 (m), 1348 (m), 1304 (m), 1267 (s), 1116 (s), 1078 (s), 1022 (s), 905 (m), 731 cm^{-1} (m); ^1H NMR δ 6.78 (dd, J_1=J_2=1.6 Hz, 4H), 4.86/4.83 (2d, J=10.3 Hz, 2H), 4.75 (m, 2H), 4.60 (dt, J_1=22.9 Hz, J_2=10 Hz, 4H), 4.50/4.48 (2d, J=10.3 Hz, 2H), 4.15 (m, 4H), 3.94–3.99 (m, 2H), 3.80–3.82 (m, 12H), 3.56–3.69 (m, 18H), 2.20 (AB quartet, $\Delta\delta$=0.059 ppm, J=7.1 Hz, 4H), 1.48–1.60 (m, 12H); ^{13}C NMR δ 150.20/150.17 (2s), 150.02/150.00 (2s), 143.74/143.72 (2s), 143.63/143.60 (2s), 142.58/142.55 (2d), 128.24/128.16/128.13 (3s), 98.64/98.60 (2d), 70.55/70.47 (2t), 69.61 (t), 68.52 (t), 64.38 (t), 62.36/62.29 (2q), 62.07/62.04 (2t), 61.05/61.01 (2t), 47.73/47.68 (2d), 30.69/30.67 (2t), 25.49 (t), 19.46/19.45 (2t); MS (FAB, NBA) *m/z* (%) 850 (M^+, 4), 427 (44), 229 (100), 228 (92). HRMS (FAB) calcd for $C_{48}H_{66}O_{13}$: 850.4503. Found: 850.4512.

4.6. Hydrolysis of ditetrahydropyranyl-substituted ethers 16b–d. Formation of bis-benzylic diols 17b–d

The procedure for hydrolysis of bis-ω-tetrahydropyranyl ethers **12a–c** to form ω,ω′-diols **13a-c** was generally followed.

4.6.1. 1,9-Bis[7-hydroxymethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8-trioxanonane (17b). Yield 96%. R_f=0.50 (EtOAc/*n*-Hex, 1:1); IR 3491 (br), 2929 (s), 2857 (m), 1460 (m), 1380 (w), 1267 (s), 1121 (m), 1072 (m), 1023 cm^{-1} (w); ^1H NMR δ 6.80 (dd, J_1=J_2=1.7 Hz, 4H), 4.62–4.68 (m, 8H), 4.16–4.20 (m, 4H), 3.85 (s, 6H), 3.76 (s, 6H), 3.68–3.71 (m, 4H), 3.58–3.60 (m, 4H), 2.21 (AB quartet, $\Delta\delta$=0.063 ppm, J=7.2 Hz, 4H); ^{13}C NMR δ 149.8 (s), 149.3 (s), 143.9 (s), 143.0 (s), 142.7 (d), 142.6 (d), 132.5 (s), 127.1 (s), 70.3 (t), 69.3 (t), 68.7 (t), 64.9 (t), 62.5 (q), 62.4 (q), 56.7 (t), 47.8 (d), 47.7 (d); MS (FAB) *m/z* (%) 595 (M^++H, weak), 441 (34), 245 (100), 229 (97). HRMS (FAB) calcd for $C_{34}H_{42}O_9{\cdot}H^+$: 595.2912. Found: 595.2910.

4.6.2. 1,12-Bis[7-hydroxymethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8,11-tetraoxadodecane (17c). Yield 93%. R_f=0.33 (EtOAc); IR 3485 (br), 2934 (m), 2869 (m), 1460 (m), 1304 (m), 1266 (s), 1219 (m), 1085 (s), 1021 cm^{-1} (s); ^1H NMR δ 6.81 (dd, J_1=J_2=1.5 Hz, 4H), 4.61–4.65 (m, 8H), 4.16–4.19 (m, 4H), 3.85 (s, 6H), 3.77 (s, 6H), 3.58–3.66 (m, 12H), 2.21 (AB quartet, $\Delta\delta$=0.065 ppm, J=7.1 Hz, 4H); ^{13}C NMR δ 149.8 (s), 149.3 (s), 144.0 (s), 143.0 (s), 142.8 (d), 142.6 (d), 132.5 (s), 127.1 (s), 70.4 (t), 70.3 (t), 69.2 (t), 68.7 (t), 64.8 (t), 62.6 (q), 62.4 (q), 56.8 (t), 47.7 (d); MS (FAB, NBA) *m/z* (%) 639 (M^++1), 620 (M^+-H_2O, 16), 429 (35), 427 (40), 377 (37), 246 (50), 245 (100), 244 (79), 243 (96), 230 (45), 229 (100), 215 (54), 213 (35), 163 (42), 154 (67), 136 (56), 128 (30), 115 (32), 89 (35), 77 (36). HRMS (FAB) calcd for $C_{36}H_{46}O_{10}{\cdot}H^+$: 639.3163. Found: 639.3166.

