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Synthesis and alkali metal binding properties of novel *N*-adamantylaza-crown ethers

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Abstract—New *N*-adamantylaza-crown ethers **1**–**8** have been synthesized and their respective alkali metal picrate extraction profiles have been obtained. These results are compared with the results obtained for the parent aza-18-crown-6 and *N*-benzylaza-18-crown-6. Among the crown hosts studied, **2**, and **6**, proved to be the best alkali metal picrate extractants and displayed significant levels of complexation with K^+ and Rb^+.

1. Introduction

Since their discovery[1] the crown ethers have played an important role in a number of areas in chemistry and serve as synthetic receptors for organic and inorganic cations, anions and neutral molecules.[2] Different kinds of crown ethers have been synthesized in order to find molecules with superior properties and proper application in various areas. Relatively small numbers of crown ethers, which have been synthesized thus far, contain polycyclic moiety as a part of the crown-backbone. Incorporation of a rigid polycyclic moiety such as cubane,[3] pentacycloundecane,[4] 3,5-disubstituted-4-oxahexacyclododecane,[5] adamantane[5a,6,7] and oxaadamantane[8] into crown ethers should affect not only their lipophilicity but also their conformational mobility and therefore their complexing power. To our knowledge, only a few examples of crown ethers with a polycyclic cage compound as a part of the side chain have been prepared.[9]

In this paper, we report the synthesis of novel lariat-crown ethers (**1**–**8**)[10] with the adamantyl system attached to the aza-crown ether. We have also investigated their binding ability and selectivity toward alkali metals compared with that of aza-18-crown-6 and *N*-benzylaza-18-crown-6. The linkage of the adamantane molecule to the aza-18-crown-6 is realized either by using an amide bond (**1**,**3**,**5**,**7**) or a methylene group (**2**,**4**,**6**,**8**). In the former, the CO linkages should impose rigidity and thus preorganise the receptor, but on the other hand, strongly reduces the binding properties of the nitrogen atom of the macrocyclic ring. In the latter case, the methylene group would preserve the complexation ability of the macrocycle, but the ligand would be more flexible and, therefore, less preorganized.

2. Results and discussion

2.1. Synthesis of aza-crown ethers 1–8

The synthetic strategy to prepare compounds **1**–**8** was based on the coupling reactions of the aza-18-crown-6 with corresponding adamantane derivatives [i.e. 1-(chloroethanoyl)-adamantane (**9**), 1-(chloropropanoyl)adamantane (**10**), 1,3-bis(chloroethanoyl)adamantane (**11**), 1,3-bis(chloropropanoyl)adamantane (**12**)] or adamantane tosylates [i.e. 1-(2-tosyloxyethyl)adamantane (**13**), 1-(3-tosyloxypropyl)adamantane (**14**), 1,3-bis(2-tosyloxyethyl)adamantane (**15**), 1,3-bis(3-tosyloxypropyl)adamantane (**16**)] (Scheme 1).

The synthesis of the lariat-crowns **1**,**3**,**5** and **7** were carried out in a straightforward way by mixing the reactants and triethylamine as the base, and THF as the solvent, in 85, 79, 72 and 45% yield, respectively. A closely analogous reaction, using sodium carbonate in dry CH_3CN, was employed to prepare the lariat-crown ethers **2**,**4**,**6** and **8** in good to modest yields (24, 54, 59, and 57% respectively). Crown ethers **2** and **4** were also prepared using a Na^+ templated Williamson synthesis. Reaction of the tetraethylene glycol ditosylate with the conjugate base of 2-(1-adamantyl)ethyldiethanolamine (**17**) or 3-(1-adamantyl)propyldiethanolamine (**18**) resulted in the formation of **2** or **4** in 36 or 21% yield, respectively. Aza-18-crown-6,[11] *N*-benzylaza-18-crown-6,[11] as well as adamantane precursors **9**,[12] **10**,[13] **11**,[14] and **12**[13] were prepared according to the published procedures. The synthesis of hitherto unknown adamantane derivatives **13**–**18** are described in Section 4.

Keywords: adamantanes; crown ethers; complexation.

