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Host–Guest Complexes of Nitro-Substituted *N*-Alkylbenzoaza-18-crowns-6

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Abstract—A number of *N*-alkyl(nitrobenzo)aza-18-crowns-6 in which the nitrogen atom in the macroring is conjugated with the benzene ring were synthesized, and their complexing power was compared with that of model nitro derivatives of benzo-18-crown-6 and *N*-phenylaza-18-crown-6 using ^{1}H NMR spectroscopy and DFT/PBE quantum-chemical calculations. The stability constants of the complexes formed by crown ethers with NH_4^+, $EtNH_3^+$, Li^+, Na^+, and K^+ in CD_3CN were determined by ^{1}H NMR titration. The complexing power of *N*-alkyl(nitrobenzo)aza-18-crowns-6 toward metal and ammonium cation was considerably higher than that of *N*-(4-nitrophenyl)aza-18-crown-6 and *N*-alkyl(nitrobenzo)aza-15-crown-5 and was comparable or higher than that of nitrobenzo-18-crown-6.

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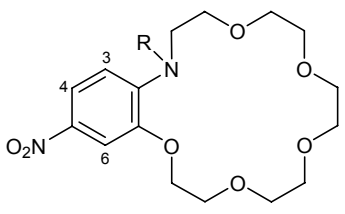
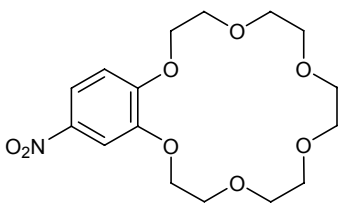
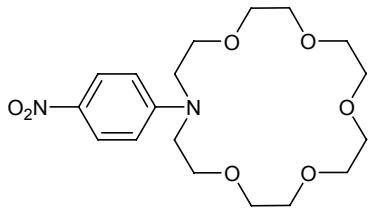
Crown ethers are known to form stable host–guest complexes with metal ions, organic cations, and neutral polar molecules. The ability to form such complexes underlies application of crown ethers as selective ligands toward metal cations, in particular for extraction of metal ions, in ion-selective electrodes and light-sensitive systems, etc. [1–3]. Synthesis of aza crown compounds containing different numbers of nitrogen and oxygen atoms in the macroring attracts persistent interest [1–3]. From the viewpoint of potential application of aza crown compounds as structural fragments of light-sensitive ligands, specific attention is given to those possessing a nitrogen atom conjugated with a chromophore. Such compounds absorb light at considerably longer wavelengths as compared to common crown ether derivatives, which is especially important for photometric and fluorescent analysis, photocontrolled extraction, ion transport through membranes, and design of light-sensitive molecular devices. At present, phenyl aza crown ethers are used most widely for the above purposes; however, a considerable disadvantage is that their complex formation constants with metal ions are not high. In this respect, benzo-fused aza crown ethers may be appreciably more advantageous; on the other hand, derivatives of 1-aza-2,3-benzocrown ethers have been studied fairly poorly, and most their functional derivatives are almost inaccessible despite simple structure [3, 4]. We previously developed a procedure for the synthesis of *N*-methyl benzo aza crown compounds with different sizes of the macroring (both unsubstituted at the benzene ring and formyl-substituted) [5–7] and nitro-



Ia–Id



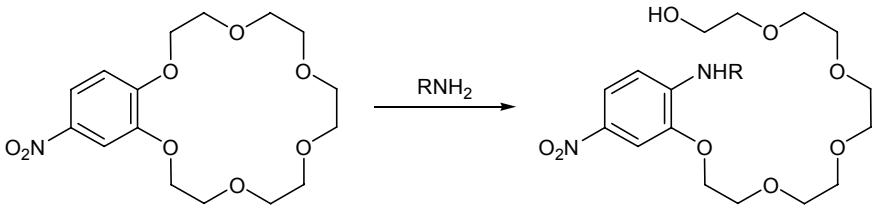
II



III

I, R = Me (**a**), Et (**b**), *n*-Pr (**c**), $PhCH_2$ (**d**).

Scheme 1.



IV, R = Me (**a**), Et (**b**), *n*-Pr (**c**), $PhCH_2$ (**d**), *i*-Pr (**e**), PhCH(Me) (**f**).

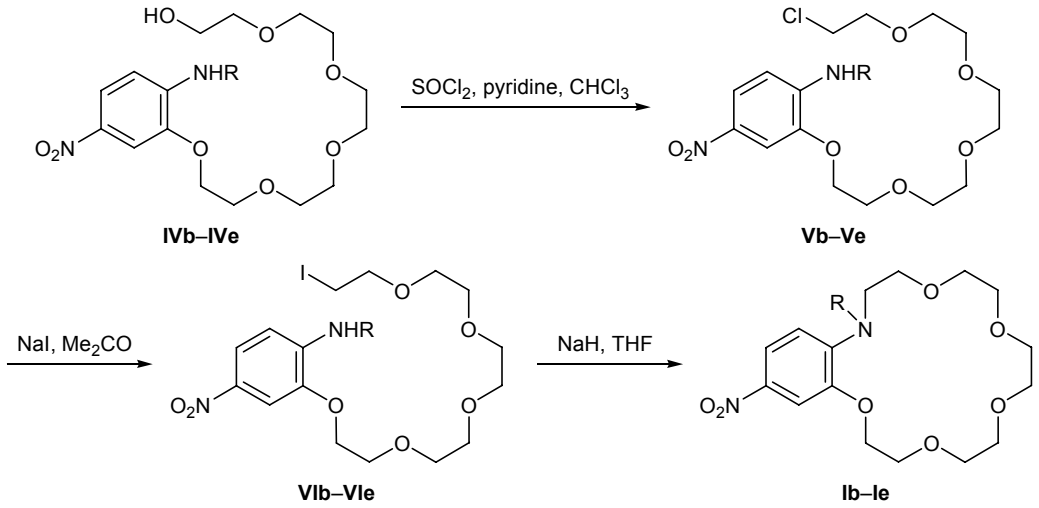
substituted *N*-alkylbenzoaza-15-crowns-5 via stepwise transformations of macroring in benzocrown ethers [8, 9]. The developed synthetic approach to functionalized aza crown ether derivatives seems to be a promising alternative to the known methods of synthesis of 1-aza-2,3-benzocrown ethers [3, 4].

In the present article we report on the synthesis of *N*-alkyl(nitrobenzo)aza-18-crowns-6 **Ib**–**Id** and their ability to form host–guest complexes in comparison with model nitro derivatives of benzo-18-crown-6 and *N*-phenylaza-18-crown-6 **II** and **III**. The complexing power of the compounds under study was estimated by ^{1}H NMR spectroscopy and DFT quantum-chemical calculations. The stability constants of crown ether complexes with alkali and alkaline-earth metal and ammonium ions were determined by ^{1}H NMR titration.

We previously showed that nitro derivatives of benzocrown ethers undergo nucleophilic opening of the macroring by the action of methylamine and that cleavage of the macroring in nitrobenzo-15-crown-5 occurs by the action of alkylamines having hydrocarbon radicals of different lengths and structure; as a result, nitrogen-containing podands were formed [10, 11], e.g., **IVa** (Scheme 1). It was found that increase in the length and degree of branching of the alkyl group in alkylamine is accompanied by reduction of the conversion of benzo-15-crown-5 into podands and that the complete conversion may be achieved by increasing the reaction time (due to the absence of side reactions) [11]. The resulting aza podands can be used for the synthesis of *N*-methylbenzoazacrown ethers such as **Ia** [8, 12, 13] and *N*-alkyl(nitrobenzo)-aza-15-crowns-5 [9] in which the nitrogen atom in the macroring is conjugated with the benzene ring. Following the proposed approach, in the present work we synthesized a series of *N*-alkyl(nitrobenzo)aza-18-crowns-6 (Scheme 2).

Nitro-substituted benzo-18-crown-6 (**II**) was also expected to undergo opening of the macroring by the action of alkylamines. The reactions were carried out according to a modified procedure, which was analogous to that proposed previously for nitrobenzo-15-crown-5 [11], but the reaction temperature and time were increased to attain higher conversion. By heating

Scheme 2.



R = Et (**b**), *n*-Pr (**c**), $PhCH_2$ (**d**), *i*-Pr (**e**).

crown ether **II** with alcoholic solutions of alkylamines we obtained nitrogen-containing podands **IVb–IVf** in 45–100% yield (Scheme 1; see Experimental). The reactions with amines containing bulky alkyl groups [R = *i*-Pr, $PhCH_2$, PhCH(Me)] required considerably longer time to ensure complete conversion of compound **II**, as compared to unbranched alkylamines (R = Et, *n*-Pr).

The presence in molecules **IVb–IVe** of a secondary amino group and terminal hydroxy group made it possible to effect their intramolecular cyclization to previously unknown *N*-alkyl(nitrobenzo)azacrown ethers **Ib–Ie** (Scheme 2). Aza podand **IVf** having the bulkiest substituent on the nitrogen atom was not subjected to analogous transformations, taking into account unsuccessful attempt to obtain the corresponding product from 15-membered benzoazacrown ether [9]. To ensure successful cyclization of aza podands **IVb–IVe** to benzoazacrown ethers, the terminal hydroxy group therein should be replaced by a readily departing group or atom. For this purpose, by treatment of compounds **IVb–IVe** with thionyl chloride in the presence of pyridine we obtained chloro derivatives **Vb–Ve** (yield 73–93%), and the latter were converted into iodides **VIb–VIe** (89–95%) via reaction with sodium iodide in acetone. Cyclization of **VIb–VIe** by the action of sodium hydride in tetrahydrofuran gave the target *N*-alkyl(nitrobenzo)azacrown ethers **Ib–Ie**. The yields of **Ib–Ie** are given in Table 1. For comparison, the yields of previously synthesized *N*-methyl derivative **Ia** are also given [8, 13]. Apart from compounds **Ia–Id**, the cyclization of iodides **VI** gave the corresponding vinyl ethers (products of HI elimination) [13] which were not isolated.