4.6.3. 1,15-Bis[7-hydroxymethyl-5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalen-6-yl]-2,5,8,11,14-pentaoxadodecane (17d). Yield 99%. R_f=0.18 (EtOAc); IR 3486 (br), 2935 (m), 2869 (m), 1459 (m), 1304 (m), 1267 (s), 1218 (m), 1089 (s), 1021 (s), 732 cm^{-1} (m); ^1H NMR δ 6.81 (dd, J_1=J_2=1.2 Hz, 4H), 4.62–4.66 (m, 8H), 4.16–4.19 (m, 4H), 3.85 (s, 6H), 3.77 (s, 6H), 3.58–3.67 (m, 16H), 2.21 (AB quartet, $\Delta\delta$=0.065 ppm, J=7.2 Hz, 4H); ^{13}C NMR δ 149.8 (s), 149.3 (s), 144.0 (s), 142.9 (s), 142.7 (d), 142.6 (d), 132.5 (s), 127.0 (s), 70.5 (t), 70.4 (t), 70.3 (t), 69.2 (t), 68.7 (t), 64.8 (t), 62.5 (q), 62.4 (q), 56.8 (t), 47.7 (d); MS (FAB, NBA) *m/z* (%) 705 (M^++Na, 40), 429 (26), 229 (100), 215 (84). HRMS (FAB) calcd for $C_{38}H_{50}O_{11}{\cdot}Na^+$: 705.3251 Found: 705.3259.

4.7. Synthesis of crown ethers 14b–d

Method A. From dibromide **7** and ω,ω′-diols **13a–c**. Under

N_2 atmosphere, a solution of ω,ω′-diols **14a–c** (0.14 mmol) in dried THF (20 mL) was added NaH (0.84 mmol) and the reaction mixture was heated under gentle reflux. Dibromide **7** (0.14 mmol) in THF (10 mL) was added dropwise into the reaction mixture. After refluxing for 2 h, the reaction mixture was cooled down to room temperature and methanol (10 mL) was added. Solvent (THF) was removed prior to the addition of water (20 mL) and the resulting solution was extracted with ethyl acetate (20 mL×4). The combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. Removal of solvent left a pale yellow viscous liquid, which was subjected to purification via column chromatography to afford pure **14a** as a white solid in 47% yield, and **14b** and **14c** as colorless oil in 78 and 64% yields, respectively.

Method B. From diols **17b–d** and bis-toluene-*p*-sulfonate **11b–d**. A solution of bis-benzyl alcohol **17b–d** (0.10 mmol) in dried THF (10 mL) was added NaH (0.50 mmol) under N_2 atmosphere and the reaction mixture was heated under gentle reflux. Bis-toluene-*p*-sulfonate **11b–d** (0.10 mmol) in THF (5 mL) was added dropwise into the reaction mixture. After refluxing for 10 h, another portion of NaH (0.5 mmol) was added, and the reaction mixture was refluxed for additional 20 h, and cooled down to room temperature. Methanol (10 mL) was added. Solvent (THF) was removed prior to the addition of water (30 mL) and the resulting solution was extracted with EtOAc (20 mL×3). The combined organic layers were washed with brine, dried ($MgSO_4$), and filtered. Removal of solvent left a pale yellow viscous liquid, which was subjected to purification via column chromatography to afford **14b**, **14c**, and **14d** as colorless oil in 78, 83, and 65% yields, respectively.

4.7.1. 9,16,25,32-Tetramethoxy-3,6,19,22-tetraoxaheptacyclo[22.8.0.1^{11,14}.1^{27,30}.0^{8,17}.0^{10,15}.0^{27,30}]tetratriaconta-1(24),8,10(15),12,16,25,28,31-octene (14a). Mp 176–177°C (CH_2Cl_2/acetone); R_f=0.31 (EtOAc/*n*-Hex, 1:1); IR 2936 (m), 2870 (m), 1460 (s), 1267 (s), 1097 (s), 1019 (s), 975 (m), 735 cm^{-1} (w); ^1H NMR and ^{13}C NMR (see Table 1); MS *m*/*z* (%) 576 (M^+, 3), 501 (8), 300 (9), 288 (53), 287 (34), 229 (85), 228 (100), 213 (40), 199 (40), 141 (32), 128 (38). HRMS calcd for $C_{34}H_{40}O_8$: 576.2723. Found: 576.2729.

