

**BIS(MONOAZACROWN ETHERS): EFFECTS OF BRIDGE LENGTH AND RING SIZE ON STABILITY AND SELECTIVITY IN ALKALI ION SANDWICH COMPLEX FORMATION\***

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Sodium, potassium, rubidium and caesium ion complex formation was investigated in two homologous series of bis(azacrown ether)s *Ia–Ic* and *IIa–IIc*. Three complementary bis(azacrown ether)s series *IIIa–IIIc*, *IVa–IVc* and *Va–Vc* were employed for a more detailed study of sodium complexation. Very pronounced effects of bridge length as well as macroring size were found in the investigated series and interpreted mainly in terms of various proclivity of individual ligands and alkali ions to sandwich complex formation. Remarkably high selectivities in alkali ion formation were noted for the shortest bridge ligands *Ia* and *Ib*, the former preferring strongly sodium and the latter potassium complex formation.

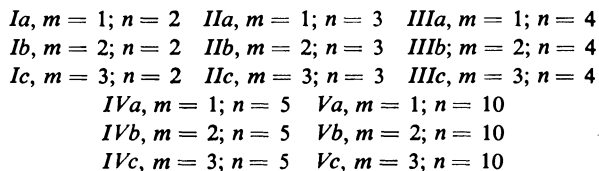
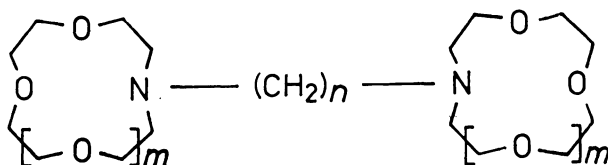
Macrocyclic polyether ligands carrying two crown ether units at the end of bridge, customarily referred to as bis(crown ether)s, exhibit sometimes remarkably different cation-complexing properties than the corresponding monocyclic analogues<sup>1–8</sup>. Ability of bis(crown ether)s to form intramolecular sandwich complexes, in which both adjacent crown units cooperate, is assumed to be responsible factor. As a result of the sandwich formation, unusually high selectivity towards some cations has been occasionally observed<sup>8–11</sup> providing a promising prospect for exploitation in construction of ion selective sensors.

As it appears, the bis(crown ether)s principle may be extended to azacrown derivatives, in which an oxygen is replaced by nitrogen in each crown unit. Easy accessibility<sup>12–14</sup> makes from the bis(monoazacrown ether)s a very convenient subject of a systematic study. As a continuation of our earlier investigation<sup>14</sup>, we now report on the effect of bridge length ( $n = 2, 3, 4, 5, 10$ ) and macroring size (12, 15, 18) observed in the alkali ion ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Rb}^+$ ,  $\text{Cs}^+$ ) complex formation with the homologous series of bis(azacrown ether)s *I–V*. A comparison has been made with the

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corresponding data obtained in the parent monocyclic series of azacrown ethers *VIa–VIc*.



## EXPERIMENTAL

N-methyl substituted *VIa–VIc* as well as unsubstituted *VIIa–VIIc* azacrown ethers were available from the previous studies<sup>13,14</sup>. Bis(monoazacrown ether)s *Ia*, *Ila–Ilc*, *IIIb–IIIc* and *IVb–IVc*, are also known compounds prepared by described procedures<sup>12,19</sup>.

### General Procedure for Preparation of Bis(monoazacrown ether)s *Ib–Ic*, *Va* and *Vb*

An appropriate unsubstituted monoazacrown ether *VIIa–VIIc* (12 mmol) was stirred with the corresponding  $\alpha,\omega$ -alkanediol-di-*p*-toluenesulfonate (6.5 mmol) and anhydrous sodium carbonate (2.0 g; 19 mmol) under reflux in acetonitrile (20 ml) for 10 h. The solvent was taken down at reduced pressure and the product was isolated by a column chromatography on alumina (Merck, act. II, 200 g/mmol). Data are in Tables I–III.

### General Procedure for Preparation of Bis(monoazacrown ether)s *IIIa* and *IVa*

To a solution of an appropriate unsubstituted monoazacrown ether *VIIa–VIIc* (12 mmol) in chloroform (50 ml) and triethylamine (1.32 g; 13 mmol) was dropwise added succinic (or glutaric) dichloride (6.5 mmol) in chloroform (20 ml). After 2 h stirring at ambient temperature the reaction mixture was washed with water ( $2 \times 20$  ml), dried with magnesium sulfate and the solvent was distilled off. The crude diamide was dissolved in dry tetrahydrofuran (30 ml) and treated with lithiumaluminiumhydride (2 g) dissolved in the same solvent (30 ml). After 2 h reflux the mixture was decomposed with aqueous tetrahydrofuran, solids were filtered off and washed (500 ml chloroform). After evaporation of the solvents the crude product was separated by a column chromatography on alumina (Reanal, act. II, 200 g/mmol). Data are in Tables I–III.

