Synthesis of azacrown ethers and benzocryptands by macrocyclization of podands at high concentrations of reactants

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The reactions of 1,2-bis(2-Y-ethoxy)benzenes, *N*,*N*-bis(2-Y-ethyl)-*N*-phenylamines, or 2,6-bis(Y-methyl)pyridines (Y = I, Br, or OTs) with α,ω-polyoxaalkanediamines or diazacrown ethers in the presence or absence of alkali carbonates in a concentrated acetonitrile solution of the reactants afforded the corresponding azacrown ethers or cryptands in high yields.

Key words: macrocyclization of azapolyethers, diamines, alkali carbonates, azacrown ethers, cryptands, crown compounds.

The replacement of oxygen atoms in macroheterocyclic crown ether compounds by nitrogen atoms affords complexes capable of being coordinated to different types of metal cations (alkali, alkaline earth, heavy, and transition),[1—7] due to which this class of ligands has attracted interest.[8—12] Macrocyclic azapolyethers can be derivatized at the nitrogen atom, with the result that they can be used as intermediates in the synthesis of ion-selective dyes,[13—17] biologically active compounds,[17—19] bicyclic analogs, and polymer-bound reagents.[20,21]

There are various methods for the synthesis of azamacroheterocyclic compounds.[22—30] Nevertheless, the development of new facile methods for the synthesis of benzoazacrown compounds, particularly, of functionalized derivatives, is an important problem.

Earlier,[31] we have developed a method for the synthesis of formyl derivatives of benzodiazacrown ethers and benzocryptands based on the condensation of 3,4-bis(2-iodoethoxy)benzaldehyde with α,ω-polyoxaalkanediamines and diazacrown ethers in the presence of alkali metal carbonates at high dilutions in different organic solvents and their mixtures with water. However, the reactions of unsubstituted terminal diamines with diazacrown ethers are accompanied by partial resinification of the starting reactants and, consequently, the purification of the reaction products presents considerable difficulties.

With the aim of preventing resinification and extending the range of the reactants, in the present study we developed a procedure for the synthesis of derivatives of benzoazacrown compounds by the condensation of acyclic precursors under mild conditions. The main difference between this method and the method described earlier[31] is that the reaction is performed at room temperature (as opposed to the refluxing of the starting compounds in acetonitrile) and in a concentrated acetonitrile solution of the reactants (as opposed to the high dilution technique used in the method developed earlier[31]). The formation of azamacrocyclic compounds can occur even in the absence of alkali carbonates, which has not been observed earlier in the syntheses of azacrown ethers. The advantages of the new method are that the reaction products are formed in good or high yields and are characterized by higher purity.

We studied the condensation of substituted 1,2-bis(2-iodoethoxy)benzenes **1a**,**b** and related dielectrophiles designed on diethylphenylamine **1c**,**d** and 2,6-lutidine **1e**,**f** with diamines **2a**—**f** and diazacrown ethers **2g**,**h** and **3d** in the presence of alkali carbonates (Scheme 1).

The condensation occurs with linear dielectrophiles **1a**—**f** and dinucleophiles **2a**—**h** or **3d** in a concentrated acetonitrile solution at room temperature within 70—75 h (in the presence of alkali carbonates) or 250—300 h (in their absence) with TLC monitoring until the reactants were completely consumed. To study the substrate dependence, the reactions were carried out under the same conditions (the reaction time, the temperature, and the concentrations of the reactants). In particular, the presence of the formyl group in the starting compound **1b** has no substantial effect on the macrocyclization outcome.

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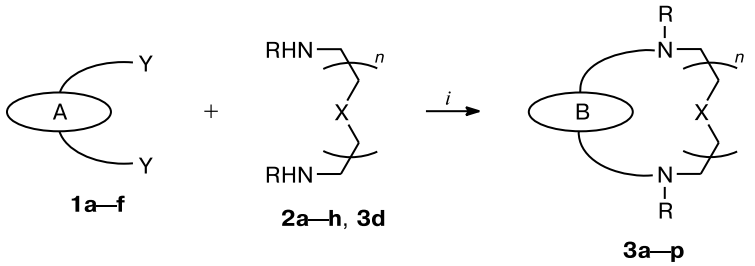
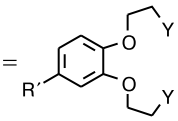
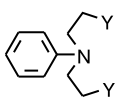
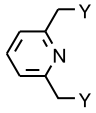
Scheme 1



i. M_2CO_3 or without the salt, MeCN.

1: A =  (**a**, **b**),  (**c**, **d**),  (**e**, **f**) M = Na, K

R′ = H (**a**), CHO (**b**)
Y = I (**a**, **b**, **d**), OTs (**c**, **e**), Br (**f**)

2: X = O (**a**—**c**, **e**, **g**, **h**), $CH_2(NMe)CH_2$ (**d**), NH (**f**);
R = H (**b**, **c**, **d**, **f**), Me (**a**, **e**);
R—R = $CH_2(CH_2OCH_2)_2CH_2$ (**g**, **h**); *n* = 1 (**a**, **b**, **d**, **g**), 2 (**c**, **e**, **f**, **h**)

