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# Synthesis of Polyaza Macrocycles by Palladium-Catalyzed Amination of 1,2-Dibromobenzene and 2-Bromo-1,3-dichlorobenzene

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**Abstract**—Palladium-catalyzed amination of 1,2-dibromobenzene with equimolar amounts of linear polyamines leads to the formation of polyaza macrocycles in low yields. The use of 2-bromo-1,3-dichlorobenzene as starting compound ensures considerably larger yields of the target macrocycles, and the reaction is accompanied by side formation of *N*-aryl- and *N*,*N*′-diaryl-substituted polyamines, as well as of cyclic oligomers. The yields strongly depend on the polyamine chain length. Reactions of excess 2-bromo-1,3-dichlorobenzene with a series of polyamines gave the corresponding *N*,*N*′-diarylpolyamines in high yields, and the latter reacted with the second polyamine molecule to form cyclic dimers. A relation between the yield of cyclic dimers and polyamine structure was revealed.

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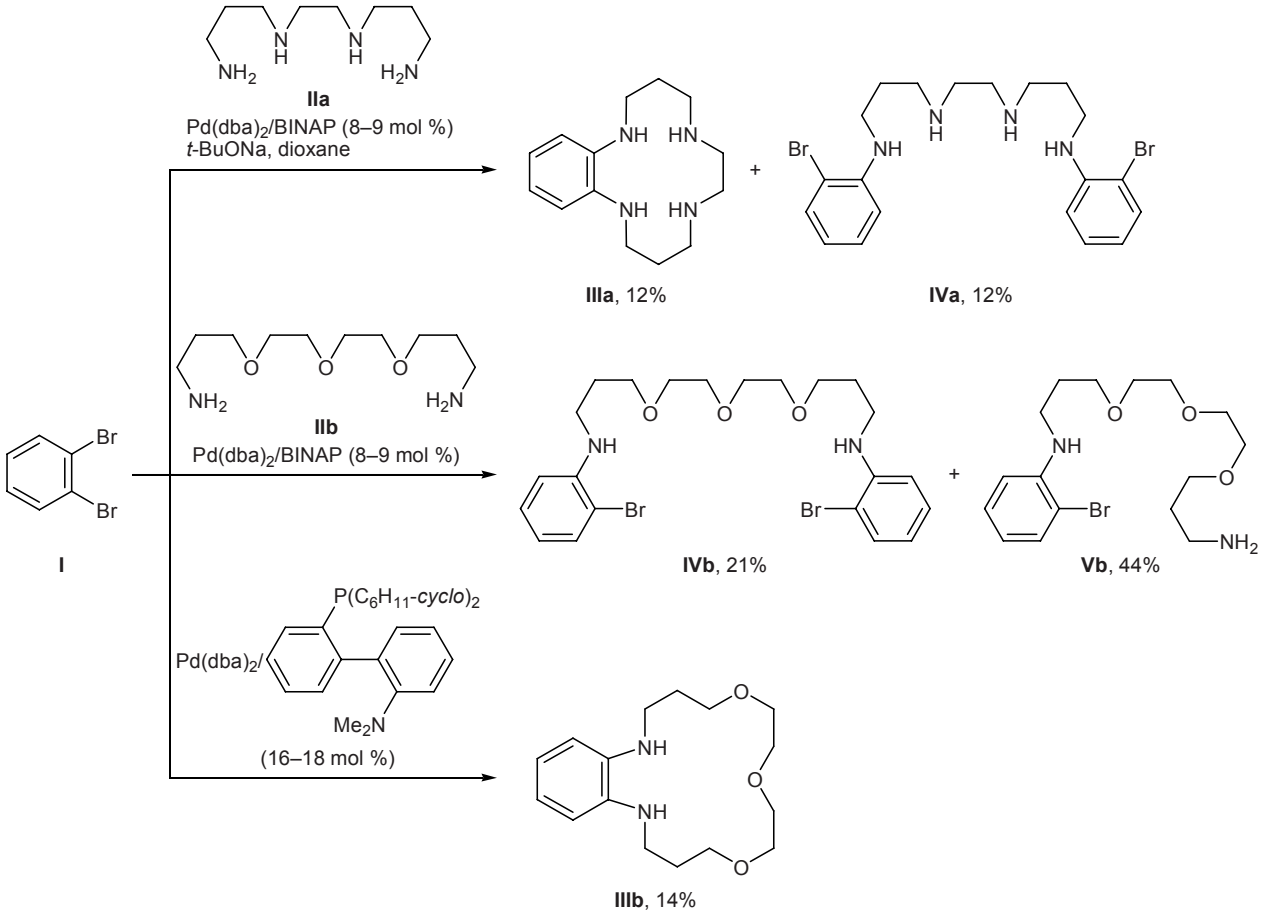
Polyaza macrocycles (aza crown ethers) attract persistent interest due to their ability to effectively bind various inorganic and organic ions, as well as some polar molecules. During the past decades, hundreds of such compounds containing nitrogen, oxygen, and sulfur atoms in the macroring have been synthesized [1]. However, the main problem is that such syntheses are multistep and laborious; therefore, the yields of the target products are often poor [2–5]. Many polyaza macrocycles can be used as chemical sensors due to photochemical or redox properties of aromatic fragments therein. Aromatic groups capable of providing a detectable response to coordination with metal ions may be present as substituents on the nitrogen atoms or incorporated into the macroring. In most cases, aromatic substituents are linked to endocyclic nitrogen atoms through methylene or methine bridges [6–11]. According to published data, the best response is obtained when an aromatic group is directly attached to nitrogen atom in the macroring; however, only a few examples of such compounds have been reported up to now [12–14].

We recently developed an effective procedure for arylation of linear polyamines with aryl halides [15] via palladium-catalyzed amination of dihaloarenes according to Buchwald–Hartwig [16]. This approach was applied to the synthesis of polyaza and polyazapolyoxa macrocycles containing 1,3-disubstituted benzene [17], 2,6- and 3,5-disubstituted pyridine [18, 19], and 1,8- and 1,5-disubstituted anthracene and anthraquinone fragments [20]. Macrocycles having anthracene and anthraquinone fragments attract specific interest, for their electronic absorption spectra lie in the visible region, while anthracene derivatives show strong luminescence which makes them promising as molecular sensors.