### Potentiometric Measurements

Formation of alkali ion complexes was followed potentiometrically in 99% aqueous methanol basified with 0.01M tetramethylammonium hydroxide. The values of sodium, rubidium, and caesium complex stability were determined by titration of bis(crown ether)s with 0.01M solution

of the appropriate alkali metal chloride, employing sodium ion selective electrode (Radiometer G 502 Na); rubidium and caesium were determined competitively<sup>20</sup> against sodium. Tacussel PKV electrode was employed for potassium ion complexes. Stability constants were calculated by MINQUAD program<sup>21</sup>.

## RESULTS AND DISCUSSION

### *Alkali Ion – Bis(azacrown ether) Sandwich Complex Stability*

Table IV summarizes the stability constants determined potentiometrically in the complex-forming reaction of bis(azacrown ether)s *I–V* with sodium chloride in 99% aqueous methanol. As the Table IV shows, both bridge length as well as ring size of the macrocyclic units profoundly affect stability of the resulting sodium ion complexes. The most stable complex ( $\log K_s = 8.18$ ) is formed from the bis(crown ether) *Ia* possessing the shortest bridge ( $n = 2$ ) and at the same time the smallest ( $m = 1$ ) macrorings. A very steep decrease of the complex stability is induced in the twelve-membered ring series *Ia–Va* on lengthening the bridge. A drop greater than

TABLE I  
Bis(monoazacrown ether)s *Ia, Ic, IIIa, IVa, Va–Vc*

Compound	Yield %	Eluent <sup>a</sup>	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
<i>Ib</i>	70	CHCl <sub>3</sub>	C <sub>22</sub> H <sub>44</sub> N <sub>2</sub> O <sub>8</sub> (464.6)	56.87 56.56	9.55 9.72	6.03 5.99
<i>Ic</i>	64	CHCl <sub>3</sub> : CH <sub>3</sub> OH 99 : 1	C <sub>26</sub> H <sub>52</sub> N <sub>2</sub> O <sub>10</sub> (552.7)	56.50 56.32	9.48 9.52	5.07 5.01
<i>IIIa</i>	68	C <sub>6</sub> H <sub>6</sub> : CH <sub>3</sub> OH 98 : 2	C <sub>20</sub> H <sub>40</sub> N <sub>2</sub> O <sub>6</sub> (404.6)	59.38 59.21	9.97 9.92	6.92 6.59
<i>IVa</i>	65	C <sub>6</sub> H <sub>6</sub> : CH <sub>3</sub> OH 98 : 2	C <sub>21</sub> H <sub>42</sub> N <sub>2</sub> O <sub>6</sub> (418.6)	60.26 60.30	10.11 10.17	6.69 6.58
<i>Va</i>	77	CHCl <sub>3</sub>	C <sub>26</sub> H <sub>52</sub> N <sub>2</sub> O <sub>6</sub> (488.7)	63.90 63.72	10.73 10.86	5.73 5.60
<i>Vb</i>	82	CHCl <sub>3</sub> : CH <sub>3</sub> OH 99.5 : 0.5	C <sub>30</sub> H <sub>60</sub> N <sub>2</sub> O <sub>8</sub> (576.8)	62.47 62.39	10.49 10.32	4.86 4.79
<i>Vc</i>	46	CHCl <sub>3</sub> : CH <sub>3</sub> OH 99 : 1	C <sub>34</sub> H <sub>68</sub> N <sub>2</sub> O <sub>10</sub> (664.9)	61.42 61.30	10.31 10.16	4.21 4.16

<sup>a</sup> CHCl<sub>3</sub> stabilized by CH<sub>3</sub>OH.

