Building up of Macroring in the New Synthesis of Azacrown Ethers. Structure and Complex Formation of Nitrobenzoazacrown Ethers

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Received November 5, 2003

Abstract—A cyclization of azapodand haloderivatives into nitrobenzoazacrown ethers under treatment with various bases and in their absence was investigated. The nitrobenzoazacrown ethers obtained and their complexes with metal cations were studied by X-ray diffraction method and by ^{1}H NMR titration. In nitrobenzoaza-15-crown-5 a capability to complex Ca^{2+} cation was found that significantly exceeded similar ability of nitrobenzocrown ether with the same size of the macroring.

The most important feature of crown compounds is their capability to form stable complexes with metal ions, organic cations, and neutral polar molecules. This property underlies the application of crown compounds as selective ligands for metal cations, in particular, for extraction [1, 2], in ion-selective electrodes [3], in photosensitive systems [4–9] etc.

Of special interest for the use of crown compounds in the composition of photosensitive ligands are those with the nitrogen conjugated to a chromophore. These azacrowns absorb light at notably longer waves than the crown ethers derivatives. This feature is important for photometry and fluorescence analysis, in photo-controlled extraction and transport through membranes, in building up photosensitive molecular devices. Nowadays for these purposes the most commonly are used derivatives of phenylazacrown ethers possessing one important drawback: They have small stability constants of complexes with metal ions. In this respect the derivatives of azacrown ethers with fuzed benzene rings may have significant advantages. However the 1-aza-2,3-benzocrown ethers are poorly documented, and the majority of their functional derivatives are inaccessible in spite of simple structure. The preparation methods of these compounds are limited to the so-called

1+1 condensations (building up of a macroring from two acyclic fragments), that afford 1-aza-2,3-benzocrown ethers in poor yields [10–13]. Synthetic procedures involving cyclization of a suitable linear precursor (podand) are not used in the chemistry of 1-aza-2,3-benzocrown ethers due to practical inaccessibility of the initial compounds.

We develop a new approach to the synthesis of functionally-substituted derivatives of azacrown ethers from nitrogen-containing podands obtained by nucleophilic opening by amines of the macroring in available crown ethers used as synthons. This procedure we consider to be a promising alternative to existing methods of 1-aza-2,3-benzocrown ethers synthesis [14. 15].

It was established that a nitro group located in the *para*-position to one of the oxygens in the benzocrown ether activated a regioselective opening of macroring under the action of methylamine. At heating (4-nitrobenzo)crown ethers **Ia–c** with ethanol solution of $MeNH_2$ podands **IIa–c** formed in up to 100% yield (Scheme 1) [16]. To perform cyclization of podands **IIa–c** into benzoazacrown ethers **IIIa–c** the hydroxy group in podands **IIa–c** was in 98% yield replaced by chlorine or iodine [98], i.e. by easily departing groups.

Scheme 1.

Ia–c   IIa–c   IIIa–c

n = 0–2.
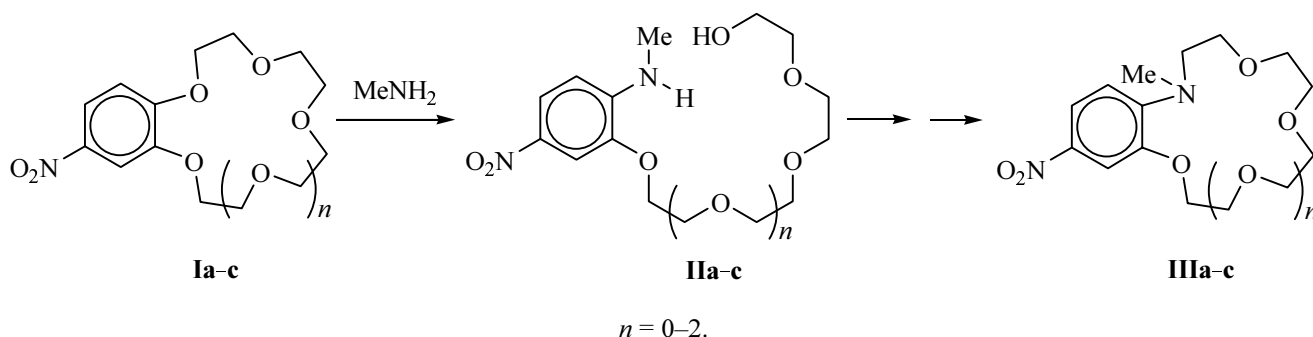
Scheme 2.
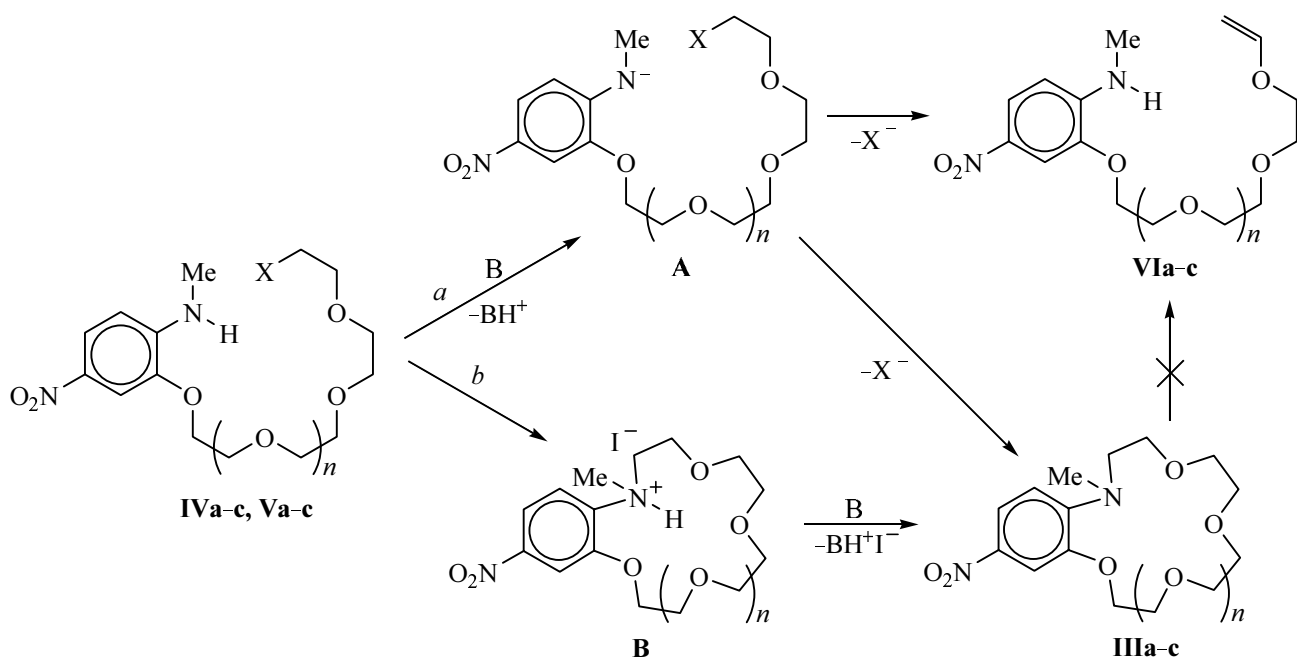
X = Cl (**IV**), I (**V**); *n* = 0 (**a**), 1 (**b**), 2 (**c**).