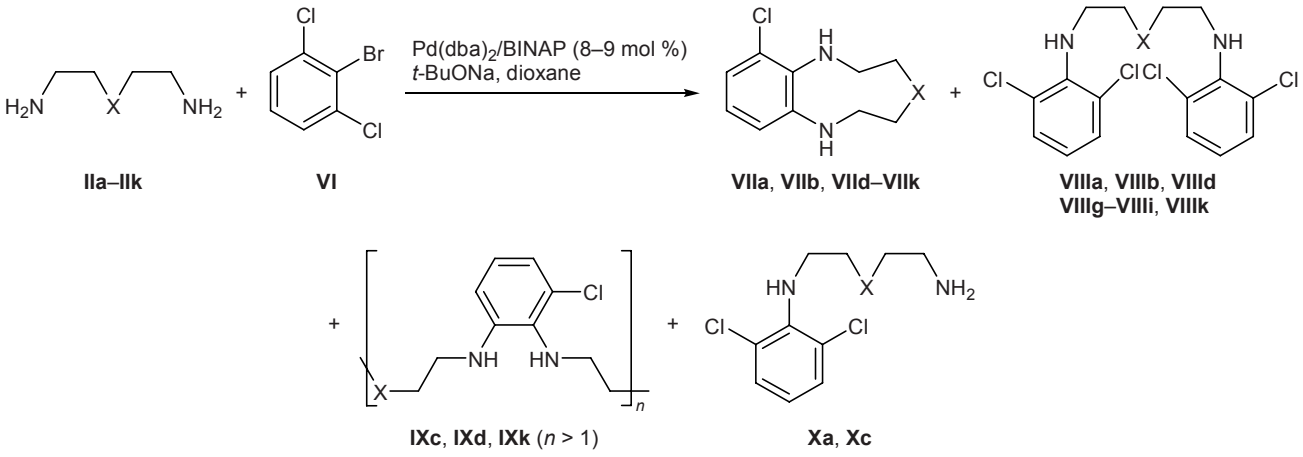
In the present work we tried to synthesize macrocyclic compounds on the basis of 1,2-disubstituted benzene with a view to determine the scope of application of the developed procedure since catalytic *ortho*-diamination is known to be the most problematic owing to ready reduction at the C–Hlg bond. It was also important to elucidate how the yield of the target macrocycles depends on the polyamine chain length and to synthesize macrocyclic compounds each having two benzene and two polyamine fragments (cyclic dimers).

As catalytic system we selected $Pd(dba)_2$/BINAP, taking into account that this system ensured good results in both amination of various haloarenes [21]

**Scheme 1.**




**Scheme 2.**




X = $CH_2NH(CH_2)_2NHCH_2$ (**a**), $CH_2O(CH_2)_2O(CH_2)_2OCH_2$ (**b**), NH (**c**), $CH_2NHCH_2$ (**d**), $NH(CH_2)_2NH$ (**e**), $NH(CH_2)_3NH$ (**f**), $CH_2NH(CH_2)_3NHCH_2$ (**g**), $NH(CH_2)_2NH(CH_2)_2NH$ (**h**), $NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH$ (**i**), $O(CH_2)_2O$ (**j**), $CH_2O(CH_2)_4OCH_2$ (**k**).

and catalytic synthesis of macrocycles. To synthesize macrocycles containing an *o*-phenylenediamine fragment we tried initially the simplest starting compound, 1,2-dibromobenzene (**I**), which was brought into reactions with polyamines **II**. The reactions were carried out by heating fairly dilute solutions ($c$ = 0.02–0.04 M) of the reactants in dioxane in the presence of sodium *tert*-butoxide as a base. The reaction of equimolar

**Table 1.** Synthesis of macrocycles by amination of 2-bromo-1,3-dichlorobenzene (**VI**)

| Run no. | Polyamine | Product | Yield, % |
|---|---|---|---|
| 1 | $NH_2(CH_2)_3NH(CH_2)_2NH(CH_2)_3NH_2$ (**IIa**) | **VIIa** | 47 |
| 2 | $NH_2(CH_2)_3NH(CH_2)_2NH(CH_2)_3NH_2$ (**IIa**) | **VIIa**<br>**VIIIa**<br>**Xa** | 11<br>20<br>19 |
| 3 | $NH_2(CH_2)_3O(CH_2)_2O(CH_2)_2O(CH_2)_3NH_2$ (**IIb**) | **VIIb**<br>**VIIIb**<br>**IXb** ($n$ = 2) | 24<br>12<br>17 |
| 4 | $NH_2(CH_2)_3O(CH_2)_2O(CH_2)_2O(CH_2)_3NH_2$ (**IIb**) | **VIIb**<br>**VIIIb**<br>**IXb** ($n$ = 2)<br>**IXb** ($n$ = 3–5) | 23<br>6<br>17<br>27[a] |
| 5 | $NH_2(CH_2)_2NH(CH_2)_2NH_2$ (**IIc**) | **Xc** | 37 |
| 6 | $NH_2(CH_2)_3NH(CH_2)_3NH_2$ (**IId**) | **VIIId** | 9 |
| 7 | $NH_2(CH_2)_3NH(CH_2)_3NH_2$ (**IId**)[b] | **VIId**<br>**IXd** ($n$ = 2–5) | 8<br>50 |
| 8 | $NH_2(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$ (**IIe**) | **VIIe** | 14 |
| 9 | $NH_2(CH_2)_2NH(CH_2)_3NH(CH_2)_2NH_2$ (**IIf**) | **VIIf** | 17 |
| 10 | $NH_2(CH_2)_3NH(CH_2)_3NH(CH_2)_3NH_2$ (**IIg**) | **VIIg**<br>**VIIIg** | 27<br>7 |
| 11 | $NH_2(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$ (**h**) | **VIIh**<br>**VIIIh** | 12<br>17 |
| 12 | $NH_2(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$ (**IIi**) | **VIIi**<br>**VIIIi** | 10<br>21 |
| 13 | $NH_2(CH_2)_2O(CH_2)_2O(CH_2)_2NH_2$ (**IIj**) | **VIIj** | 12 |
| 14 | $NH_2(CH_2)_3O(CH_2)_4O(CH_2)_3NH_2$ (**IIk**) | **VIIk**<br>**VIIIk**<br>**IXk** ($n$ = 2)<br>**IXk** ($n$ > 2) | 17<br>10<br>10<br>11 |

[a] In a mixture with acyclic oligomers.
[b] In the presence of 16 mol % of the catalyst.

amounts of *o*-dibromobenzene with tetraamine **IIa** in the presence of 8 mol % of the catalyst gave 12% of macrocycle **IIIa** and *N*,*N*′-diaryl tetraamine derivative **IVa** (Scheme 1).

The reaction of *o*-dibromobenzene with trioxadiamine **IIb** did not lead to the desired macrocycle **IIIb** in the presence of the same amount of the catalyst. We isolated only linear *N*,*N*′-di- and *N*-monoaryl-substituted derivatives **IVb** and **Vb** in 21 and 44% yield, respectively. No compound **IIIb** was formed when the amount of the catalyst was increased to 16 mol %; in this case, only the fraction of linear product **IVb** in the reaction mixture was greater. We succeeded in obtaining macrocycle **IIIb** in 14% yield using DavePHOS (L) as donor ligand. The low yield of macrocyclic compounds having a 1,2-diaminobenzene fragment may be rationalized taking into account that replacement of the first bromine atom by amino group hampers replacement of the second bromine atom owing to positive mesomeric effect of the first amino group.

