

## Synthesis, Characterization and Complexation Behavior Investigations of Novel Bis- and Tris-crown Ethers

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Novel bis- and tris-crown ethers were synthesized from 1-aza and diaza-crown ethers with 2-acryloyloxymethyl crown ethers through Michael addition. The synthesized bis- and tris-crown ethers were characterized by their elemental analyses, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, mass spectra, IR spectra, respectively. The complexation behavior of the bis- and tris-crown ethers with Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup>, Cs<sup>+</sup> was examined by <sup>1</sup>H-NMR, FAB mass, and UV spectrometry.

**Key Words** : 2-Acryloyloxymethyl crown ether, Aza-crown ether, Bis-crown ether, Tris-crown ether

### Introduction

The chemistry of bis-crown ethers has attracted considerable attentions during the last two decades because of both their fascinate structures and high abilities in complex with guest cations. A wide variety of bis-crown ethers were synthesized and reported.<sup>1-34</sup> Recently, significant research interest has been devoted to the design of multi-site crown ethers, several tris-crown ethers have been synthesized.<sup>35-38</sup> The construction of multi-site molecular receptor molecules capable of binding two or more guest metal cations is one current area of interest in this field.<sup>39-48</sup>

Crown ether moiety is one of the most popular host compounds in host-guest chemistry field. When the metal cations radii exactly fit the size of the crown ether unit, it always forms a 1 : 1 host/guest complex. However, compounds that consist of more than one crown ether units in the same molecule, it may produce "sandwich type" complexes with the metal cations. When the size exceeds that of the crown ether cavity such as the "butterfly crown ethers",<sup>1-4</sup> it may form a host/guest 2 : 1 sandwich type complex.<sup>49-52</sup>

Aza-crown ethers have been acted as important building blocks in host-guest and supra-molecular chemistry fields. Armed crown ethers are characterized by a parent crown ring such as 1-aza crown ethers and diaza crown ethers. As our continuing effort to make new bis- and tris-crown ethers, 1-aza and diaza crown ethers were used as starting material to react with 2-acryloyloxymethyl crown ethers. The structure of the novel bis- and tris-crown ethers are shown in Figure 1 and Figure 2. In addition, these host compounds of bis- and tris-crown ethers showed interesting complexation ability with various size of alkali metal cations such as Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup> and Cs<sup>+</sup>. In this paper, the synthesis, characterization and complexation behavior of a new type of bis- and tris-crown ethers are reported. The bis- and tris-crown ethers lead to original applications for the preparation of novel host-guest complexes. The properties can be applied in various areas, such as synthetic and medical

chemistry, host-guest and supra-molecular chemistry.

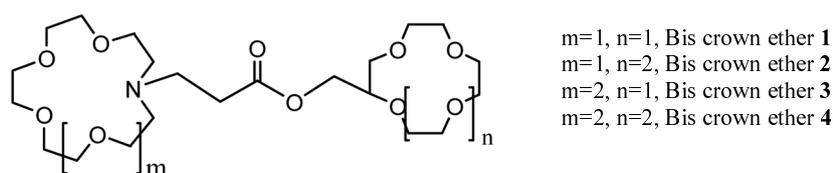
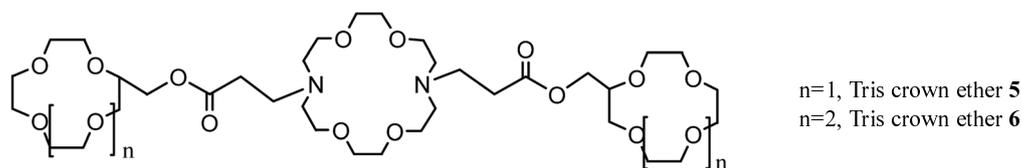
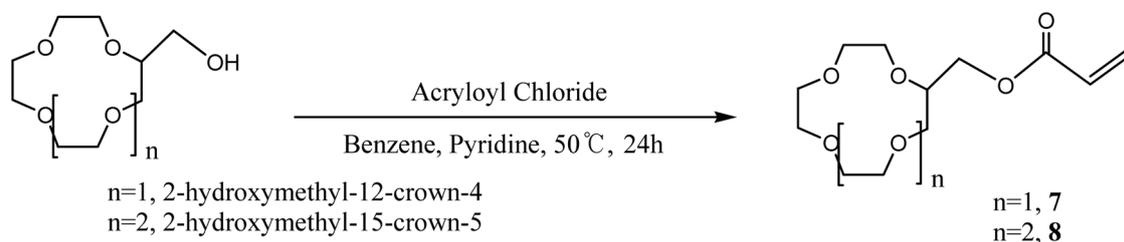
### Results and Discussion