The key stage in the synthesis of benzoazacrown ethers **IIIa–c** is cyclization of chlorides **IVa–c** and iodides **Va–c**. Presumably the reaction would either occur through intermediate formation of anion **A** (path *a*) that arises by elimination of a proton from amino group effected by a base, or by intramolecular N-alkylation of the secondary amino group resulting in macrocyclic ammonium salt **B** (path *b*). In the first case in the anion **A** occurs intramolecular nucleophilic substitution of iodine atom with the negatively charged nitrogen providing a macroheterocycle (Scheme 2). In the second case reaction is finished by deprotonation of the ammonium salt **B** by the base.

The realization of path *a* with formation of anion **A** under the action of bases would be facilitated by the presence in halides **IVa–c** and **Va–c** of electron-withdrawing nitro group. The cyclization via intermediate anion formation, providing it forms in sufficient amount, should be fast due to the higher nucleophilicity of the negatively charged nitrogen as compared to neutral one.

The formation of the second reaction product, vinyl ethers **VIa–c**, is also more probably taking path *a* since the macroring opening by bases hardly occurs in benzoazacrown ethers **IIIa–c**.

The reaction along path *b* would be slow since the nitrogen atom in compounds **IVa–c** and **Va–c** is inactive toward N-alkylation for its lone electron pair is conjugated to the electron-withdrawing nitro group. The formation of benzoazacrown ethers **IIIa–c** along this path would have occurred by N-deprotonation of the ammonium salt **B**.

Table 1. Cyclization of halides **IVa–c** and **Va–c** into nitro-benzoazacrown ethers **IIIa–c** and vinyl ethers **VIa–c**

Compd. no.	Base	Solvent	Reaction time, h [a]	Yield, %
IVa	NaH	THF	18	**IIIa** (0), **VIa** (0)
IVb	NaH	THF	50	**IIIb** (23), **VIb** (12)
IVc	NaH	THF	7	**IIIc** (1), **VIc** (22)
	NaOH	Dioxane	9	**IIIc** (0), **VIc** (0)
Va	NaOH	Dioxane	20	**IIIa** (22), **VIa** (34)
	NaH	THF	2	**IIIa** (36), **VIa** (33)
	NaH	THF	50[b]	**IIIa** (18), **VIa** (50)
Vb	–	CH₃CN	150	**IIIb** (22), **VIb** (0)
	Na₂CO₃	CH₃CN	150	**IIIb** (54), **VIb** (0)
	NaOH	Dioxane	60	**IIIb** (39), **VIb** (18)
	NaH	THF	0.5	**IIIb** (80), **VIb** (19)
	NaH	THF	2.5[b]	**IIIb** (74), **VIb** (22)
Vc	NaOH	Dioxane	2	**IIIc** (56), **VIc** (16)
	NaH	THF	0.5	**IIIc** (71), **VIc** (20)
	NaH	THF	1.5[b]	**IIIc** (71), **VIc** (29)

[a] At reflux. [b] At room temperature.

In order to make a justified choice of iodide **Vb** cycliz-ation mechanism and to develop optimum conditions for the synthesis of target compounds **III** we carried out experiments under comparable conditions in the absence of base and in the presence of a weak base Na₂CO₃ for 150 h (Table 1). The time was not sufficient for complete conversion of compound **Vb** into reaction products. In the absence of bases we isolated from the reaction mix-ture alongside the unreacted iodide **Vb** also nitrobenzo-azacrown ether **IIIb** in 22% yield. Here the cyclization apparently occurred through intramolecular N-alkylation with intermediate formation of macrocyclic cation **B**. The low efficiency of the process is due to hampering the reaction along path *b* by the electron-withdrawing character of the nitro group in the *para*-position to amino group. The reaction in the presence of Na₂CO₃ unexpect-edly resulted in the yield of benzoazacrown ether **IIIb** as high as 54%. This result apparently is caused by reac-tion taking both paths *a* and *b*. The long reaction time indicates that the main process consists in the intramolec-ular N-alkylation. However the significant increase in the yield of the cyclization product is hardly understand-able without suggestion that the reaction in part occurs through intermediate formation of anion **A**. Consequently the basicity of Na₂CO₃ proved to be sufficient for deprotonation to a small extent of the amino group of iodide **Vb** and occurrence of reaction along path *a*.

It was presumable that the application of stronger bases would reduce the reaction time and increase the yield of the target products. We studied the cyclization of chlorides **IVa–c** and iodides **Va–c** into benzoazacrown ethers **IIIa–c** effected by sodium hydroxide or hydride. The reaction were carried out till total consumption of the initial halide (TLC monitoring). The data on the yields of benzoazacrown ethers **IIIa–c** and concurrently formed vinyl ethers **VIa–c** are presented in Table 1. In keeping with the reaction mechanism along path *a* the efficiency of the intramolecular cyclization should depend on the strength of the base capable to generate sufficiently high stationary concentration of arylamide anion **A** and on the character of the departing group. It turned out that chlorides **IVa–c** did not undergo cyclization in the presence of sodium or potassium hydroxide. The use of still stronger base, sodium hydride, led to cyclization only of chloride **IVb**, but the corresponding nitrobenzoaza-crown ether **IIIb** was obtained in low yield (23%).

The target result was obtained by replacement of chlorine by more nucleofugic iodine. Here the cyclization in the presence of sodium hydroxide in anhydrous dioxane at reflux afforded benzoazacrown ethers **IIIa–c** in 22–56% yield. Maximum yields (36–80%) of benzoazacrown ethers **IIIa–c** were obtained in a short time in THF at reflux using sodium hydride as base. Reducing the reaction temperature to ambient somewhat decreses the yields of benzoazacrown ethers **IIIa–c** and significantly increases the reaction time. Among nitrobenzoazacrown ethers **IIIa–c** the highest yields were obtained at cyclization of iodides **Vb, c** that possessed sufficiently long oligo(ethylene glycol) chain. Apparently here the transition state for intramolecular nucleophilic substitution resulting in the macroring formation can be realized with a minimal steric strain.

The mechanisms leading to formation of vinyl ethers **VIa–c** are also of importance in view of understanding the routes of iodides **Va–c** transformations. It turned out that the yields of vinyl ethers **VI** depend rather strong on the length of the oligo(ethylene glycol) chain. This may occur only in the case of intramolecular character of HI elimination, namely, when the negatively charged nitrogen of arylamide anion **A** acts as a base. It is likely that at treatment with bases anion **A** is relatively fast generated from iodides **Va–c**, and then it is slowly transformed by attack either of ω carbon or of hydrogen atom in the ψ position of the oligo(ethylene glycol) chain affording respectively benzoazacrown ethers **IIIa–c** and vinyl ethers **VIa–c**.