Increase in the length and size of the alkyl radical on the nitrogen atom in **VIb–VIe** reduces the yield of aza crown ethers **I**, so that longer reaction time is necessary. The maximal yield (40%) was obtained for *N*-ethyl derivative **Ib**, but it was considerably smaller than the yield of *N*-methyl analog **Ia** (71%). The yields of compounds **Ib–Id** differed insignificantly from each other (40, 37, and 34%, respectively). No cyclization product was isolated in the reaction with iodide **VIe** having an isopropyl group on the nitrogen atom. When the reactions were carried out at room temperature, the yields of **Ib–Id** were somewhat lower than in boiling tetrahydrofuran.

Table 1. Cyclization of iodides **VIa–VIe** by the action of sodium hydride in tetrahydrofuran

Iodide	R	Time, h	Temperature, °C	Yield, %
VIa[a]	Me	0.5	64	71
		1.5	25	71
VIb	Et	4	64	40
		48	25	34
VIc	*n*-Pr	1	64	37
		48	25	30
VId	$PhCH_2$	8	64	34
VIe	*i*-Pr	96	25	0

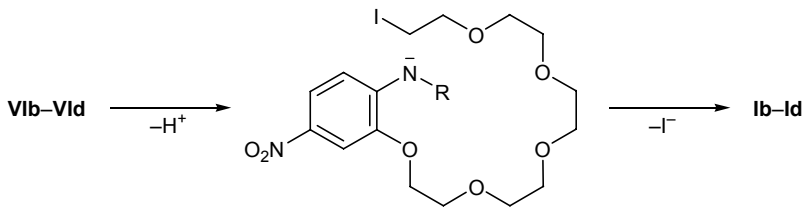
[a] Data of [8, 13].

Presumably, the mechanism of cyclization of iodides **VIb–VId** into aza crown ethers **Ib–Id** is as follows. Sodium hydride as a strong base abstracts proton from the nitrogen atom in **VI** to give reactive arylamide ion **VII**, and intramolecular nucleophilic attack by the nitrogen atom on the terminal CH_2I carbon atom leads to cyclization product **I** provided that there are no considerable steric hindrances at the reaction center (Scheme 3).

Model *N*-(4-nitrophenyl)aza-18-crown-6 (**III**) was synthesized according to the procedure described in [14]. The structure of the synthesized compounds was confirmed by their ^1H and ^{13}C NMR, IR, and mass spectra (including high-resolution mass spectra).

We previously showed [5–7, 13] that benzo aza crown ethers and their derivatives having one tertiary nitrogen atom conjugated with the benzene ring give rise to fairly stable host–guest complexes with alkali,

Scheme 3.



VIIb–VIId

R = Et (**b**), *n*-Pr (**c**), $PhCH_2$ (**d**).

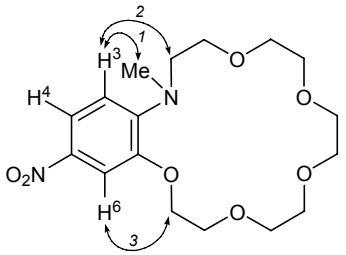


Fig. 1. Couplings between aromatic and aliphatic protons, observed in the NOESY spectrum of aza crown ether **Ia** (CD_3CN, temperature 30°C).

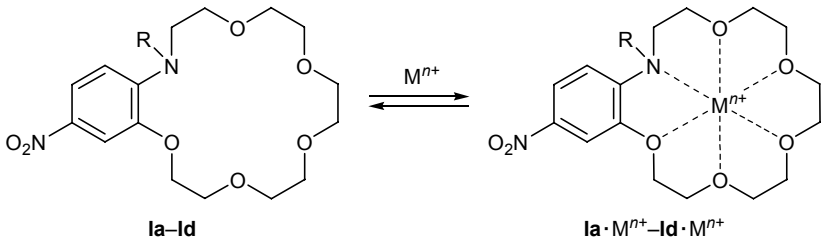
alkaline-earth, and heavy metal ions, as well as with ammonium ions. Therefore, such crown compounds may be efficient as ionophore blocks in optical chemosensors. It was interesting to estimate under comparable conditions the stability of host–guest complexes formed by nitrobenzoaza-18-crowns-6 **Ia**–**Id** with Groups I and II metal ions and ammonium ions, reveal structural specificity of the resulting complexes and selectivity for different ions, and compare the complexing abilities of nitrobenzoazacrowns having different alkyl groups on the nitrogen atom and related compounds, such as *N*-(4-nitrophenyl)aza-18-crown-6 (**III**) and nitrobenzo-18-crown-6 (**II**).

The steric structure of macrocyclic ligands **Ia**–**Id** was determined by NOESY experiments. In all cases, strong cross peaks were observed between protons in the methyl or methylene groups on the nitrogen atom and 3-H in the benzene ring (Fig. 1, *1*), as well as between the C**H**$_2$OAr protons and 6-H (Fig. 1, *3*), which indicated close positions of the corresponding protons. The cross peak formed by the CH_2N protons in the macroring and 3-H (Fig. 1, *2*) is less intense due to longer distance between the interacting protons; however, that distance is shorter than 3.5 Å. Unlike 18-membered *N*-alkylbenzoazacrown ethers, their 15-membered analogs [9] displayed in the NOESY spectra cross peaks due to 3-H$\cdots$R interactions (R is the substituent on the nitrogen), whereas interaction between 3-H and NCH_2 protons in the macroring is very weak. This means that the alkyl and alkoxy groups on the nitrogen atom in **Ia**–**Id** appear at similar distances from the *ortho*-proton (3-H) and that the above substituents deviate by similar distances from the benzene ring plane, i.e., the contribution of sp^3-state of the nitrogen atom is considerable. The lone electron pair (LEP) on the nitrogen atom is most likely to be forced out from conjugation with the π-electron system of the benzene ring and is thus directed toward the macroring center, which should favor formation of stable complexes with metal and ammonium ions (see below).

The ^{1}H NMR spectra of aza crown ethers **Ia**–**Ic** and model compounds **II** and **III** in CD_3CN revealed an appreciable downfield shift ($\Delta\delta_H$) of signals from most protons in the ligand molecule upon addition of excess metal (Li, Na, K, Ca, Ba) or ethylammonium perchlorate. This behavior is typical of inclusion complexes where M^{n+} ion is linked to most heteroatoms in the macroring (Scheme 4) via hydrogen bonds and/or ion–dipole interactions; as a result, electron density is transferred from all atoms in the ligand molecule toward the cation (electron-withdrawing effect of cation). The $\Delta\delta_H$ values for doubly charged cations were generally larger (up to 0.45 ppm) than those observed for singly charged cations, obviously due to higher charge density on alkaline earth cations.

Presumably, the formation of complexes of compounds **Ia**–**Id** with, e.g., Na^+, Ca^{2+}, and Ba^{2+} ions is accompanied by only minor conformational reorganization of the host molecule in the vicinity of the nitrogen atom. This is reflected in the NOESY spectra in leveling of the intensities of cross peaks corresponding to interactions between 3-H in the aromatic ring, on the one hand, and α-protons in the substituent on the nitrogen atom and protons in the endocyclic NCH_2 group, on the other (Fig. 2, *1*, *2*). Approximately equal deviations of the N-substituents from the benzene ring in the complex may be presumed, which implies even larger contribution of sp^3-hybridization of the nitrogen

Scheme 4.



Ia–**Id** **Ia**·M^{n+}–**Id**·M^{n+}

M^{n+} stands for metal or ethylammonium ion, n = 1, 2.

atom as compared to free ligands **Ia**–**Id**. Analogous conclusion was drawn by analysis of the NOESY spectra of *N*-methyl(formylbenzo)aza-18-crown-6 and crystalline structure of its complex with $Ba(ClO_4)_2$ [7]. The larger deviation of the N-substituents from the benzene ring plane also follows from the upfield shift ($\Delta\delta_H$ up to –0.29 ppm) of signals from all CH_2N and MeN groups as a result of complex formation (except for the lithium complex). Analogous pattern was observed previously while studying complex formation of benzoaza-15(18)-crowns-5(6) and their derivatives having a formyl group in the benzene ring [5, 7].

The stability of the complexes formed by nitrobenzo aza crown ethers with metal and ethylammonium perchlorates was estimated by ^{1}H NMR titration. The stability constants were calculated from the dependences of ^{1}H chemical shifts of the ligand upon the amount of added metal (ammonium) salt (15 points) using HYPNMR program [15]. The calculated stability constants were very consistent with the formation of 1:1 complexes $L \cdot M^{n+}$:

$$L + M^{n+} \underset{}{\overset{K}{\rightleftharpoons}} L \cdot M^{n+}$$

Here, L stands for aza crown ether, M^{n+} is metal or ethylammonium cation (n = 1, 2), and K (l mol^{-1}) is the stability constant. For comparison, we estimated the complexing ability toward the same salts of the closest structural analogs of ligands **I**, benzo crown **II** and phenyl aza crown **III**, which are characterized by the same size of the macroring. The results are given in Table 2.

The presence of a nitro group in the examined compounds is responsible for slightly lower (by 0.1–1.7 order of magnitude) stability constants as compared to formyl-substituted analogs [7] due to strong electron-withdrawing effect of the nitro group. The stability constants of the complexes formed by *N*-alkylnitrobenzoaza-18-crowns-6 are considerably higher (by 0.9–3 orders of magnitude) than those for analogous *N*-alkylnitrobenzoaza-15-crowns-5 [9], which may be due to larger number of donor heteroatoms in 18-membered crown compounds as compared to 15-membered. It was also found that the complexing power of the examined crown ethers depends on the nature (size and charge) of the cation and substituent on the nitrogen atom and probably on the degree of conjugation between the nitrogen atom and the benzene ring.