3	B	R or R—R	R′	X	*n*
a		Me	H	O	1
b		H	H	O	1
c		Me	H	O	2
d		H	H	O	2
e		$CH_2(CH_2OCH_2)_2CH_2$	H	O	1
f		$CH_2(CH_2OCH_2)_2CH_2$	H	O	2
g		H	H	NH	2
h		H	H	$CH_2(NMe)CH_2$	1
i		Me	CHO	O	1
j		Me	CHO	O	2
k		$CH_2(CH_2OCH_2)_2CH_2$	CHO	O	1
l		$CH_2(CH_2OCH_2)_2CH_2$	CHO	O	2

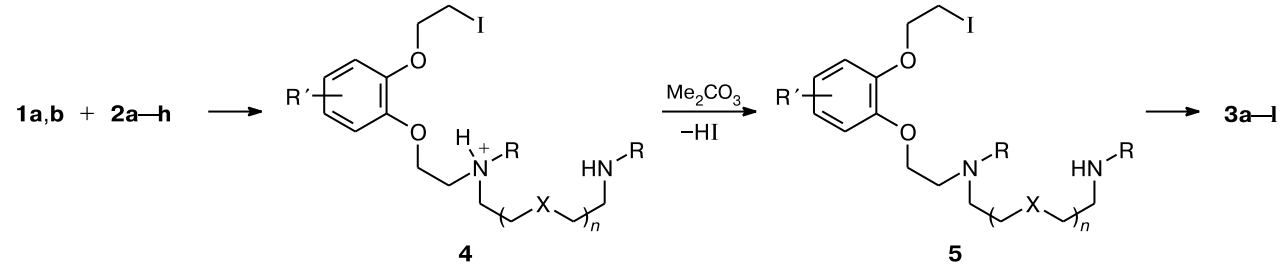
3	B	R or R—R	R′	X	*n*
m		Me	—	O	1
n		Me	—	O	1
o		Me	—	O	2
p		1,2-$C_6H_4(OCH_2CH_2)_2$	—	O	2

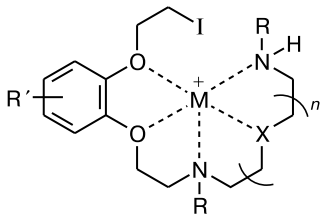
The reaction in the absence of the bases occurs slowly (~280 h), but the yields of the corresponding benzodiazacrown compounds vary from good to high (Table 1). The addition of alkali carbonates makes it possible to reduce the reaction time to 75 h. Apparently, the formation of azacrown compounds **3a**—**l** occurs in several steps (Scheme 2).

The *N*-alkylation of compounds **2a**—**h** with **1a**,**b** affords ammonium derivative **4**, whose deprotonation gives aza podand **5**. The final step involves the cyclization of the aza podand to form macrocycles **3a**—**l**. In the reactions in the presence of alkali carbonates, the metal cations are involved in the formation of intermediate template complex **6** (see Ref. 31).

In the absence of carbonates, the starting diamine can serve as a base. This is confirmed by the fact that diamine hydroiodide **2a** was isolated from the reaction mixture. Compound **2a** was characterized by X-ray diffraction

Scheme 2





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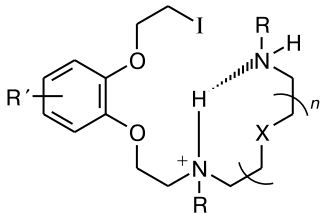

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(Fig. 1). Apparently, the cyclization of aza podand **4** to the macrocycle occurs through the formation of a complex having structure **7**, in which a proton is coordinated to the terminal amino group. On the one hand, the formation of this complex facilitates the intramolecular cyclization as a result of the rearrangement of the podand to the pseudomacrocycle and the location of the terminal reacting groups in close proximity to each other. On the other hand, this coordination should hinder the final step of the reaction, *viz.*, the alkylation of the terminal amino group, which is manifested in the longer reaction time.

The formation of the azamacrocyclic compound that occurs with the involvement of the hydrogen bond between the hydrogen atom of the terminal group and the nitrogen atom of the podand was documented.[32] It was noted[32] that the yield of the macrocyclization product in the absence of alkali carbonates was higher.

The yields of benzodiaza-15-crown-5 compounds **3a**,**b**, benzodiaza-17-crown-5 compound **3h**, and benzodiaza-18-crown-6 compounds **3c**,**d**,**j** are relatively high (see Table 1). The reaction with tetramine **2f** affords the target product **3g** in low yield, which is apparently attributed to the possible reaction at any of the nitrogen atoms of the tetramine chain and the formation of a wide range of products (see Table 1).

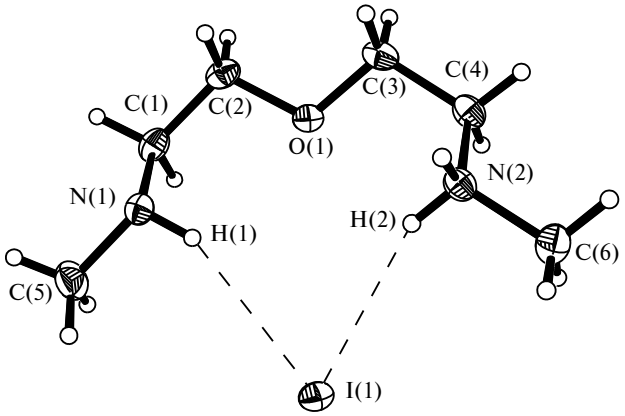

Fig. 1. Structure of the asymmetric unit in the crystal structure of salt **2a**.