We made an attempt to enhance the reactivity of aryl halide via introduction of an additional halogen atom. The reaction of 2-bromo-1,3-dichlorobenzene (**VI**) with tetraamine **IIa** in the presence of 8% of $Pd(dba)_2$/BINAP gave 47% of macrocyclic compound **VIIa** (Scheme 2; Table 1, run no. 1). Analogous reaction of **VI** with trioxa diamine **IIb** afforded 24% of **VIIb**; in addition, *N*,*N*′-diaryl diamine **VIIIb** (12%) and cyclic dimer **IXb** (17%) were formed (Table 1, run no. 3). Increase in the reactant concentration differently affected the reaction outcome, depending on the polyamine nature. In the reaction with tetraamine **IIa**

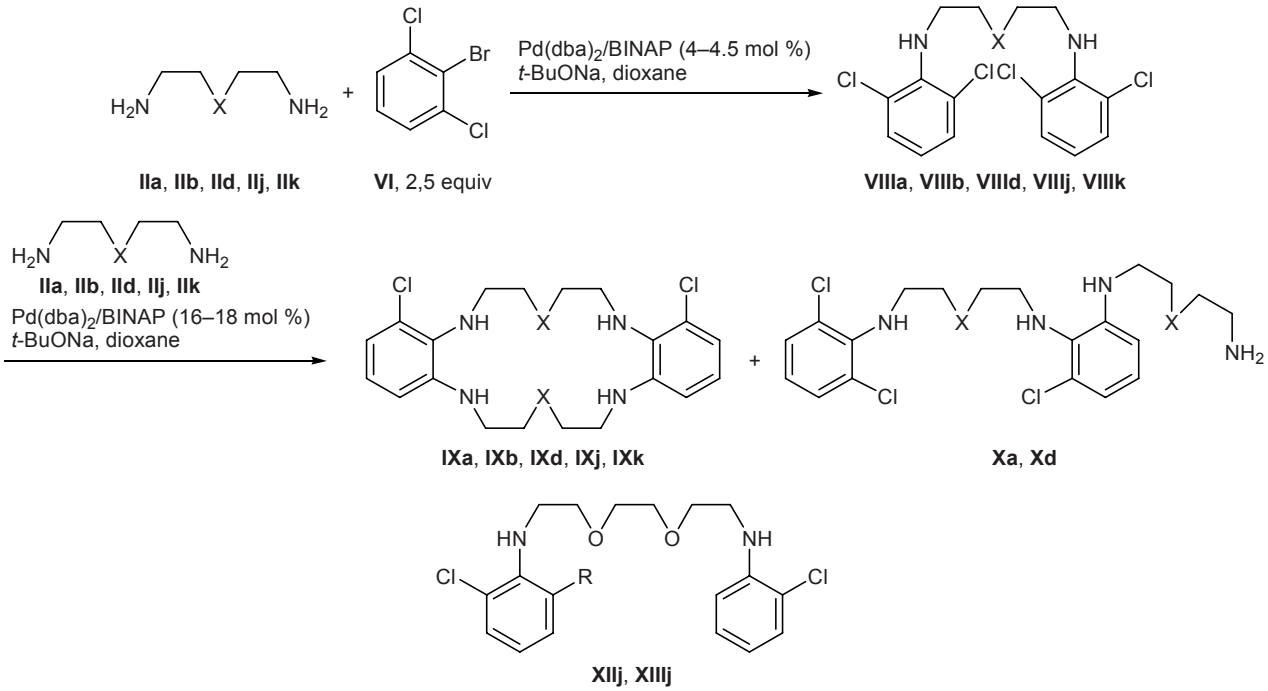
**Table 2.** Synthesis of cyclic dimers **IX**

| Run no. | Polyamine | Product | Yield, % |
|---|---|---|---|
| 1 | $NH_2(CH_2)_3NH(CH_2)_2NH(CH_2)_3NH_2$ (**IIa**) | **XIa** | 33 |
| 2 | $NH_2(CH_2)_3NH(CH_2)_3NH_2$ (**IId**) | **IXd**<br>**XId** | 9<br>19 |
| 3 | $NH_2(CH_2)_2O(CH_2)_2O(CH_2)_2NH_2$ (**IIj**) | **IXj**<br>**XIIj**<br>**XIIIj** | 6<br>12<br>6 |
| 4 | $NH_2(CH_2)_3O(CH_2)_4O(CH_2)_3NH_2$ (**IIk**) | **IXk** | 23 |
| 5 | $NH_2(CH_2)_3O(CH_2)_2O(CH_2)_2O(CH_2)_3NH_2$ (**IIb**) | **IXb** | 27 |

small variation of the reactant concentration resulted in significant decrease of the yield of **VIIa**, whereas appreciable amounts of linear arylation products **VIIIa** and **Xa** were obtained (Table 1; run nos. 1, 2). By contrast, even strong increase of the reactant concentration in the reaction with diamine **IIb** almost did not change the yield of compound **VIIb** (Table 1; run nos. 3, 4).

We also examined how the polyamine chain length and the number of nitrogen and oxygen atoms therein affect the yield of macrocyclic compounds and by-products. Obviously, the chain length of triamine **IIc** (seven atoms), is insufficient for ring closure, and the reaction of **IIc** with haloarene **VI** gave only monoaryl derivative **Xc** (Table 1, run no. 5). Triamine **IId** with a longer chain gave rise to 8% of the corresponding macrocyclic product (Table 1, run no. 7) in addition to considerable amounts of cyclic oligomers **IXd** ($n$ = 2–5; 50% in the reaction mixture). This result was obtained only in the presence of a double amount of the catalyst (16 mol %). In the reaction with 8 mol % of the catalyst, *N*,*N*′-diaryl derivative **VIIId** was the only product (Table 1, run no. 6). Tetraamines **IIe**–**IIg** gave rise to the corresponding macrocycles **VIIe**–**VIIg** in 14–27% yield (Table 1, run nos. 8–10), while in going to pentaamine **IIh** and hexaamine **IIi** the yields decreased to 12 and 10%, respectively. Simultaneously, the yields of linear compounds **VIIh** and **VIIi** increased. Probable reasons are greater conformational

**Scheme 3.**




**XIIj**, R = Cl; **XIIIj**, R = H.

mobility of longer polyamine chains and increased number of ethylenediamine units capable of chelating palladium which is thus removed from the catalytic series. In the reaction with dioxa diamine **IIj** the yield of macrocycle **VIIj** was also poor (12%; Table 1, run no. 13), presumably owing to insufficient chain length in the initial diamine. In going to longer dioxa diamine **IIk** the yield of the macrocyclic product increased to 17% (Table 1, run no. 14). In addition, 10% of cyclic dimer **IXk** ($n$ = 2) and 11% of a mixture of higher cyclic oligomers ($n$ > 2) were obtained. The above data indicate that intramolecular diamination processes leading to the target macrocycles do not go to completion even in the presence of a considerable amount of the catalyst (8 mol %).