All benzo aza crown ethers **Ia**–**Id**, like previously described nitro-substituted 15-membered aza crown

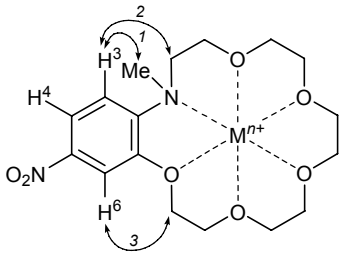


Fig. 2. Couplings between aromatic and aliphatic protons, observed in the NOESY spectra of compound **Ia** in the presence of excess $NaClO_4$, $Ca(ClO_4)_2$, or $Ba(ClO_4)_2$ (CD_3CN, temperature 30°C).

ethers [9], formed more stable complexes than those derived from phenylazacrown **III**. This indicates more rigid (and hence more suited to bind cations) structure of the macroring in ligands **I** and different contributions of the nitrogen atom in **Ia**–**Id** and **III** to complex formation. Presumably, the nitrogen atom in **III** is essentially sp^2-hybridized and involved in effective conjugation with the benzene ring, which prevents participation of its LEP in complex formation. This assumption is confirmed by the X-ray diffraction data for structurally related *N*-(4-formylphenyl)aza-18-crown-6 [7]. By contrast, the nitrogen atom in **Ia**–**Id** is largely contributed by sp^3 state as a result of spatial interactions between the N-substituents and CH_2OAr group, so that it tends to donate its LEP for coordination of guest species.

The examined compounds showed no clearly defined relation between the stability of host–guest complexes and the size of singly charged cation (except for Li^+ ion whose diameter is small relative to the cavity in the 18-membered macroring; therefore, the stability

Table 2. Stability constants of complexes of crown ethers **Ia**–**Id**, **II**, and **III** with metal, ammonium, and ethylammonium perchlorates[a]

Ligand	log K[b]						
	NH_4^+	$EtNH_3^+$	Li^+	Na^+	K^+	Ca^{2+}	Ba^{2+}
II	3.7	3.4	3.3	3.5	4.1	> 5	> 5
Ia	3.8	3.6	2.5	3.6	4.2	> 5	> 5
Ib	4.3	3.5	2.4	4.4	4.2	> 5	> 5
Ic	4.5	3.2	2.4	4.3	4.1	> 5	> 5
Id	3.9	2.9	2.2	3.7	4.1	> 5	> 5
III	2.3	1.5	1.7	3.2	2.1	4.2	4.6

[a] ^{1}H NMR titration in acetonitrile-d_3, 30°C.

[b] $K = [L \cdot M^{n+}]/([L]\,[M^{n+}])$, l/mol; error in the determination of stability constants ±20%.

constants of lithium complexes were appreciably lower). The nitrogen atom in 18-membered compounds **Ia**–**Id** is likely to weakly participate in coordination of lithium cation, as follows from appreciably smaller shifts of signals from protons in the vicinity of that nitrogen atom. For example, complexation of Li^+ with crown ether **Ia** is accompanied by downfield shift of the aromatic 3-H proton by only 0.07 ppm, whereas the corresponding shift for the complex with Na^+ reaches 0.33 ppm. The NOESY spectrum of the complex of **Ia** with lithium perchlorate displayed almost the same proton interaction pattern as that typical of free crown ether **Ia** (Fig. 1).

The complexes with ammonium were generally more stable than the complexes with ethylammonium. This may be due to positive inductive effect of the ethyl group, which reduces the effective positive charge on the nitrogen atom. The stability constants for the complexes with doubly charged cations were considerably higher than those for the corresponding complexes with singly charged cations. Obviously, higher charge density on doubly charged cations compared to singly charged favors stronger ion–dipole interaction between heteroatoms in the macroring and the cation residing in its cavity. The stability constants of the complexes of nitrobenzo-18-(aza)crowns-6 with calcium and barium perchlorates exceed the upper limit for ^{1}H NMR titration ($\log K > 5$).

Quantum-chemical calculations were performed with a view to interpret the experimental data on a qualitative level. Quantitative energy parameters, such as relative conformational energy or binding energy of cation to macroring, can be used only to demonstrate a tendency; therefore, they are not given here. However, structural parameters of molecules (e.g., conformations, interatomic distances, and angles) can be directly correlated with available experimental (X-ray diffraction and 2D NMR) data. In the present work we focused primarily just on structural parameters of the compounds under study.

Geometric parameters of a large number of conformations of free crown ether and its various complexes were optimized in terms of the density functional theory. Though comprehensive conformational analysis of crown ethers and their complexes at the DFT level is an extremely intricate problem, we hope that the most important groups of conformers have been covered in such a way. Analogous approach was used by us previously to simulate the structure and properties of a wide series of crown ethers and their complexes [16–23].

Further consideration included only the most stable (with a relative energy not higher than 3 kcal/mol) conformers of free crown ether, its solvates with water and acetonitrile, calcium complex, and solvates of the complex containing two molecules of water or acetonitrile in the inner coordination sphere. The energy difference 3 kcal/mol at room temperature corresponds to about ~150-fold excess of more stable conformer over less stable. The conformational equilibrium constant (**A** ↔ **B**) $K = [\mathbf{B}]/[\mathbf{A}] = \exp(-\Delta F/RT)$, where F is the Helmholtz free energy; $\Delta F = \Delta U - T\Delta S$, where U is the internal energy (determined by quantum-chemical calculations), and S is the entropy. Different conformers of the same molecule are characterized by approximately equal entropies, so that $\Delta S \approx 0$, $\Delta F \approx \Delta U$. Substituting ΔU into the eqaution for the equilibrium constant gives $K = [\mathbf{B}]/[\mathbf{A}] \approx 0.006$, i.e., the concentration of conformer **A** exceeds the concentration of **B** by a factor of more than 150. We believe that a particular conformer can be detected in solution (e.g., by NMR spectroscopy) when its concentration is larger than 1%. Thus it is sufficient to known the energies of conformers to judge on the presence of one or another conformer in equilibrium mixture.

It is known [24] that interactions between protons at distances longer than 4 Å are not reflected in the NOESY spectra. Therefore, among the calculated structures, specific attention was given to those in which interproton distances were consistent with the data of NOESY experiments. Unfortunately, this procedure does not allow us to unambiguously determine conformation of macroring in solution. Nevertheless, provided that relevant X-ray diffraction data are lacking, a combination of 2D NMR data and quantum-chemical calculations could partly elucidate some specificity of the structure of crown ethers and their complexes.

Figure 3 shows structures of the most stable conformers of free *N*-methyl(nitrobenzo)aza-18-crown-6 (**Ia**). Structure **A** is characterized by the lowest energy. It resembles the structure of free 18-crown-6 with C_i symmetry. Here, strong coupling between the 3-H proton and protons in the NMe group is possible (the shortest distance is ~2.2 Å), whereas coupling of 3-H with protons in the CH_2N group should be much weaker due to considerably longer interproton distance (~ 4.0 Å).

The energy of conformer **B** is only slightly higher (by 0.8 kcal/mol), and the structure of **B** is similar to that of free 18-crown-6 with D_{3d} symmetry. The

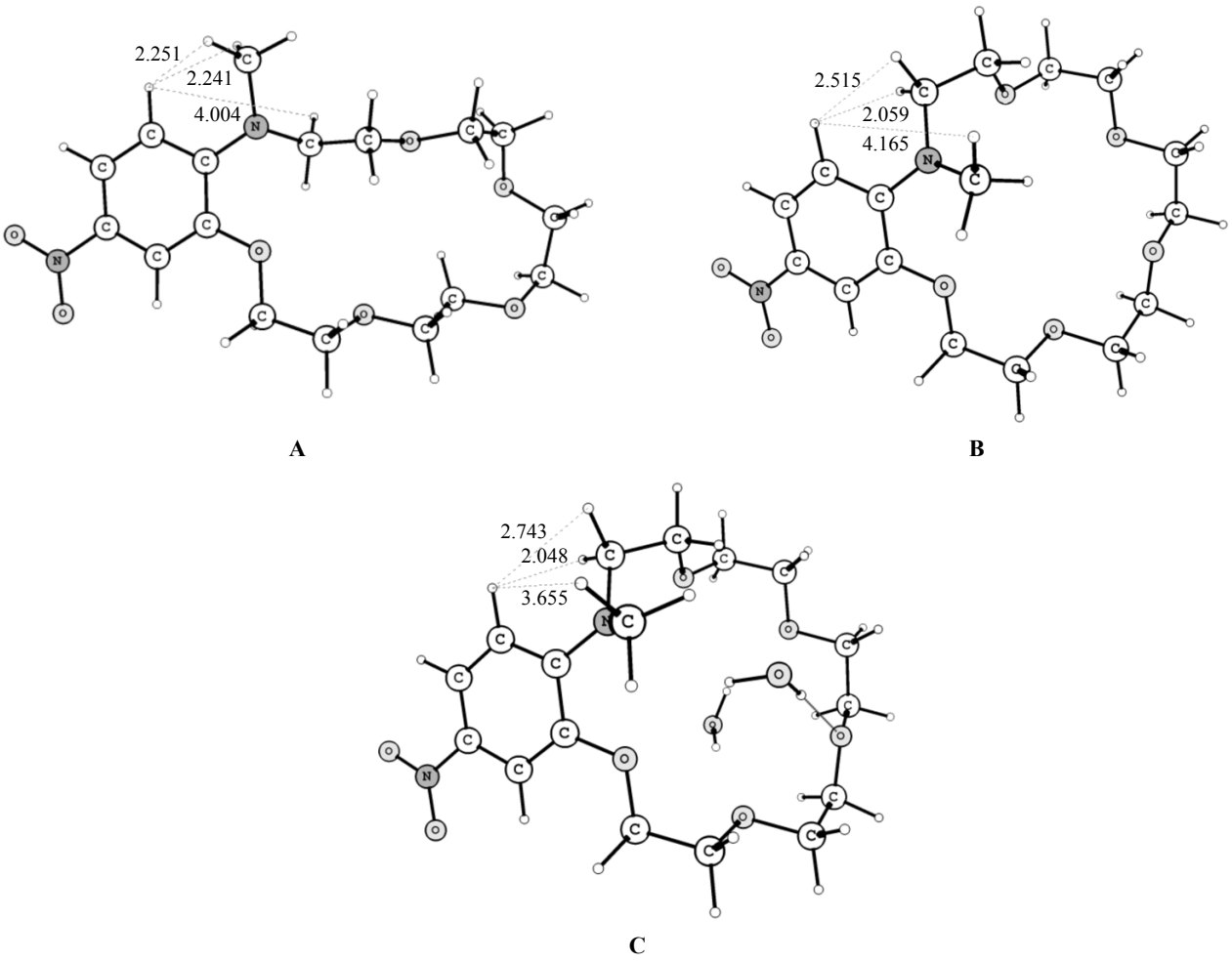
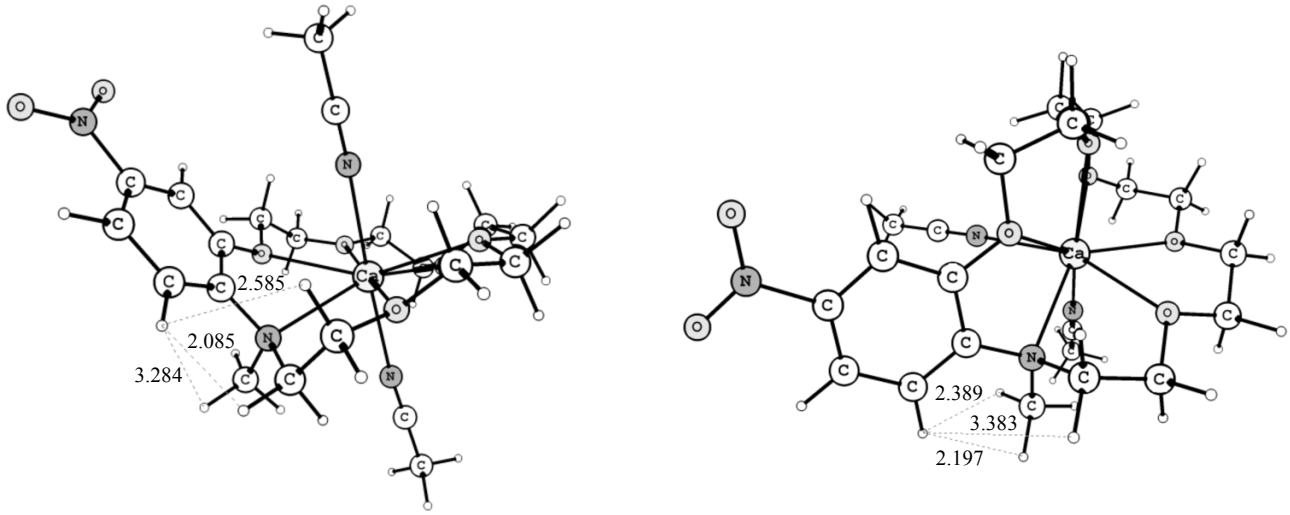