Table 1. Reaction conditions and yields of crown compounds **3a**—**p**

Crown-compound	Starting dinucleophile	Reaction time/h	Base	Yield (%)
3a	**1a**	280	—	74
	1a	75	K_2CO_3	79
3b	**1a**	280	—	58
	1a	75	K_2CO_3	76
3c	**1a**	280	—	76
	1a	75	K_2CO_3	80
3d	**1a**	280	—	56
	1a	75	Na_2CO_3	72
	1a	75	K_2CO_3	77
3e	**1a**	280	—	63
3f	**1a**	280	—	69
3g	**1a**	280	—	10
	1a	75	K_2CO_3	28
3h	**1a**	280	—	54
	1a	75	K_2CO_3	73
3i	**1b**	280	—	73
	1b	75	Na_2CO_3	83
	1b	75	K_2CO_3	77
3j	**1b**	280	—	71
	1b	75	Na_2CO_3	86
3k	**1b**	280	—	80
	1b	75	Na_2CO_3	26
3l	**1b**	280	—	40
	1b	75	Na_2CO_3	24
3m	**1c**	280	—	78*
	1c	75	K_2CO_3	77*
	1d	280	—	Traces
	1d	75	K_2CO_3	7
3n	**1e**	280	—	Traces
	1e	75	K_2CO_3	18
	1f	280	—	Traces
	1f	75	K_2CO_3	22
3o	**1f**	75	K_2CO_3	53
3p	**1f**	75	Na_2CO_3	41

* The yield is given based on the azacrown ether.

It was shown by an example of benzocryptands **3k**,**l** that the reaction performed in the presence of sodium carbonate gives the product in lower yield compared to the reaction in the absence of the base (see Table 1). Apparently, the reaction producing cryptands is accompanied by the strong binding of the alkali metal cation to the starting diazacrown ether through coordination to the nitrogen and oxygen atoms. This leads to a reduction of the nucleophilicity of the nitrogen atoms and a decrease in the activity in the reactions with dihalides.

In the case of phenylazacrown ether **3m**, the reaction occurs only with the use of *N*,*N*-bis[2-(*p*-toluenesulfonyloxy)ethyl]-*N*-phenylamine (**1c**) as the starting compound, whereas the corresponding diiodide **1d** proved to be insufficiently active (see Table 1).

The condensation of 1,5-bis(methylamino)-3-oxapentane (**2a**) with 2,6-pyridinedimethanol ditosylate (**1e**) or 2,6-bis(bromomethyl)pyridine (**1f**) was accompanied by substantial resinification of the reaction mixture, and, consequently, the target product **3n** was obtained in low yield. The reactions with larger diamino compounds **2e** and **3d** gave target products **3o**,**p** in higher yields (see Table 1).

Compounds **3a**—**p** were characterized by physicochemical methods. The physicochemical characteristics of formyl derivatives **3i**—**l** have been described in our earlier study.[31]

Compound **2a** is diamine hydroiodide (see Fig. 1). Both nitrogen atoms have a tetrahedral bond configuration, but one of the nitrogen atoms, N(2), is protonated and bears a positive charge. Both nitrogen atoms form a N—H...I hydrogen bond with the iodide anion. The hydrogen bond with the positively charged nitrogen atom is somewhat shorter. The I(1)...N(1), I(1)...N(2) and I(1)...H(1), I(1)...H(2) distances are 3.663(1), 3.602(1) and 2.86(2), 2.78(2) Å, respectively. The angles at the H(1) and H(2) atoms are 157(2) and 156(2)°, respectively.

The central C(1)—C(2)—O(1)—C(3)—C(4) fragment of the cation is almost planar, and the nitrogen atoms are located on the same side of the plane. The N(1)—C(1)—C(2)—O(1) and N(2)—C(4)—C(3)—O(1) torsion angles are almost equal in magnitude (60.7 and −58.6°, respectively).

These anions are linked into centrosymmetric dimers by two N—H...N hydrogen bonds with the participation of the second hydrogen atom at the protonated nitrogen atom.

In the crystal structure, two complexes are linked into centrosymmetric dimers by the N(2)—H...N(1) hydrogen bond with the participation of the second proton at the nitrogen atom N(2) (Fig. 2). The geometric parameters of this bond are as follows: the N(2A)...N(1B) and H(22A)...N(1B) distances are 2.762(2) and 1.84(3) Å, respectively, the N(2A)—H(22)...N(1B) angle is 172(2)°.

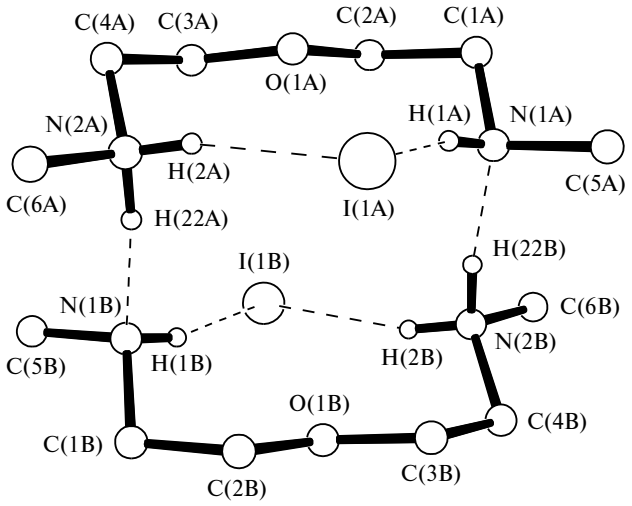

Fig. 2. Structure of the dimer formed by N—H...N hydrogen bonds.