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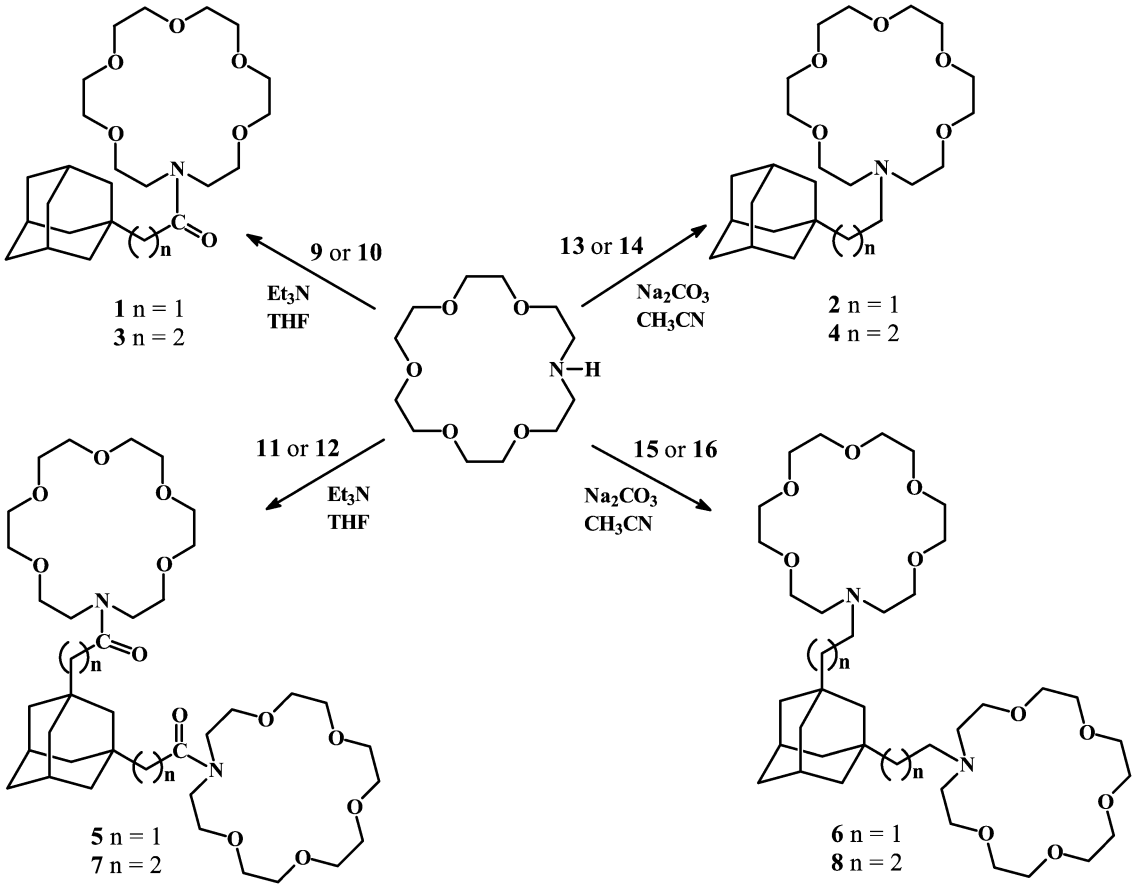

Scheme 1.

2.2. Alkali metal ion selectivities of aza-crown ethers 1–8

The picrate extraction studies with novel *N*-adamantylaza-crown ethers **1**–**8** were carried out by solvent extraction of alkali metal picrates from aqueous solution into chloroform. Since picrate ion concentration can be easily determined by UV, extractions of aqueous alkali metal picrates (Li^+, Na^+, K^+, Rb^+ and Cs^+; 5×10^{-3} M) were carried out at 25°C with chloroform solutions of crown ethers **1**–**8** (5×10^{-3} M). The results were compared with those obtained using parent aza-18-crown-6 and *N*-benzylaza-18-crown-6. In addition 'blank' experiments in which $CHCl_3$ contained no aza-crown ether were carried out for each alkali metal picrate salt. The results are shown in Table 1.

The extraction technique used in this study has been described elsewhere.[8c,15] Consideration of the results of the alkali metal picrate extraction experiments shown in Table 1 led to the following observations. The extraction abilities of aza-crown ethers **1**,**3**,**5**, and **7** are very low, almost negligible toward any of the alkali cations studied.[16] However, all of the aza-crown ethers with the alkyl-side arms [i.e. **2**,**4**,**6** and **8**] showed lower avidity toward the extraction of Li^+, Na^+ and Cs^+ picrate vis-à-vis corresponding parent aza-18-crown-6 but somewhat greater avidity for those cations than *N*-benzylaza-18-crown-6. At the same time, lariat-crown ethers **2**,**4**,**6** and **8** displayed both high avidity and high selectivity toward the extraction of K^+ and Rb^+ picrates. The enhanced extractability of potassium