Fig. 3. Structures of the most stable conformers of compound **Ia** optimized by the DFT method.

methyl group on the nitrogen in conformer **B** is oriented toward the center of the cavity, so that NOE is possible for 3-H and CH_2N protons in the macroring, whereas interaction between 3-H and protons in the methyl group on the nitrogen should be considerably weakened. In the experimental NOESY spectrum of **Ia** the intensities of the 3-H/NCH_2 and 3-H/NMe cross peaks differ only slightly (the latter is more intense; Fig. 1). Therefore, the presence in solution of both conformers at comparable concentrations may be presumed. The same also follows from the small difference in their energies.

An alternative explanation implies the presence of another conformer in which strong interaction between 3-H and MeN is also possible. However, conformers that differ appreciably from **A** and **B** are characterized by considerably higher energy. Appearance of a different conformer may be favored by solvation. Such polar solvent as acetonitrile always contains some amount of water; therefore, possible formation of hydrated structures should be taken into account. An example is conformer **C** which is fairly similar to **B**, but the N-methyl group declines from the cavity center due to formation of hydrogen bonds between water molecules and oxygen atoms in the macroring. As a result, the distances between 3-H and α-protons in both substituents on the nitrogen become more leveled than in structure **B**. Simultaneously, the contribution of sp^3-hybridization of the nitrogen atom slightly increases: the sum of the bond angles at the nitrogen atom in structure **C** is 347.3° against 349.0° in **A** and 355.4° in **B**.

The results of calculations also showed that solvation of **Ia** with acetonitrile is less energetically favorable and that it almost does not affect conformation of the macroring. On the other hand, solvation with acetonitrile (as well as with water) of conformer **B** is more favorable than solvation of **A**. This means that solvation should displace the equilibrium **A** ↔ **B**



D **E**

Fig. 4. Structures of acetonitrile solvates of host–guest complexes of compound **Ia** with Ca^{2+} ion, optimized by the DFT method. Distances from 3-H to protons in the MeN group and α- and β-methylene protons in the CH_2CH_2N fragment are given (Å).

toward conformer **B**. We can conclude that conformational equilibrium of free *N*-methyl(nitrobenzo)aza-18-crown-6 (**Ia**) can involve three structures **A**–**C**.

Calcium complex with crown ether **Ia** in solution could give rise to different solvates with solvent molecules in the coordination sphere of the cation. Impurity water molecules are also capable of being coordinated to metal cation. We calculated a number of conformers of Ca^{2+} complex with **Ia**, which contained 0 to 4 molecules of water or 2 acetonitrile molecules in the metal coordination sphere. Conformers in which the cation is linked to all donor atoms in the macroring can include no more than two water molecules in the inner coordination sphere. The nitrogen atom in some conformers does not participate in coordination to the metal ion, while the latter is linked to five oxygen atoms in the macroring and three water molecules. However, these so-called recoordinated structures turned out to be quite unfavorable from the viewpoint of energy (E_{rel} = 6 kcal/mol and more).

We then considered solvate structures containing only two molecules of water or acetonitrile, which corresponded to completed inner coordination sphere of the metal ion. Solvent molecules can reside at the same or opposite sides with respect to the mean-square plane of the macroring, as well as at the same or different sides with respect to the MeN group (asymmetric arrangement). Energetically favorable is either symmetric orientation of solvent molecules (one molecule at each side of the macroring) or asymmetric (at the same side with respect to the MeN group). The relative conformational energy of these structures is lower than 3 kcal/mol; therefore, they can be present in the equilibrium mixture.

The NOESY spectrum of a mixture of crown ether (**Ia**) and excess $Ca(ClO_4)_2$ contained three intense cross peaks corresponding to interactions of 3-H and protons in the MeN group and α- and β-methylene groups (CH_2CH_2N). Among low-energy conformers of the calcium complex, structures were found where protons in the MeN and CH_2CH_2N groups appeared spatially close to 3-H (the corresponding distances were sufficiently short to ensure NOE). In other structures the 3-H proton and β-methylene group in the CH_2CH_2N fragment were distant from each other. We considered the possibility for stabilization of conformers via interaction of the cation with solvent inside the macroring cavity. It was found that symmetric arrangement of solvent molecules stabilized structures like **D** and that their asymmetric arrangement stabilized structures like **E** (Fig. 4). The distance from 3-H to protons in the N-methyl group in structure **D** is 3.28 Å, while the distances from 3-H to the α- and β-methylene protons in the CH_2CH_2N fragment are even shorter, 2.09, and 2.59 Å, respectively. These distances are sufficiently short to ensure fairly strong interactions between the corresponding protons. The β-methylene protons in the CH_2CH_2N fragment of structure **E** is remote from 3-H by more than 4 Å, whereas the distances from 3-H to protons in the MeN group and α-methylene protons in the CH_2CH_2N group are 2.2–2.4 and 3.38 Å, respectively. In this case, the

3-H/N-Me cross peak should be more intense than that observed for structure **D**, while 3-H/β-CH_2 cross peak should be absent.

Structures **D** and **E** of acetonitrile solvates are characterized by almost similar energies, the difference being as small as ~0.2 kcal/mol. Therefore, the concentrations of **D** and **E** in the equilibrium mixture should be almost equal. Insofar as external environment of the complex was not taken into account in our calculations, it is quite possible that just structure **D** would predominate in acetonitrile solution as a result of nonspecific solvation.

To conclude, a number of *N*-alkyl(nitrobenzo)aza-18-crowns-6 with the nitrogen atom linked to the benzene ring were synthesized by stepwise transformations of accessible nitrobenzo-18-crown-6. Determination of the stability constants clearly demonstrated high efficiency of complexation of nitro-substituted *N*-alkylbenzoaza-18-crowns-6 with metal and ammonium cations. Their complexing power was comparable or superior to nitrobenzo-18-crown-6, and it considerably exceeded that of *N*-(4-nitrophenyl)aza-18-crown-6 and nitro-substituted *N*-alkylbenzoaza-15-crowns-5. DFT quantum-chemical calculations revealed conformers of azacrown ether and its complex, whose structures were consistent with the experimental NOESY spectra. The results of the present study may be useful for the design of promising chromoionophores with a strong optical response to complex formation with metal and ammonium cations on the basis of nitrobenzoaza-18-crowns-6.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer at 500.13 and 125.76 MHz, respectively, using $CDCl_3$ as solvent and reference ($CHCl_3$, δ 7.27 ppm; $CDCl_3$, δ_C 77.00 ppm). Signals were assigned with the aid of two-dimensional homonuclear (^{1}H–^{1}H COSY, NOESY) and heteronuclear (^{1}H–^{13}C COSY, HSQC, HMBC) correlation techniques. The NOESY mixing period was 300 μs, and HMBC experiment was optimized for J_{CH} = 8 Hz. The IR spectra were measured on a Bruker IFS-113V spectrometer from films. The mass spectra were obtained on Varian MAT-311A (quadrupole mass analyzer) and Finnigan MAT-212 instruments (magnetic mass analyzer), and the high-resolution mass spectra were obtained on a Finnigan MAT-212 mass spectrometer using perfluorokerosene as reference (electron impact, 70 or 60 eV, direct sample admission into the ion source). The elemental composition of compound **Ia** was determined at the Microanalysis Laboratory, Nesmeyanov Institute of Organometallic Compounds, Russian Academy of Sciences. The melting points were measured in capillaries on an MEL-Temp II melting point apparatus. Silica gel Kieselgel 60 (0.063–0.100 or 0.063–0.200 mm, Merck) was used for column chromatography. The progress of reactions was monitored by TLC on DC-Alufolien Kieselgel 60 F_{254} plates (Merck).