The synthetic approach to 2-acryloyloxymethyl crown ethers is shown in Scheme 1. 2-Acryloyloxymethyl crown ethers **7** and **8** were synthesized from 2-hydroxymethyl-12-crown-4 and 2-hydroxymethyl-15-crown-5 with acryloyl chloride in benzene, respectively. Pyridine was used as catalyst. The acrylic double bond was very reactivity, in order to avoid polymerization and to obtain relatively high yield of crown ether **7** and **8**, the reaction temperature was kept under 50 °C. Bis-crown ether **1** to **4** was prepared from 1-aza 15-crown-5 and 1-aza 18-crown-6 with **7** and **8**. Tris-crown ether **5** and **6** was obtained from the diaza 18-crown-6 with **7** and **8**, respectively.

All the compounds **1** to **8** were characterized by <sup>1</sup>H- and <sup>13</sup>C-NMR spectra, mass spectrometry, IR spectrometry and elemental analyses (C, H, N).

In the <sup>1</sup>H-NMR spectra, each proton signal of the new compounds was at the expected chemical shift. For example in the bis-crown ethers, the ethereal protons of the crown ether groups appeared as multiplets at 3.57-3.98 ppm. The 1-aza-crown ether -CH<sub>2</sub>-N-CH<sub>2</sub>- protons were at 2.75 ppm (triplets). The newly formed -CH<sub>2</sub>-N bond protons which connected the 2-acryloyloxymethyl crown ethers with the 1-aza crown ether nitrogen atoms were at 2.88 ppm (triplets). The case of the tris-crown ethers was similar to that of the bis-crown ethers. At the 5.8-6.5 ppm region, the double bond proton signals of 2-acryloyloxy-methyl crown ethers were not found, indicating that the Michael addition accomplished.

The <sup>13</sup>C-NMR spectra revealed the removal of the double bond carbon signals which were located at 128 ppm and 131 ppm, and the C=O carbon chemical shift moved from 165 ppm to 173 ppm. The crown ether carbon chemical shifts were seen at 70 ppm region. All the other carbon atoms' chemical shifts of the bis- and tris-crown ethers were as

**Figure 1.** The structure of bis-crown ethers.**Figure 2.** The structure of tris-crown ethers.**Scheme 1**

expected.

The crown ethers **1** to **8** were checked by mass spectrometry. The results of mass spectroscopy further supported the structures of the bis- and tris-crown ethers. In the FAB mass spectra of the new tris-crown ethers **5** and **6**, which came from the diaza-18-crown-6 ether, the fragment ion peaks could be easily observed. For instance, in the FAB mass spectra of the tris-crown ether **5**, the molecular ion peak was found at  $m/z$  783.4  $[M+H]^+$  (calc. for  $C_{36}H_{66}N_2O_{16}$ : M, 782.4). An ion peak at  $m/z$  435.3 corresponds to a decomposition product formed by removing of two [12-crown-4 ring] ions. Another ion peak at  $m/z$  609.3 corresponds to a decomposition product formed by cleavage of one [12-crown-4 ring] ion. The case of tris-crown ether **6** was similar to that of **5**.

In IR spectra, the crown ether C-O-C group absorption peaks were observed around  $1120\text{--}1130\text{ cm}^{-1}$  region. In the elemental analyses, all the C, H, N values of the bis- and tris-crown ethers were within acceptable ranges.

The binding interactions of the host compounds of bis- and tris-crown ethers with the alkali metal cations were examined with  $^1\text{H}$  NMR spectroscopy, FAB mass spectrometry and absorption investigation on UV spectrometry.

In the  $^1\text{H}$  NMR analysis, the LiSCN, NaSCN, KSCN, RbSCN and CsSCN were dissolved in acetone- $d_6$  to make a  $2 \times 10^{-2}$  M solution, respectively. **1** to **6** were dissolved in acetone- $d_6$  to make  $5 \times 10^{-3}$  M solutions. The gradually downfield shift or upfield shift was observed with increasing concentration of the alkali metal thiocyanate salt in the bis- and tris-crown solutions. The stoichiometry of the