Hence the sum of data obtained on cyclization of iodides **Va–c** into benzoazacrown ethers **IIIa–c** and on formation from iodides **Va–c** of vinyl ethers **VIa–c** suggests that the reaction effected by strong bases takes the path *a*. The efficient occurrence of reaction along path *b* is apparently hampered by decrease in nucleophilicity of the methylamino group due to the strong electron-withdrawing effect of the nitro group located in the *para*-position to the nitrogen.

The structure of compounds obtained was established using ^{1}H and ^{13}C NMR spectroscopy and confirmed by the data of high-resolution mass spectrometry

The molecular structure of nitrobenzoaza-15-crown-5 **IIIb** was established by X-ray diffraction analysis. The general view of the molecule and numbering of atoms are presented on Fig.1, some bond lengths and bond angles are given in Table 2.

Benzene ring of molecule **IIIb** is a little distorted as compared to the geometry of an ideal hexagon. The C^{10}–C^{15} bond common for two rings is considerably elongated and equals to 1.443(6) E. This elongation of the bond may be caused by repulsion of atoms O^1 and N^1 located in reciprocal *ortho*-position. The distance between these

Table 2. Some bond lengths and bond angles in molecule **IIIb**

Bond	d, Å	Angle	ω, deg
O^1–C^{15}	1.364(5)	$C^{15}O^1C^1$	117.2(3)
O^1–C^1	1.443(6)	$C^2O^2C^3$	113.2(3)
O^2–C^3	1.433(5)	$C^4O^3C^5$	112.7(4)
O^2–C^2	1.421(6)	$C^6O^4C^7$	113.3(3)
O^3–C^4	1.422(6)	$C^8N^1C^9$	112.0(3)
O^3–C^5	1.432(6)	$C^8N^1C^{10}$	120.4(4)
O^4–C^6	1.426(6)	$C^9N^1C^{10}$	117.0(4)
O^4–C^7	1.426(5)	$N^1C^{10}C^{11}$	120.9(4)
N^1–C^8	1.474(6)	$N^1C^{10}C^{15}$	121.6(4)
N^1–C^9	1.458(6)	$C^{11}C^{10}C^{15}$	117.4(4)
N^1–C^{10}	1.386(6)	$O^1C^{15}C^{14}$	123.8(4)
C^{10}–C^{11}	1.398(6)	$O^1C^{15}C^{10}$	116.2(4)
C^{11}–C^{12}	1.384(7)	$C^{10}C^{15}C^{14}$	120.0(4)
C^{12}–C^{13}	1.386(7)		
C^{13}–C^{14}	1.397(7)		
C^{14}–C^{15}	1.384(6)		
C^{10}–C^{15}	1.443(6)		

atoms equal to 2.774 Å is actually somewhat shorter than the sum of van der Waals radii (~2.9 Å). However the character of distortion of bond angles $C_{Ar}C_{Ar}O$ and $C_{Ar}C_{Ar}N$ at the carbons C^{10} and C^{15} of the benzene ring does not correspond to such repulsion. These bond angles at C^{10} have similar values [121.6(4) and 120.9(4)°] close to an ideal one 120°, and analogous bond angles at C^{15} are strongly distorted. Just the angle $C^{10}C^{15}O^1$ inside the macroring is decreased [116.2(4)°] and not the external with respect to macroring angle $C^{14}C^{15}O^1$ [123.8(4)°]. Likewise was distorted the geometry of a benzene ring
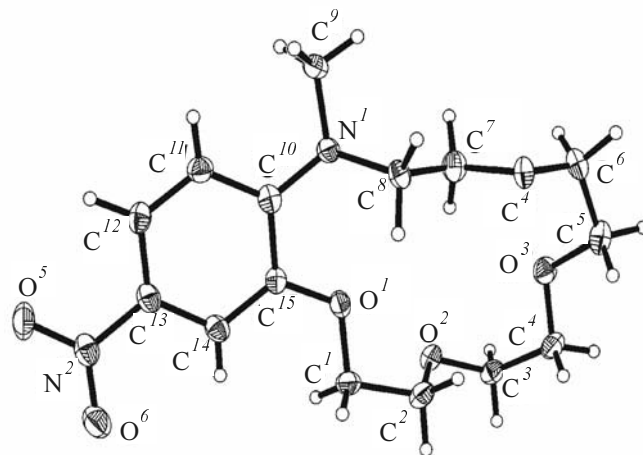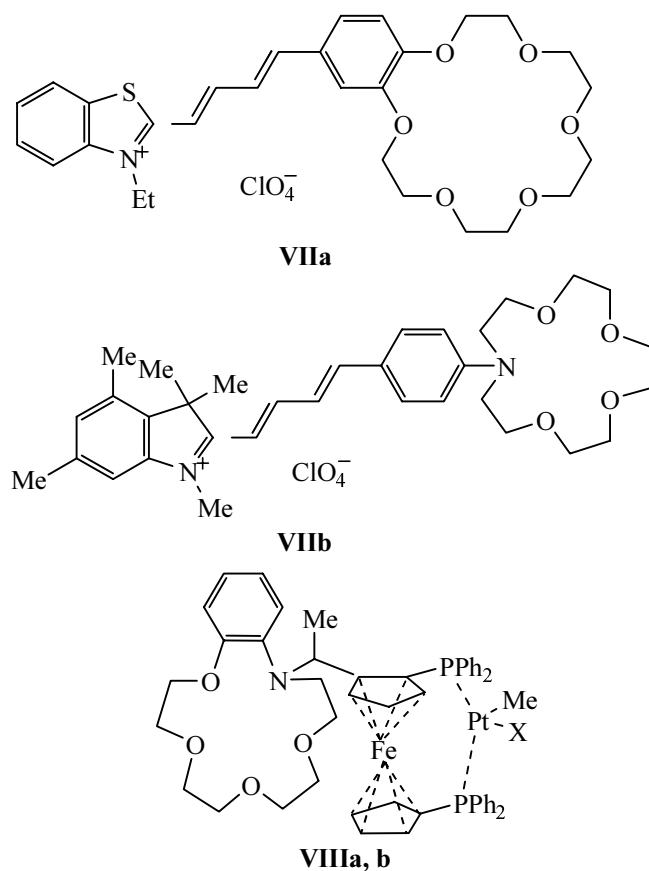