Insofar as the polyamine chain in macrocycles **VII** appears to be unsymmetrically substituted (a chlorine atom is present in position *3* of the benzene ring), all methylene groups showed nonequivalence in the $^1$H and $^{13}$C NMR spectra. The difference in the chemical shifts of protons in the methylene groups nearest to the benzene ring reached 0.3 ppm.

We have developed a procedure for the synthesis of cyclic dimers **IX**. It included formation of intermediate *N*,*N*′-diaryl polyamines **VIIIa**, **VIIIb**, **VIIId**, **VIIIj**, and **VIIIk** and their subsequent reaction with the second polyamine molecule (Scheme 3). In the first step the amount of the catalyst was smaller (4 mol %), and the reactions were carried out in more concentrated solutions (dioxane, $c$ = 0.1 M) using 2.5 equiv of 2-bromo-1,3-dichlorobenzene (**VI**). Intermediate compounds **VIII** were formed in 85–90% yield and were brought into reactions with polyamines **IIa**, **IIb**, **IId**, **IIj**, and **IIk** without isolation from the reaction mixture. The second step was carried out in more dilute solutions ($c$ = 0.04–0.05 M) using 16 mol % of the catalyst. The yields of cyclic dimers **IX** very strongly depended on the polyamine nature. No target macrocycle was obtained from tetraamine **IIa**; instead, linear compound **XIa** was isolated (Table 2, run no. 1). In the reaction with triamine **IId**, the yield of macrocycle **IXd** was 9% (Table 2, run no. 2), and 19% of linear compound **XId** was formed. The yield of cyclic dimer **IXj** from diamine **IIj** was also poor (6%; Table 2, run no. 3); in this case, partially reduced *N*,*N*′-diaryl dioxa diamines **XIIj** and **XIIIj** were obtained as by-products (yield 6 and 12%, respectively). Another dioxa diamine, compound **IIk**, gave rise to a higher yield of cyclic dimer **IXk** (23%; Table 2, run no. 4). The best yield of cyclic dimer (27%) was obtained in the reaction with trioxa diamine **IIb** (Table 2, run no. 5).

Cyclic dimers **IX**, as well as the corresponding macrocycles **VII**, possess unsymmetrically substituted polyamine chains. In addition, most signals in the $^{13}$C NMR spectrum of cyclic dimer **IXb** are doubled, which may be due to existence of different stable conformers fixed by intramolecular hydrogen bonding with participation of six oxygen atoms and four amino groups. Analogous pattern was observed previously for cyclic dimers containing 1,3-disubstituted benzene [17] and 2,6-disubstituted pyridine fragments [18].

## EXPERIMENTAL

The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Avance-400 spectrometer at 400 and 100.6 MHz, respectively, using $CDCl_3$ as solvent unless otherwise stated. The chemical shifts were determined relative to the residual proton and carbon signals of the solvent ($CHCl_3$, δ 7.25; $CDCl_3$, $\delta_C$ 77.0 ppm). The mass spectra (MALDI-TOF, positive ion detection) were obtained on a Bruker Daltonics Ultrafex instrument using 1,8,9-trihydroxyanthracene as matrix. Preparative column chromatography was performed on Merck silica gel (40–60 μm). Commercial 1,2-dibromobenzene (**I**), 2-bromo-1,3-dichlorobenzene (**VI**), polyamines **IIa**–**IIk**, sodium *tert*-butoxide, BINAP, and DavePHOS were used without additional purification; $Pd(dba)_2$ was synthesized according to the procedure described in [22] and was not additionally recrystallized. Dioxane was distilled first over alkali and then over metallic sodium; methylene chloride and methanol were purified by distillation.

**Macrocycles IIIa, IIIb, VIIa, VIIb, and VIId–VIIk (*general procedure*).** Anhydrous dioxane, 25 ml, amine **IIa**–**IIk**, 0.5 mmol, and sodium *tert*-butoxide, 1.5 mmol (144 mg), were added to a mixture of 0.5 mmol of 1,2-dibromobenzene (**I**) (118 mg) or 2-bromo-1,3-dichlorobenzene (**VI**) (113 mg), 0.04 mmol (23 mg) of $Pd(dba)_2$, and 0.045 mol (28 mg) of BINAP, and the mixture was heated for 24–72 h under reflux in an argon atmosphere. The mixture was cooled, the solution was separated by decanting, the precipitate was washed with a small amount of methylene chloride, the washings were combined with the organic phase and evaporated under reduced pressure, and the solid residue was subjected to chromatographic separation on silica gel using the following solvents as eluents (in succession): $CH_2Cl_2$, $CH_2Cl_2$–MeOH (200:1 to 3:1), $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:1 to 10:4:1). The yields of compounds **VII**–**XIII** are given in Tables 1 and 2.

**1,2,3,4,5,6,7,8,9,10,11,12-Dodecahydro-1,5,8,12-benzotetraazacyclotetradecine (IIIa)** was synthesized from 0.5 mmol (118 mg) of 1,2-dibromobenzene (**I**) and 0.5 mmol (87 mg) of tetraamine **IIa**. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Yield 15 mg (12%), light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.82 quint (4H, $^3J$ = 6.5 Hz), 2.69 t (4H, $^3J$ = 6.5 Hz), 2.75 s (4H), 3.28 t (4H, $^3J$ = 6.5 Hz), 6.58–6.61 m (2H), 6.61–6.64 m (2H) (four NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 27.7 (2C), 43.0 (2C), 48.2 (2C), 49.5 (2C), 111.1 (2C), 118.0 (2C), 138.2 (2C). Mass spectrum: *m*/*z* 248.91 $[M + H]^+$.

***N*$^1$,*N*$^{1'}$-Ethane-1,2-diylbis[*N*$^3$-(2-bromophenyl)-propane-1,3-diamine] (IVa)** was isolated as the second product in the synthesis of compound **IIIa**. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1. Yield 20 mg (16%), light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.82 quint (4H, $^3J$ = 6.7 Hz), 2.76 t (4H, $^3J$ = 6.7 Hz), 2.86 s (4H), 3.23 t (4H, $^3J$ = 6.6 Hz), 6.52 t.d (2H, $^3J$ = 7.9, $^4J$ = 1.4 Hz), 6.63 d (2H, $^3J$ = 8.0 Hz), 7.15 (2H, $^3J$ = 7.8 Hz), 7.39 d.d (2H, $^3J$ = 7.9, $^4J$ = 1.4 Hz) (four NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 29.2 (2C), 42.7 (2C), 52.7 (4C), 109.5 (2C), 111.3 (2C), 117.4 (2C), 128.4 (2C), 132.3 (2C), 145.2 (2C).