complexation between the bis-crown ether with the alkali cation was confirmed to be 1 : 2, and the tris-crown ether was confirmed to be 1 : 3 by the molar ratio. For example, with the addition of LiSCN to bis-crown ether **1** solution, the chemical shift of H-1 (O-CO-CH $_2^1$ -CH $_2^2$ -N) downfield shifted from  $\delta$  2.427 ppm (triplets) (chemical shift  $\delta$  was relative to TMS  $\delta$  0 ppm) to  $\delta$  2.661 ppm,  $\Delta\delta = 0.234$  ppm. H-2 shifted from  $\delta$  2.801 ppm (triplets) to  $\delta$  2.874 ppm,  $\Delta\delta = 0.073$  ppm. The chemical shift of 1-aza-crown unit CH $_2$ -N-CH $_2$ - protons downfield shifted from  $\delta$  2.687 ppm (triplets) to  $\delta$  2.768 ppm,  $\Delta\delta = 0.081$  ppm. The crown ether ring proton multiple peaks all downshifted, the changed average chemical shift  $\Delta\delta = 0.118$  ppm. The shape of the peaks became more complicated. The association constants  $K_a$  ( $M^{-1}$ ) was determined by a nonlinear curve-fitting method.<sup>53</sup> The chemical shift change was due to the interaction of crown ether rings with metal cations, which indicates that a new complex was formed.

The case of bis-crown ethers **1** to **4** interacted with Li $^+$ , Na $^+$ , K $^+$ , Rb $^+$ , Cs $^+$  were similar to the above. The changes of  $^1\text{H}$  NMR chemical shifts  $\Delta\delta$  of H-1, H-2, 1-aza-crown unit CH $_2$ -N-CH $_2$ , the changed crown ring proton average chemical shift and the association constant  $K_a$  are summarized in Table 1.

The  $^1\text{H}$  NMR chemical shifts changes of the tris-crown ethers **5** and **6** interacted with Li $^+$ , Na $^+$ , K $^+$ , Rb $^+$ , Cs $^+$  were similar to the bis-crown ethers. The changes of  $^1\text{H}$  NMR chemical shifts  $\Delta\delta$  of H-3, H-4, diaza-crown unit CH $_2$ -N-CH $_2$ , the changed crown ring proton average chemical shift and the association constant  $K_a$  are summarized in Table 2.

We had attempted to obtain the crystal of the new host/guest complexes, but we did not succeed. The FAB mass spectrometry was used to check the formation of the host/guest complexes. It was observed that there were several peaks appeared after the new host bis- and tris-crown ethers were added with the guest alkali metal cations which in exactly fit the size of the crown ether unit. For example, after bis-crown ether **1** was added with LiSCN and NaSCN, an ion peak was observed at  $m/z$  486, which corresponds to a fragmentary product formed by  $[1+Li^+]$ . The second peak at  $m/z$  502 corresponds to  $[1+Na^+]$ . The third peak at  $m/z$  509 was  $[1+Li^++Na^+]$ . The peak at  $m/z$  625 was  $[1+LiSCN+NaSCN]$ . It indicating that the bis-crown ether **1** had formed the 1 : 2 host/guest complex.

When the bis- and tris-crown ethers were added with the ideal sizes cations for the crown ether cavities, the FAB mass spectra all showed more than one peaks, respectively. Only one peak appeared when the bis-crown ethers complexed with the cations which their sizes exceed that of the crown ether cavity. It was ascribed to the formation of intra-molecular sandwich type complexes between the larger size guest cations with the bis-crown ethers. The FAB mass spectrum data of the complexes are indicated in Table 3. All the results of mass spectroscopy of the complexes were evident and all correct as expected.

From the results of the FAB mass spectrum outlined in Table 3, it was noticed that when tris-crown ether **5** and **6** interacted with  $K^+$ , both of them can bind two  $K^+$  cations. Due to the cavity of the diaza-18-crown-6 unit is exactly fit the size of  $K^+$  cation, we suppose that one 1 : 2 host/guest complex has been formed. In the Table 3, it was found that when tris-crown ether **5** interacted with  $Rb^+$  and **6** interacted

**Table 1.** Changes of  $^1H$  NMR chemical shifts of bis-crown ethers with various metal salts

	$\Delta\delta$ of H-1	$\Delta\delta$ of H-2	$\Delta\delta$ of CH <sub>2</sub> -N-CH <sub>2</sub>	$\Delta\delta$ of crown H	$K_a$ (M <sup>-1</sup> )
<b>1</b> + LiSCN	0.234	0.073	0.081	0.118	1190 ± 42
<b>1</b> + NaSCN	0.132	0.031	0.023	0.071	987 ± 12
<b>1</b> + KSCN	0.090	0.040	-0.007	0.047	346 ± 13
<b>1</b> + RbSCN	0.072	0.055	-0.002	0.029	214 ± 21
<b>1</b> + CsSCN	0.062	0.063	-0.004	0.047	251 ± 64
<b>2</b> + NaSCN	0.128	0.030	0.022	0.064	1324 ± 31
<b>2</b> + KSCN	0.123	0.053	-0.006	0.081	907 ± 27
<b>2</b> + RbSCN	0.084	0.066	-0.004	0.072	475 ± 17
<b>2</b> + CsSCN	0.058	0.059	-0.004	0.046	223 ± 11
<b>3</b> + LiSCN	0.044	0.036	0.025	0.043	886 ± 68
<b>3</b> + NaSCN	0.019	0.006	-0.004	0.050	102 ± 3
<b>3</b> + KSCN	0.072	0.030	0.016	0.088	919 ± 52
<b>3</b> + RbSCN	0.061	0.030	0.027	0.083	792 ± 33
<b>3</b> + CsSCN	0.062	0.022	0.016	0.054	586 ± 6
<b>4</b> + NaSCN	0.089	0.003	-0.005	0.064	1041 ± 30
<b>4</b> + KSCN	0.056	0.083	0.021	0.083	889 ± 54
<b>4</b> + RbSCN	0.039	0.063	0.006	0.074	633 ± 9
<b>4</b> + CsSCN	0.050	0.073	-0.001	0.051	402 ± 6