4.7.2. 12,19,31,38-Tetramethoxy-3,6,9,22,25,28-hexaoxaheptacyclo[28.8.0.1^{14,17}.1^{33,36}.0^{11,20}.0^{13,18}.0^{32,37}]tetraconta-1(30),11,13(18),15,19,31,34,37-octene (14b). R_f=0.71 (EtOAc); IR 2930 (s), 2869 (s), 1461 (m), 1355 (m), 1303 (m), 1267 (m), 1136 (m), 1093 (m), 732 cm^{-1} (s); ^1H NMR and ^{13}C NMR (see Table 1); MS (FAB) *m*/*z* (%) 664 (M^+, 6), 452 (6), 332 (45), 243 (53), 228 (100), 213 (18), 199 (15), 127 (17). HRMS calcd for $C_{38}H_{48}O_{10}$: 664.3247. Found: 664.3254.

4.7.3. 15,22,37,44-Tetramethoxy-3,6,9,12,25,28,31,34-octaoxaheptacyclo[34.8.0.1^{17,20}.1^{39,42}.0^{14,23}.0^{16,21}.0^{38,43}]hexatetraconta-1(36),14,16(21),18,22,37,40,43-octene (14c). R_f=0.76 (EtOAc); IR 2925 (s), 1461 (m), 1267 (m), 1093 (s), 1020 (m), 754 cm^{-1} (s); ^1H NMR and ^{13}C NMR (see Table 1); MS *m*/*z* (%) 752 (M^+, 1), 452 (4), 377 (17), 376 (20), 375 (12), 243 (46), 229 (100), 199 (22), 133 (20). HRMS calcd for $C_{42}H_{56}O_{12}$: 752.3772. Found: 752.3776.

4.7.4. 18,25,43,50-Tetramethoxy-3,6,9,12,15,28,31,34,37,40-decaoxaheptacyclo[40.8.0.1^{20,23}.1^{45,48}.0^{17,26}.0^{19,24}.0^{44,49}]dopentaconta-1(42),17,19(24),25,43,46,49-octene (14d). R_f=0.29 (EtOAc); IR 2930 (s), 2871 (s), 1462 (m), 1267 (m), 1098 (s), 1018 cm^{-1} (m); ^1H NMR and ^{13}C NMR (see Table 1); MS (FAB) *m*/*z* (%) 840 (M^+, 8), 647 (34), 243 (90), 229 (100). HRMS calcd for $C_{46}H_{64}O_{14}$: 840.4296. Found: 840.4305.

4.8. X-Ray crystallography

Single crystals of crown ether **14a** suitable for X-ray crystallographic analysis were obtained from a mixture of ether–dichloromethane. It crystallized in a monoclinic form, space group *Cc* (No. 9). The X-ray crystallographic data were recorded with a Bruker Smart APEX CCD diffractometer. Graphite monochromatized Mo Kα radiation [λ=0.71073 Å] and temperature of 273(2) K were used. The CCD data were processed with SAINT and the structures were solved by direct method (SHELXS-97[21]) and refined on F^2 by full-matrix least-squares techniques (SHELXL-97[22]). The hydrogen atoms were located from the difference Fourier and refined isotropically. Crystallographic data (excluding structure factors) for **14a** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 216665. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Compound **14a**. $C_{34}H_{40}O_8$, monoclinic, space group *Cc*, *a*=9.0852(12) Å, *b*=25.122(3) Å, *c*=26.700(4) Å; α=91.585(4)°, *V*=6091.5(15) Å^3, *Z*=8 (two independent molecules), D_{calcd}=1.258 Mg/m^3, crystal size 0.3×0.2×0.1 mm^3. A total of 34983 reflections (−35≤*h*≤34, −12≤*k*≤11, −32≤*l*≤32) were collected at *T*=300(2) K in the range from 1.53 to 28.3°, of which 14360 were unique (R_{int}=0.0508); All nonhydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated idealized positions. The residual peak and hole of electron densities were 1.169 and −0.204 e Å^{-3}. The final *R* indices [($I>2\sigma(I)$)]: $R(F)$=0.0638, $wR(F^2)$=0.1745; GOF=0.855 (for 345 parameters).