**1,2,3,4,6,7,9,10,12,13,14,15-Dodecahydro-5,8,11,1,15-benzotrioxadiazacycloheptadecine (IIIb)** was synthesized from 0.5 mmol (118 mg) of 1,2-dibromobenzene (**I**) and 0.5 mmol (110 mg) of trioxadiamine **IIb** in the presence of 0.08 mmol (48 mg) of $Pd(dba)_2$ and 0.08 mmol (31 mg) of 2′-(dicyclohexyl-λ$^3$-phosphanyl)-*N*,*N*-biphenyl-2-amine (DavePHOS) in 12 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 100:1. Yield 20 mg (14%), light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.93 quint (4H, $^3J$ = 5.5 Hz), 3.28 q (4H, $^3J$ = 5.5 Hz), 3.62–3.66 m (4H), 3.67–3.72 m (8H), 3.94 br.s (2H), 6.59–6.63 m (2H), 6.71–6.75 m (2H). $^{13}$C NMR spectrum, $\delta_C$, ppm: 28.7 (2C), 42.7 (2C), 70.8 (4C), 71.1 (2C), 110.2 (2C), 118.2 (2C), 137.1 (2C). Mass spectrum: *m*/*z* 294.1990 $[M]^+$. $C_{16}H_{26}N_2O_3$. Calculated: *M* 294.1943.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bisoxy]-bis(propane-3,1-diyl)}bis(2-bromoaniline) (IVb)** was synthesized from 0.5 mmol (118 mg) of 1,2-dibromobenzene (**I**) and 0.5 mmol (110 mg) of trioxadiamine **IIb** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 200:1. Yield 28 mg (21%), light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.93 quint (4H, $^3J$ = 6.2 Hz), 3.27 q (4H, $^3J$ = 5.5 Hz), 3.57–3.64 m (8H), 3.65–3.70 m (4H), 4.63 br.s (2H), 6.53 t (2H, $^3J$ = 7.6 Hz), 6.62 d (2H, $^3J$ = 8.0 Hz), 7.15 t (2H, $^3J$ = 7.7 Hz), 7.39 d.d (2H, $^3J$ = 7.9, $^4J$ = 1.1 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 29.0 (2C), 41.6 (2C), 69.6 (2C), 70.4 (2C), 70.6 (2C), 109.6 (2C), 111.1 (2C), 117.3 (2C), 128.4 (2C), 132.3 (2C), 145.2 (2C). Mass spectrum: *m*/*z* 528.0649 $[M]^+$. $C_{22}H_{30}Br_2N_2O_3$. Calculated: *M* 528.0623.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}-propyl)-2-bromoaniline (Vb)** was isolated as the second product in the synthesis of **IVb**. Elyuent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1 to 10:4:1. Yield 83 mg (44%), light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.71 quint (2H, $^3J$ = 6.7 Hz), 1.93 quint (2H, $^3J$ = 6.0 Hz), 2.77 t (2H, $^3J$ = 6.7 Hz), 3.27 q (2H, $^3J$ = 5.9 Hz), 3.53 t (2H, $^3J$ = 6.1 Hz), 3.55–3.68 m (10H), 4.64 br.s (1H), 6.53 t (1H, $^3J$ = 7.6 Hz), 6.62 d (1H, $^3J$ = 8.1 Hz), 7.15 t (1H, $^3J$ = 7.7 Hz), 7.39 d (1H, $^3J$ = 7.8 Hz) (two NH proton signals cannot be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 28.9, 33.0, 39.4, 41.4, 69.5, 70.0, 70.3, 70.4 (2C), 70.5, 109.4, 110.9, 117.2, 128.3, 132.2, 145.1. Mass spectrum: *m*/*z* 374.1270 $[M]^+$. $C_{16}H_{27}BrN_2O_3$. Calculated: *M* 374.1205.

**13-Chloro-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-1,5,8,12-benzotetraazacyclotetradecine (VIIa)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (87 mg) of tetraamine **IIa** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.81 quint (2H, $^3J$ = 5.3 Hz), 1.84 quint (2H, $^3J$ = 5.5 Hz), 2.75–2.79 m (2H), 2.80–2.84 m (2H), 2.85–2.92 m (4H), 2.94 t (2H, $^3J$ = 5.5 Hz), 3.19 t (2H, $^3J$ = 5.3 Hz), 6.43 d (1H, $^3J$ = 8.0 Hz), 6.64 d.d (1H, $^3J$ = 8.0, $^4J$ = 1.1 Hz), 6.86 t (1H, $^3J$ = 8.0 Hz) (four NH proton signals cannot be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 27.1, 28.9, 45.7, 46.6, 47.0, 47.8, 48.5, 50.2, 108.5, 116.5, 125.3, 129.3, 134.4, 145.6. Mass spectrum: *m*/*z* 282.1622 $[M]^+$. $C_{14}H_{23}ClN_4$. Calculated: *M* 282.1611.

***N*$^1$,*N*$^{1'}$-(Ethane-1,2-diyl)bis[*N*$^3$-(2,6-dichlorophenyl)propane-1,3-diamine] (VIIIa)** was isolated as by-product in the synthesis of **VIIa** from 2 mmol (452 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 2 mmol (348 mg) of tetraamine **IIa** in the presence of 0.04 mmol (96 mg) of $Pd(dba)_2$ and 0.045 mmol (112 mg) of BINAP in 75 ml of dioxane. Eluent

$CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1, light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.71 quint (4H, $^3J$ = 6.7 Hz), 2.67 s (4H), 2.68 t (4H, $^3J$ = 6.8 Hz), 3.36 q (4H, $^3J$ = 6.1 Hz), 4.24 br.s (2H), 6.70 t (2H, $^3J$ = 8.0 Hz), 7.16 d (4H, $^3J$ = 8.0 Hz) (two NH proton signals cannot be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 30.9 (2C), 46.0 (2C), 47.7 (2C), 49.5 (2C), 121.3 (2C), 125.9 (4C), 128.7 (4C), 142.9 (2C). Mass spectrum: *m*/*z* 462.0877 $[M]^+$. $C_{20}H_{26}Cl_4N_4$. Calculated: *M* 462.0912.