<sup>a</sup>H-1 and H-2 are protons (O-CO-CH<sub>2</sub><sup>1</sup>-CH<sub>2</sub><sup>2</sup>-N) in bis-crown ethers **1-4**.

**Table 2.** Changes of  $^1H$  NMR chemical shifts of tris-crown ethers with various metal salts

	$\Delta\delta$ of H-3	$\Delta\delta$ of H-4	$\Delta\delta$ of CH <sub>2</sub> -N-CH <sub>2</sub>	$\Delta\delta$ of crown H	$K_a$ (M <sup>-1</sup> )
<b>5</b> + LiSCN	0.082	0.098	0.046	0.072	1038 ± 35
<b>5</b> + NaSCN	0.175	0.076	0.011	0.102	361 ± 17
<b>5</b> + KSCN	0.109	0.074	-0.031	0.088	833 ± 8
<b>5</b> + RbSCN	0.095	0.080	-0.030	0.061	741 ± 62
<b>5</b> + CsSCN	0.060	0.090	-0.019	0.095	624 ± 15
<b>6</b> + NaSCN	0.078	0.077	0.012	0.122	1047 ± 9
<b>6</b> + KSCN	0.109	0.073	-0.032	0.068	712 ± 7
<b>6</b> + RbSCN	0.097	0.080	-0.044	0.067	491 ± 14
<b>6</b> + CsSCN	0.070	0.100	-0.030	0.091	470 ± 11

<sup>a</sup>H-3 and H-4 are protons (O-CO-CH<sub>2</sub><sup>3</sup>-CH<sub>2</sub><sup>4</sup>-N) in tris-crown ethers **5** and **6**.

**Table 3.** The FAB mass data of the complexes and the corresponding ion peaks indication

Complex	Ion peaks and the corresponding fragment
<b>1</b> + LiSCN + NaSCN	486 ( <b>1</b> + Li <sup>+</sup> ); 502 ( <b>1</b> + Na <sup>+</sup> ); 509 ( <b>1</b> + Li <sup>+</sup> + Na <sup>+</sup> ); 537 ( <b>1</b> + LiSCN); 625 ( <b>1</b> + LiSCN + NaSCN);
<b>1</b> + KSCN	518 ( <b>1</b> + K <sup>+</sup> );
<b>1</b> + RbSCN	564 ( <b>1</b> + Rb <sup>+</sup> );
<b>1</b> + CsSCN	612 ( <b>1</b> + Cs <sup>+</sup> );
<b>2</b> + NaSCN	685 ( <b>2</b> + 2NaSCN);
<b>2</b> + KSCN	562 ( <b>2</b> + K <sup>+</sup> );
<b>2</b> + RbSCN	608 ( <b>2</b> + Rb <sup>+</sup> );
<b>2</b> + CsSCN	656 ( <b>2</b> + Cs <sup>+</sup> );
<b>3</b> + LiSCN + KSCN	568 ( <b>3</b> + Li <sup>+</sup> + K <sup>+</sup> ); 627 ( <b>3</b> + Li <sup>+</sup> + KSCN);
<b>3</b> + NaSCN	546 ( <b>3</b> + Na <sup>+</sup> );
<b>3</b> + KSCN	562 ( <b>3</b> + K <sup>+</sup> );
<b>3</b> + RbSCN	608 ( <b>3</b> + Rb <sup>+</sup> );
<b>3</b> + CsSCN	656 ( <b>3</b> + Cs <sup>+</sup> );
<b>4</b> + NaSCN + KSCN	590 ( <b>4</b> + Na <sup>+</sup> ); 606 ( <b>4</b> + K <sup>+</sup> ); 647 ( <b>4</b> + NaSCN); 663 ( <b>4</b> + KSCN); 687 ( <b>4</b> + KSCN + Na <sup>+</sup> );
<b>4</b> + RbSCN	653 ( <b>4</b> + Rb <sup>+</sup> );
<b>4</b> + CsSCN	700 ( <b>4</b> + Cs <sup>+</sup> );
<b>5</b> + LiSCN	790 ( <b>5</b> + Li <sup>+</sup> );
<b>5</b> + NaSCN	860 ( <b>5</b> + Na <sup>+</sup> );
<b>5</b> + KSCN	822 ( <b>5</b> + K <sup>+</sup> ); 978 ( <b>5</b> + 2KSCN);
<b>5</b> + RbSCN	868 ( <b>5</b> + Rb <sup>+</sup> ); 952 ( <b>5</b> + 2Rb <sup>+</sup> );
<b>5</b> + CsSCN	916 ( <b>5</b> + Cs <sup>+</sup> );
<b>6</b> + NaSCN	894 ( <b>6</b> + Na <sup>+</sup> ); 973 ( <b>6</b> + NaSCN + Na <sup>+</sup> );
<b>6</b> + KSCN	910 ( <b>6</b> + K <sup>+</sup> ); 950 ( <b>6</b> + 2K <sup>+</sup> ); 1006 ( <b>6</b> + KSCN + K <sup>+</sup> );
<b>6</b> + RbSCN	956 ( <b>6</b> + Rb <sup>+</sup> );
<b>6</b> + CsSCN	1003 ( <b>6</b> + Cs <sup>+</sup> ); 1194 ( <b>6</b> + CsSCN + Cs <sup>+</sup> );

