1,2-BIS(AZACROWN)ETHANES: EFFECT OF BRIDGE SUBSTITUTION AND RING SIZE ON FORMATION OF SANDWICH COMPLEXES WITH SODIUM AND POTASSIUM IONS*

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Dedicated to Professor Václav Horák on the occasion of his 70th birthday.

The title problem was investigated potentiometrically using four homologous series of bis(azacrown)s *I* – *IV*. A surprisingly large destabilizing effect of bridge substituent was found in the intramolecular sandwich complex formation and ascribed to symmetry violation.

Previously, some bis(azacrown)alkanes have been found to exhibit much higher selectivity in complexation of alkali ions than the starting (monocyclic) azacrown ethers[1 – 5]. Cooperation of both adjacent crown units in the sandwich complex formation has been proposed to be the responsible factor.

Our recent study[5] revealed that the bis(azacrown) selectivity depends strongly on the length of the alkane bridge connecting the participating azacrown units, the two-carbon bridge giving rise to the most promising results.

Aiming to enhance lipophilicity of the parent bis(azacrown) compounds *Ia* – *Ic*, which deemed to be a prerequisite for application in ion-selective sensors, we have now prepared two series of benzyloxymethyl and 1-naphthyloxymethyl analogues *IIa* – *IIc* and *IIIa* – *IIIc* and investigated potentiometrically their ability to complex sodium and potassium ions. At the same time, we have investigated also the corresponding derivatives *IVa* – *IVc* bearing a hydrophilic rather than lipophilic hydroxymethyl substituent at the bridge.

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EXPERIMENTAL

Bis(azacrown)s *Ia* – *Ic* and azacrowns *Va* – *Vc* were available from the previous work[4,5].

Bis(azacrown)s *IIa* – *IIc*

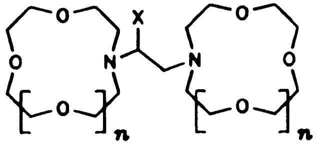
An appropriate azacrown ether *Va* – *Vc* (12 mmol) in dioxane (20 ml) was stirred under reflux with 1-benzyloxy-2,3-bis(*p*-toluenesulfonyloxy)propane[6] (2.94 g, 6 mmol) and anhydrous sodium carbonate (2.0 g, 19 mmol) for 50 h, the mixture was diluted with chloroform (50 ml) and the precipitated salts were filtered off. The solvents were taken down in vacuo and the product was isolated by column chromatography on alumina (Reanal, act. II) using chloroform as eluent. Treatment with 0.1 M ethanolic solution of perchloric acid afforded the corresponding perchlorates as glassy solids. Results are summarized in Table I.

Bis(azacrown)s *IIIa* – *IIIc*

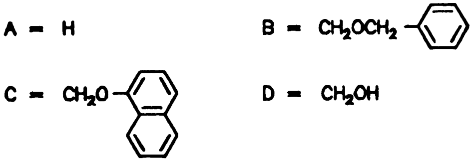
Prepared analogously[6] as the bis(azacrown)s *IIa* – *IIc* from the corresponding azacrown ethers *Va* – *Vc* and 1-(1-naphthoxy)-2,3-bis(*p*-toluenesulfonyloxy)propane. Crystalline perchlorates were obtained on treatment with 0.1 M ethanolic solution of perchloric acid. Results are summarized in Table I.

Bis(azacrown)s *IVa* – *IVc*

The perchlorate of bis(azacrown)s *IIa* – *IIc* (5 mmol) dissolved in ethanol (10 ml) was treated with 10% Pd/C catalyst (250 mg) and hydrogenated under stirring at atmospheric pressure at 50 °C. The crude product was recrystallized from 0.1 M ethanolic solution of perchloric acid. Results are summarized in Table I.



Ia, *n* = 1; X = A
Ib, *n* = 2; X = A
Ic, *n* = 3; X = A
IIa, *n* = 1; X = B
IIb, *n* = 2; X = B
IIc, *n* = 3; X = B
IIIa, *n* = 1; X = C
IIIb, *n* = 2; X = C
IIIc, *n* = 3; X = C
IVa, *n* = 1; X = D
IVb, *n* = 2; X = D
IVc, *n* = 3; X = D

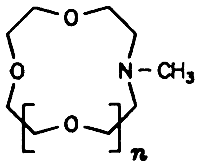


Potentiometric Measurements

Formation of alkali ion complexes was followed potentiometrically in 0.01 M tetramethylammonium hydroxide in 99% methanol. The values of sodium and potassium complex stability were determined by titration of bis(azacrown)s with 0.01 M solution of the appropriate alkali metal chloride, employing sodium (Radiometer G 502 Na) or potassium (Tacussel PKV) ion selective electrode. Stability constants were calculated using MINIQUAD programme[7].

RESULTS AND DISCUSSION

Table II summarizes the stability constants K_s determined potentiometrically for the 1 : 1 complex formation from the bis(azacrown)s *I* – *IV* with sodium and potassium chloride in 99% aqueous methanol. A comparison is simultaneously made with the corresponding K_s values reported[8,9] for the parent monoazacrown *Va* – *Vc*.



V	*n*
a	1
b	2
c	3

As the comparison shows, cooperation of two azacrown units in the bis(crown) compounds provides in most instances an extra-stabilization of the complex resulting assumedly from the intramolecular sandwich formation. It is seen that the extent of stabilization depends greatly on the alkali ion identity, ring size of the azacrown unit as well as on the bridge substituent.

As it concerns the sodium ion the greatest stabilization is provided by unsubstituted twelve-membered bis(azacrown) *Ia*, the $\log K_s^{Na^+}(Ia) - \log K_s^{Na^+}(Va)$ difference being greater than 6. Much smaller stabilization is provided by the larger bis(azacrown) homologues, the $\log K_s^{Na^+}(Ib) - \log K_s^{Na^+}(Vb)$ and $\log K_s^{Na^+}(Ic) - \log K_s^{Na^+}(Vc)$ values being only 1.2 and 0.3, respectively.