N-(4-Nitrophenyl)aza-18-crown-6 (**III**) was synthesized according to the procedure described in [14]. (4-Nitrobenzo)-18-crown-6 (**II**) was purchased from Bogatskii Physicochemical Institute, National Academy of Sciences of Ukraine (Odessa, Ukraine). Ethanamine (70% aqueous solution), propan-1-amine, propan-2-amine, phenylmethanamine, and 1-phenylethanamine (Aldrich) were used without additional purification. Commercial NH_4ClO_4, $NaClO_4$, $KClO_4$, $Ca(ClO_4)_2$, and $Ba(ClO_4)_2$ (Aldrich) were dried under reduced pressure at 60°C (NH_4ClO_4) or 200°C (other salts). Ethylammonium perchlorate $EtNH_3ClO_4$ was synthesized by neutralization of a 70% aqueous solution of ethylamine with 70% $HClO_4$ (Aldrich), followed by drying of the salt under reduced pressure at 60°C.

^{1}H NMR titration. Acetonitrile-d_3 (water content <0.05%; *Prikladnaya khimiya* Russian Research Center, St. Petersburg) was used as solvent. The composition and stability constants of complexes formed by crown compounds with $M^{n+}(ClO_4^-)_n$ were determined from variation of the position of signals from protons in the ligand (L) depending on the concentration of added salt. The concentration of L was maintained constant at $\sim 5 \times 10^{-3}$ M, and the concentration of salt was varied from zero to a maximal M^{n+}/L ratio of ~3. In the titration with NH_4ClO_4 and $KClO_4$, the overall ligand concentration was maintained at $\sim 1 \times 10^{-3}$ M because of limited solubility of the salts. The Δδ values were measured with an accuracy of ±0.001 ppm. The stability constants were calculated using HYPNMR program [15].

Quantum-chemical calculations. Geometric parameters of crown ether **Ia** and its complexes were optimized by the DFT method with Perdew–Burke–Ernzerhof (PBE) functional [25] and triple zeta basis set (PBE/3z) using PRIRODA program [26, 27] built in NANOMODEL software package. Contracted Gaussian-type orbital basis sets (5*s*1*p*)/[3*s*1*p*] for H, (11*s*6*p*2*d*)/[6*s*3*p*2*d*] for C, O, and N, and (17*s*13*p*)/[12*s*9*p*] for Ca were used, as well as auxiliary uncon-

tracted Gaussian basis sets for representation of electron density, (5*s*1*p*) for H, (10*s*3*p*3*d*1*f*) for C, N, and O, and (18*s*3*p*2*d*) for Ca. The initial structures were generated by molecular mechanics and on the basis of X-ray diffraction data for structurally related compounds. The detailed calculation procedure is described in [16–23].

Aza podands IVb–IVf (*general procedure*). A mixture of 313 mg (1 mmol) of crown ether **II** and 0.04 mol of a 45% solution of the corresponding amine in anhydrous ethanol was heated in a sealed ampule at 130°C for 100 h (**IVb**, **IVc**) or 300 h (**IVd**–**IVf**). The ampule was cooled and opened, and the mixture was evaporated under reduced pressure. The products were isolated as follows.

a. The residue containing compound **IVb**, **IVc**, or **IVe** was subjected to column chromatography on silica gel using first ethyl acetate and then ethyl acetate–ethanol (5 : 1) as eluent.

b. The residue containing compound **IVd** or **IVf** was treated with 50 ml of water, and concentrated hydrochloric acid was added dropwise until pH 3. The mixture was extracted with chloroform, the extract was evaporated, and the residue was purified as described above in *a*.

Podands **IVb**–**IVf** were isolated as yellow oily substances.

14-(2-Ethylamino-5-nitrophenoxy)-3,6,9,12-tetraoxatetradecan-1-ol (IVb). Yield 100%. IR spectrum, ν, cm^{-1}: 3403 (NH), 1494 (NO_2). ^1H NMR spectrum, δ, ppm: 1.23 m (3H, Me), 3.21 m (2H, CH_2N), 3.54 m (2H, CH_2O), 3.57 s (8H, CH_2O), 3.61 m (6H, CH_2O), 3.82 m (2H, C**H**$_2$$CH_2OAr$), 4.14 m (2H, C**H**$_2$OAr), 5.33 br.s (1H, NH), 6.40 d (1H, 3-H, J = 9.2 Hz), 7.27 br.s (1H, 6-H), 7.80 br.d (1H, 4-H, J = 9.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.79 (Me), 37.03 (CH_2N), 61.06 (CH_2OH), 68.09 (CH_2O), 68.88 (CH_2O), 69.77 (CH_2O), 70.04 (4C, CH_2O), 70.11 (CH_2O), 72.06 (CH_2O), 106.08 and 106.18 (C^3, C^6), 119.88 (C^4), 135.88 (C^5), 143.64 and 144.47 (C^1, C^2). Mass spectrum, *m*/*z* (I_{rel}, %): 402 (54) $[M]^+$, 270 (18), 226 (15), 182 (37), 181 (15), 167 (16), 135 (17), 133 (22), 89 (100), 78 (13). Found: *m*/*z* 402.2011 $[M]^+$. $C_{18}H_{30}N_2O_8$. Calculated: *M* 402.2002.

14-(5-Nitro-2-propylaminophenoxy)-3,6,9,12-tetraoxatetradecan-1-ol (IVc). Yield 100%. IR spectrum, ν, cm^{-1}: 3412 (NH), 1495 (NO_2). ^1H NMR spectrum, δ, ppm: 0.88 t (3H, Me, J = 7.4 Hz), 1.57 m (2H, CH_2), 3.09 br.t (2H, CH_2N), 3.30 br.s (1H, OH), 3.47 m (2H, CH_2O), 3.53 m (8H, CH_2O), 3.59 m (6H, CH_2O), 3.77 m (2H, C**H**$_2$$CH_2OAr$), 4.10 m (2H, C**H**$_2$OAr), 5.51 br.s (1H, NH), 6.35 d (1H, 3-H, J = 9.0 Hz), 7.49 d (1H, 6-H, J = 2.3 Hz), 7.74 d.d (1H, 4-H, J = 9.0, 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.08 (Me), 21.79 (CH_2), 44.27 (CH_2N), 61.06 (CH_2OH), 67.96 (CH_2O), 68.93 (CH_2O), 69.41 (CH_2O), 69.72 (CH_2O), 70.00 (3C, CH_2O), 70.14 (CH_2O), 72.27 (CH_2O), 106.13 (C^3, C^6), 120.00 (C^4), 135.79 (C^5), 143.71 and 144.76 (C^1, C^2). Mass spectrum, *m*/*z* (I_{rel}, %): 416 (60) $[M]^+$, 387 (15), 284 (16), 196 (15), 195 (14), 193 (30), 167 (31), 133 (28), 119 (15), 89 (100). Found: *m*/*z* 416.2150 $[M]^+$. $C_{19}H_{32}N_2O_8$. Calculated: *M* 416.2159.

14-(2-Benzylamino-5-nitrophenoxy)-3,6,9,12-tetraoxatetradecan-1-ol (IVd). Yield 86%. IR spectrum, ν, cm^{-1}: 3418 (NH), 1495 (NO_2). ^1H NMR spectrum, δ, ppm: 3.50 m (2H, CH_2O), 3.52–3.60 m (10H, CH_2O), 3.62 m (4H, CH_2O), 3.83 m (2H, C**H**$_2$$CH_2OAr$), 4.18 m (2H, C**H**$_2$OAr), 4.43 d (2H, C**H**$_2$Ph, J = 5.5 Hz), 6.15 t (1H, NH, J = 5.5 Hz), 6.36 d (1H, 3-H, J = 8.8 Hz), 7.21 m (1H, 4′-H), 7.27–7.30 m (4H, 2′-H, 3′-H, 5′-H, 6′-H), 7.59 d (1H, 6-H, J = 2.1 Hz), 7.73 d.d (1H, 4-H, J = 8.8, 2.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 46.50 (**C**H_2Ph), 61.22 (CH_2OH), 68.18 (CH_2O), 69.01 (CH_2O), 69.80 (CH_2O), 70.11 (4C, CH_2O), 70.21 (CH_2O), 72.31 (CH_2O), 106.32 and 107.08 (C^3, C^6), 119.86 (C^4), 126.68 ($C^{2'}$, $C^{6'}$), 127.09 ($C^{4'}$), 128.42 ($C^{3'}$, $C^{5'}$), 136.54 and 137.70 ($C^{1'}$, C^5), 144.08 and 144.52 (C^1, C^2). Mass spectrum, *m*/*z* (I_{rel}, %): 464 (26) $[M]^+$, 448 (20), 447 (76), 433 (6), 332 (6), 288 (6), 133 (8), 92 (13), 91 (100), 89 (37). Found: *m*/*z* 464.2151 $[M]^+$. $C_{23}H_{32}N_2O_8$. Calculated: *M* 464.2159.

14-(2-Isopropylamino-5-nitrophenoxy)-3,6,9,12-tetraoxatetradecan-1-ol (IVe). Yield 84%. IR spectrum, ν, cm^{-1}: 3391 (NH), 1497 (NO_2). ^1H NMR spectrum, δ, ppm: 1.18 d (6H, Me, J = 6.7 Hz), 3.50 m (2H, CH_2O), 3.55 m (8H, CH_2O), 3.58–3.65 m (7H, CH_2O, CHN), 3.80 m (2H, C**H**$_2$$CH_2OAr$), 4.13 m (2H, C**H**$_2$OAr), 5.20 br.s (1H, NH), 6.40 d (1H, 6-H, J = 9.0 Hz), 7.54 d (1H, 3-H, J = 2.3 Hz), 7.77 d.d (1H, 5-H, J = 9.0, 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.12 (Me), 43.59 (CHN), 61.18 (CH_2OH), 68.14 (CH_2O), 69.03 (CH_2O), 69.82 (CH_2O), 70.13 (4C, CH_2O), 70.27 (CH_2O), 72.31 (CH_2O), 106.63 and 106.48 (C^3, C^6), 120.10 (C^5), 135.81 (C^4), 143.72 and 143.83 (C^1, C^2). Mass spectrum, *m*/*z* (I_{rel}, %): 416 (66) $[M]^+$, 401 (28), 284 (14), 207 (22), 196 (22), 181 (32), 165 (13), 133 (33), 89 (100), 73 (15). Found: *m*/*z* 416.2142 $[M]^+$. $C_{19}H_{32}N_2O_8$. Calculated: *M* 416.2159.