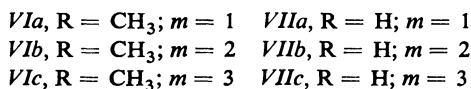
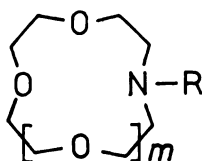
four orders of magnitude takes place on going from the two carbon to three carbon bridge analogue (*Ia* and *IIa*, respectively), followed by a much smaller decrease on going to the four-carbon homologue (*IIIa*). Levelling out of the  $\log K_s$  values is observed on further bridge elongation ( $n = 5$  and  $10$ ; *IVa* and *Va*, respectively). In this way, it follows that both the adjacent crown units cooperate strongly only when the bridge is very short (*Ia*, *IIa*). In the higher homologues *IIIa*–*Va* possessing four or more carbon bridge we assume that sandwich complexes play only insignificant, if any role. A support for this view is provided by a comparison with the corresponding (parent) monoazacrown *VIa*.

Next, it may be noted that much smaller differences due to bridge length than we found in the twelve-membered series *Ia*–*Va* occur in the fifteen-membered bis-(crown)s *Ib*–*Vb*, a significant enhancement of sodium complex stability (by c. 1.7 log units relative to the corresponding monocrown *VIb*) being found only in the homologue with the shortest bridge (*Ib*;  $n = 2$ ). In the eighteen-membered ring series

TABLE II  
<sup>1</sup>H NMR spectra of bis(monoazacrown ether)s<sup>a</sup>

Compound	Solvent	$\delta$ in ppm
<i>Ib</i>	CD <sub>3</sub> OD	2.85 s, 4 H (NCH <sub>2</sub> CH <sub>2</sub> N); 2.93 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 6$ Hz); 3.84 m, 24 H (CH <sub>2</sub> O)
<i>Ic</i>	CD <sub>3</sub> OD	2.87 s, 4 H (NCH <sub>2</sub> CH <sub>2</sub> N); 2.97 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 5.5$ Hz); 3.84 m, 30 H (CH <sub>2</sub> O)
<i>IIIa</i>	CDCl <sub>3</sub>	1.49 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> N); 2.52 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ); 2.69 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 5$ Hz); 3.6–3.75 m, 24 H (CH <sub>2</sub> O)
<i>IVa</i>	CDCl <sub>3</sub>	1.35–1.65 m, 6 H (NCH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> N); 2.52 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ); 2.61 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 5.0$ Hz); 3.6–3.8 m, 24 H (CH <sub>2</sub> O)
<i>Va</i>	CDCl <sub>3</sub>	1.34 m, 16 H (NCH <sub>2</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> N); 2.3–2.6 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ); 2.68 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 8$ Hz); 3.5–3.75 m, 24 H (CH <sub>2</sub> O)
<i>Vb</i>	CDCl <sub>3</sub>	1.25 m, 16 H (NCH <sub>2</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> N); 2.3–2.6 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ); 2.72 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 10$ Hz); 3.5–3.75 m, 32 H (CH <sub>2</sub> O)
<i>Vc</i>	CDCl <sub>3</sub>	1.35 m, 16 H (NCH <sub>2</sub> (CH <sub>2</sub> ) <sub>8</sub> CH <sub>2</sub> N); 2.3–2.6 m, 4 H (NCH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ); 2.75 t, 8 H (NCH <sub>2</sub> CH <sub>2</sub> O, $J = 10$ Hz); 3.45 to 3.8 m, 40 H (CH <sub>2</sub> O)

<sup>a</sup> Measured on Tesla BS 497 instrument (100 MHz) with tetramethylsilane as internal standard, in FT mode.



*Ic–Vc* the cooperative effect is already virtually absent indicating thus a general reluctance to sodium ion – sandwich complex formation.

Table V compares the corresponding potentiometric data we obtained in the homologous bis(azacrown ether) series *Ia–Ic* and *IIa–IIc* for a wider range of alkali metal ions ( $Na^+$ ,  $K^+$ ,  $Rb^+$ ,  $Cs^+$ ). A qualitatively similar pattern of complex stability variation with bridge length as we noted above for sodium is now reproduced also for the other investigated alkali ions, the  $\log K_s$  values obtained for the *Ia* and *Ib* being always significantly higher than those for the longer bridge homologues (*IIa* and *IIb*, respectively).