The components of the asymmetric unit in the crystal structure of Na complex **3´k** containing ligand molecule **3k** are presented in Fig. 3. The crystal contains the ligand coordinated to the Na^+ cation by all heteroatoms, the iodide anion disordered over two closely spaced sites I(1)

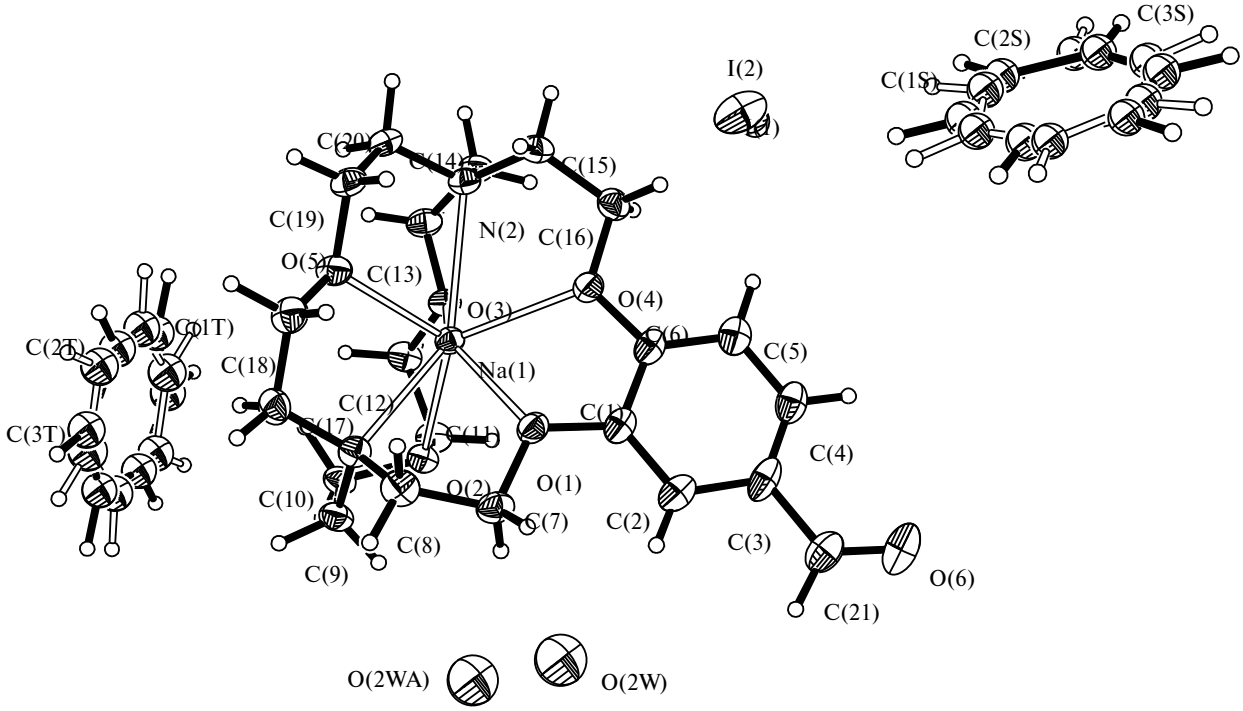

Fig. 3. Crystal structure of cryptand complex **3´k**.

and I(2), two benzene solvent molecules occupying centers of symmetry, and a water molecule disordered over two sites (O(2W) and O(2WA)). Each benzene molecule is also disordered over two sites.

The Na^+ cation is seven-coordinated and is located in the cavity of the cryptand. The distances from the cation to the heteroatoms O(1), O(2), O(3), O(4), O(5), N(1), and N(2) are 2.460(2), 2.496(2), 2.453(2), 2.458(2), 2.352(2), 2.596(2), and 2.616(2) Å, respectively, and are in usual ranges. As a result, the sodium cation is somewhat more distant from the nitrogen atoms.

To sum up, we developed a convenient procedure for the preparation of azacrown compounds and benzocryptands under mild conditions at room temperature, suitable for reactants with different oxygen and nitrogen content. This method holds the most promise for the synthesis of azacrown ethers conjugated with complex molecules, since under mild conditions of the condensation, the moiety of the complex molecule would remain intact. The method provides an approach to the synthesis of optical chelating agents, catalytic systems based on organometallic complexes, and extractants for the selective extraction of metal salts.

Experimental

Commercial 1,2-bis(2-hydroxyethoxy)benzene, 2,2′-(ethylenedioxy)bis(ethylamine), 4,13-diaza-18-crown-6 ether, anhydrous acetonitrile, anhydrous sodium and potassium carbonates (Aldrich), anhydrous sodium iodide (Aldrich), 1,8-bis(methylamino)-3,6-dioxaoctane, 1,5-bis(methylamino)-3-oxapentane, and 1,7-diaza-15-crown-5 ether (Janssen) were used as purchased. 1,2-Bis(2-iodoethoxy)benzene (**1a**), 3,4-bis(2-iodoethoxy)benzaldehyde (**1b**),[31,33] *N*,*N*-bis[2-(*p*-toluenesulfonyloxy)ethyl]-*N*-phenylamine (**1c**),[34] *N*,*N*-bis(2-iodoethyl)-*N*-phenylamine (**1d**),[35] 2,6-pyridinedimethanol ditosylate (**1e**),[36] and 2,6-bis(bromomethyl)pyridine (**1f**)[37] were synthesized according to known procedures. The reagents and solvents used for the synthesis were purchased from Fluka, Merck, and Aldrich. The staring compounds and solvents were not purified before use.