VIIa

VIIb

VIIIa, b

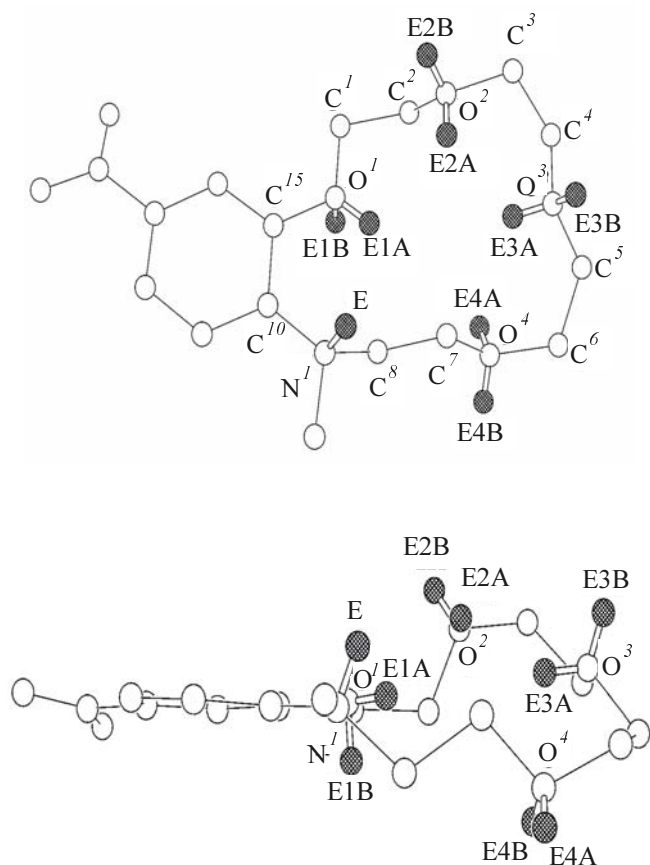**Fig. 1**. Molecular structure of compound **IIIb**.

Fig. 2. Lone electron pairs orientation for heteroatoms of macroring **IIIb**. Front and side elevations. Lone electron pairs designated by E.
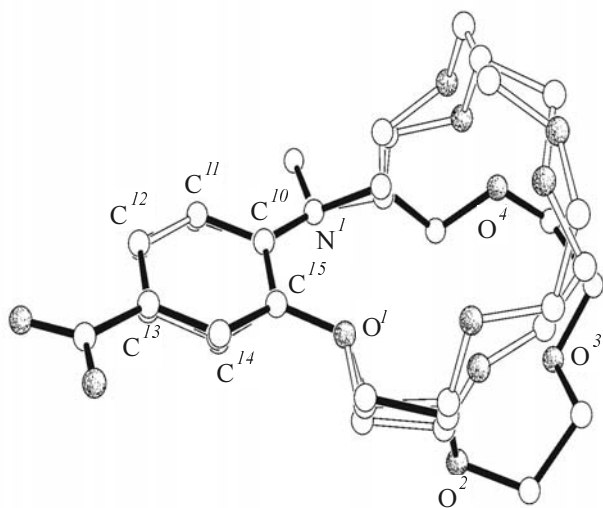

Fig. 3. Superposition of benzene rings of benzoaza-15-crown-5 fragments of molecules **IIIb** and **VIIIa, b**.

in 18-crown-6 butadienyl dye **VIIa** where the C–C bond common for the benzene ring and macroring was lengthened to 1.414(4) Å, both internal angles $C_{Ar}C_{Ar}O$ decreased to ~115°, whereas both external angles $C_{Ar}C_{Ar}O$ increased to ~125° [17].

This distortion of benzene ring in **VIIa** molecule may be ascribed to an effect of conjugation between the lone electron pairs of oxygen atoms occupying *p*-orbitals and the π- system of the benzene ring. The bond angles at these oxygen atoms (~118°) are consistent with sp^2-hybridization unlike the bond angles at the rest of oxygen atoms of the crown ether macroring (~112°) typical of sp^3-hybridization. Note that the torsion angles $COC_{Ar}C_{Ar}$ are close to 180 or 0° also in agreement with the mentioned conjugation. In structure **IIIb** the similar torsion angle $C^1O^1C^{15}C^{14}$ amounts only to –5.0°, and the bond angle at O^1 atom [117.2(3)°] is larger than the bond angles at the other three oxygens of the macroring [112.7(4)–113.3(4)°]. Hence the lone electron pairs of atom O^1 are effectively conjugated with the π system of benzene ring.

Atom N^1 posesses unsymmetrical pyramidal configuration of bonds where the sum of bond angles equals 349.4(4)° and the angles proper vary in the range 112.0(3)–120.4(4)°; therewith the bond angle $C^8N^1C^{10}$ inside the macroring has the largest value. The torsion angle $C^8N^1C^{10}C^{15}$ is –42.1°. This geometry shows that the orientation of the lone pair on the nitrogen atom is not feasible for its conjugation with the benzene ring of compound **IIIb**.

According to Cambridge Structural Database [18] a structure of only two similar benzoazacrown ethers **VIIIa, b** [19] was investigated. These compounds contained as a substituent on nitrogen a bulky bicyclic organometallic complex. Like in the structure of crown ether **IIIb** the nitrogen atom in compounds **VIIIa, b** has a nonplanar configuration of bonds with the sum of bond angles 348.0 and 343.9° respectively while the individual angle values vary within 112.5–119.4 and 110.4–118.5°. It is noteworthy that among these angles the largest is also the intracyclic angle. In macrorings **VIIIa, b** torsion angles $CNC_{Ar}C_{Ar}$ are 40.8 and –36.6° thus being quite close to the same parameter found in **IIIb** molecule. This reproducibility of the geometric parameters under consideration in compounds containing at the nitrogen atom side substituents of different volume means that the structure of 1-aza-2,3-benzo-15crown-5 ether around nitrogen atom is fairly rigid. Therefore the lone pair of the nitrogen cannot take the orientation required for conjugation with the benzene ring and remains available

for participation in coordinating metal cation in the course of complex formation.

The geometry of nitrogen atom found in aza-15-crown-5 **VIIb** was different [20]. The configuration of bonds at the nitrogen in the macroring corresponds sp^2-hybridization, and therewith the plane of bonds at nitrogen is virtually coplanar with the benzene ring. The lone pair of nitrogen in **VIIb** molecule is effectively conjugated with the benzene ring as seen from the definite *para*-quinoid distribution of bond lengths in the benzene ring of this dye.

Orientations of lone electron pairs on all heteroatoms of macroring **IIIb** are shown on Fig. 2 in two projections. As seen, the lone electon pairs of nitrogen and lone pairs E1A, E2A, and E3A of oxygen atoms are oriented to the center of the macroring and approximately in the same direction. Thus the conformation of macroring **IIIb** in the crystal to a significant extent predetermines its coordination with a metal cation.

$$L + M^{n+} \xrightleftharpoons{K_1} (LM)^{n+} \qquad (1)$$

$$(LM)^{n+} + L \xrightleftharpoons{K_2} (L_2M)^{n+} \qquad (2)$$
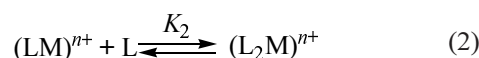
It should be remembered that the macroring conformation in the region of aliphatic carbon atoms remains fairly labile as is clear from Fig. 3 where the superposition is shown of benzoazacrown ether fragments of molecules **IIIb** and **VIIIa, b** along the benzene ring. The macroring conformations strongly differ even in two related molecules **VIIIa, b** but remain about the same in the region of the $CCOC_6H_{3(4)}N(C)C$ fragment.