with Cs<sup>+</sup>, the ion peaks of [**5** + 2Rb<sup>+</sup>] and [**6** + CsSCN + Cs<sup>+</sup>] appeared. Because the cations radii of Rb<sup>+</sup> and Cs<sup>+</sup> is much larger than the crown cavity of 18-crown-6. It was supposed that the double armed tris-crown ethers could form 1 : 2 host/guest complex with Rb<sup>+</sup> and Cs<sup>+</sup>.

As described above, the newly synthesized bis- and tris-

**Table 4.** The increased absorbance order of the bis- and tris-crown ethers interacted with alkali metal picrate salts in MeOH solution

Bis- and tris-crown ether	The increased absorbance order of the cations
Bis-crown ether <b>1</b>	Na <sup>+</sup> < K <sup>+</sup> < Cs <sup>+</sup>
Bis-crown ether <b>2</b>	Na <sup>+</sup> < K <sup>+</sup> < Cs <sup>+</sup>
Bis-crown ether <b>3</b>	Na <sup>+</sup> < K <sup>+</sup> < Cs <sup>+</sup>
Bis-crown ether <b>4</b>	Na <sup>+</sup> ≈ K <sup>+</sup> < Cs <sup>+</sup>
Tris-crown ether <b>5</b>	Na <sup>+</sup> < K <sup>+</sup> < Cs <sup>+</sup>
Tris-crown ether <b>6</b>	Na <sup>+</sup> ≈ K <sup>+</sup> < Cs <sup>+</sup>

crown ethers could capture not only the metal cations which are in ideal size for the crown rings, but also larger size metal cation such as Rb<sup>+</sup> and Cs<sup>+</sup>.

In the absorption investigation of UV spectrometry, the bis- and tris-crown ethers were made into  $2 \times 10^{-3}$  M solutions in methanol. The sodium picrate, potassium picrate and cesium picrate were dissolved in methanol to make very low concentration solutions, respectively. The absorption maximum of the picrate anion in methanol was observed at 354 nm. Interestingly, with the addition of the bis- or tris-crown ether solution into the alkali picrate salt solutions, the absorption intensity at 354 nm all increased. The increased ratio of the absorption intensity was different. In bis-crown ether **1** case, the increased intensity ratio were Na<sup>+</sup> < K<sup>+</sup> < Cs<sup>+</sup>, the increased intensity order of the bis- and tris-crown ethers are outlined in Table 4. The results indicated that interactions of the host bis- and tris-crown ethers with the guest alkali metal cations of Na<sup>+</sup>, K<sup>+</sup> and Cs<sup>+</sup> have taken place in the methanol solution.

### Conclusions

We have successfully used the Michael addition to develop an efficient approach to synthesize novel host compounds of bis- and tris-crown ethers. The synthesis and characterization of the bis- and tris-crown ethers were described. The structures are novel, the reaction condition is gentle, and the yield was good. The reactions could take place directly without protection-deprotection. The interaction between the bis- and tris-crown ethers with alkali metal cations such as Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup> and Cs<sup>+</sup> was investigated. The association constant  $K_a$  was obtained. The result showed that the bis- and tris-crown ethers could capture not only the ideal size metal cations Li<sup>+</sup>, Na<sup>+</sup> and K<sup>+</sup>, but also larger size cations than that of the crown ether ring cavity like Rb<sup>+</sup> and Cs<sup>+</sup> to form sandwich type complexes.