The ^{1}H NMR spectra were recorded on a Bruker DRX-400 spectrometer (operating at 400.13 MHz) using $CDCl_3$, DMSO-d_6, and CD_3CN as the solvents and the residual protons of the deuterated solvent as the internal standard. The chemical shifts and the spin-spin coupling constants were measured with an accuracy of 0.01 ppm and 0.1 Hz, respectively. The electron-impact mass-spectrometric analysis was performed on a Finnigan MAT 311S instrument (the ionizing electron energy was 70 eV) equipped with a quartz capillary column (L = 60 m, d = 0.25 mm) coated with the DB-1 stationary phase in the temperature-programmed mode; helium was used as the carrier gas. The elemental analysis was performed at the Laboratory of Microanalysis of the A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences (Moscow). The melting points (uncorrected) were measured on a Mel-temp II instrument. The TLC monitoring was carried out on DC-Alufolien Kieselgel 60 F_{254} and DC-Alufolien Aluminiumoxid 60 F_{254} neutral (Typ E) plates. The column chromatography was performed with the use of Kieselgel 60 (0.0063—0.100 mm), Kieselgel 60 (0.0063—0.200 mm), Aluminium oxide 150 basic (type T) (0.0063—0.200 mm), Aluminium oxide 90 active, neutral (activity 1) (0.0063—0.200 mm), and HPTLC-Alufolien Cellulose (Merck).

Benzoazacrown compounds 3a—d,g—j,m and benzocryptands 3e,f,k,n—p (general procedure). ***A. Synthesis in the presence of K_2CO_3 (Na_2CO_3).*** Compound **2a—h** or **3d** (0.23 mmol) was added with stirring to a mixture of dielectrophile **1a—f** (0.23 mmol), K_2CO_3 (Na_2CO_3) (1.15 mmol), and MeCN (3 mL). The reaction mixture was then kept without stirring at ~20 °C for 75 h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane (3×20 mL) and washed with water. The extract was concentrated *in vacuo*. The product was extracted with boiling hexane. Cryptands **3k**,**l** were washed off from the starting compound **1b** with benzene and then recrystallized from an acetonitrile—benzene system. The yields of the compounds are given in Table 1.

B. Synthesis in the absence of bases. Diamino compound **2a—h** (0.05 mL, 0.25 mmol) was added with stirring to a solution of dielectrophile **1a—f** (0.23 mmol) in MeCN (3 mL). The reaction mixture was kept without stirring at ~20 °C for 280 h. The solvent was evaporated *in vacuo*. The residue was extracted with dichloromethane (3×20 mL) and then washed with a 3% K_2CO_3 solution (20 mL) and water. The extract was concentrated *in vacuo*. The product was extracted with boiling hexane. Cryptands **3k**,**l** were washed off from the starting compound **1b** with benzene and then recrystallized from an acetonitrile—benzene system. The yields of the products are given in Table 1.

1,10-Dimethyl-1,7,13,4,10-benzotrioxadiazacyclopentadecene (3a), yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.24 (s, 6 H, 2 NMe); 2.59 (m, 4 H, 2 CH_2N); 2.74 (m, 4 H, 2 CH_2N); 3.57 (m, 4 H, 2 CH_2O); 3.96 (m, 4 H, 2 CH_2O); 6.85 (m, 2 H, H(1)); 6.92 (m, 2 H, H(2)). The ^{1}H NMR spectrum is consistent with the published data.[24]

1,7,13,4,10-Benzotrioxadiazacyclopentadecene (3b) was obtained as a powder, m.p. 97—100 °C. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.72 (s, 2 H, 2 NH); 2.87 (t, 4 H, 2 CH_2N, J = 5.0 Hz); 3.02 (t, 4 H, 2 CH_2N, J = 5.0 Hz); 3.63 (t, 4 H, 2 CH_2O, J = 5.0 Hz); 4.11 (t, 4 H, 2 CH_2O, J = 5.0 Hz); 6.88 (s, 4 H, Ar). The physicochemical parameters are consistent with the published data.[26]

4,13-Dimethyl-1,7,10,16,4,13-benzotetraoxadiazacyclooctadecene (3c), yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.37 (s, 6 H, NMe); 2,82 (t, 4 H, CH_2N, J = 5.68 Hz); 3.00 (t, 4 H, CH_2N, J = 5.86 Hz); 3.60 (s, CH_2O); 3.66 (m, 4 H, CH_2O, J = 5.68 Hz); 4.08 (t, 4 H, CH_2O, J = 5.86 Hz); 6.87 (m, 4 H, 2 H(1), 2 H(2)). The ^{1}H NMR spectrum is consistent with the published data.[24]

1,7,10,16,4,13-Benzotetraoxadiazacyclooctadecene (3d) was obtained as a powder, m.p. 86—92 °C. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.62 (s, 2 H, 2 NH); 2.87 (t, 4 H, 2 CH_2N, J = 4.8 Hz); 3.06 (t, 4 H, 2 CH_2N, J = 4.6 Hz); 3.61 (s, 4 H, 2 CH_2O); 3.67 (t, 4 H, 2 CH_2O, J = 4.8 Hz); 4.13 (t, 4 H, 2 CH_2O, J = 4.6 Hz); 6.88 (s, 4 H, Ar). The physicochemical parameters are consistent with the published data.[26]