For the potassium ion, on the other hand, the greatest energy gain from the sandwich is obtained with the unsubstituted fifteen-membered bis(azacrown) *IIb*, the $\log K_s^{Na^+}(IIb) - \log K_s^{Na^+}(Vb)$ value being greater than 4.2. Markedly smaller stabilization of potassium ion arises with the twelve- as well as eighteen-membered homologues. As a consequence of the differences between the two alkali ions, the twelve-membered bis(azacrown) *Ia* strongly prefers sodium over potassium ion (log $K_s^{Na^+}(Ia)$ – log $K_s^{K^+}(Ia)$ ~ 4), whereas the opposite holds for the fifteen-membered homologue *Ib*.

A surprisingly large and not easily predictable effect on sandwich complex formation arises from introduction of a substituent at the ethane bridge. As Table II shows, the bridge substitution in twelve-membered bis(azacrown)s *IIa*, *IIIa*, *IVa* decreases stability of the sodium complexes by 3 – 4 orders of magnitude. A similar but less uniform effect is observed in the twelve- and also fifteen-membered bis(azacrown) series *IIb*, *IIIb*, *IVb* for the potassium ion.

TABLE I
Analytical data of compounds *II* – *IV*

Compound	Yield[a] (%)	M. p. °C	Formula (M. w.)	Calculated/Found			
				% C	% H	% N	% Cl
IIa	82	[b]	$C_{26}H_{44}N_2O_7 \cdot 2\,HClO_4$	44.77	6.65	4.02	10.16
	(42)		(697.6)	44.40	6.41	3.90	10.35
IIb	50	[b]	$C_{30}H_{52}N_2O_9 \cdot 2\,HClO_4 \cdot H_2O$	44.83	7.02	3.48	8.82
	(41)		(803.7)	45.10	6.78	3.47	8.78
IIc	23	[b]	$C_{34}H_{60}N_2O_{11} \cdot 2\,HClO_4 \cdot 2\,H_2O$	44.89	7.31	3.08	7.79
	(15)		(909.8)	44.61	6.97	2.87	8.07
IIIa	[b]	237 – 239	$C_{29}H_{44}N_2O_7 \cdot 2\,HClO_4$	47.48	6.32	3.82	9.62
	(42)		(733.6)	47.43	6.21	3.75	9.60
IIIb	[b]	115 – 117	$C_{33}H_{52}N_2O_9 \cdot 2\,HClO_4 \cdot 2\,H_2O$	46.20	6.81	3.26	8.27
	(10)		(857.7)	45.80	6.66	3.31	8.29
IIIc	30	109 – 111	$C_{37}H_{60}N_2O_{11} \cdot 2\,HClO_4 \cdot 2\,H_2O$	46.98	7.03	2.96	7.50
	(24)		(697.6)	46.96	6.81	2.80	7.70
IVa	[b]	196 – 198	$C_{19}H_{38}N_2O_7 \cdot 2\,HClO_4$	37.57	6.64	4.61	11.67
	(70)		(607.5)	37.79	6.51	4.79	11.52
IVb	[b]	160 – 162	$C_{23}H_{46}N_2O_9 \cdot 2\,HClO_4 \cdot H_2O$	38.71	7.06	3.93	9.94
	(40)		(713.6)	39.16	6.98	3.88	9.51
IVc	[b]	83 – 84	$C_{27}H_{54}N_2O_{11} \cdot 2\,HClO_4 \cdot 2\,H_2O$	39.56	7.38	3.42	8.65
	(68)		(819.7)	40.02	7.12	3.38	8.64

[a] Free base and perchlorate (in parenthesis). [b] Not determined.

Since similar effects are produced in most instances by a lipophilic (benzyloxymethyl, 1-naphthyloxymethyl) as well as hydrophilic (hydroxymethyl) substituents, solvophobicity apparently does not play an essential role. Also steric bulk of the substituents can be probably ruled out as the causative factor.

Instead we are inclined to suggest that violation of symmetry due to substitution of the ethane bridge is responsible for destabilization of the intramolecular sandwich complex. It is in accord with the proposition that practically none substituent effect is observed in the complexation of the fifteen-membered bis(azacrown)s *IIb*, *IIIb*, *IVb* with sodium and the eighteen-membered bis(azacrown)s *IIc*, *IIIc*, *IVc* with sodium as well as potassium ions. The intramolecular sandwich complexes are here expected[5] to play only a minor if any role.

TABLE II
Stability of 1 : 1 complexes of crown compounds *I* – *V* with sodium and potassium ion: effects of crown structure

Compound	$\log K_s(1:1)^a$		$\log K_s^{Na^+} - \log K_s^{K^+}$
	Na^+	K^+	
Ia	8.18	4.21	3.97
IIa	5.18	3.21	1.97
IIIa	3.48	3.62	-0.14
IVa	4.77	2.86	1.91
Va	2.04	1.80	0.24
Ib	4.62	7.10	-2.48
IIb	4.90	6.55	-1.65
IIIb	4.32	6.54	-2.22
IVb	4.25	6.23	-1.98
Vb	3.41	2.90	0.50
Ic	3.80	5.57	-1.77
IIc	4.31	5.44	-1.13
IIIc	4.92	5.37	-1.45
IVc	4.71	4.99	-0.28
Vc[b]	3.50	4.92	-1.42

[a] A correction on the competitive formation of the intermolecular (2 : 1) sandwich complex formation has been made in the calculation and the minor contributions obtained were disregarded. [b] n-Propyl analogue.

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