Table 1. Extractions of alkali picrates with $CHCl_3$ containing crown ethers

Crown ether	Percent of picrate extracted (%)[a]				
	Li^+	Na^+	K^+	Rb^+	Cs^+
Aza-18-crown-6	11.6±0.3	35.5±0.6	42.9±0.6	37.0±0.6	39.8±0.5
N-Benzylaza-18-crown-6	<1	15.0±0.8	51.3±0.5	35.9±0.4	18.4±0.8
1	1.8±0.3	<1	<1	1.0±0.4	1.3±0.4
2	2.2±0.2	24.7±0.7	52.8±0.5	44.3±0.6	28.3±0.4
3	1.2±0.5	3.9±0.5	3.4±0.4	3.7±0.5	3.0±0.6
4	<1	18.7±0.3	34.9±0.6	29.8±0.3	21.6±0.2
5	<1	2.0±0.6	1.9±0.6	2.8±0.2	3.6±0.2
6	4.7±0.3	32.4±0.3	79.0±0.5	66.2±0.3	40.9±0.4
7	<1	2.5±0.6	<1	3.8±0.7	4.7±0.7
8	5.4±0.3	31.0±0.5	69.2±0.3	57.2±0.4	35.7±0.6

[a] Defined as percent of picrate extracted into organic phase. Each value is the average of five independent extraction experiments.

picrate with the adamantylaza-crowns could be attributed to the lipophilicity of adamantane moiety. Among those four aza-crown ethers, **2** and **6** proved to be the best extractands and displayed significant levels of complexation with K^+ and Rb^+. It appears that the complexing capabilities of adamantylaza-crown ethers are influenced by length of the chain between the adamantane moiety and the macrocyclic ring.

3. Conclusions

In the course of this study, several new lariat aza-crown ethers **1**–**8** have been synthesized and their cation-binding abilities were evaluated using a solvent extraction technique. Besides, hitherto unknown adamantane derivatives [i.e. **13**–**18**] have also been prepared and their structures confirmed spectroscopically.

The results obtained by extraction experiments of alkali metal picrates indicate that the extraction capabilities of aza-crown ethers **1**,**3**,**5** and **7**, in which the linkage of the adamantane molecule to the aza-18-crown-6 is realized using the amide bond, are poor towards all the alkali metal cations. Lariat aza-crown ethers **2**,**4**,**6** and **8** have complexing abilities at the same level or better than the referent aza-18-crown-6 and *N*-benzylaza-18-crown-6. The length of the chain between the adamantane moiety and the crown ring also plays a role for complexation. Aza-crown ethers **2** and **6** where chain length is three C–C bonds display enhanced avidity toward all alkali cations than aza-crown ethers **4** and **8**, respectively, in which the chain length is four C–C bonds. Also, the enhanced extractability could be attributed to the lipophilicity of adamantane moiety.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were obtained by using Varian Gemini 300 nuclear magnetic resonance spectrometer. The assignment of the NMR signals was done by a combination of 2D NMR techniques (^1H–^1H COSY and ^1H–^{13}C HETCOR). IR spectra were recorded on a Perkin–Elmer M-297 spectrophotometer. UV-spectra were recorded on Philips P 8730 spectrophotometer. The purity of adamantyl compounds was determined by GLC analysis carried out on a Varian 3300 gas chromatograph equipped with a DB-210 capillary column. Melting points were determined on Kofler apparatus and are uncorrected. Elemental analyses were performed at Central Analytical Laboratory, IRB, Zagreb. Unless stated otherwise, reagent grade solvents were employed.

4.2. General procedure for the synthesis of *N*-adamantylaza-crown ethers 1,3,5 and 7

The solution of aza-18-crown-6 (1.0 mmol for the synthesis of **1** and **3** or 2.0 mmol for compounds **5** and **7**) in THF (6 or 12 mL) was stirred under nitrogen atmosphere and triethylamine (1.5 or 2.5 mmol) was added. The resulting mixture was stirred at ambient temperature for 10 min, and then a solution of **9**,**10**,**11** or **12** (1 mmol) in THF (6 mL) was added dropwise. The reaction mixture was stirred at the ambient temperature for additional 24 h, filtered and the filtrate was evaporated under reduced pressure. The solid residue was diluted in CH_2Cl_2 (20–40 mL), washed with saturated solution of NaCl (3×20–40 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and the residue thereby obtained was purified via column chromatography.

4.2.1. *N*-[1-Oxo-2-(1-adamantyl)ethyl]aza-18-crown-6 (1). By following the general procedure, compound **1** was obtained via reaction of aza-18-crown-6 (1.40 g, 5.3 mmol) with 1-(chloroethanoyl)adamantane (**9**, 1.13 g, 5.3 mmol). The crude product was purified on a silica gel column using 2→20% MeOH in CH_2Cl_2 as an eluent to give 1.98 g (85%) of product **1** as a slightly yellow oil. An analytically pure sample was obtained by HPLC (column: μ-porasil 3.9×300 mm; eluent: 2% MeOH in CH_2Cl_2) as a colorless oil. IR (KBr-film) ν: 2900 (s), 2850 (s), 1640 (s), 1455 (m), 1415 (m), 1350 (m), 1120 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.60–1.76 (m, 12H), 1.96 (br s, 3H), 2.14 (br s, 2H), 3.50–3.75 (m, 24H). ^{13}C NMR ($CDCl_3$) δ: 28.45 (d, 3C), 33.37 (s, 1C), 36.60 (t, 3C), 42.47 (t, 3C), 45.56 (t, 1C), 46.60 (t, 1C), 49.38 (t, 1C), 69.20 (t, 1C), 70.00 (t, 1C), 70.18 (t, 1C), 70.36 (t, 1C), 70.45 (t, 3C), 70.55 (t, 2C), 70.60 (t, 1C), 171.64 (s, 1C). Anal. calcd for $C_{24}H_{41}NO_6$ (M_r=439.597): C, 65.57; H, 9.40; N, 3.19. Found: C, 65.39; H, 9.68; N, 3.33.