To get additional proof of a preliminary organization in the molecules of nitrobenzoazacrown ethers **IIIa–c** we studied their ability of complex formation with metal and ammonium perchlorates in CD_3CN at 30°C by means of ^1H NMR titration. Two different titration procedures were used in the study of complex formation: direct titration with salts, and concurrent titration. The dependences of chemical shift variations of protons in the spectra of azacrown ethers **IIIa–c** on the amount of the added salt agree well with two schemes of complexes formation of composition $1(L):1(M^{n+})$ and $2(L):1(M^{n+})$. Here L is crown ether, M^{n+} is metal or ammonium cation ($n = 1, 2$), K_1 and K_2 (1 mol^{-1}) are stability constants of the corresponding complexes. The stability constants of complexes with metal and ammonium cations for nitrobenzoaza-15-crown-5 **IIIb** were calculated with the use of program HYPNMR [21] and are given below.

IIIb	Li$^+$	Na$^+$	K$^+$	NH$_4^+$	Mg^{2+}	Ca^{2+}	Ba^{2+}
logK_1	3.1 ± 0.1	2.7 ± 0.1	1.9 ± 0.1	1.7 ± 0.1	3.2 ± 0.1	3.3 ± 0.1	4.2 ± 0.2
logK_2	2.7 ± 0.2	–	–	–	–	2.5 ± 0.2	1.6 ± 0.3

For the sake of comparison we measured the stability constant of the complex with Ca^{2+} of nitrobenzo-15-crown-5 ether **Ib** for it was the nearest oxygen structural analog of benzoazacrown ether **IIIb**. The K_1 value for benzo-aza-18-crown-6 ether **IIIc** and Ca^{2+} proved to be larger than the upper limit for application of the direct ^1H NMR titration. To evaluate this value more accurately we carried out a concurrent titration (c.t.) of this compound complex with $Ca(ClO_4)_2$ using as competing substance crown ether **Ib** whose K_1 value was known from direct titration. Below are presented the calculated stability constants for complexes of nitrobenzoazacrown ethers **IIIa–c** and nitrobenzo-15-crown-5 ether **Ib** with $Ca(ClO_4)_2$.

Ligand	**IIIa**	**IIIb**	**IIIc** (c. t.)	**Ib**
log K_1	1.1 ± 0.1	3.3 ± 0.1	5.8 ± 0.3	2.9 ± 0.1
log K_2	–	2.5 ± 0.2	–	–

We established that ability to complex formation significantly differed in the series of compounds studied both with respect to each other and as regards various cations. The estimated stability constants of calcium complexes of 1:1 composition significantly grow with the size of the macroring in the homolog series of azacrown ethers **III**, and compound **IIIb** notably stronger binds Ca^{2+} ions as compared with crown ether **Ib** with the same size of the macroring. In going from compound **Ib** to nitrobenzoaza-15-crown-5 **IIIb** the stability constant K_1 increased 2.5-fold. This fact testifies to the accessibility of the lone electron pair belonging to nitrogen in macrorings **III** for taking part in a coordination bond with metal cation and presumably evidences better conformational readiness to complexing of the macroring in benzoazacrown ether **IIIb**.

The stability constant value of complexes with **IIIb** depends on the charge of cation. It was established that two-charge cations of alkaline-earth metals form stronger complexes than ions of alkali metals and ammonium. Of two cations with about the same size the two-charge one formed in acetonitrile a stronger complex than that of the single-charge cation: for Na$^+$ K_1 = 500, for Ca^{2+} 2000 l mol^{-1}.

As seen from the above data, in the case of benzoazacrown ether **IIIb** the K_1 value grows in the series K$^+$–

Na^+–Li^+ and Mg^{2+}–Ca^{2+}–Ba^{2+}. A similar dependence of K_1 on the size of alkali metal cation and a reverse one for alkaline-earth metals was observed for benzo-15-crown-5 and some among its derivatives [17]. The reversed order for alkaline-earth cations may be due to the relatively high water content in the CD_3CN solvent since these cations are more prone to hydration competing with complex formation than alkali metal cations, and the tendency to hydration grows with decreasing cation size.

It is known that large cations, first of all like K^+, Cs^+, Sr^{2+}, and Ba^{2+} , form sandwich complexes with derivatives of benzo-15-crown-5 with a stoichiometric ratio 2(L):1(M^{n+}) [22, 23]. Similar complexes were obtained from azacrown ether **IIIb** and ions Ca^{2+} and Ba^{2+}. Unusual fact is formation of a complex 2:1 from compound **IIIb** with the smallest alkali metal cation, lithium, and with relatively small cation, calcium, and lack of such complex with potassium.

Spectrum NOESY of compound **IIIb** revealed that in solution the distance $C^{11}H \cdots H_3C^9$ is considerably shorter than the distance $C^{11}H \cdots H_2C^8$; thus the macroring conformation in the neighborhood of the nitrogen is similar to that in the crystal where these distances are respectively 2.228 and 4.159 Å. The structure of the macroring fragment around atom N^1 likely brings about formation of a smaller cavity in compound **IIIb** compared to that in compound **Ib**. As show X-ray diffraction data the lone electron pairs of the heteroatoms are directed mainly to the apex of a distorted pyramid having for base oxygens and nitrogen of the macroring. This is the reason why benzoazacrown ether **IIIb** better binds cations of smaller size and is more inclined to form complexes of partially inclusive type of composition 2(L):1(M^{n+}) with cations of larger size or with those having higher charge density. The discovery of this type complexes for benzoazacrown ether **IIIb** and ions Li^+, Ca^{2+}, and Ba^{2+} gives a hope for feasibility of purposeful synthesis of ligands containing two fragments of benzoaza-15-crown-5 possessing high selectivity with respect to these cations.

Thus we developed reagents and conditions for cyclizing azapodands haloderivatives in the presence or absence of bases into nitrobenzoazacrown ethers. The cyclization reaction takes either of two paths, an intermediate formation of arylamide anion, or intramolecular N-alkylation affording macrocyclic ammonium salt. The analysis of specific features in the structure of the synthesized benzoazacrown ether nitro derivative was performed by X-ray diffraction study. The high degree of preliminary organization in benzoazacrown ethers for complexing was established. This feature was due to disrupture of conjugation between the lone electron pair of nitrogen and the benzene ring and to spatial fixing of the *ortho*-aminophenol fragment in conformation favorable for complexing. We established for the first time the high capability of 1 aza-2,3-benzocrown ether of complex formation exceeding that of benzocrown ether with the same size of the macroring.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on spectrometer Bruker DRX-500 at 30°C using solvent as internal refernce. Assignment of signals from protons and carbon atoms was performed with the help of homonuclear ^1H ^1H COSY and NOESY and heteronuclear ^1H ^{13}C COSY spectra. Chemical shifts were measured with an accuracy to 0.01ppm, coupling constants to 0.1Hz. IR spectra were recorded on spectrophotometer Bruker IFSV. Mass spectra were measured on Varian MAT 311A instrument, high resolution mass spectra were obtained on Finnigan MAT-95XL and Finnigan MAT-8430 instruments (with perfluorokerosene as standard) at ionizing electrons energy 70 eV, with direct sample admission into the ion source. The column chromatography was performed on silica gel Kieselgel 60 (0.063–0.100 mm), Merck. The reaction progress was monitored by TLC on plates DC Alufolien Kieselgel 60 F_{254}, Merck. CD_3CN (with water content <0.05%) was purchased from Merck. Metal perchlorates and ammonium perchlorate were dried in a vacuum at 240 and 70°C respectively.