**$N^1$-[2-(3-Aminopropylamino)ethyl]-$N^3$-(2,6-dichlorophenyl)propane-1,3-diamine (Xa)** was isolated as as the second by-product in the synthesis of **VIIa**. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 10:4:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.57 quint (2H, $^3J$ = 6.7 Hz), 1.67 quint (2H, $^3J$ = 6.6 Hz), 2.59 t (2H, $^3J$ = 6.9 Hz), 2.63 br.s (6H), 2.70 t (2H, $^3J$ = 6.6 Hz), 3.08 br.s (4H), 3.30 t (2H, $^3J$ = 6.6 Hz), 4.18 br.s (1H), 6.66 t (1H, $^3J$ = 8.0 Hz), 7.11 d (2H, $^3J$ = 8.0 Hz). Mass spectrum: *m*/*z* 318.1400 $[M]^+$. $C_{14}H_{24}Cl_2N_4$. Calculated: *M* 318.1378.

**16-Chloro-1,2,3,4,6,7,9,10,12,13,14,15-dodecahydro-5,8,11,1,15-benzotrioxadiazacycloheptadecine (VIIb)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (110 mg) of trioxadiamine **IIb** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 200:1 to 100:1, light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.86 quint (2H, $^3J$ = 5.7 Hz), 1.89 quint (2H, $^3J$ = 5.9 Hz), 3.04 t (2H, $^3J$ = 6.5 Hz), 3.30 q (2H, $^3J$ = 5.1 Hz), 3.60–3.66 m (4H), 3.67 s (4H), 3.70–3.74 m (4H), 4.86 br.s (1H), 6.46 d (1H, $^3J$ = 8.1 Hz), 6.64 d (1H, $^3J$ = 7.9 Hz), 6.84 t (1H, $^3J$ = 8.0 Hz) (the NH proton signal could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 28.9, 30.6, 40.4, 43.3, 68.3, 69.1, 70.6, 70.9, 71.0 (2C), 108.1, 116.3, 124.5, 128.4, 131.4, 144.1. Mass spectrum: *m*/*z* 328.1594 $[M]^+$. $C_{16}H_{25}ClN_2O_3$. Calculated: *M* 328.1554.

Compounds **VIIIb** and **IXb** were isolated as by-products.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(2,6-dichloroaniline) (VIIIb).** Eluent $CH_2Cl_2$–MeOH, 100:1–50:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.84 quint (4H, $^3J$ = 6.4 Hz), 3.44 q (4H, $^3J$ = 6.7 Hz), 3.57 t (4H, $^3J$ = 6.2 Hz), 3.57–3.60 m (4H), 3.62–3.66 m (4H), 4.21 t (2H, $^3J$ = 6.4 Hz), 6.73 t (2H, $^3J$ = 8.0 Hz), 7.19 d (4H, $^3J$ = 8.0 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 30.6 (2C), 45.0 (2C), 69.2 (2C), 70.4 (2C), 70.6 (2C), 121.2 (2C), 125.8 (4C), 128.8 (4C), 142.8 (2C). Mass spectrum: *m*/*z* 507.87 $[M]^+$.

**1,23-Dichloro-5,6,7,8,10,11,13,14,16,17,18,19,24,25,26,27,29,30,32,33,35,36,37,38-tetracosahydrodibenzo[*l*,$c_1$][1,4,7,18,21,24,11,14,28,31]hexaoxatetraazacyclotetratriacontine (IXb).** Eluent $CH_2Cl_2$–MeOH, 50:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.80–1.86 m (4H), 1.89 quint (4H, $^3J$ = 6.6 Hz), 2.95 t (4H, $^3J$ = 7.0 Hz), 3.19 t (4H, $^3J$ = 5.6 Hz), 3.54–3.70 m (24H), 4.71 br.s (1H), 4.89 br.s (1H), 6.43–6.47 m (2H), 6.64 d.d (2H, $^3J$ = 7.9, $^4J$ = 1.1 Hz), 6.84 t (2H, $^3J$ = 8.0 Hz) (two NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 29.1 and 29.5 (2C), 30.4 and 30.5 (2C), 41.2 and 41.4 (2C), 44.2 and 44.5 (2C), 69.3 and 69.4 (2C), 69.6 (2C), 70.2 (2C), 70.3 and 70.4 (2C), 70.6 (4C), 108.3 and 108.5 (2C), 116.4 and 116.5 (2C), 124.6 and 124.7 (2C), 128.4 and 128.5 (2C), 131.3 (2C), 144.7 (2C). Mass spectrum: *m*/*z* 656.3075 $[M]^+$. $C_{32}H_{50}Cl_2N_4O_6$. Calculated: *m*/*z* 656.3107.

**Mixture of cyclic oligomers IXb (*n* = 3–5).** Eluent $CH_2Cl_2$–MeOH, 10:1–3:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.78–1.85 m (2*n*H), 1.88 quint (2*n*H, $^3J$ = 6.5 Hz), 2.93 t (2*n*H, $^3J$ = 5.6 Hz), 3.18 t (2*n*H, $^3J$ = 5.7 Hz), 3.52–3.66 m (12*n*H), 4.69 br.s (*n*H), 6.46 d (*n*H, $^3J$ = 7.8 Hz), 6.63 d (*n*H, $^3J$ = 7.9 Hz), 6.84 t (*n*H, $^3J$ = 8.0 Hz) (signals from *n* NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 29.5 (*n*C), 30.5 (*n*C), 41.2 (*n*C), 44.4 (*n*C), 69.3 (*n*C), 69.7 (*n*C), 70.2 (*n*C), 70.3 (*n*C), 70.6 (2*n*C), 108.5 (*n*C), 116.5 (*n*C), 124.7 (*n*C), 128.8 (*n*C), 131.3 (*n*C), 144.7 (*n*C). Mass spectrum: *m*/*z* 984.35 $[M]^+$ (*n* = 3), 1312.73 $[M]^+$ (*n* = 4), 1641.09 $[M]^+$ (*n* = 5).

**$N^1$-(2-Aminoethyl)-$N^2$-(2,6-dichlorophenyl)-ethane-1,2-diamine (Xc)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (52 mg) of triamine **IIc** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2 to 100:20:3. Light yellow oily substance. $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 3.16 t (2H, $^3J$ = 6.2 Hz), 3.22 t (4H, $^3J$ = 6.0 Hz), 3.44 br.s (2H), 4.90 br.s (1H), 6.91 t (1H, $^3J$ = 8.0 Hz), 7.33 d (2H, $^3J$ = 8.0 Hz) (three NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum (DMSO-$d_6$), $\delta_C$, ppm: 35.5 (1C), 43.1 (1C), 44.5 (1C), 47.6 (1C), 122.7 (1C), 126.0 (2C), 129.1 (2C), 141.9 (1C). Mass spectrum: *m*/*z* 247.11 $[M]^+$.