4.2.2. *N*-[1-Oxo-3-(1-adamantyl)propyl]aza-18-crown-6 (3). By following the general procedure, crown ether **3** was obtained via reaction of aza-18-crown-6 (0.53 g, 2.0 mmol) with 1-(chloropropanoyl)adamantane (**10**, 0.48 g, 2.0 mmol). The crude product was purified on silica gel column using 2→20% MeOH in CH_2Cl_2 as an eluent. Product **3** (0.72 g, 79%) was obtained as slightly yellow oil. Analytically pure sample was obtained as a colorless oil by HPLC (column: μ-porasil 3.9×300 mm; eluent: 2% MeOH in CH_2Cl_2). IR (KBr-film) ν: 2900 (s), 2850 (s), 1645 (s), 1450 (m), 1420 (m), 1355 (m), 1120 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.35–1.45 (m, 2H), 1.48 (br s, 6H), 1.55–1.75 (m, 6H), 1.95 (br s, 3H), 2.25–2.35 (m, 2H), 3.55–3.80 (m, 24H). ^{13}C NMR ($CDCl_3$) δ: 28.29 (t, 1C), 28.37 (d, 3C), 31.71 (s, 1C), 36.88 (t, 3C), 39.23 (t, 1C), 41.96 (t, 3C), 46.67 (t, 1C), 48.77 (t, 1C), 69.35 (t, 1C), 69.86 (t, 1C), 70.14 (t, 1C), 70.38 (t, 1C), 70.47 (t, 3C), 70.56 (t, 1C), 70.60 (t, 2C), 174.26 (s, 1C). Anal. calcd for $C_{25}H_{43}NO_6$ (M_r=453.625): C, 66.19; H, 9.56; N, 3.09. Found: C, 66.01; H, 9.76; N, 3.12.

4.2.3. 1,3-Bis[*N*-(2-oxoethyl)aza-18-crown-6]adamantane (5). By following the general procedure, product **5** was obtained via reaction of aza-18-crown-6 (0.50 g, 1.9 mmol) with 1,3-bis(chloroethanoyl)adamantane (**11**, 0.27 g, 0.9 mmol). The crude product was purified via column chromatography on silica gel with 2→20% MeOH in CH_2Cl_2 as an eluent to obtain 0.48 g (72%) yellow oily product **5**. Analytically pure sample of crown ether **5** was obtained as a colorless oil by HPLC (column: μ-porasil 3.9×300 mm; eluent: 5% MeOH in CH_2Cl_2). IR (KBr-film) ν: 2900 (br s), 1635 (s), 1455 (m), 1415 (m), 1350

(m), 1120 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.50–1.75 (m, 12H), 2.03 (bs, 2H), 2.16 (s, 4H), 3.50–3.75 (m, 48H). ^{13}C NMR ($CDCl_3$) δ: 28.75 (d, 2C), 34.04 (s, 2C), 35.67 (t, 1C), 41.39 (t, 4C), 45.10 (t, 2C), 46.58 (t, 2C), 48.25 (t, 1C), 49.27 (t, 2C), 69.23 (t, 2C), 69.90 (t, 2C), 70.13 (t, 2C), 70.33 (t, 2C), 70.41 (t, 6C), 70.52 (t, 4C), 70.56 (t, 2C), 171.43 (s, 2C). Anal. calcd for $C_{38}H_{66}N_2O_{12}$ (M_r=742.956): C, 61.43; H, 8.95; N, 3.77. Found: C, 61.33; H, 8.91; N, 3.92.