8-Methyl-1,15,4,8,12-benzodioxatriazacycloheptadecene (3h), viscous pale-yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 1.64 (m, 4 H, CH_2); 2.12 (s, 3 H, NMe); 2.30 (t, 4 H, 2 CH_2N, J = 6.06 Hz); 2.81 (t, 4 H, 2 CH_2N, J = 6.06 Hz); 3.03 (t, 4 H, 2 CH_2N, J = 4.50 Hz); 4.08 (t, 4 H, 2 CH_2O, J = 4.50 Hz); 6.88 (m, 4 H, 2 H(1), 2 H(2)). ^{13}C NMR ($CDCl_3$), 25 °C, δ: 26.6,

40.8, 47.3, 48.8, 55.7, 68.9, 113.3, 120.9, 148.7. Electrospray-ionization mass spectrum (ESI-MS): m/z 308 $[MH]^+$. Found (%): C, 66.48; H, 9.55. $C_{17}H_{29}N_3O_2$. Calculated (%): C, 66.42; H, 9.51.

4,11,17,20,25-Pentaoxa-1,14-diazatricyclo[12.8.5.0^{5,10}]-heptacosa-5,7,9-triene (3e) was obtained as a powder, m.p. 74—75 °C. ^{1}H NMR (CD_3CN), 25 °C, δ: 2.46—3.06 (m, 12 H, CH_2); 3.44—4.18 (m, 16 H, CH_2); 6.90 (s, 4 H, 2 H(1), 2 H(2)). The physicochemical parameters are consistent with the published data.[30]

4,11,17,20,25,28-Hexaoxa-1,14-diazatricyclo[12.8.8.0^{5,10}]-triaconta-5,7,9-triene (3f) was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.6—3.1 (m, 12 H, NCH_2); 3.3—3.8 (m, 16 H, OCH_2); 4.1 (m, 4 H, $ArOCH_2$); 7.2 (m, 4 H, 2 H(1), 2 H(2)). The ^{1}H NMR spectrum is consistent with the published data.[29]

1,16,4,7,10,13-Benzodioxatetraazacyclooctadecene (3g), viscous yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.63—3.01 (m, 16 H, 2 CH_2N); 4.05—4.11 (m, 4 H, 2 CH_2O); 6.87 (m, 4 H, H(1), H(2)). ^{13}C NMR ($CDCl_3$), δ: 47.6, 49.1, 55.8, 69.1, 112.3, 120.6, 148.2. ESI-MS, m/z: 309 $[MH]^+$. Found (%): C, 62.42; H, 9.10. $C_{16}H_{28}N_4O_2$. Calculated (%): C, 62.31; H, 9.15.

4,10-Dimethyl-1,7,13,4,10-benzotrioxadiazacyclopentadecene-15-carbaldehyde (3i), yellowish powder, m.p. 70—73 °C (heptane). ^{1}H NMR (CD_3CN), 30 °C, δ: 2.29 (s, 6 H, 2 NMe); 2.64 (t, 4 H, C(5)H_2N, C(9)H_2N, J = 5.6 Hz); 2.82 (m, 4 H, C(3)H_2N, C(11)H_2N); 3.62 (m, 4 H, C(6)H_2O, C(8)H_2O); 4.08 (m, 2 H, C(12)H_2O); 4.11 (m, 2 H, C(2)H_2O); 7.06 (d, 1 H, H(17), J = 8.3 Hz); 7.32 (d, 1 H, H(14), J = 1.7 Hz); 7.49 (dd, 1 H, H(16), J = 8.3 Hz, J = 1.7 Hz); 9.83 (s, 1 H, CH=O). The physicochemical parameters are consistent with the published data.[31]

4,13-Dimethyl-1,7,10,16,4,13-benzotetraoxadiazacyclooctadecene-18-carbaldehyde (3j), yellow oil. ^{1}H NMR (CD_3CN), 25 °C, δ: 2.85 (m, 4 H, C(5)H_2N, C(12)H_2N); 3.05 (m, 4 H, C(3)H_2N, C(14)H_2N); 3.57 (s, 4 H, C(8)H_2O, C(9)H_2O); 3.59 (m, 4 H, C(6)H_2O, C(11)H_2O); 4.19, 4.22 (2 m, 4 H, C(2)H_2O, C(15)H_2O); 7.13 (d, 1 H, H(20), J = 8.3 Hz); 7.43 (d, 1 H, H(17), J = 1.9 Hz); 7.43 (dd, 1 H, H(19), J = 8.3 Hz, J = 1.9 Hz); 9.84 (s, 1 H, CH=O). The ^{1}H NMR spectrum is consistent with the published data.[31]

4,11,17,20,25-Pentaoxa-1,14-diazatricyclo[12.8.5.0^{5,10}]-heptacosa-5,7,9-triene-7-carbaldehyde (3k), yellow crystals, m.p. 255—257 °C (with decomp.). ^{1}H NMR (DMSO-d_6), 30 °C, δ: 2.34 (m, 4 H, 2 CH_2N); 2.98 (m, 4 H, 2 CH_2N); 3.15 (m, 2 H, CH_2N); 3.28 (m, 2 H, CH_2N); 3.42 (m, 4 H, 2 CH_2O); 3.55 (s, 4 H, 2 CH_2O); 3.68 (m, 4 H, 2 CH_2O); 4.18 (m, 4 H, 2 C$\underline{H}_2$OAr); 7.24 (d, 1 H, H(9), J = 8.3 Hz); 7.45 (d, 1 H, H(6), J = 1.7 Hz); 7.62 (dd, 1 H, H(8), J = 8.3 Hz, J = 1.7 Hz); 9.88 (s, 1 H, CH=O). The physicochemical parameters are consistent with the published data.[31]

Complex **3k** with the Na cation (**3´k**) was synthesized according to the method ***A*** and was used for the X-ray diffraction study.