### Experimental Section

**General methods.** Elemental analyses (C, H, N) were performed using a Vario EL Elementar. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were obtained on a Varian Mercury 300 NMR spectrometer in CDCl<sub>3</sub>. The chemical shifts were expressed in ppm ( $\delta$  scale) using tetramethylsilane as an internal standard. GC-MS data were obtained from Shimadzu GC-

Mass Spectrometer GCMSD-QP5050. FAB MS data were obtained from a Jeol JMS 700 Mass Spectrometer at the Korea Basic Science Institute (Daegu, Korea). FT-IR spectra were recorded on a Mattson Instrument Genesis II spectrometer. The absorption spectra was taken on Hewlett Packard UV-visible spectrophotometer UV-8453.

**Material.** All the crown ethers and reagents were purchased from Aldrich Company and used as received. The solvents were analytical grade, purchased from DC Chemical Co. Ltd. of Korea, and used without further purification. Spectral grade solvents were obtained from Junsei Chemical Co. Ltd. of Japan.

**2-Acryloyloxymethyl-12-crown-4 (7).** 2-Hydroxymethyl-12-crown-4 (0.50 g, 2.4 mmol) was dissolved in benzene (30 mL). Pyridine (2 mL) was added and the mixture stirred for 30 min. In an ice bath acryloyl chloride (0.4 g) was dropped into the flask over 1 h. The reaction was stirred below 50 °C. After 24 h the solution was washed with aqueous K<sub>2</sub>CO<sub>3</sub> (2 N, 5 mL), water (10 mL  $\times$  3), and dried over magnesium sulfate. Evaporation of solvent gave 0.55 g **7** as yellow oil, yield 87.3%. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 3.46-3.93 (m, 15H), 4.13-4.21 (m, 2H), 5.86 (d,  $J$  = 10.5 Hz, 1H), 6.15 (dd,  $J_1$  = 17.1 Hz,  $J_2$  = 10.2 Hz, 1H), 6.43 (d,  $J$  = 17.4 Hz, 1H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 165.98, 131.17, 128.41, 77.60, 71.19, 70.93, 70.75, 70.65, 70.57, 70.29, 70.17, 64.03; IR (NaCl, cm<sup>-1</sup>): 2914.9, 2867.6, 1724.1, 1634.8, 1619.9, 1449.3, 1408.8, 1361.5, 1294.0, 1275.7, 1194.7, 1135.9, 1102.1, 1025.0, 984.5, 915.1, 855.3, 810.9; GC-MS:  $m/z$  260.1 [M]<sup>+</sup> (calc. for C<sub>12</sub>H<sub>20</sub>O<sub>6</sub>: M, 260.1). Anal. calc. for C<sub>12</sub>H<sub>20</sub>O<sub>6</sub>: C, 55.37; H, 7.74. Found: C, 55.33; H, 7.69.

**2-Acryloyloxymethyl-15-crown-5 (8).** 2-Hydroxymethyl-15-crown-5 (0.5 g, 2 mmol) was dissolved in benzene (30 mL). Operated the same as **7**, affording 0.53 g **8** as yellow oil, yield 87.2%. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 3.50-3.83 (m, 19H), 4.12-4.23 (m, 2H), 5.78 (d,  $J$  = 10.5 Hz, 1H), 6.11 (dd,  $J_1$  = 17.1 Hz,  $J_2$  = 10.5 Hz, 1H), 6.35 (d,  $J$  = 17.1 Hz, 1H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 165.00, 129.92, 127.28, 76.64, 70.14, 70.07, 69.84, 69.76, 69.69, 69.55, 69.48, 69.41, 69.32, 63.42; IR (NaCl, cm<sup>-1</sup>): 2916.3, 2869.6, 1725.0, 1634.4, 1618.9, 1451.2, 1408.7, 1352.8, 1294.0, 1273.8, 1194.7, 1129.1, 986.4, 943.0, 842.7, 810.9; GC-MS:  $m/z$  304.2 [M]<sup>+</sup> (calc. for C<sub>14</sub>H<sub>24</sub>O<sub>7</sub>: M, 304.1). Anal. calc. for C<sub>14</sub>H<sub>24</sub>O<sub>7</sub>: C, 55.25; H, 7.95. Found: C, 55.04; H, 8.02.