4.2.4. 1,3-Bis[*N*-(3-oxopropyl)aza-18-crown-6]adamantane (7). By following the general procedure, product **7** was obtained via reaction of aza-18-crown-6 (0.60 g, 2.3 mmol) with 1,3-bis(chloropropanoyl)adamantane (**12**, 0.37 g, 1.2 mmol). The crude product **7** was purified via column chromatography on Al_2O_3 (act. II–III) using 0⟶5% MeOH in CH_2Cl_2 as an eluent thereby affording 0.42 g (45%) of product **7** as a colorless oil. IR (KBr-film) ν: 2900 (s), 1630 (s), 1450 (m), 1350 (m), 1110 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.19 (br s, 2H), 1.30–1.50 (m, 12H), 1.58 (br s, 2H), 2.02 (s, 2H), 2.25–2.35 (m, 4H), 3.55–3.75 (m, 48H). ^{13}C NMR ($CDCl_3$) δ: 26.37 (t, 2C), 28.69 (d, 2C), 32.46 (s, 2C), 36.27 (t, 1C), 38.90 (t, 2C), 41.93 (t, 4C), 46.61 (t, 2C), 46.96 (t, 1C), 48.74 (t, 2C), 69.35 (t, 2C), 69.84 (t, 2C), 70.13 (t, 2C), 70.38 (t, 4C), 70.46 (t, 6C), 70.58 (t, 4C), 174.09 (s, 2C). Anal. calcd for $C_{40}H_{70}N_2O_{12}$ (M_r=771.010): C, 62.31; H, 9.15; N, 3.63. Found: C, 62.25; H, 9.07; N, 3.75.

4.3. General procedures for synthesis of *N*-adamantylaza-crown ethers 2,4,6 and 8

Adamantyl tosylate or ditosylate (1 mmol) and aza-18-crown-6 (1.0 mmol for the synthesis of **2** and **4** or 2 mmol for crowns **6** and **8**) were diluted in dry acetonitrile (60–120 mL) under nitrogen atmosphere. Na_2CO_3 (2.0 mmol or 4.0 mmol) was added and the reaction mixture was refluxed for 5 days. Then, the reaction mixture was cooled to the ambient temperature and concentrated in vacuo. The solid residue was suspended in CH_2Cl_2 (50–100 mL) and filtered through a plug of celite. The combined filtrates were concentrated under reduced pressure to afford crude product, which was purified via column chromatography.

4.3.1. *N*-[2-(1-Adamantyl)ethyl]aza-18-crown-6 (2). By following the general procedure, compound **2** was obtained via reaction of 1-(2-tosyloxyethyl)adamantane (**13**, 0.33 g, 1.0 mmol) and aza-18-crown-6 (0.26 g, 1.0 mmol). The crude product was purified via column chromatography on silica gel using 2⟶20% MeOH in CH_2Cl_2 as an eluent thereby affording 0.10 g (24%) of product **2** as a colorless oil. Analytically pure sample was obtained by re-chromatography on a small column of silica gel using 0⟶10% MeOH in CH_2Cl_2 as an eluent. IR (KBr-film) ν: 2900 (s), 2850 (s), 1670 (w), 1450 (m), 1355 (m), 1115 (s), 955 (w) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.20–1.30 (m, 2H), 1.48 (br s, 6H), 1.60–1.75 (m, 6H), 1.93 (br s, 3H), 2.50–2.60 (m, 2H), 2.76 (t, 4H, J=5.62 Hz), 3.55–3.70 (m, 20H). ^{13}C NMR ($CDCl_3$) δ: 28.32 (d, 3C), 31.41 (s, 1C), 36.86 (t, 3C), 40.21 (t, 1C), 42.21 (t, 3C), 49.27 (t, 1C), 53.48 (t, 2C), 69.32 (t, 2C), 70.06 (t, 2C), 70.41 (t, 6C). Anal. calcd for $C_{24}H_{43}NO_5$ (M_r=425.614): C, 67.73; H, 10.18; N, 3.29. Found: C, 67.66; H, 10.02; N, 3.27.

4.3.2. *N*-[3-(1-Adamantyl)propyl]aza-18-crown-6 (4). By following the general procedure, compound **4** was obtained via reaction of 1-(3-tosyloxypropyl)adamantane (**14**, 0.60 g, 1.7 mmol) and aza-18-crown-6 (0.45 g, 1.7 mmol). The crude product was purified via column chromatography on silica gel using 2⟶20% MeOH in CH_2Cl_2 as an eluent thereby affording 0.40 g (54%) of product **4** as a colorless oil. Analytically pure sample was obtained by re-chromatography through a small column of silica gel using 0⟶10% MeOH in CH_2Cl_2 as an eluent. IR (KBr-film) ν: 2900 (s), 2850 (s), 1450 (m), 1380 (m), 1355 (m), 1250 (w), 1105 (s), 955 (m), 925 (m) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.95–1.05 (m, 2H), 1.45 (br s, 6H), 1.55–1.75 (m, 6H), 1.93 (br s, 3H), 2.45–2.55 (m, 2H), 2.77 (t, 4H, J=5.89 Hz), 3.55–3.70 (m, 22H). ^{13}C NMR ($CDCl_3$) δ: 19.65 (t, 1C), 28.51 (d, 3C), 31.92 (s, 1C), 37.03 (t, 3C), 41.95 (t, 1C), 42.29 (t, 3C), 53.66 (t, 2C), 56.71 (t, 1C), 69.43 (t, 2C), 70.23 (t, 2C), 70.61 (t, 4C), 70.69 (t, 2C). Anal. calcd for $C_{25}H_{45}NO_5$ (M_r=439.641): C, 68.30; H, 10.32; N, 3.19. Found: C, 68.47; H, 10.38; N, 3.27.