TABLE III  
Mass spectra of bis(monoazacrown ether)s<sup>a</sup>

Compound	<i>m/z</i> (%)
<i>Ib</i>	464 ( $M^+$ , 6); 234 (12), 232 (100), 100 (10), 71 (8), 56 (12), 45 (12)
<i>Ic</i>	552 ( $M^+$ , 8); 276 (100), 232 (15), 100 (12), 73 (8), 57 (12), 45 (10)
<i>IIIa</i>	404 ( $M^+$ , 6); 285 (18), 230 (20), 228 (22), 214 (52), 190 (100), 188 (50), 160 (17), 97 (25), 86 (25), 84 (20), 56 (17)
<i>IVa</i>	418 ( $M^+$ , 15); 188 (100), 124 (40), 110 (38), 100 (42), 98 (65), 57 (52), 56 (44), 43 (39), 41 (34)
<i>Va</i>	488 ( $M^+$ ); 383 (45), 353 (35), 339 (30), 189 (30), 188 (100), 186 (20), 158 (22), 149 (20), 100 (38)
<i>Vb</i>	576 ( $M^+$ , 12); 383 (18), 232 (100), 203 (16), 73 (22), 72 (18), 57 (31), 56 (25), 45 (20), 43 (24)
<i>Vc</i>	278 (18), 276 (100), 246 (25), 186 (14), 100 (18), 69 (14), 58 (16), 57 (18), 55 (16), 45 (20)

<sup>a</sup> Measured on ZAB-EQ instrument, EI ionization (70 eV).

As it concerns complex stability variation with ring size in Table V, some dependence on alkali ion diameter becomes apparent, the most stable complexes with the bulkier alkali ions ( $K^+$ ,  $Rb^+$ ,  $Cs^+$ ) being formed with fifteen-rather than twelve-membered bis(crown)s.

While the observed effect of ring size does not come as a surprise and agrees well with the earlier experience that sandwich type of complexes are most likely to form when metal ion is a little larger<sup>5</sup> than the crown cavity, the very pronounced effect of bridge length found in the series *Ia–Va* and *Ib–Vb*, respectively, disagrees

TABLE IV

Effect of bridge length (*n*) and ring size (*S*) on stability  $\log K_s$  of sodium ion — bis(crown ether) complexes<sup>a</sup>

Compound	<i>n</i>	$\log K_s^b$		
		<i>S</i> = 12	<i>S</i> = 15	<i>S</i> = 18
<i>I</i>	2	8.18	4.62	3.80
<i>II</i>	3	3.95	3.44	3.75
<i>III</i>	4	2.44	3.29	3.77
<i>IV</i>	5	2.06	3.35	3.74
<i>V</i>	10	2.39	3.32	3.79
<i>VI</i>	—	2.04	3.41	3.79

<sup>a</sup> Determined in 99% aqueous methanol basified with 0.01M tetramethylammonium hydroxide;

<sup>b</sup>  $K_s$  in  $\text{mol l}^{-1}$ .

TABLE V

Values of  $\log K_s$  in bis(crown ether) series *Ia–Ic* and *IIa–IIc*. The effects of metal ion identity ( $M^+$ ), bridge length (*n*) and ring size<sup>a</sup>

$M^+$	$\log K_s$					
	<i>Ia</i>	<i>IIa</i>	<i>Ib</i>	<i>IIb</i>	<i>Ic</i>	<i>IIc</i>
$Na^+$	8.18	3.95	4.62	3.44	3.80	3.75
$K^+$	4.21	2.28	7.10	3.76	5.57	5.26
$Rb^+$	3.42	2.83	5.98	3.73	4.85	5.15
$Cs^+$	— <sup>b</sup>	— <sup>b</sup>	4.88	3.01	3.70	3.35

<sup>a</sup> Determined in 99% aqueous methanol basified with 0.01M tetramethylammonium hydroxide;

<sup>b</sup> immeasurably low values.

markedly with earlier scattered evidence from some other bis(crown ether) series exhibiting only an insignificant<sup>15-18</sup> complex stability variation with bridge length. A closer examination of the literature data however reveals that a heteroatom grouping (imino-<sup>15</sup>, amido-<sup>16</sup>, carbalkoxy-<sup>17</sup> or alkoxy<sup>18</sup>) was invariantly involved as a part of the bridge in the earlier studies. Accordingly, we propose as an explanation that lariat type rather than sandwich type of alkali ion complex formation prevailed in such bis(crown ether) series where the electron-donating heteroatom grouping provides a more efficient participation than the adjacent macroring.

#### *Selectivity in Alkali-Ion – Bis(azacrown ether) Complex Formation*

So far we have focussed attention on stability rather than selectivity in bis(crown ether) complex formation. A closer examination of data in Table V reveals a very pronounced selectivity of bis(crown ether)s *Ia* and *Ib* in alkali ion complex formation, the former strongly preferring sodium and the latter potassium.

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