**Bis-crown ether (1) – N-(2-propionyloxymethyl-12-crown-4)-aza-15-crown-5.** 1-Aza-15-crown-5 (44 mg, 0.2 mmol) and crown ether **7** (52 mg, 0.2 mmol) were dissolved in methanol (5 mL). The mixture was stirred below 50 °C. After 24 h the solvent was evaporated in *vacuo* and was subjected to flash chromatography on silica gel (EtOAc) affording 85 mg **1** as yellow oil, yield 88.5%. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 2.48 (t,  $J$  = 7.2 Hz, 2H), 2.75 (t,  $J$  = 6.0 Hz, 4H), 2.88 (t,  $J$  = 7.2 Hz, 2H), 3.59-3.67 (m, 33H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, ppm)  $\delta$ : 173.13, 79.97, 71.60, 70.93, 70.91, 70.67, 70.65, 70.60, 70.36, 70.27, 70.23, 70.14, 70.12, 69.94, 69.89, 69.78, 69.54, 62.40, 54.39,

51.56, 32.52; IR (NaCl,  $\text{cm}^{-1}$ ): 2941.4, 2864.5, 1737.4, 1441.7, 1353.3, 1295.7, 1250.9, 1199.1, 1123.1, 988.1, 944.7, 840.6; GC-MS:  $m/z$  479.2  $[\text{M}]^+$  (calc. for  $\text{C}_{22}\text{H}_{41}\text{NO}_{10}$ : M, 479.3). Anal. calc. for  $\text{C}_{22}\text{H}_{41}\text{NO}_{10}$ : C, 55.10; H, 8.62; N, 2.92. Found: C, 55.41; H, 8.67; N, 2.88.

**Bis-crown ether (2) – N-(2-propionyloxymethyl-15-crown-5)-aza-15-crown-5.** 1-Aza-15-crown-5 (44 mg, 0.2 mmol) and crown ether **8** (61 mg, 0.2 mmol) were dissolved in methanol (5 mL). Bis-crown ether **2** was prepared from the same method as described above, affording 92 mg **2** as yellow oil, yield 87.6%.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 2.48 (t,  $J = 7.2$  Hz, 2H), 2.77 (t,  $J = 6.0$  Hz, 4H), 2.88 (t,  $J = 7.8$  Hz, 2H), 3.57–3.89 (m, 37H);  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 173.13, 79.65, 71.49, 71.16, 70.93, 70.79, 70.57, 70.51, 70.45, 70.35, 70.32, 70.11, 70.05, 69.92, 63.03, 54.39, 51.56, 32.49; IR (NaCl,  $\text{cm}^{-1}$ ): 2940.9, 2866.1, 1737.9, 1442.1, 1354.1, 1294.1, 1251.3, 1198.2, 1124.2, 989.3, 941.3, 841.2; GC-MS:  $m/z$  523.4  $[\text{M}]^+$  (calc. for  $\text{C}_{24}\text{H}_{45}\text{NO}_{11}$ : M, 523.3). Anal. calc. for  $\text{C}_{24}\text{H}_{45}\text{NO}_{11}$ : C, 55.05; H, 8.66; N, 2.68. Found: C, 54.98; H, 8.53; N 2.67.

**Bis-crown ether (3) – N-(2-propionyloxymethyl-12-crown-4)-aza-18-crown-6.** 1-Aza-18-crown-6 (52 mg, 0.2 mmol) and crown ether **7** (52 mg, 0.2 mmol) were dissolved in methanol (5 mL). The same as above, affording 92 mg **3** as yellow oil, yield 88.4%.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 2.48 (t,  $J = 6.9$  Hz, 2H), 2.77 (t,  $J = 6.0$  Hz, 4H), 2.88 (t,  $J = 7.5$  Hz, 2H), 3.59–3.68 (m, 37H);  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 173.17, 79.95, 71.61, 70.90, 70.81, 70.71, 70.69, 70.66, 70.64, 70.58, 70.39, 70.35, 70.26, 70.18, 70.14, 69.79, 69.62, 62.39, 53.82, 51.54, 32.43; IR (NaCl,  $\text{cm}^{-1}$ ): 2942.7, 2870.4, 1735.3, 1443.2, 1351.8, 1296.7, 1255.3, 1196.4, 1120.9, 986.4, 939.8, 838.7; GC-MS:  $m/z$  523.3  $[\text{M}]^+$  (calc. for  $\text{C}_{24}\text{H}_{45}\text{NO}_{11}$ : M, 523.3). Anal. calc. for  $\text{C}_{24}\text{H}_{45}\text{NO}_{11}$ : C, 55.05; H, 8.66; N, 2.68. Found: C, 55.23; H, 8.59; N 2.61.