4.3.3. 1,3-Bis(*N*-ethylaza-18-crown-6)adamantane (6). By following the general procedure, compound **6** was obtained via reaction of 1,3-bis(2-tosyloxyethyl)adamantane (**15**, 0.53 g, 1.0 mmol) and aza-18-crown-6 (0.53 g, 2.0 mmol). The crude product was chromatographed on column of silica gel using 2⟶20% MeOH in CH_2Cl_2 as an eluent to obtain 0.42 g (59%) product **6** as a colorless oil. Analytically pure sample was obtained by re-chromatography on a column of Al_2O_3 (act. II–III) using 5% MeOH in CH_2Cl_2 as an eluent. IR (KBr-film) ν: 2900 (br s), 1450 (m), 1355 (m), 1250 (w), 1110 (s), 955 (m) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.18 (br s, 2H), 1.20–1.25 (m, 4H), 1.30–1.50 (m, 8H), 1.56 (br s, 2H), 1.97 (br s, 2H), 2.45–2.55 (m, 4H), 2.65–2.85 (m, 8H), 3.58–3.75 (m, 40H). ^{13}C NMR ($CDCl_3$) δ: 28.63 (d, 2C), 32.09 (s, 2C), 36.30 (t, 1C), 40.07 (t, 2C), 41.67 (t, 4C), 47.34 (t, 1C), 49.54 (t, 2C), 53.62 (t, 4C), 69.52 (t, 4C), 70.09 (t, 4C), 70.27 (t, 2C), 70.43 (t, 8C), 70.50 (t, 2C). Anal. calcd for $C_{38}H_{70}N_2O_{10}$ (M_r=714.989): C, 63.89; H, 9.87; N, 3.92. Found: C, 63.82; H, 10.09; N, 4.01.

4.3.4. 1,3-Bis(*N*-propylaza-18-crown-6)adamantane (8). By following the general procedure, compound **8** was obtained via reaction of 1,3-bis(3-tosyloxypropyl)adamantane (**16**, 0.56 g, 1.0 mmol) and aza-18-crown-6 (0.55 g, 2.1 mmol). The crude product was chromatographed on column of Al_2O_3 (act. II–III) using 5% MeOH in CH_2Cl_2 as an eluent thereby affording 0.42 g (57%) of product **8** as a colorless oil. Analytically pure sample was obtained after re-chromatography on column of Al_2O_3 (act. II–III) by eluting with 5% MeOH in CH_2Cl_2. IR (KBr-film) ν: 2910 (s), 2850 (s), 1455 (m), 1355 (m), 1250 (w), 1105 (s), 955 (m) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.95–1.05 (m, 4H), 1.13 (br s, 2H), 1.20–1.40 (m, 12H), 1.55 (br s, 2H), 1.98 (br s, 2H), 2.35–2.50 (m, 4H), 2.77 (t, 8H, J=5.90 Hz), 3.50–3.75 (m, 40H). ^{13}C NMR ($CDCl_3$) δ: 19.93 (t, 2C), 28.86 (d, 2C), 32.61 (s, 2C), 36.52 (t, 1C), 41.70 (t, 2C), 41.84 (t, 4C), 47.28 (t, 1C), 53.70 (t, 4C), 56.83 (t, 2C), 69.69 (t, 4C), 70.21 (t, 4C), 70.36 (t, 2C), 70.60 (t, 8C), 70.67 (t, 2C). Anal. calcd for $C_{40}H_{74}N_2O_{10}$ (M_r=743.043): C, 64.66; H, 10.04; N, 3.77. Found: C, 64.72; H, 10.17; N, 3.64.