Benzoazacrown ethers IIIa–c and vinyl ethers VIa–c. (a) A mixture of 0.35 mmol of iodide **Va–c**, 15 ml of anhydrous THF, and 0.14 g (3.5 mmol) of 60% NaH in paraffin was heated at reflux while stirring for 2 h (**Va**) or 0.5 h (**Vb, c**). On cooling the reaction mixture was diluted with water, and the reaction products were extracted into benzene. The extract was washed with water, evaporated in a vacuum, the residue was purified by column chromatography on SiO_2. Compound **IIIa** was eluted with a mixture benzene–AcOEt, 5:1, compound **IIIb** was eluted in succession first with a mixture benzene–AcOEt, 5:1, then with a mixture benzene–AcOEt, 1:1, and eluent for compound **IIIc** was AcOEt. We obtained benzoazacrown ethers **IIIa–c** and vinyl ethers **VIa–c** as orange and yellow oily substances respectively. Benzoazacrown ethers **IIIa, b** crystallized

at standing. Yields of reaction products are given in Table1.

(b) Iodides **Va–c** and NaH in THF were stirred at room temperature for 50 h (**Va**), 2.5 h (**Vb**), and 1.5 h (**Vc**). The isolation of compounds **IIIa–c** and **VIa–c** was carried out as described in (a).

(c) A mixture of 0.35 mmol of chloride **IVb, c**, 15 ml of anhydrous THF, and 0.14 g (3.5 mmol) of 60% NaH in paraffin was heated at reflux while stirring for 50 h (**IVb**) or 7 h (**IVc**). The reaction mixture was worked up as in (a).

(d) A mixture of 0.14 mmol of iodide **Va–c**, 10 ml of anhydrous dioxane, and 56 mg (1.4 mmol) of NaOH was heated at reflux while stirring for 20 h (**Va**), 60 h (**Vb**), and 2 h (**Vc**). The reaction mixture was worked up as in (a).

(e) A mixture of 50 mg (0.11 mmol) of iodide **Vb**, and 5 ml of anhydrous acetonitrile was heated for 150 h in a sealed ampule on a boiling water bath (100°C). The reaction mixture was evaporated in a vacuum, the residue was purified as described in (a). Yield of benzo-azacrown ether **IIIb** 22%.

(f) A mixture of iodide **Vb** and 117 mg (1.1 mmol) of Na_2CO_3 was heated in acetonitrile as described in (e). The reaction mixture was filtered, the solvent was distilled off in a vacuum, and the residue was purified as described in *a*. Yield of benzoazacrown ether **IIIb** 54%.

10-Methyl-13-nitro-2,3,5,6,9,10-hexahydro-8*H*-1,4,7,10-benzotrioxaazacyclodecin (IIIa). Yield 36% (procedure *a*), mp 108–109°C (hexane–CH_2Cl_2) [16], R_f 0.53 (AcOEt), R_f 0.35 (C_6H_6–AcOEt, 1:1).

13-Methyl-16-nitro-2,3,5,6,8,9,12,13-octahydro-11*H*-1,4,7,10,13-benzotetraoxaazacyclopentadecin (IIIb). Yield 80% (procedure *a*), mp 93–95°C (hexane–CH_2Cl_2) [16], R_f 0.38 (AcOEt).

16-Methyl-19-nitro-2,3,5,6,8,9,11,12,15,16-decahydro-14*H*-1,4,7,10,13,16-benzopentaoxaazacyclooctadecin (IIIc). Yield 71% (procedure *a*), R_f 0.38 (AcOEt–MeOH, 5:1), R_f 0.10 (AcOEt). Orange oily substance. ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 3.04 s (3H, MeN), 3.63 m (6H, CH$_2$N, 2CH$_2$O), 3.65 br.s (4H, 2CH$_2$O), 3.70 br.s (4H, 2CH$_2$O), 3.83 m (2H, CH$_2$O), 3.92 m (2H, C$\underline{H}_2$CH$_2$OAr), 4.20 m (2H, C$\underline{H}_2$OAr), 6.73 d (1H, H^{17}, *J* 9.0 Hz), 7.65 d (1H, H^{20}, *J* 2.3 Hz), 7.82 d.d (1H, H^{18}, *J* 9.0, 2.3 Hz) [16].

N-Methyl-N-(4-nitro-2-{2-[2-(vinyloxy)ethoxy]-ethoxy}phenyl)amine (VIa). Yield 50% (procedure *b*), R_f 0.70 (C_6H_6–AcOEt, 1:1), R_f 0.54 (C_6H_6–AcOEt, 5:1).

Yellow oily substance. IR spectrum (KBr), ν, cm^{-1}: 3368 (NH), 1495 (NO$_2$). ^{1}H NMR spectrum (C$_6$D$_6$), δ, ppm: 2.29 d (3H, MeN, *J* 5.2 Hz), 3.46 m (4H, 2CH$_2$O), 3.67 m (4H, 2CH$_2$O), 4.12 d.d (1H, OCH=C$\underline{H}_2$-*trans*, *J* 6.8, 1.8 Hz), 4.32 d.d (1H, OCH=C$\underline{H}_2$-*cis*, *J* 14.3, 1.8 Hz), 4.92 br.s (1H, NH), 6.10 d (1H, H^6, *J* 8.8 Hz), 6.55 d.d (1H, OC$\underline{H}$=CH$_2$, *J* 14.3, 6.8 Hz), 7.81 d (1H, H^3, *J* 2.3 Hz), 8.16 d.d (1H, H^5, *J* 8.8, 2.3 Hz). ^{13}C NMR spectrum (C$_6$D$_6$), δ, ppm: 28.92 (MeN), 67.65 (CH$_2$O), 68.29 (CH$_2$O), 69.37 (CH$_2$O), 69.53 (CH$_2$O), 86.77 (OCH=$\underline{C}$H$_2$), 106.49 (C^6), 106.98 (C^3), 120.18 (C^5), 137.67 (C^4), 144.46 (C^2), 145.40 (C^1), 152.06 (O$\underline{C}$H=CH$_2$). Mass spectrum, *m/z* (I_{rel}, %): 282 (100) [*M*]$^+$, 168 (42), 67 (47), 121 (33), 93 (33), 92 (22), 79 (18), 78 (65), 73 (68), 71(23). High resolution mass spectrum, [*M*]$^+$, *m/z*: found 282.1210. $C_{13}H_{18}N_2O_5$. Calculated 282.1215.