14-[5-Nitro-2-(1-phenylethylamino)phenoxy]-3,6,9,12-tetraoxatetradecan-1-ol (IVf). Yield 45% (on the reacted compound **II**; conversion 36%). IR spectrum, ν, cm^{-1}: 3417 (NH), 1495 (NO_2). ^1H NMR spectrum, δ, ppm: 1.61 d (3H, Me, J = 6.7 Hz), 3.57–3.65 m (17H, CH_2O, OH), 3.93 m (2H, C**H**$_2$CH$_2$OAr), 4.28 m (2H, C**H**$_2$OAr), 4.58 m (1H, CHN), 5.80 d (1H, NH, J = 5.4 Hz), 6.24 d (1H, 3-H, J = 8.7 Hz), 7.24 m (1H, 4′-H), 7.30–7.35 m (4H, 2′-H, 3′-H, 5′-H, 6′-H), 7.65 d (1H, 6-H, J = 2.0 Hz), 7.71 d.d (1H, 4-H, J = 8.7, 2.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 24.51 (Me), 52.94 (CHN), 61.58 (CH_2OH), 68.49 (CH_2O), 69.32 (CH_2O), 70.09 (CH_2O), 70.40 (CH_2O), 70.44 (3C, CH_2O), 70.58 (CH_2O), 72.53 (CH_2O), 106.67 (C^3), 108.32 (C^6), 119.95 (C^4), 125.56 ($C^{2'}$, $C^{6'}$), 127.25 ($C^{4'}$), 128.77 ($C^{3'}$, $C^{5'}$), 136.83 (C^5), 143.59 (C^2), 143.66 ($C^{1'}$), 144.12 (C^2). Mass spectrum, m/z (I_{rel}, %): 478 (38) $[M]^+$, 464 (4), 463 (15), 461 (10), 269 (4), 133 (9), 106 (9), 105 (100), 89 (21), 79 (5). Found: m/z 478.2315 $[M]^+$. $C_{24}H_{34}N_2O_8$. Calculated: M 478.2315.

Chlorides Vb–Ve (*general procedure*). A solution of 3.2 ml (43.9 mmol) of thionyl chloride in 5 ml of chloroform was slowly added under stirring at 0°C (ice bath) to a solution of 1.8 mmol of compound **IVb**–**IVf** and 0.16 ml (2 mmol) of anhydrous pyridine in 15 ml of chloroform. The mixture was heated for 6–7 h under reflux and cooled, treated with 50 ml of 5% hydrochloric acid, and extracted with chloroform. The extracts were combined, washed with a 5% aqueous solution of sodium carbonate and with water, and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel using as eluent benzene–ethyl acetate (1 : 1 for compounds **Vb**–**Vd** or 5 : 1 and then 1 : 1 for **Ve**). Chlorides **Vb**–**Ve** were isolated as yellow oily substances.

2-(14-Chloro-3,6,9,12-tetraoxatetradecyloxy)-*N*-ethyl-4-nitroaniline (Vb). Yield 90%. IR spectrum, ν, cm^{-1}: 3413 (NH), 1497 (NO_2). ^1H NMR spectrum, δ, ppm: 1.33 t (3H, Me, J = 7.3 Hz), 3.30 q (2H, CH_2N, J = 7.3 Hz), 3.63 t (2H, CH_2Cl, J = 5.9 Hz), 3.64 s (8H, CH_2O), 3.71 m (4H, CH_2O), 3.75 t (2H, C**H**$_2$CH$_2$Cl, J = 5.9 Hz), 3.90 m (2H, C**H**$_2$CH$_2$OAr), 4.24 m (2H, C**H**$_2$OAr), 5.25 br.s (1H, NH), 6.50 d (1H, 6-H, J = 8.7 Hz), 7.66 d (1H, 3-H, J = 2.2 Hz), 7.93 d.d (1H, 5-H, J = 8.7, 2.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.59 (Me), 38.03 (CH_2N), 43.13 (CH_2Cl), 68.93 (CH_2O), 69.68 (CH_2O), 70.82 (5C, CH_2O), 70.93 (CH_2O), 71.55 (CH_2O), 106.93 and 107.17 (C^3, C^6), 120.51 (C^5), 136.75 (C^4), 144.40 (C^2), 144.54 (C^1). Mass spectrum, m/z (I_{rel}, %): 422 (9) $[M]^+$ (^{37}Cl), 420 (25) $[M]^+$ (^{35}Cl), 226 (11), 182 (24), 181 (11), 151 (14), 135 (13), 109 (15), 107 (53), 65 (34), 63 (100). Found: m/z 420.1671 $[M]^+$. $C_{18}H_{29}ClN_2O_7$. Calculated: M 420.1663 (^{35}Cl).

2-(14-Chloro-3,6,9,12-tetraoxatetradecyloxy)-4-nitro-*N*-propylaniline (Vc). Yield 93%. IR spectrum, ν, cm^{-1}: 3414 (NH), 1495 (NO_2). ^1H NMR spectrum, δ, ppm: 0.89 t (3H, Me, J = 7.4 Hz), 1.57 m (2H, CH_2), 3.08 t (2H, CH_2N, J = 7.1 Hz), 3.50 t (2H, CH_2Cl, J = 5.8 Hz), 3.54 s (8H, CH_2O), 3.58 m (4H, CH_2O), 3.62 t (2H, C**H**$_2$CH$_2$Cl, J = 5.8 Hz), 3.77 m (2H, C**H**$_2$CH$_2$OAr), 4.09 m (2H, C**H**$_2$OAr), 5.20 br.s (1H, NH), 6.36 d (1H, 6-H, J = 9.0 Hz), 7.50 d (1H, 3-H), 7.75 d.d (1H, 5-H, J = 9.0, 2.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.05 (Me), 21.81 (CH_2), 42.37 (CH_2Cl), 44.24 (CH_2N), 68.23 (**C**H$_2$OAr), 68.94 (**C**H$_2$CH$_2$OAr), 70.05 (CH_2O), 70.12 (4C, CH_2O), 70.20 (CH_2O), 70.85 (CH_2O), 106.18 (C^6), 106.28 (C^3), 119.91 (C^5), 135.90 (C^4), 143.69 (C^2), 144.64 (C^1). Mass spectrum, m/z (I_{rel}, %): 436 (16) $[M]^+$ (^{37}Cl), 434 (40) $[M]^+$ (^{35}Cl), 196 (20), 195 (14), 193 (21), 167 (17), 151 (20), 109 (20), 107 (58), 65 (31), 63 (100). Found: m/z 434.1826 $[M]^+$. $C_{19}H_{31}ClN_2O_7$. Calculated: M 434.1820 (^{35}Cl).

***N*-Benzyl-2-(14-chloro-3,6,9,12-tetraoxatetradecyloxy)-4-nitroaniline (Vd).** Yield 90%. IR spectrum, ν, cm^{-1}: 3420 (NH), 1496 (NO_2). ^1H NMR spectrum, δ, ppm: 3.53 t (2H, CH_2Cl, J = 5.8 Hz), 3.56 m (8H, CH_2O), 3.58 m (2H, CH_2O), 3.63 m (2H, CH_2O), 3.65 t (2H, C**H**$_2$CH$_2$Cl, J = 5.8 Hz), 3.83 m (2H, C**H**$_2$CH$_2$OAr), 4.16 m (2H, C**H**$_2$OAr), 4.42 br.s (2H, C**H**$_2$Ph), 6.37 d (1H, 6-H, J = 8.7 Hz), 7.21 m (1H, 4′-H), 7.25–7.30 m (4H, 2′-H, 3′-H, 5′-H, 6′-H), 7.59 d (1H, 3-H, J = 2.3 Hz), 7.73 d.d (1H, 5-H, J = 8.7, 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 42.41 (CH_2Cl), 46.48 (**C**H$_2$Ph), 68.40 (CH_2O), 68.96 (CH_2O), 70.13 (5C, CH_2O), 70.21 (CH_2O), 70.87 (CH_2O), 106.55 (C^3), 107.06 (C^6), 119.76 (C^5), 126.64 ($C^{2'}$, $C^{6'}$), 127.08 ($C^{4'}$), 128.37 ($C^{3'}$, $C^{5'}$), 136.56 (C^4), 137.53 ($C^{1'}$), 144.03 (C^2), 144.38 (C^1). Mass spectrum, m/z (I_{rel}, %): 84 (7) $[M]^+$ (^{37}Cl), 482 (15) $[M]^+$ (^{35}Cl), 467 (11), 466 (9), 465 (30), 109 (8), 107 (23), 92 (10), 91 (100), 65 (16), 63 (52). Found: m/z 482.1825 $[M]^+$. $C_{23}H_{31}ClN_2O_7$. Calculated: M 482.1820 (^{35}Cl).

2-(14-Chloro-3,6,9,12-tetraoxatetradecyloxy)-*N*-isopropyl-4-nitroaniline (Ve). Yield 73%. IR spectrum, ν, cm^{-1}: 3400 (NH), 1497 (NO_2). ^1H NMR spectrum, δ, ppm: 1.17 m (6H, Me, J = 4.6 Hz), 3.51 m (2H, CH_2O), 3.55 s (8H, CH_2O), 3.61 m (7H, CHN, CH_2O), 3.79 m (2H, C**H**$_2$CH$_2$OAr), 4.11 m (2H,

C**H**$_2$OAr), 6.39 d (1H, 6-H, J = 9.0 Hz), 7.53 d (1H, 3-H, J = 2.4 Hz), 7.77 d.d (1H, 5-H, J = 9.0, 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.07 (Me), 42.38 (CH_2Cl), 43.52 (CHN), 68.35 (CH_2O), 68.97 (CH_2O), 70.10 (CH_2O), 70.17 (4C, CH_2O), 70.27 (CH_2O), 70.89 (CH_2O), 106.66 (C^3, C^6), 119.94 (C^5), 135.86 (C^4), 143.64 and 143.69 (C^1, C^2). Mass spectrum, m/z (I_{rel}, %): 436 (16) $[M]^+$ (^{37}Cl), 434 (35) $[M]^+$ (^{35}Cl), 419 (16), 207 (16), 196 (15), 181 (20), 151 (19), 109 (21), 107 (65), 65 (34), 63 (100). Found: m/z 434.1825 $[M]^+$. $C_{19}H_{31}ClN_2O_7$. Calculated: M 434.1820 (^{35}Cl).