4,11,17,20,25,28-Hexaoxa-1,14-diazatricyclo[12.8.8.0^{5,10}]-triaconta-5,7,9-triene-7-carbaldehyde (3l), yellow powder, m.p. 134—138 °C (MeOH—Et_2O). ^{1}H NMR (DMSO-d_6), 25 °C, δ: 2.55—2.70 (m, 8 H, 4 CH_2N); 2.76 (m, 4 H, 2 CH_2N); 3.49 (m, 8 H, 4 CH_2O); 3.57 (s, 8 H, 4 CH_2O); 4.26 (m, 2 H, C$\underline{H}_2$OAr); 4.30 (m, 2 H, C$\underline{H}_2$OAr); 7.32 (d, 1 H, H(9), J = 7.9 Hz); 7.51 (s, 1 H, H(6)); 7.60 (d, 1 H, H(8), J = 7.9 Hz); 9.87 (s, 1 H, CH=O). The physicochemical parameters are consistent with the published data.[31]

Complex of 4,10-dimethyl-7-phenyl-1-oxa-4,7,10-triazacyclododecane with 4-methylbenzenesulfonic acid (3m), white crystals, m.p. 134—138 °C. ^{1}H NMR (DMSO-d_6), 30 °C, δ: 2.29 (s, 3 H, Me_{Ts}); 2.60 (s, 1 H, MeN); 3.12 (t, 2 H, H_δ, J = 0.01 Hz); 3.20 (s, 6 H, 2 MeN); 3.46 (m, 2 H, H_β); 3.56 (m, 2 H, $H_{\beta'}$); 3.59 (m, 4 H, 2 H_α, 2 $H_{\alpha'}$); 3.70 (m, 2 H, $H_{\delta'}$); 3.75 (m, 2 H, $H_{\gamma'}$); 3.92 (m, 2 H, H_γ); 6.88 (t, 1 H, H(4), J = 7.32 Hz); 7.01 (dd, 2 H, H(2), H(6), J = 3.8 Hz, J = 8.0 Hz); 7.11 (d, 2 H, CH_{Ts}, J = 7.9 Hz, J = 7.3 Hz); 7.29 (t, 2 H, H(3), H(5), J = 7.9 Hz); 7.48 (d, 2 H, CH_{Ts}, J = 7.9 Hz). ESI-MS, m/z: 278 $[MH]^+$. Found (%): C, 61.49; H, 7.84; N, 9.57. $C_{23}H_{35}N_3O_4S$. Calculated (%): C, 61.44; H, 7.85; N, 9.35.

3,9-Dimethyl-6-oxa-3,9,15-triazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (3n), viscous pale-yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.26 (s, 6 H, 2 NMe); 2.62 (m, 4 H, 2 CH_2N); 3.54 (m, 4 H, 2 CH_2N); 3.65 (s, 4 H, 2 CH_2); 7.25 (m, 2 H, H(3´)); 7.55 (m, 2 H, H(4´)). ^{13}C NMR ($CDCl_3$), 25 °C: 46.3, 57.1, 64.3, 69.3, 121.7, 137.1, 158.7. ESI-MS, m/z: 236 $[MH]^+$. Found (%): C, 66.74; H, 9.09. $C_{13}H_{21}N_3O$. Calculated (%): C, 66.35; H, 8.99.

3,12-Dimethyl-6,9-dioxa-3,12,18-triazabicyclo[12.3.1]-octadeca-1(18),14,16-triene (3o), viscous yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 2.47 (s, 6 H, 2 NMe); 2.62 (t, 4 H, 2 CH_2N, J = 6.06 Hz); 3.49 (s, 4 H, CH_2O); 3.61—3.58 (m, 4 H, CH_2O); 3.70 (s, 4 H, 2 CH_2); 7.17 (d, 2 H, H(3´), J = 7.63 Hz); 7.58 (t, 1 H, H(4´), J = 7.63 Hz). ^{13}C NMR ($CDCl_3$), 25 °C, δ: 44.9, 55.7, 64.0, 68.3, 70.3, 122.4, 136.3, 158.2. ESI-MS, m/z: 280 $[MH]^+$. Found (%): C, 65.03; H, 8.91. $C_{15}H_{25}N_3O_2$. Calculated (%): C, 64.49; H, 9.02.