4.4. Synthesis of mono- and disubstituted adamantane derivatives

4.4.1. 1-(2-Tosyloxyethyl)adamantane (13). To a stirred, cooled (ice/water) suspension of TsCl (0.32 g, 1.7 mmol) in dry pyridine (1.0 mL) 1-(2-hydroxyoxyethyl)adamantane[12] (0.25 g, 1.4 mmol) was added in small portions. The reaction mixture was stirred over night at 4°C, then diluted with water (15 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extract was washed with 6 M HCl (3×20 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and product **13** (0.4 g, 85%) of was obtained as a colorless oil. IR (KBr) ν: 2900 (s), 2850 (m), 1600 (w), 1450 (w), 1360 (m), 1190 (m), 1175 (m), 1095 (w), 955 (m), 935 (m), 810 (m) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.40–1.50 (m, 6H), 1.55–1.75 (m, 8H), 1.91 (br s, 3H), 2.45 (s, 3H), 4.09 (t, 2H, J=7.18 Hz), 7.35 (d, 2H, J=7.95 Hz), 7.79 (d, 2H, J=7.95 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.40 (q, 1C), 28.18 (d, 3C), 31.51 (s, 1C), 36.60 (t, 3C), 42.09 (t, 3C), 42.22 (t, 1C), 67.20 (t, 1C), 127.82 (d, 2C), 129.75 (d, 2C), 133.18 (s, 1C), 144.61 (s, 1C). Anal. calcd for $C_{19}H_{26}O_3S$ (M_r=334.481): C, 68.23; H, 7.83. Found: C, 68.22; H, 7.95.

4.4.2. 1-(3-Tosyloxypropyl)adamantane (14). To a stirred, cooled (ice/water) suspension of TsCl (0.48 g, 2.5 mmol) in dry pyridine (1.5 mL) 1-(3-hydroxypropyl)adamantane[13] (0.45 g, 2.3 mmol) was added in small portions. The reaction mixture was stirred over night at 4°C, then diluted with water (15 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extract was washed with 6 M HCl (3×20 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and 0.67 g (78%) of product **14** was obtained as a colorless microcrystalline solid, mp 61–65°C. IR (KBr) ν: 2900 (s), 2850 (m), 1600 (w), 1450 (w), 1355 (s), 1185 (m), 1170 (s), 950 (s), 954 (m) 835 (s), 815 (m) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.00–1.05 (m, 2H), 1.39 (br s, 6H), 1.50–1.70 (m, 8H), 1.92 (br s, 3H), 2.45 (s, 3H), 3.99 (t, 2H, J=6.67 Hz), 7.35 (d, 2H, J=7.95 Hz), 7.79 (d, 2H, J=7.95 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.39 (q, 1C), 22.08 (t, 1C), 28.37 (d, 3C), 31.63 (s, 1C), 36.87 (t, 3C), 39.56 (t, 1C), 42.01 (t, 3C), 71.61 (t, 1C), 127.85 (d, 2C), 129.74 (d, 2C), 133.17 (s, 1C), 144.59 (s, 1C). Anal. calcd for $C_{20}H_{28}SO_3$ (M_r=348.508): C, 68.93; H, 8.10. Found: C, 68.96; H, 8.21.

4.4.3. 1,3-Bis(2-tosyloxyethyl)adamantane (15). To a stirred, cooled (ice/water) suspension of TsCl (3.91 g, 21 mmol) in dry pyridine (7 mL) 1,3-bis(2-hydroxyethyl)-adamantane[17] (2.0 g, 8.9 mmol) was added in small portions. The reaction mixture was stirred over night at 4°C, diluted with water (50 mL) and then extracted with CH_2Cl_2 (3×30 mL). The combined organic extract was washed with 6 M HCl (3×100 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and 4.71 g (99%) of product **15** was obtained as a colorless microcrystalline solid, mp 76–77°C. IR (KBr) ν: 3080 (w), 3000 (w), 2900 (s), 2850 (s), 1600 (m), 1355 (s), 1175 (s), 1100 (m), 950 (s), 815 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.08 (br s, 2H), 1.20–1.55 (m, 14H), 1.94 (br s, 2H), 2.46 (s, 6H), 4.05 (t, 4H, J=7.18 Hz), 7.36 (d, 4H, J=8.20 Hz), 7.78 (d, 4H, J=8.20 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.26 (q, 2C), 28.15 (d, 2C), 31.99 (s, 2C), 35.55 (t, 1C), 41.10 (t, 4C), 41.65 (t, 2C), 46.79 (t, 1C), 66.72 (t, 2C), 127.66 (d, 4C), 129.68 (d, 4C), 132.98 (s, 2C), 144.59 (s, 2C). Anal. calcd for $C_{28}H_{36}O_6S_2$ (M_r=532.724): C, 63.13; H, 6.81. Found: C, 63.27; H, 6.64.