**10-Chloro-2,3,4,5,6,7,8,9-octahydro-1*H*-1,4,8-benzotriazacycloundecine (VIId)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (66 mg) of triamine **IIb** in the presence of 0.08 mmol (48 mg) of $Pd(dba)_2$ and 0.09 mmol (56 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.71 quint (2H, $^3J$ = 5.0 Hz), 1.86 quint (2H, $^3J$ = 5.4 Hz), 3.03 t (2H, $^3J$ = 5.6 Hz), 3.07 t (2H, $^3J$ = 5.3 Hz), 3.16 t (2H, $^3J$ = 4.7 Hz), 3.26 t (2H, $^3J$ = 5.5 Hz), 4.70 br.s (1H), 6.61 d (1H, $^3J$ = 7.6 Hz), 6.79 d (1H, $^3J$ = 8.0 Hz), 6.87 t (1H, $^3J$ = 7.9 Hz) (two NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 26.0, 28.1, 40.4, 44.7, 47.6, 49.1, 108.3, 116.9, 122.9 (three quaternary carbon signals could not be assigned unambiguously). Mass spectrum: *m*/*z* 239.18 $[M]^+$.

A mixture of cyclic oligomers **IXd** ($n$ = 2–5) was isolated as by-product. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2 to 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.06 br.s (4$n$H), 2.82–3.22 m (8$n$H), 6.33 d ($^3J$ = 8.2 Hz) and 6.34 d ($^3J$ = 8.0 Hz) ($n$H), 6.62 t ($^3J$ = 7.6 Hz) and 6.64 t ($^3J$ = 7.4 Hz) ($n$H), 6.82 t ($^3J$ = 8.1, $n$H) (NH proton signals could not be assigned unambiguously). Mass spectrum: *m*/*z* 478.20 $[M]^+$ ($n$ = 2), 717.26 $[M]^+$ ($n$ = 3), 956.18 $[M]^+$ ($n$ = 4), 1196.01 $[M]^+$ ($n$ = 5).

***N*-(2,6-Dichlorophenyl)-*N*′-[3-(2,6-dichlorophenylamino)propyl]propane-1,3-diamine (VIIId)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (66 mg) of triamine **IIb** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 10:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.73 quint (4H, $^3J$ = 6.8 Hz), 2.70 t (4H, $^3J$ = 6.8 Hz), 3.37 t (4H, $^3J$ = 6.7 Hz), 4.21 br.s (2H), 6.71 t (2H, $^3J$ = 8.0 Hz), 7.17 d (4H, $^3J$ = 8.0 Hz) (NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 30.9 (2C), 46.0 (2C), 47.9 (2C), 121.3 (2C), 126.0 (4C), 128.7 (4C), 142.8 (2C). Mass spectrum: *m*/*z* 419.10 $[M]^+$.

**11-Chloro-1,2,3,4,5,6,7,8,9,10-decahydro-1,4,7,10-benzotetraazacyclododecine (VIIe)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (73 mg) of tetraamine **IIe** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.68 t (2H, $^3J$ = 6.1 Hz), 2.78 t (2H, $^3J$ = 6.1 Hz), 2.80–2.87 m (6H), 3.36 t (2H, $^3J$ = 6.7 Hz), 4.24 br.s (1H), 6.49 d (1H, $^3J$ = 8.0 Hz), 6.53 t (1H, $^3J$ = 7.9 Hz), 6.62 d (1H, $^3J$ = 7.9 Hz) (three NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 40.8, 42.1, 46.8, 48.6, 52.5, 52.9, 110.1, 118.1, 118.5, 130.5, 130.8, 136.3. Mass spectrum: *m*/*z* 254.76 $[M + H]^+$.

**12-Chloro-2,3,4,5,6,7,8,9,10,11-decahydro-1*H*-1,4,8,11-benzotetraazacyclotridecine (VIIf)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (80 mg) of tetraamine **IIf** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.76 quint (2H, $^3J$ = 6.6 Hz), 2.67 t (4H, $^3J$ = 6.6 Hz), 2.80 br.s (4H), 3.31 br.s (4H), 6.42 d (1H, $^3J$ = 7.9 Hz), 6.51 t (1H, $^3J$ = 7.9 Hz), 6.58 d (1H, $^3J$ = 7.9 Hz) (four NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 26.4, 40.3, 43.7, 47.3, 47.5, 49.4, 51.8, 109.2, 117.2, 118.0, 128.7, 130.2, 135.6. Mass spectrum: *m*/*z* 268.80 $[M + H]^+$.

**14-Chloro-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-1*H*-1,5,9,13-benzotetraazacyclopentadecine (VIIg)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (94 mg) of tetraamine **IIg** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1 to 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.80 quint (2H, $^3J$ = 6.5 Hz), 1.87 quint (2H, $^3J$ = 5.3 Hz), 1.96 quint (2H, $^3J$ = 5.9 Hz), 2.82–2.86 m (4H), 2.89 t (2H, $^3J$ = 5.2 Hz), 2.95 t (2H, $^3J$ = 5.5 Hz), 2.99 t (2H, $^3J$ = 5.8 Hz), 3.33 t (2H, $^3J$ = 5.0 Hz), 5.07 br.s (1H), 6.47 d (1H, $^3J$ = 8.0 Hz), 6.70 d (1H, $^3J$ = 8.1 Hz), 6.86 t (1H, $^3J$ = 8.0 Hz) (three NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 25.9, 26.2, 27.7, 42.6, 43.0, 46.0, 48.4, 49.0, 50.6, 108.7, 117.5, 124.9, 130.1, 131.7, 144.3. Mass spectrum: *m*/*z* 296.07 $[M]^+$.

***N*$^1$,*N*$^{1'}$-(Propane-1,3-diyl)bis[*N*$^3$-(2,6-dichlorophenyl)propane-1,3-diamine] (VIIIg)** was isolated as by-product. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.91–2.00 m (6H), 2.74–2.81 m (8H), 3.19 t (4H, $^3J$ = 6.5 Hz), 6.75 t (2H, $^3J$ = 8.0 Hz), 7.19 t (4H, $^3J$ =

8.0 Hz) (four NH proton signals could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 29.6 (2C), 29.9 (1C), 45.8 (2C), 47.8 (2C), 48.6 (2C), 121.9 (2C), 127.7 (4C), 128.8 (4C), 142.1 (2C). Mass spectrum: *m*/*z* 475.95 $[M]^+$.

**14-Chloro-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-1*H*-1,4,7,10,13-benzopentaazacyclopentadecine (VIIh)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (95 mg) of pentaamine **IIh** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.61–2.85 m (12H), 3.35 br.s (2H), 3.43 br.s (2H), 6.47 d.d (1H, $^3J$ = 7.9, $^4J$ = 1.4 Hz), 6.52 t (1H, $^3J$ = 7.9 Hz), 6.62 d.d (1H, $^3J$ = 7.9, $^4J$ = 1.4 Hz) (signals from five NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 40.4, 46.2, 48.2, 48.9 (2C), 49.4, 51.8, 51.9, 109.5, 117.7, 118.0, 128.7, 130.4, 135.7. Mass spectrum: *m*/*z* 296.86 $[M]^+$.

