# SYNTHESIS OF TWO-ARMED MACROCYCLES VIA N,N'-DISUBSTITUTED $\omega,\omega'$ -DIAMINOETHER PRECURSORS

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> Received November 28, 1994 Accepted December 15, 1995

N,N'-Dialkyldiazacrowns and their precursors, bis(alkylamino) derivatives of tri- and tetraethylene glycols, are synthesized and characterized.

Key words: Diazacrowns; Oligoethylene glycols, derivatives.

Crown ethers were first described by Pedersen<sup>1</sup>. Since that time the chemistry of these neutral complexing agents has undergone a rapid development. Besides the monocyclic compounds, a large number of oligo- and polycyclic derivatives have been synthesized and studied<sup>2</sup>. For many of those preparations, oligo(oxoethylenes) with amino end groups have been used as intermediates because the nitrogen atoms allow further controlled reaction during the synthesis<sup>3</sup>. In the resultant complexing molecules the nitrogen atoms are electron donor atoms as well as branching points.

The azacrowns possess complexation properties that are intermediate between those of the all-oxygen crowns, which strongly complex alkali and alkaline-earth metal ions, and those of the all-nitrogen cyclams, which strongly complex heavy metal cations. These mixed complexation properties make the azacrowns interesting for research in many areas. The azacrowns have important uses as synthetic receptors in molecular recognition processes<sup>1</sup> and, in some cases, their anion complexation properties are similar to those in certain biological systems<sup>4–6</sup>. They show an enhanced complexing ability for ammonium salts<sup>7,8</sup> and for transition-metal ions<sup>7,9</sup> over the all-oxygen crown compounds. Anion-promoted two-phase reactions can be successfully performed by using as catalysts crown ethers of suitable structure which continuously transfer the anion from the aqueous to organic phase<sup>10</sup>.

For this reason we have prepared a series of diazacrowns **2** substituted with long alkyl chains. The synthesis of bis(secondary amine) precursors derived from oligoe-thylene glycols is illustrated in Scheme 1. This alkylation procedure, originally developed by Krespan<sup>11</sup> is more straightforward than the synthesis by other methods<sup>12–16</sup>. Some of these compounds were obtained previously and tested as drugs<sup>17,18</sup>, pes-

ticides<sup>19</sup> and extraction agents for mercury(II) chloride, alkali metals and alkaline earth metals<sup>12</sup>.



### Scheme 1

In previous studies<sup>10,12,20,21</sup>, most of N,N'-dialkyl derivatives of 1,10-diaza-18-crown-6 such as butyl, hexyl, octyl, dodecyl and benzyl ones were synthesized by alkylation or acylation of ring nitrogen atoms using the expensive diazacrown.

In this study all *N*,*N*'-dialkyl derivatives of 1,10-diaza-18-crown-6 were synthesized by reaction of triethylene glycol ditosylate and an appropriate diazadioxaalkane. This cyclization is illustrated in Scheme 2.



#### **EXPERIMENTAL**

Infrared spectra were recorded on a Midac 1700 instrument in KBr pellets. <sup>1</sup>H and <sup>13</sup>C NMR spectra at 200 and 50.2 MHz, respectively, were recorded on a Bruker-AC spectrometer in CDCl<sub>3</sub> and are reported in ppm ( $\delta$ ) downfield from internal tetramethylsilane. Elemental analyses were performed on a Carlo–Erba model 1200 instrument. All reactions were performed under dry nitrogen atmosphere.

## Azaoxaalkanes 1a-1e

A solution of amine and 1,2-bis(2-chloroethoxy)ethane or related dichloro derivative (mole ratio 4 : 1) was heated and stirred at 140–160 °C under nitrogen atmosphere for 4 h. The reaction mixture was then dissolved in hot benzene and the starting amine salt precipitated was filtered off. The filtrate was extracted with 10% aqueous sodium hydroxide. The benzene extracts were dried with anhydrous

# TABLE I

Characteristics	of	dipicrates	of	azaoxaalkanes	1a–1e
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Compound	B.p. <sup><i>a</i></sup> , °C/kPa	M.p., °C	Formula	Calculated/Found		
	Yield, %		(M.w.)	% C	% H	% N
<b>1</b> a	180-182/0.02	95–97	C32H50N8O16	47.90	6.27	13.95
	46		(802.8)	48.03	6.04	13.39
1b	194–201/0.11 <sup>b</sup>	99–103	$C_{34}H_{54}N_8O_{16}$	49.15	6.55	13.49
	46		(830.8)	49.53	6.73	14.02
1c	208-209/0.04	101-103	C <sub>36</sub> H <sub>58</sub> N <sub>8</sub> O <sub>16</sub>	50.34	6.80	13.04
	32		(858.9)	50.52	7.08	13.00
1d	254–258/0.07 <sup>c</sup>	102-104	$C_{42}H_{70}N_8O_{16}$	53.50	7.48	11.88
	46		(943.1)	53.49	7.57	11.55
1e	230-237/0.12	174–176 <sup>d</sup>	$\mathrm{C}_{22}\mathrm{H}_{34}\mathrm{Cl}_{2}\mathrm{N}_{2}\mathrm{O}_{3}{}^{d}$	59.32	7.69	6.25
	43		(445.4)	59.62	7.63	6.05

<sup>a</sup> Free base. <sup>b</sup> 167 °C/0.002 kPa (ref.<sup>12</sup>). <sup>c</sup> M.p. 38–39 °C (refs<sup>12,14</sup>). <sup>d</sup> Dihydrochloride.