N-Methyl-N-[4-nitro-2-(2-{2-[2-(vinyloxy)-ethoxy]ethoxy}ethoxy)phenyl]amine (VIb). Yield 22% (procedure *b*), R_f 0.73 (AcOEt), R_f 0.50 (C_6H_6–AcOEt, 1:1).Yellow oily substance.IR spectrum (KBr), ν, cm^{-1}: 3406 (NH), 1494 (NO$_2$). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 2.96 d (3H, MeN, *J* 5.1 Hz), 3.72 m (4H, 2CH$_2$O), 3.75 m (2H, CH$_2$O), 3.85 m (2H, CH$_2$O), 3.89 m (2H, CH$_2$O), 4.02 d.d (1H, OCH=C$\underline{H}_2$-*trans*, *J* 6.8, 2.0 Hz), 4.19 d.d (1H, OCH=C$\underline{H}_2$-*cis*, *J* 14.4, 2.0 Hz), 4.22 m (2H, CH$_2$OAr), 5.34 br.m (1H, NH), 6.47 d (1H, H^6, *J* 8.9 Hz), 6.49 d.d (1H, OC$\underline{H}$=CH$_2$, *J* 14.4, 6.8 Hz), 7.64 d (1H, H^3, *J* 2.2 Hz), 7.93 d.d (1H, H^5, *J* 8.9, 2.2 Hz). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 29.58 q (MeN, *J* 137.2 Hz), 67.18 (CH$_2$O), 68.50 t (CH$_2$OAr, *J* 144.7 Hz), 69.42 t (CH$_2$O, *J* 141.4 Hz), 69.65 t (CH$_2$O, *J* 144.5 Hz), 70.62 t (CH$_2$O, *J* 142.9 Hz), 70.70 t (CH$_2$O, *J* 141.1 Hz), 86.72 d.d.d (OCH=$\underline{C}$H$_2$, *J* 158.9, 156.4, 9.6 Hz), 106.30 d.d (C^6, *J* 162.0, 5.7 Hz), 106.57 d.d (C^3, *J* 163.2, 5.1 Hz), 120.46 d.d (C^5, *J* 167.0, 4.4 Hz), 136.68 (C^4), 144.16 and 145.72 (C^2, C^1), 151.62 d (O$\underline{C}$H=CH$_2$, *J* 180.2 Hz). Mass spectrum, *m/z* (I_{rel}, %): 326 (62) [*M*]$^+$, 168 (90), 167 (70), 149 (61), 121 (70), 115 (60), 93 (68), 78 (78), 73 (85), 71 (100). High resolution mass spectrum, [*M*]$^+$, *m/z*: found 326.1488. $C_{15}H_{22}N_2O_6$. Calculated 326.1477.

N-Methyl-N-[4-nitro-2-(3,6,9,12-tetraoxa-13-tetradecenyloxy)phenyl]amine (VIc). Yield 29% (procedure *b*), R_f 0.58 (AcOEt), R_f 0.40 (C_6H_6–AcOEt, 1:1).Yellow oily substance.IR spectrum (KBr),ν, cm^{-1}: 3401 (NH), 1496 (NO$_2$). ^{1}H NMR spectrum (CDCl$_3$), δ, ppm: 2.96 d (3H, MeN, *J* 5.2 Hz), 3.66–3.75 m (10H, 5CH$_2$O), 3.84 m (2H, CH$_2$O), 3.89 m (2H, CH$_2$O),

4.01 d.d (1H, OCH=C$\underline{H}_2$-*trans*, *J* 6.8, 2.0 Hz), 4.18 d.d (1H, OCH=C$\underline{H}_2$-*cis*, *J* 14.4, 2.0 Hz), 4.23 m (2H, CH$_2$OAr), 5.39 br.m (1H, NH), 6.47 d (1H, H^6, *J* 8.8 Hz), 6.48 d.d (1H, OC$\underline{H}$=CH$_2$, *J* 14.4, 6.8 Hz), 7.64 d (1H, H^3, *J* 2.3 Hz), 7.93 d.d (1H, H^5, *J* 8.8, 2.3 Hz). ^{13}C NMR spectrum (CDCl$_3$), δ, ppm: 29.58 q (MeN, *J* 137.1 Hz), 67.18 t (CH$_2$O, *J* 139.4 Hz), 68.52 t (CH$_2$OAr, *J* 144.4 Hz), 69.39 t (CH$_2$O, *J* 141.2 Hz), 69.59 (CH$_2$O), 70.59 (CH$_2$O), 70.62 t (2CH$_2$O, *J* 141.7 Hz), 70.69 (CH$_2$O), 86.66 d.d.d (OCH=$\underline{C}$H$_2$, *J* 158.9, 156.0, 9.2 Hz), 106.30 d.d (C^6, *J* 161.8, 6.0 Hz), 106.58 d.d (C^3, *J* 163.2, 4.8 Hz), 120.48 d.d (C^5, *J* 166.7, 4.1 Hz), 136.67 (C^4), 144.18 and 145.76 (C^1, C^2), 151.66 d (O$\underline{C}$H=CH$_2$, *J* 184.7 Hz). Mass spectrum, *m/z* (I_{rel}, %): 370 (19) [M]$^+$, 168 (74), 167 (40), 149 (36), 138 (35), 121 (39), 115 (49), 89 (50), 73 (100), 71 (85), 58 (100). High resolution mass spectrum, *m/z*: found 370.1752. C$_{17}$H$_{26}$N$_2$O$_7$. Calculated 370.1740.

X-ray diffraction analysis. A single crystal of compound **IIIb** suitable for X-ray study was grown by slow evaporation of a solution in hexane. The crystallographic parameters and parameters of the X-ray experiment, solution and refinement of structure are given below.

Empirical formula	C$_{15}$H$_{22}$N$_2$O$_6$
Molecular weight	326.35
Color, appearance	Colorless plate
Crystal habit mm	0.26×0.24×0.06
Crystal system	monoclinic
Space group	$P2_1/n$
Unit cell parameters	
a, Å	15.055(3)
b, Å	4.4509(9)
c, Å	23.668(5)
α, deg	90
β, deg	97.39(3)
γ, deg	90
V, Å^3	1572.7(5)
Z	4
ρ_{calc}, g cm^{-3}	1.378
μ(MoK_α), mm^{-1}	0.107
$F(000)$	696
Temperature, K	150.0(2)
Range of θ, deg	1.71≤Θ≤27.00
Spherical segment	$-21 \le h \le 21$, $-6 \le k \le 6$, $-33 \le l \le 31$

Total number of reflections	7041
Number of independent reflections	3404, R$_{int}$ = 0.0615
Number of reflections with I > 2 σ (I)	3140
Number of refined parameters	297
Divergence factor by F2	1/195
R-factors by I > 2σ (I)	0.0887, 0.2531
R-factors by all data	0.1166, 0.2705
Residual electron density (min./max.), e/Å3	0.398/–0.321

The structure **IIIb** was solved and refined with the use of programs SHELXS 86 [24] and SHELXL 97 [25] respectively.