**Bis-crown ether (4) – N-(2-propionyloxymethyl-15-crown-5)-aza-18-crown-6.** 1-Aza-18-crown-6 (52 mg, 0.2 mmol) and crown ether **8** (61 mg, 0.2 mmol) were dissolved in methanol (5 mL). The same as above affording 96 mg **4** as yellow oil, yield 85.0%.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 2.48 (t,  $J = 7.5$  Hz, 2H), 2.77 (t,  $J = 6.0$  Hz, 4H), 2.88 (t,  $J = 7.5$  Hz, 2H), 3.55–3.69 (m, 41H);  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 173.17, 79.78, 71.53, 71.13, 70.80, 70.76, 70.70, 70.68, 70.53, 70.50, 70.45, 70.40, 70.34, 70.25, 70.03, 70.01, 69.77, 68.49, 62.82, 53.81, 51.55, 32.41; IR (NaCl,  $\text{cm}^{-1}$ ): 2943.8, 2865.7, 1736.6, 1440.6, 1352.8, 1296.9, 1251.6, 1199.5, 1122.4, 990.3, 945.9, 841.8; GC-MS:  $m/z$  567.2  $[\text{M}]^+$  (calc. for  $\text{C}_{26}\text{H}_{49}\text{NO}_{12}$ : M, 567.3). Anal. calc. for  $\text{C}_{26}\text{H}_{49}\text{NO}_{12}$ : C, 55.01; H, 8.70; N, 2.47. Found: C, 54.91; H, 8.67; N 2.49.

**Tris-crown ether (5) – N,N'-di-(2-propionyloxymethyl-12-crown-4)-diaz-18-crown-6.** Diaza-18-crown-6 (26 mg, 0.1 mmol) and crown ether **7** (53 mg, 0.2 mmol) were dissolved in methanol (5 mL). The same as above affording 64 mg **5** as yellow oil, yield 81.1%.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 2.47 (t,  $J = 6.9$  Hz, 4H), 2.77 (t,  $J = 6.0$  Hz, 8H), 2.87 (t,  $J = 7.2$  Hz, 4H), 3.57–3.70 (m, 50H);  $^{13}\text{C-NMR}$

(75 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 173.34, 80.12, 71.75, 71.14, 70.90, 70.84, 70.79, 70.48, 70.32, 69.99, 68.12, 62.75, 53.92, 51.75, 32.57; IR (NaCl,  $\text{cm}^{-1}$ ): 2936.8, 2860.1, 1730.2, 1436.8, 1348.6, 1293.3, 1249.6, 1195.7, 1125.9, 983.4, 940.2, 836.7; MS (FAB):  $m/z$  783.4  $[\text{M}+\text{H}]^+$  (calc. for  $\text{C}_{36}\text{H}_{66}\text{N}_2\text{O}_{16}$ : M, 782.4). Anal. calc. for  $\text{C}_{36}\text{H}_{66}\text{N}_2\text{O}_{16}$ : C, 55.23; H, 8.50; N, 3.58. Found: C, 55.57; H, 8.52; N, 3.53.

**Tris-crown ether (6) – N,N'-di-(2-propionyloxymethyl-15-crown-5)-diaz-18-crown-6.** Diaza-18-crown-6 (26 mg, 0.1 mmol) and crown ether **8** (61 mg, 0.2 mmol) were dissolved in methanol (5 mL). The same as above to obtain 71 mg **6** as yellow oil, yield 81.6%.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 2.47 (t,  $J = 6.9$  Hz, 4H), 2.78 (t,  $J = 6.0$  Hz, 8H), 2.87 (t,  $J = 7.2$  Hz, 4H), 3.62–3.84 (m, 58H);  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ , ppm)  $\delta$ : 173.16, 79.75, 71.49, 71.16, 70.80, 70.78, 70.66, 70.57, 70.51, 70.47, 70.34, 70.03, 69.79, 62.95, 53.72, 51.59, 32.38; IR (NaCl,  $\text{cm}^{-1}$ ): 2935.7, 2861.5, 1733.4, 1435.7, 1349.3, 1294.7, 1249.1, 1196.9, 1124.7, 981.2, 940.7, 835.3; MS (FAB):  $m/z$  871.2  $[\text{M}+\text{H}]^+$  (calc. for  $\text{C}_{40}\text{H}_{74}\text{N}_2\text{O}_{18}$ : M, 870.5). Anal. calc. for  $\text{C}_{40}\text{H}_{74}\text{N}_2\text{O}_{18}$ : C, 55.16; H, 8.56; N, 3.22. Found: C, 55.06; H, 8.48; N, 3.20.

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