4.4.4. 1,3-Bis(3-tosyloxypropyl)adamantane (16). To a stirred, cooled (ice/water) suspension of TsCl (1.2 g, 6.3 mmol) in dry pyridine (2.5 mL) 1-(3-hydroxypropyl)-adamantane[18] (0.67 g, 2.7 mmol) was added in small portions. The reaction mixture was stirred over night at 4°C, then diluted with water (25 mL) and extracted with CH_2Cl_2 (3×15 mL). The combined organic extract was washed with 6 M HCl (3×50 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and 1.21 g (80%) of product **16** was obtained as a colorless microcrystalline solid, mp 135–138°C. IR (KBr) ν: 2900 (s), 2845 (s), 1600 (m), 1365 (s), 1190 (s), 1170 (s), 1095 (m), 1010 (m), 960 (s), 905 (s), 810 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.95–1.05 (m, 4H), 1.2–1.45 (m, 10H), 1.50–1.60 (m, 6H), 1.94 (br s, 2H), 2.43 (s, 6H), 3.96 (t, 4H, J=6.67 Hz), 7.33 (d, 4H, J=7.95 Hz), 7.77 (d, 4H, J=7.95 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.36 (q, 2C), 22.11 (t, 2C), 28.57 (d, 2C), 32.27 (s, 2C), 36.16 (t, 1C), 39.18 (t, 2C), 41.36 (t, 4C), 46.73 (t, 1C), 71.43 (t, 2C), 127.79 (d, 4C), 129.74 (d, 4C), 133.12 (s, 2C), 144.61 (s, 2C). Anal. calcd for $C_{30}H_{40}O_6S_2$ (M_r=560.778): C, 64.26; H, 7.19. Found: C, 64.23; H, 7.14.

4.4.5. 2-(1-Adamantyl)ethyldiethanolamine (17). Suspension of diethanolamine (1.0 g, 1.9 mmol) and Na_2CO_3 (0.5 g, 4.75 mmol) in acetonitrile (4 mL) was stirred at 80°C under nitrogen atmosphere and a solution of 1-(2-bromoethyl)adamantane[13] (2.3 g, 9.5 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was stirred at the same temperature for additional 20 h. After cooling to ambient temperature, CH_2Cl_2 (50 mL) was added and the reaction mixture was filtered. Filtrate was concentrated in vacuo and residue was purified through a small column of florisil using CH_2Cl_2 as an eluent to give 2.00 g (79%) of product **17** as a yellow microcrystalline solid, mp 48–50°C. IR (KBr) ν: 3380 (s), 2900 (s), 2840 (s), 1450 (m), 1040 (s) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.20–1.35 (m, 2H), 1.48 (br s, 6H), 1.55–1.75 (m, 6H), 1.94 (br s, 3H), 2.60–2.70 (m, 2H), 2.74 (t, 4H, J=5.35 Hz), 3.62 (br s, 2H, OH), 3.67 (t, 4H, J=5.35 Hz). ^{13}C NMR ($CDCl_3$) δ: 28.29 (d, 3C), 31.47 (s, 1C), 36.79 (t, 3C), 39.61 (t, 1C), 42.17 (t, 3C), 48.37 (t, 1C), 55.72 (t, 2C), 58.84 (t, 2C). Anal. calcd for $C_{16}H_{29}NO_2$ (M_r=267.415): C, 71.86; H, 10.93; N, 5.24. Found: C, 71.93; H, 10.85; N, 5.05.

4.4.6. 3-(1-Adamantyl)propyldiethanolamine (18). A suspension of diethanolamine (0.7 g, 1.9 mmol) and Na_2CO_3 (0.37 g, 3.5 mmol) in acetonitrile (3 mL) was stirred at 80°C under nitrogen atmosphere and solution of 1-(bromopropyl)adamantane[13] (1.72 g, 6.7 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise. The reaction mixture was stirred at the same temperature for additional 20 h. After cooling to the ambient temperature, CH_2Cl_2 (50.0 mL) was added and the reaction mixture was filtered. Filtrate was concentrated in vacuo and residue was purified through a small column of Al_2O_3 (act. II–III) using 0→5% MeOH in CH_2Cl_2 as an eluent to give 1.67 g (89%) of product **18** as a yellow microcrystalline solid, mp

32–34°C. IR (KBr) ν: 3380 (s), 2895 (s), 2840 (s), 1450 (m), 1040 (m), 875 (w) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.95–1.05 (m, 2H), 1.30–1.55 (m, 8H), 1.55–1.75 (m, 6H), 1.94 (br s, 3H), 2.45–2.60 (m, 2H), 2.68 (t, 4H, J=5.34 Hz), 3.31 (br s, 2H, OH), 3.64 (t, 4H, J=5.34 Hz). ^{13}C NMR ($CDCl_3$) δ: 19.11 (t, 1C), 28.44 (d, 3C), 31.87 (s, 1C), 36.95 (t, 3C), 41.82 (t, 1C), 42.25 (t, 3C), 55.48 (t, 1C), 55.69 (t, 2C), 59.03 (t, 2C). Anal. calcd for $C_{17}H_{31}NO_2$ (M_r=281.442): C, 72.55; H, 11.10; N, 4.98. Found: C, 72.43; H, 11.39; N, 5.15.

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