Measurement of ^{1}H NMR spectra during titration was carried out at 30 ± 1°C. At direct titration to a solution of a crown ether in CD$_3$CN (0.5 ml, *c* 5.0×10^{-3} M) was added by portions a solution in CD$_3$CN (0.5 ml) of a mixture of crownether (*c* 5.0×10^{-3} M) and M^{n+}(ClO$_4$)$_n$ (*c* 0.03 M). We failed to perform under common conditions the titration at the use of azacrown ether **IIIb** and salts NH$_4$ClO$_4$ and KClO$_4$ because either the stability constants of the complexes were low and a large excess of the salt was required or a salt (KClO$_4$) was less soluble in acetonitrile than the other perchlorates. At titration with NH$_4$ClO$_4$ 1.5 ml of solution in CD$_3$CN was added containing salt (*c* 0.033 M) and crown ether **IIIb** (*c* 1.67×10^{-3} M) to a solution of crown ether **IIIb** (0.5 ml, *c* 5.0×10^{-3} M); at titration with KClO$_4$ 1.0 ml of solution was added containing salt (*c* 7.5×10^{-3} M) and crown ether **IIIb** (*c* 1.25×10^{-3} M) to solution of crown ether **IIIb** (0.5 ml, *c* 2.5×10^{-3}M). The variation of chemical shifts of crown ether protons was measured as a function of the amount of salt added. At concurrent titration 0.5 ml of solution containing azacrown ether **IIIc** (*c* 5.0×10^{-3} M), Ca(ClO$_4$)$_2$ (*c* 5.0×10^{-3} M), and crown ether **Ib** (*c* 0.08 M) in CD$_3$CN was added by portions to 0.5 ml of solution containing crown ether **IIIc** (*c* 5.0×10^{-3} M) and Ca(ClO$_4$)$_2$ (*c* 5.0×10^{-3} M) in CD$_3$CN. By the use of routine HYPNMR [21] in calculation of equilibrium (1) or a sum of equilibriums (1) and (2) we obtained stability constants (*K*) of complexes; for calculation of concurrent titration results were used simultaneously two equilibriums (1) with a fixed value log $K_{(Ib)}$ 2.9 measured by direct titration.

REFERENCES

1. Yordanov, A.T. and Roundhill, D.M., *Coord. Chem. Rev.,* 1998, vol. 170, p. 93.

2. Gloe, K., Graubaum, H., Wust, M., Rambusch, T., and Seichter, W., *Coord. Chem. Rev.,* 2001, vol. 222, p. 103.

3. Buhlmann, P., Pretsch, E., and Bakker, E., *Chem. Rev.,* 1998, vol. 98, p. 1593.

4. De, Silva, A.P., Gunaratne, H.Q.N., Gunnlaugsson, T., Huxley, A.J.M., McCoy, C.P., Rademacher, J.T., and Rice, T.E., *Chem. Rev.,* 1997, vol. 97, p. 1515.

5. Alfimov, M.V. and Gromov, S.P., in *Applied Fluorescence in Chemistry Biology and Medicine*, Rettig, W., Strehmel, B., Schrader, S., and Seifert, H., Eds., Berlin: Springer-Verlag, 1999, p. 161.

6. Valeur, B. and Leray, I., *Coord. Chem. Rev.,* 2000, vol. 205, p. 3.

7. Shinkai, S., in *Comprehensive Supramolecular Chemistry*, Gokel, G.W., Ed., Oxford: Pergamon, 1996, vol. 1, p. 671.

8. Gromov, S.P. and Alfimov, M.V., *Izv. Akad. Nauk, Ser. Khim.,* 1997, p. 641.

9. Mishra, A., Behera, R.K., Behera, P.K., Mishra, B.K., and Behera, G.B., *Chem. Rev.,* 2000, vol. 100, p. 1973.

10. Lockhart, J.C., Robson, A.C., Thompson, M.E., Furtado, S.D., Kaura, C.K., and Allan, A.R., *J. Chem. Soc., Perkin, Trans. I*, 1973, p. 577.

11. Pedersen, C.J., and Bromels, M.H., US Patent 3 847 949, 1974; *Chem. Abstr.*, 1975, vol. 82, 73049.

12. Hogberg, S.A.G. and Cram, D.J., *J. Org. Chem.*, 1975, vol. 40, p. 151.

13. Lockhart, J.C. and Thompson, M.E., *J. Chem. Soc., Perkin Trans. I,* 1977, p. 202.

14. Gromov, S.P., Vedernikov, A.I., and Dmitrieva, S.N., RF Patent 2161153, 2000; RF *Byull. Izobr.,* 2000, p. 36.

15. Gromov, C.P., Dmitrieva, S.N., and Churakova, M.V., Patent 2215738, 2003; RF *Byull. Izobr.,* 2003, no. 31.

16. Gromov, S.P., Dmitrieva, S.N., and Churakova, M.V., *Synthesis*, 2003, p. 593.

17. Gromov, S.P., Vedernikov, A.I., Ushakov, E.N., Kuz'mina, L.G., Feofanov, A.V., Avakyan, V.G., Churakov, A.V., Alaverdyan, Yu.S., Malysheva, E.V., Alfimov, M.V., Howard, J.A.K., Eliasson, B., and Edlund, U.G., *Helv. Chim. Acta.,* 2002, vol. 85, p. 60.

18. Allen, F.H. and Kennard, O., *Chem. Design Autom. News., 19*93, vol. 8, p. 1.

19. Landis, C.R., Sawyer, R.A., and Somsook, E., *Organometallics,* 2000, vol. 19, p. 994.

20. Gromov, S.P., Sergeev, S.A., Druzhinin, S.I., Rusalov, M.V., Uzhinov, B. M., Kuz'mina, L. G., Churakov, A.V., Khovard, Dzh.A.K., and Alfimov, M.V., *Izv. Akad. Nauk, Ser. Khim.,* 1999, p. 530.

21. Frassineti, C., Ghelli, S., Gans, P., Sabatini, A., Moruzzi, M.S., and Vacca, A., *Anal. Biochem.*, 1995, vol. 231, p. 374.

22. Solotnov, A.F., Solov'ev, V.P., Govorkova, L.V., Kudrya, T.N., Chaikovskaya, A.A., and Raevskii, O.A., *Koord. Khimiya,* 1989, vol. 15, p. 319.

23. Hiraoka, M., *Crown Compounds. Their Characteristics and Applications,* Tokyo: Kodansha, 1982.

24. Sheldrick, G.M., *Acta Crystallogr. A.,* 1990, vol. 46, p. 467.

25. Sheldrick, G.M., *SHELXL-93, Program for the Refinement of Crystal Structures. University of Gottingen, Germany*, 1997.