Iodides VIb–VIe (*general procedure*). A solution of 1.6 mmol of compound **Vb**–**Ve** and 4.8 g (32 mmol) of sodium iodide in 50 ml of anhydrous acetone was heated for 100 h under reflux with stirring. The mixture was evaporated under reduced pressure, and the residue was treated with 50 ml of water and extracted with benzene. The combined extracts were evaporated under reduced pressure, and the residue was subjected to chromatography on silica gel using benzene–ethyl acetate (5:1) as eluent. Compounds **VIb**–**VIe** were isolated as yellow oily substances.

***N*-Ethyl-2-(14-iodo-3,6,9,12-tetraoxatetradecyloxy)-4-nitroaniline (VIb).** Yield 94%. IR spectrum, ν, cm^{-1}: 3413 (NH), 1495 (NO_2). ^{1}H NMR spectrum, δ, ppm: 1.23 t (3H, Me, J = 7.1 Hz), 3.17 t (2H, CH_2I, J = 6.9 Hz), 3.20 q (2H, CH_2N, J = 7.1 Hz), 3.57 s (4H, CH_2O), 3.58 s (4H, CH_2O), 3.62 m (4H, CH_2O), 3.65 t (2H, C**H**$_2$CH$_2$I, J = 6.9 Hz), 3.81 m (2H, C**H**$_2$CH$_2$OAr), 4.14 m (2H, C**H**$_2$OAr), 6.40 d (1H, 6-H, J = 8.9 Hz), 7.54 d (1H, 3-H, J = 2.3 Hz), 7.79 d.d (1H, 5-H, J = 8.9, 2.3 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 2.75 (CH_2I), 13.09 (Me), 37.23 (CH_2N), 68.26 (CH_2O), 69.04 (CH_2O), 69.80 (CH_2O), 70.21 (5C, CH_2O), 71.55 (CH_2O), 106.35 and 106.28 (C^3, C^6), 120.06 (C^5), 136.09 (C^4), 143.76 and 144.55 (C^1, C^2). Mass spectrum, m/z (I_{rel}, %): 512 (29) $[M]^+$, 270 (9), 199 (14), 182 (18), 181 (8), 167 (7), 155 (100), 135 (9), 128 (5), 78 (6). Found: m/z 512.1028 $[M]^+$. $C_{18}H_{29}IN_2O_7$. Calculated: M 512.1020.

2-(14-Iodo-3,6,9,12-tetraoxatetradecyloxy)-4-nitro-*N*-propylaniline (VIc). Yield 89%. IR spectrum, ν, cm^{-1}: 3411 (NH), 1496 (NO_2). ^{1}H NMR spectrum, δ, ppm: 0.91 t (3H, Me, J = 7.7 Hz), 1.60 m (2H, CH_2), 3.10 t (2H, CH_2N, J = 7.4 Hz), 3.15 t (2H, CH_2I, J = 6.9 Hz), 3.55 m (8H, CH_2O), 3.60 m (4H, CH_2O), 3.64 t (2H, C**H**$_2$CH$_2$I, J = 6.9 Hz), 3.79 m (4H, C**H**$_2$CH$_2$OAr), 4.12 m (2H, C**H**$_2$OAr), 5.34 br.s (1H, NH), 6.38 d (1H, 6-H, J = 8.9 Hz), 7.52 d (1H, 3-H, J = 2.3 Hz), 7.77 d.d (1H, 5-H, J = 8.9, 2.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 3.28 (CH_2I), 11.69 (Me), 21.41 (CH_2), 44.84 (CH_2N), 68.81 (CH_2O), 69.54 (CH_2O), 70.2 (CH_2O), 70.71 (CH_2O), 70.81 (CH_2O), 72.03 (CH_2O), 106.78, 106.89 (C^3, C^6), 120.52 (C^5), 136.48 (C^4), 144.24 and 145.21 (C^1, C^2). Mass spectrum, m/z (I_{rel}, %): 526 (48) $[M]^+$, 284 (10), 253 (9), 199 (18), 196 (15), 195 (11), 193 (16), 167 (15), 155 (100), 119 (9). Found: m/z 526.1168 $[M]^+$. $C_{19}H_{31}IN_2O_7$. Calculated: M 526.1176.

***N*-Benzyl-2-(14-iodo-3,6,9,12-tetraoxatetradecyloxy)-4-nitroaniline (VId).** Yield 95%. IR spectrum, ν, cm^{-1}: 3412 (NH), 1496 (NO_2). ^{1}H NMR spectrum, δ, ppm: 3.17 t (2H, CH_2I, J = 6.7 Hz), 3.56 s (4H, CH_2O), 3.58 s (4H, CH_2O), 3.61 m (2H, CH_2O), 3.65 m (4H, C**H**$_2$CH$_2$I, CH_2O), 3.85 m (2H, C**H**$_2$CH$_2$OAr), 4.18 m (2H, C**H**$_2$OAr), 4.44 d (2H, C**H**$_2$Ph, J = 4.2 Hz), 6.03 br.t (1H, NH), 6.37 d (1H, 6-H, J = 9.2 Hz), 7.24 m (1H, 4′-H), 7.25–7.31 m (4H, 2′-H, 3′-H, 5′-H, 6′-H), 7.60 d (1H, 3-H, J = 1.8 Hz), 7.75 br.d (1H, 5-H, J = 9.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 3.42 (CH_2I), 47.04 (**C**H$_2$Ph), 68.84 (CH_2O), 69.54 (CH_2O), 70.27 (CH_2O), 70.71 (4C, CH_2O), 70.81 (CH_2O), 72.02 (CH_2O), 106.96 (C^3), 107.61 (C^6), 120.43 (C^5), 127.21 ($C^{2'}$, $C^{6'}$), 127.69 ($C^{4'}$), 128.99 ($C^{3'}$, $C^{5'}$), 137.03 and 138.05 ($C^{1'}$, C^4), 144.54 and 144.92 (C^1, C^2). Mass spectrum, m/z (I_{rel}, %): 574 (22) $[M]^+$, 558 (7), 557 (28), 332 (6), 288 (5), 199 (8), 155 (62), 92 (11), 91 (100), 64 (6). Found: m/z 574.1175 $[M]^+$. $C_{23}H_{31}IN_2O_7$. Calculated: M 574.1176.

2-(14-Iodo-3,6,9,12-tetraoxatetradecyloxy)-*N*-isopropyl-4-nitroaniline (VIe). Yield 89%. IR spectrum, ν, cm^{-1}: 3411 (NH), 1496 (NO_2). ^{1}H NMR spectrum, δ, ppm: 1.25 d (6H, Me, J = 6.4 Hz), 3.22 t (2H, CH_2I, J = 6.8 Hz), 3.62 s (4H, CH_2O), 3.63 s (4H, CH_2O), 3.67 m (4H, CH_2O), 3.69 m (1H, CHN), 3.71 t (2H, C**H**$_2$CH$_2$I, J = 6.8 Hz), 3.86 m (2H, C**H**$_2$CH$_2$OAr), 4.20 m (2H, C**H**$_2$OAr), 6.48 d (1H, 6-H, J = 9.0 Hz), 7.62 d (1H, 3-H, J = 2.4 Hz), 7.86 d.d (1H, 5-H, J = 9.0, 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 2.81 (CH_2I), 22.38 (Me), 43.83 (CHN), 68.57 (CH_2O), 69.27 (CH_2O), 70.04 (CH_2O), 70.48 (4C, CH_2O), 70.56 (CH_2O), 71.77 (CH_2O), 106.89 and 107.04 (C^3, C^6), 120.23 (C^5), 136.28 (C^4), 143.69 and 143.93 (C^1, C^2). Mass spectrum, m/z (I_{rel}, %): 526 (47) $[M]^+$, 511 (12), 284 (8), 240 (6), 207 (10), 199 (18), 196 (12), 181 (14), 165 (6), 155 (100). Found: m/z 526.1168 $[M]^+$. $C_{19}H_{31}IN_2O_7$. Calculated: M 526.1176.

16-Methyl-19-nitro-2,3,5,6,8,9,11,12,15,16-decahydro-14*H*-1,4,7,10,13,16-benzopentaoxazacyclooctadecine (Ia) was synthesized according to the

procedure described in [8], mp 43–45°C (oily substance according to [8]). Found, %: C 55.27; H 7.09; N 7.41. $C_{17}H_{26}N_2O_7$. Calculated, %: C 55.13; H 7.08; N 7.56.

Benzo aza crowns Ib–Id (*general procedures*). *a*. A mixture of 0.35 mmol of iodide **VIb–VId**, 15 ml of anhydrous THF, and 0.14 g (3.5 mmol) of 60% NaH in paraffin was heated for 1–8 h under reflux with stirring. After cooling, the mixture was diluted with water and treated with benzene. The extract was washed with water and evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using benzene–ethyl acetate (1:1) as eluent. Compounds **Ib–Id** were isolated as yellow oily substances (Table 1).

b. A mixture of 0.35 mmol of iodide **VIb** or **IVc** in 15 ml of anhydrous THF and 0.14 g (7.0 mmol) of 60% NaH in paraffin was stirred for 48 h at room temperature. The mixture was then treated as described above in *a*.