4,11,17,20-Tetraoxa-1,14,29-triazatetracyclo-[12.8.7.1^{24,28}.0^{5,10}]nonacosa-5,7,9,24,26,28-hexaene (3p), viscous yellow oil. ^{1}H NMR ($CDCl_3$), 25 °C, δ: 3.00 (m, 4 H, CH_2N); 3.15 (m, 4 H, C(3)H_2N, C(14)H_2N); 3.65—3.80 (m, 12 H, C(6)H_2O, C(11)H_2O, C(8)H_2O, C(9)H_2O, 2 CH_2, Py); 3.95—4.05 (m, 4 H, 2 CH_2O); 7.00 (m, 4 H, Ar, 2 H(1), 2 H(2)); 7.29 (d, 2 H, Py, H(3´), J = 7.60 Hz); 7.77 (t, 1 H, Py, H(4´), J = 7.60 Hz). ^{13}C NMR ($CDCl_3$), 25 °C, δ: 52.0, 53.3, 59.3, 64.4, 67.0, 69.0, 112.9, 122.3, 122.6, 138.5, 146.8, 158.4. ESI-MS, m/z: 415 $[MH]^+$. Found (%): C, 65.21; H, 6.73. $C_{23}H_{31}N_3O_4$. Calculated (%): C, 66.81; H, 7.56.

Crystallographic characteristics and the X-ray data collection and structure refinement statistics for compounds 2a and 3´k. Single crystals of compounds **2a** and **3´k** coated with perfluorinated oil were mounted on a Bruker SMART CCD diffractometer under a cold nitrogen stream at 120 K. The experimental X-ray data were measured using graphite-monochromated Mo radiation and the ω-scanning technique. The experimental reflections were processed with the use of the Bruker SAINT software.[38] Absorption corrections were applied with the use of the SADABS program based on the intensities of equivalent reflections. The structures were solved by direct methods and refined by the full-matrix least-squares method based on F^2.

For compound **2a**, all hydrogen atoms were located in difference electron density maps. It was found that the N(2) atom bears two hydrogen atoms, whereas one hydrogen atom is attahced to the N(1) atom. The structure was finally refined by the least-squares method with anisotropic displacement parameters for all nonhydrogen atoms. The hydrogen atoms were refined isotropically.

The structure solution and refinement of **3´k** showed that the iodide anion occupies two closely spaced sites with almost

Table 2. Crystallographic characteristics and the X-ray data collection and structure refinement statistics for compounds **2a** and **3´k**

Parameter	**2a**	**3´k**
Molecular formula	$C_6H_{17}IN_2O$	$C_{27}H_{38}IN_2\ NaO_{6.2}$
M	260.12	639.68
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/n$	$P\bar{1}$
Z	4	2
a/Å	7.9301(16)	10.1009(2)
b/Å	16.014(3)	11.7577(3)
c/Å	8.5499(17)	13.1584(3)
α/deg	90	99.065(1)
β/deg	103.69(3)	109.0710(1)
γ/deg	90	95.669(1)
V/Å^3	1054.9(4)	1439.49(6)
d_{calc}/g cm^{-3}	1.638	1.476
F(000)	512	655
μ(Mo-Kα)/mm^{-1}	2.989	1.170
Crystal dimensions/mm	0.40×0.26×0.20	0.20×0.10×0.04
Absorption correction	multu-scan	multu-scan
Transmission coefficient, min/max	0.3811/0.5863	0.6138/1.0000
T/K	120.0(2)	120.0(2)
Radiation (λ/Å)	Mo-Kα (0.71073)	Mo-Kα (0.71073)
θ-Scan mode/range, deg	ω/2.54—29.98	ω/1.78—29.99
h,k,l range	$-10 \le h \le 11$, $-22 \le k \le 21$, $-11 \le l \le 12$	$-13 \le h \le 13$, $-16 \le k \le 9$, $-14 \le l \le 18$
Number of measured reflections	9470	10405
Number of independent reflections	2927 [$R_{int} = 0.0237$]	7515 [$R_{int} = 0.0254$]
Number of reflections with $I > 2\sigma(I)$	2797	6238
Number of refined parameters	160	467
R factors based on reflections with $I > 2\sigma(I)$	$R_1 = 0.0198$, $wR_2 = 0.0441$	$R_1 = 0.0440$, $wR_2 = 0.1012$
R factors based on all reflections	$R_1 = 0.0211$, $wR_2 = 0.0446$	$R_1 = 0.0559$, $wR_2 = 0.1064$
S based on F_2	1.122	1.051
Residual electron density /e·Å^{-3}, ρ_{min}/ρ_{max}	−0.772/0.671	−0.446/1.319

equal occupancies (0.51 : 0.49). Two benzene solvent molecules were found. Each molecule occupies a center of symmetry and is disordered over two sites. The occupancy ratios for the disordered sites occupied by the benzene molecules C(1S)...C(3S) and C(1T)...C(3T) are 0.80 : 0.20 and 0.51 : 0.49, respectively. In addition, a water molecule disordered over two sites related by a center of symmetry was located. The total occupancy of the water sites is 0.4. The structure was finally refined by the least-squares method with anisotropic displacement parameters for all nonhydrogen atoms, except for the nonhydrogen atoms of the solvent molecules. The hydrogen atoms were positioned geometrically. In the final steps, the hydrogen atoms of the podand were refined isotropically. The positional and thermal parameters of the hydrogen atoms of the benzene solvent molecules were fixed in the least-squares refinement.

The crystal structures were solved and refined with the use of the SHELXTL-Plus program package.[39]

The crystallographic characteristics and the X-ray data collection and structure refinement statistics for compounds **2a** and **3´k** are given in Table 2.

The atomic coordinates and other experimental data were deposited with the Cambridge Crystallographic Data Centre (CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac) and can be obtained, free of charge.

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