# TABLE II Characteristics of 1,10-dialkyl-1,10-diaza-18-crowns-6

Compound	M.p., °C Yield, %	Formula	Calculated/Found		
		(M.w.)	% C	% H	% N
2a	$-a^{a}$	$C_{26}H_{54}N_2O_4$ . Ba(ClO <sub>4</sub> ) <sub>2</sub> . H <sub>2</sub> O <sup>b</sup>	38.42	6.94	3.45
	30 <sup>c</sup>	(812.9)	38.67	7.24	3.44
2b	$-6^d$	$C_{30}H_{62}N_2O_4$ . Ba(ClO <sub>4</sub> ) <sub>2</sub> . H <sub>2</sub> O <sup>e</sup>	41.46	7.42	3.22
	$30^f$	(869.1)	41.94	7.52	3.00

 $^a$  B.p. 274–280 °C/0.09 kPa.  $^b$  M.p. 156–159 °C.  $^c$  Crude yield.  $^d$  Oil $^{20}$ .  $^e$  M.p. 104–106 °C.  $^f$  After chromatography.

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sodium sulfate, filtered, and the solvent was evaporated. Unreacted excess of amine was recovered and the product distilled. The azadioxaalkanes **1a–1e** were characterized by their dipicrates (Table I).

#### 1,10-Dialkyl-1,10-diaza-18-crowns-6 2a-2d

A mixture of 0.048 mol of 1, 0.048 mol of triethylene glycol ditosylate, and 0.173 mol of Na<sub>2</sub>CO<sub>3</sub> in MeCN–THF (800 : 200 ml) was heated at reflux under nitrogen atmosphere for 24 h. The reaction mixture was cooled, filtered, and concentrated in vacuo. Column chromatography (alumina, 2% 1-propanol–hexane) followed by a bulb-to-bulb distillation gave **2a** and **2b** as transparent oils from which crystalline barium perchlorate complexes were prepared (see Table II). Column chromatography (alumina, 2% 1-propanol–hexane) followed by recrystallization from diethyl ether gave crystalline **2c** (25%, m.p. 29–32 °C) and **2d** (27%, m.p. 50–52 °C), with physical properties identical with those reported<sup>20,21</sup>.

**2a**.  $Ba(ClO_4)_2$ .  $H_2O$ . IR spectrum: 3 438 (O–H); 2 955, 2 926, 2 857 (C–H); 1 117, 1 091, 1 061 (C–O). <sup>1</sup>H NMR spectrum: 0.87 t, 6 H (CH<sub>3</sub>); 1.28 s, 16 H (CH<sub>2</sub>); 1.8 bs, 2 H (H<sub>2</sub>O); 2.66–3.10 m, 12 H (NCH<sub>2</sub>, OCCH<sub>2</sub>N); 3.40–4.02 m, 16 H (OCH<sub>2</sub>). <sup>13</sup>C NMR spectrum: 14.53 (CH<sub>3</sub>); 23.03, 27.63, 27.67, 29.70, 32.22, 52.00 (C-4); 52.08 (C-3); 69.00 (C-2); 70.48 (C-1).

**2b**.  $Ba(ClO_4)_2$ .  $H_2O$ . IR spectrum: 3 551, 3 479 (O–H); 2 994, 2 849 (C–H); 1 140, 1 064, 1 105 (C–O). <sup>1</sup>H NMR spectrum: 0.86 t, 6 H (CH<sub>3</sub>); 1.24 s, 28 H (CH<sub>2</sub>); 2.18 bs, 2 H (H<sub>2</sub>O); 2.6–3.5 m, 12 H (NCH<sub>2</sub>, OCCH<sub>2</sub>N); 3.4–3.8 m, 16 H (OCH<sub>2</sub>). <sup>13</sup>C NMR spectrum: 14.60 (CH<sub>3</sub>); 23.14, 27.71, 29.73, 30.01, 32.35, 51.97 (C-4); 52.09 (C-3); 68.97 (C-2); 70.48 (C-1).

#### **RESULTS AND DISCUSSION**

In this study some new azaoxaalkanes **1a–1e** were synthesized and characterized by their picrates or dihydrochlorides (Table I). The chosen synthesis procedure is more straightforward than the other synthetic methods. Also, this procedure gives the corresponding diazacrowns as by-products (their isolation is not given in this study). For example, the synthesis of **1a** gave 16% of **2a** as a by-product. Other synthesis methods described in literature required protection of secondary amine with benzyl blocking group and decreasing the nucleophilic strength of primary amine by tosyl substitution. Removing the benzyl and tosyl groups required additional reaction steps and complex procedures. The reaction of azaoxaalkane precursors, triethylene glycol ditosylate and  $Na_2CO_3$  in MeCN–THF gave the diazacrowns with the physical properties identical with those reported.

We thank TÜBITAK (Scientific and Technical Research Council of Turkey) for support of this work.

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