16-Ethyl-19-nitro-2,3,5,6,8,9,11,12,15,16-decahydro-14*H*-1,4,7,10,13,16-benzopentaoxazacyclooctadecine (Ib). Yield 40% (*a*). IR spectrum: ν 1497 cm^{-1} (NO_2). ^{1}H NMR spectrum, δ, ppm: 1.18 t (3H, Me, J = 7.1 Hz), 3.48 q (2H, CH_2N, J = 7.1 Hz), 3.63 m (10H, CH_2O, 15-H), 3.68 s (4H, CH_2O), 3.73 t (2H, 14-H, J = 5.5 Hz), 3.90 m (2H, 3-H), 4.17 m (2H, 2-H), 6.70 d (1H, 17-H, J = 8.9 Hz), 7.63 d (1H, 20-H, J = 2.4 Hz), 7.78 d.d (1H, 18-H, J = 8.9, 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.52 (Me), 47.47 (CH_2N), 54.04 (C^{15}), 68.26 (CH_2O), 69.47 (CH_2O), 70.41 (CH_2O), 70.78 (3C, CH_2O), 71.14 (CH_2O), 71.38 (CH_2O), 108.20 (C^{20}), 115.00 (C^{17}), 118.70 (C^{18}), 138.97 (C^{19}), 146.27 (C^{16a}), 148.65 (C^{20a}). Mass spectrum, *m*/*z* (I_{rel}, %): 384 (50) $[M]^+$, 369 (31), 182 (49), 167 (28), 135 (28), 115 (40), 89 (35), 78 (27), 73 (79), 71 (100). Found: *m*/*z* 384.1890 $[M]^+$. $C_{18}H_{28}N_2O_7$. Calculated: *M* 384.1897.

19-Nitro-16-propyl-2,3,5,6,8,9,11,12,15,16-decahydro-14*H*-1,4,7,10,13,16-benzopentaoxazacyclooctadecine (Ic). Yield 37% (*a*). IR spectrum: ν 1511 cm^{-1} (NO_2). ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, Me, J = 7.3 Hz), 1.62 m (2H, CH_2), 3.38 t (2H, CH_2N, J = 7.0 Hz), 3.63 s (8H, CH_2O), 3.63 s (8H, CH_2O), 3.66 m (2H, 15-H), 3.70 s (4H, CH_2O), 3.77 t (2H, 14-H, J = 5.3 Hz), 3.91 m (2H, 3-H), 4.20 m (2H, 2-H), 6.40 br.s (1H, 17-H), 7.54 br.s (1H, 20-H), 7.78 d.d (1H, 18-H, J = 8.9, 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.29 (Me), 20.14 (CH_2), 52.74 (C^{15}), 54.86 (CH_2N), 68.10 (C^2), 69.28 (C^3), 70.16 (C^{14}), 70.56 (3C, CH_2O), 70.69 (CH_2O), 70.94 (2C, CH_2O), 71.14 (CH_2O), 108.11 (C^{20}), 115.06 (C^{17}), 118.38 (C^{18}), 138.76 (C^{19}), 146.06 (C^{16a}), 148.48 (C^{20a}). Mass spectrum, *m*/*z* (I_{rel}, %): 398 (42) $[M]^+$, 397 (36), 370 (20), 369 (100), 339 (6), 281 (6), 209 (11), 193 (15), 179 (6), 147 (9). Found: *m*/*z* 398.2058 $[M]^+$. $C_{19}H_{20}N_2O_7$. Calculated: *M* 398.2053.

16-Benzyl-19-nitro-2,3,5,6,8,9,11,12,15,16-decahydro-14*H*-1,4,7,10,13,16-benzopentaoxazacyclooctadecine (Id). Yield 34% (*a*). IR spectrum: ν 1496 cm^{-1} (NO_2). ^{1}H NMR spectrum, δ, ppm: 3.61–3.66 m (6H, CH_2O), 3.68–3.75 m (8H, CH_2O, 15-H), 3.88 m (4H, CH_2O, 14-H), 4.23 m (2H, 2-H), 4.76 s (2H, C**H**$_2$Ph), 6.67 d (1H, 20-H, J = 9.0 Hz), 7.24 m (3H, *o*-H, *p*-H), 7.31 m (2H, *m*-H), 7.69 d (1H, 17-H, J = 2.4 Hz), 7.73 d.d (1H, 18-H, J = 9.0, 2.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 52.32 (C^{15}), 56.62 (**C**H_2Ph), 68.20 (C^2), 69.28 (C^3), 70.16 (CH_2O), 70.60 (CH_2O), 70.68 (CH_2O), 70.77 (CH_2O), 70.85 (CH_2O), 70.97 (CH_2O), 71.34 (CH_2O), 108.02 (C^{20}), 115.77 (C^{17}), 118.34 (C^{18}), 126.94 (C^o), 127.21 (C^m), 128.48 (C^p), 138.01 (C^i), 139.29 (C^{19}), 146.27 (C^{16a}), 148.56 (C^{20a}). Mass spectrum, *m*/*z* (I_{rel}, %): 446 (46) $[M]^+$, 445 (24), 415 (4), 257 (6), 193 (6), 147 (7), 106 (5), 91 (100), 89 (7), 73 (5). Found: *m*/*z* 446.2051 $[M]^+$. $C_{23}H_{30}N_2O_5$. Calculated: *M* 446.2053.

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REFERENCES

1. Krakowiak, K.E., Bradshaw, J.S., and Zamecka-Krakowiak, D.J., *Chem. Rev*., 1989, vol. 89, p. 929.
2. Bradshaw, J.S., Krakowiak, K.E., and Izatt, R.M., *Aza-Crown Macrocycles*, New York: Wiley, 1993.
3. Gromov, S.P., Dmitrieva, S.N., and Churakova, M.V., *Usp. Khim*., 2005, vol. 74, p. 503.
4. Gromov, S.P., Dmitrieva, S.N., Vedernikov, A.I., and Churakova, M.V., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2004, p. 1362.
5. Vedernikov, A.I., Dmitrieva, S.N., Kuz'mina, L.G., Kurchavov, N.A., Strelenko, Yu.A., Howard, J.A.K., and Gromov, S.P., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2009, p. 954.
6. Gromov, S.P., Dmitrieva, S.N., Vedernikov, A.I., Kuz'mina, L.G., Churakov, A.V., Strelenko, Yu.A., and Howard, J.A.K., *Eur. J. Org. Chem*., 2003, p. 3189.
7. Gromov, S.P., Dmitrieva, S.N., Vedernikov, A.I., Kurchavov, N.A., Kuz'mina, L.G., Strelenko, Y.A., Alfi-

mov, M.V., and Howard, J.A.K., *J. Phys. Org. Chem*., 2009, vol. 22, p. 823.

8. Gromov, S.P., Dmitrieva, S.N., and Churakova, M.V., *Synthesis*, 2003, p. 593.
9. Dmitrieva, S.N., Churakova, M.V., Kurchavov, N.A., Vedernikov, A.I., Kuz'mina, L.G., Freidzon, A.Ya., Bagatur'yants, A.A., Strelenko, Yu.A., Howard, J.A.K., and Gromov, S.P., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2010, p. 1167.
10. Gromov, S.P., Dmitrieva, S.N., and Krasnovskii, V.E., *Izv. Ross. Akad. Nauk, Ser. Khim*., 1997, p. 540.
11. Gromov, S.P. and Dmitrieva, S.N., *Izv. Ross. Akad. Nauk, Ser. Khim*., 1999, p. 542.
12. Gromov, S.P., Dmitrieva, S.N., Churakova, M.V., and Turchanov, A.Yu., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2002, p. 1232.
13. Gromov, S.P., Dmitrieva, S.N., Churakova, M.V., Vedernikov, A.I., Kurchavov, N.A., Kuz'mina, L.G., Kataeva, N.A., and Howard, J.A.K., *Russ. J. Org. Chem*., 2004, vol. 40, p. 1200.
14. Sibert, J.W., Forshee, P.B., Hundt, G.R., Sargent, A.L., Bott, S.G., and Lynch, V., *Inorg. Chem*., 2007, vol. 46, p. 10913.
15. Frassineti, C., Ghelli, S., Gans, P., Sabatini, A., Moruzzi, M.S., and Vacca, A., *Anal. Biochem*., 1995, vol. 231, p. 374.
16. Freidzon, A.Ya., Bagatur'yants, A.A., Gromov, S.P., and Alfimov, M.V., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2003, p. 2505.
17. Freidzon, A.Ya., Bagatur'yants, A.A., Gromov, S.P., and Alfimov, M.V., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2005, p. 1981.
18. Freidzon, A.Ya., Bagatur'yants, A.A., and Alfimov, M.V., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2007, p. 395.
19. Freidzon, A.Ya., Bagatur'yants, A.A., Gromov, S.P., and Alfimov, M.V., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2008, p. 2009.
20. Bagatur'yants, A.A., Freidzon, A.Ya., Alfimov, M.V., Baerends, E.J., Howard, J.A.K., and Kuz'mina, L.G., *J. Mol. Struct. (Theochem)*, 2002, vol. 588, p. 55.
21. Freidzon, A.Ya., Bagatur'yants, A.A., Gromov, S.P., and Alfimov, M.V., *Int. J. Quantum Chem*., 2004, vol. 100, p. 617.
22. Freidzon, A.Ya., Vladimirova, K.G., Bagatur'yants, A.A., Gromov, S.P., and Alfimov, M.V., *J. Mol. Struct. (Theochem)*, 2007, vol. 809, p. 61.
23. Freidzon, A.Ya., Bagatur'yants, A.A., Ushakov, E.N., Gromov, S.P., and Alfimov, M.V., *Int. J. Quantum Chem*., 2011, vol. 111, p. 2649.
24. Derome, A.E., *Modern NMR Techniques for Chemistry Research*, Oxford: Pergamon, 1987.
25. Perdew, J.P., Burke, K., and Ernzerhof, M., *Phys. Rev. Lett*., 1996, vol. 77, p. 3865.
26. Laikov, D.N., *Chem. Phys. Lett*., 1997, vol. 281, p. 151.
27. Laikov, D.N. and Ustynyuk, Yu.A., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2005, p. 804.