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References

1. (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495–2496. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036. (c) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 386–391. (d) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 391–394. (e) Pedersen, C. J.; Frensdorff, H. K. *Angew. Chem.* **1972**, *84*, 16–25.
2. (a) Kyba, E. P.; Helgeson, R. C.; Madan, K.; Gokel, G. W.; Tarnowski, T. L.; Moore, S. S.; Cram, D. J. *J. Am. Chem. Soc.*

1976, *98*, 2564–2571. (b) Timko, J. M.; Moore, S. S.; Walbs, D. M.; Hiberty, P. C.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 4207–4219. (c) Moore, S. S.; Tarnowski, T. L.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398–6405. (d) Newcomb, M.; Moore, S. S.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6405–6410. (e) Newcomb, M.; Timko, J. M.; Walbs, D. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6392–6398.

3. (a) Cheney, J.; Lehn, J.-M. *Chem. Commun.* **1972**, 487–489. (b) Graf, E.; Lehn, J.-M. *J. Am. Chem. Soc.* **1975**, *97*, 5022–5024. (c) Kotzyba-Hibert, F.; Lehn, J.-M.; Vierling, P. *Tetrahedron Lett.* **1980**, *21*, 941–944. (d) Kintzinger, J.-P.; Kotzyba-Hibert, F.; Lehn, J.-M.; Pagelot, A.; Saigo, K. *J. Chem. Soc., Chem. Commun.* **1981**, 833–836. (e) Alberts, A. H.; Lehn, J.-M.; Parker, D. J. *J. Chem. Soc., Dalton Trans.* **1985**, 2311–2317.
4. (a) An, H.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1992**, *92*, 543–572. (b) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529–2586. (c) Fitzmaurice, R. J.; Kyne, G. M.; Douheret, D.; Kilburu, J. D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 841–864.
5. Cryptands: (a) Lukyanenko, N. G.; Basok, S. S.; Filonova, L. K. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3141–3148. (b) Anelli, P. L.; Montanari, F.; Quici, S.; Ciani, G.; Sironi, A. *J. Org. Chem.* **1988**, *53*, 5292–5298. (c) Fyles, T. M.; Suresh, V. V.; Fronczek, F. R.; Gandour, R. D. *Tetrahedron Lett.* **1990**, *31*, 1101–1104.
6. Lariat ethers: (a) Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 1257–1259. (b) Elshani, S.; Du, H.; Laintz, K. E.; Natale, N. R.; Wai, C. M.; Elkarim, N. S. A.; Bartsch, R. A. *Tetrahedron* **2000**, *56*, 4651–4657. (c) Liu, Y.; Zhang, H.-Y.; Bai, X.-P.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2000**, *65*, 7105–7109. (d) Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J. *Acc. Chem. Res.* **2002**, *35*, 878–886.
7. Carbocage-annelated crown ethers: (a) Marchand, A. P.; Chong, H.-S.; Alihodžić, S.; Watson, W. H.; Bodige, S. O. *Tetrahedron* **1999**, *55*, 9687–9696. (b) Marchand, A. P.; Chong, H.-S. *Tetrahedron* **1999**, *55*, 9697–9706. (c) Levitskaia, T. G.; Moyer, B. A.; Bonnesen, P. V.; Marchand, A. P.; Krishnudu, K.; Chen, Z.; Huang, Z.; Kruger, H. G.; McKim, A. S. *J. Am. Chem. Soc.* **2001**, *123*, 12099–12100.
8. Cyclophane-type crown ethers: (a) Helgeson, R. C.; Tarnowski, T. L.; Timko, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6411–6418. (b) Xu, J.; Lai, Y.-H.; He, C. *Org. Lett.* **2002**, *4*, 3911–3914.
9. Porphyrin-connected crown ethers: (a) Duggan, S. A.; Fallon, G.; Langford, S. J.; Lau, V.-L.; Satchell, J. F.; Paddon-Row, M. N. *J. Org. Chem.* **2001**, *66*, 4419–4426. (b) Martinez-Diaz, M. V.; Rodriguez-Morgade, M. S.; Feiters, M. C.; van Kan, P. J. M.; Nolte, R. J. M.; Stoddart, J. F.; Torres, T. *Org. Lett.* **2000**, *2*, 1057–1060.
10. Fullerene-connected crown ethers: (a) Nakamura, Y.; Asami, A.; Ogawa, T.; Inokuma, S.; Nishimura, J. *J. Am. Chem. Soc.* **2002**, *124*, 4329–4335. (b) Carano, M.; Corvaja, C.; Garlaschelli, L.; Maggini, M.; Marcaccio, M.; Paolucci, F.; Pasini, D.; Righetti, P. P.; Sartori, E.; Toffoletti, A. *Eur. J. Org. Chem.* **2003**, 374–384.
11. Rotaxanes: (a) Ashton, P. R.; Baxter, I.; Fyfe, M. C. T.; Raymo, F. M.; Spencer, N.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1998**, *120*, 2297–2307. (b) Cao, J.; Fyfe, M. C. T.; Stoddart, J. F.; Cousins, G. R. L.; Glink, P. T. *J. Org. Chem.* **2000**, *65*, 1937–1946.
12. Catenanes: (a) Raehm, L.; Hamann, C.; Kern, J.-M.; Sauvage, J.-P. *Org. Lett.* **2000**, *2*, 1991–1994. (b) Balzani, V.; Credi, A.; Langford, S. J.; Raymo, F. M.; Stoddart, J. F.; Venturi, M. *J. Am. Chem. Soc.* **2000**, *122*, 3542–3543. (c) Hansen, J. G.; Feeder, N.; Hamilton, D. G.; Gunter, M. J.; Becher, J.; Sanders, J. K. M. *Org. Lett.* **2002**, *4*, 449–452.
13. Perrier, S.; Kochi, J. K. *J. Chem. Soc., Perkin Trans. 2* **1993**, 825–836.
14. (a) Johnson, L. K.; Killian, C. M.; Brookhart, M. J. *J. Am. Chem. Soc.* **1995**, *117*, 6614. (b) Small, B. L.; Brookhart, M.; Bennett, A. M. A. *J. Am. Chem. Soc.* **1998**, *120*, 4049–4050.
15. (a) Grubbs, R. H.; Tumas, W. *Science* **1989**, *243*, 907–915. (b) Schrock, R. R. *Acc. Chem. Res.* **1990**, *23*, 158–165. (c) Schrock, R. R. *Tetrahedron* **1999**, *55*, 8141–8153. (d) Del Río, I.; van Koten, G. *Tetrahedron Lett.* **1999**, *40*, 1401–1404. (e) Buchmeiser, M. R. *Chem. Rev.* **2000**, *100*, 1565–1604. (f) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (g) Tsai, M.-L.; Liu, C.-Y.; Hsu, M.-A.; Chow, T. J. *Appl. Phys. Lett.* **2003**, *82*, 1–3.
16. (a) Gokel, G. W.; Durst, H. D. *Synthesis* **1976**, 168–184. (b) Reinhoudt, D. N.; Gray, R. T.; Smit, C. J.; Veenstra, M. I. *Tetrahedron* **1976**, *32*, 1161–1169. (c) An, H.; Bradshaw, J. S.; Krakowiak, K. E.; Tarbet, B. J.; Dalley, N. K.; Kou, X.; Zhu, C.; Izatt, R. M. *J. Org. Chem.* **1993**, *58*, 7694–7699.
17. (a) Bott, S. G.; Marchand, A. P.; Kumar, K. A. *J. Chem. Crystal.* **1996**, *26*, 281–286. (b) Marchand, A. P.; Ganguly, B. *Tetrahedron* **1998**, *37*, 10967–10972.
18. (a) de Vries, E. F. J.; Steenwinkel, P.; Brussee, J.; Kruse, C. G.; van der Gen, A. *J. Org. Chem.* **1993**, *63*, 3670–3677. (b) Gu, X.-P.; Ikeda, I.; Komada, S.; Masuyama, A.; Okahara, M. *J. Org. Chem.* **1986**, *51*, 5425–5427.
19. Ouchi, M.; Inoue, Y.; Liu, Y.; Wada, K.; Hakushi, T. *Bull. Chem. Soc. Jpn* **1990**, *63*, 1260–1262.
20. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772–3774.
21. Sheldrick, G. M. *SHLXS97—A Program for Automatic Solution of Crystal Structures*; University of Göttingen: Germany, 1997.
22. Sheldrick, G. M. *SHLXL97—A Program for Automatic Refinement of Crystal Structures*; University of Göttingen: Germany, 1997.