***N*$^1$-(2,6-Dichlorophenyl)-*N*$^2$-{2-[2-(2-[2,6-dichlorophenylamino]ethylamino)ethylamino]ethyl}-ethane-1,2-diamine (VIIIh)** was isolated as by-product. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.73 s (8H), 2.82 t (4H, $^3J$ = 5.7 Hz), 3.32–3.44 m (4H), 6.73 t (2H, $^3J$ = 8.1 Hz), 7.19 d (4H, $^3J$ = 8.1 Hz) (signals from five NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 46.9 (2C), 49.0 (2C), 49.4 (2C), 49.5 (2C), 121.3 (2C), 125.3 (4C), 128.8 (4C), 143.0 (2C).

**17-Chloro-1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16-hexadecahydro-1,4,7,10,13,16-benzohexaazacyclooctadecine (VIIi)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (116 mg) of hexaamine **IIi** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.75–2.85 m (16H), 3.32–3.43 m (4H), 6.47 d.d (1H, $^3J$ = 7.5, $^4J$ = 1.8 Hz), 6.52 t (1H, $^3J$ = 7.5 Hz), 6.61 d.d (1H, $^3J$ = 7.5, $^4J$ = 1.8 Hz) (signals from six NH protons could be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 40.3, 46.2, 46.5, 46.8, 48.1 (2C), 48.7 (2C), 51.8 (2C), 109.5, 117.5, 118.0, 129.5, 131.4, 135.0. Mass spectrum: *m*/*z* 340.01 $[M]^+$.

***N*$^1$-(2-Chlorophenyl)-*N*$^2$-{2-[2-(2-[2-(2,6-dichlorophenylamino)ethylamino]ethylamino)ethylamino]ethyl}ethane-1,2-diamine (VIIIi)** was isolated as by-product. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 2.75–2.85 m (16H), 3.32–3.43 m (4H), 6.73 t (2H, $^3J$ = 7.9 Hz), 7.18 t (4H, $^3J$ = 7.9 Hz) (signals from six NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 46.7 (2C), 48.5 (2C), 48.8 (2C), 49.0 (2C), 49.4 (2C), 121.3 (2C), 125.9 (4C), 128.7 (4C), 142.9 (2C).

**11-Chloro-1,2,3,5,6,8,9,10-octahydro-4,7,1,10-benzodioxadiazacyclododecine (VIIj)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (74 mg) of dioxa diamine **IIj** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 100:1. Light brown crystals, mp 85–87°C. $^1$H NMR spectrum, δ, ppm: 3.17–3.22 m (4H), 3.59 t (2H, $^3J$ = 4.3 Hz), 3.67–3.70 m (2H), 3.75–3.78 m (2H), 3.87 t (2H, $^3J$ = 4.9 Hz), 6.04 br.s (1H), 6.44 d (1H, $^3J$ = 8.0 Hz), 6.65 d (1H, $^3J$ = 7.9 Hz), 6.86 t (1H, $^3J$ = 8.0 Hz) (the NH proton signal could be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 43.4, 46.4, 69.4, 69.5, 70.3, 70.8, 108.4, 116.5, 124.8, 129.0, 130.9, 145.0. Mass spectrum: *m*/*z* 256.06 $[M]^+$.

**15-Chloro-1,2,3,4,6,7,8,9,11,12,13,14-dodecahydro-5,10,1,14-benzodioxadiazacyclohexadecine (VIIk)** was synthesized from 0.5 mmol (113 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (102 mg) of dioxa diamine **IIk** in the presence of 0.04 mmol (24 mg) of $Pd(dba)_2$ and 0.045 mmol (28 mg) of BINAP in 25 ml of dioxane. Eluent $CH_2Cl_2$–MeOH, 200:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.71–1.76 m (4H), 1.83 quint (2H, $^3J$ = 5.6 Hz), 1.84 quint (2H, $^3J$ = 5.9 Hz), 3.05 t (2H, $^3J$ = 6.2 Hz), 3.35 q (2H, $^3J$ = 5.0 Hz), 3.51–3.55 m (4H), 3.58 t (2H, $^3J$ = 5.4 Hz), 3.66 t (2H, $^3J$ = 5.5 Hz), 5.02 br.s (1H), 6.47 d (1H, $^3J$ = 8.1 Hz), 6.64 d (1H, $^3J$ = 8.0 Hz), 6.85 t (1H, $^3J$ = 8.0 Hz) (the NH proton signal could not be assigned unambiguously. $^{13}$C NMR spectrum, $\delta_C$, ppm: 26.0 (2C), 28.6, 30.3, 39.7, 43.2, 66.3, 67.5, 70.0, 70.9, 107.9, 116.1, 124.6, 129.0, 131.2, 144.1. Mass spectrum: *m*/*z* 312.06 $[M]^+$.

***N*,*N*′-{3,3′-[Butane-1,4-diylbis(oxy)]bis(propane-3,1-diyl)}bis(2,6-dichloroaniline) (VIIIk).** Eluent $CH_2Cl_2$–MeOH, 200:1 to 100:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.63 br.s (4H), 1.83 quint (4H, $^3J$ = 6.3 Hz), 3.42 br.s (4H), 3.43 t (4H, $^3J$ = 6.9 Hz), 3.51 t (4H, $^3J$ = 6.0 Hz), 4.25 t (2H, $^3J$ =

6.5 Hz), 6.72 t (2H, $^3J$ = 8.0 Hz), 7.18 t (4H, $^3J$ = 8.0 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 26.4 (2C), 30.6 (2C), 45.0 (2C), 68.7 (2C), 70.8 (2C), 121.1 (2C), 125.7 (4C), 128.7 (4C), 142.8 (2C). Mass spectrum: *m*/*z* 492.0943 $[M]^+$. $C_{22}H_{28}Cl_4N_2O_2$. Calculated: *m*/*z* 492.0905.

**1,22-Dichloro-5,6,7,8,10,11,12,13,15,16,17,18,23,-24,25,26,28,29,30,31,33,34,35,36-tetracosahydrodibenzo[*f*,*v*][1,12,17,28,5,8,21,24]tetraoxatetraazacyclododotriacontine (IXk).** Eluent $CH_2Cl_2$–MeOH, 100:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.64–1.70 m (8H), 1.82 quint (4H, $^3J$ = 6.3 Hz), 1.90 quint (4H, $^3J$ = 6.1 Hz), 2.99 t (4H, $^3J$ = 6.7 Hz), 3.22 t (4H, $^3J$ = 6.2 Hz), 3.42–3.47 m (8H), 3.54 t (4H, $^3J$ = 6.0 Hz), 3.58 t (4H, $^3J$ = 6.0 Hz), 4.95 br.s (2H), 6.46 d (2H, $^3J$ = 8.0 Hz), 6.65 d (2H, $^3J$ = 8.1 Hz), 6.85 t (2H, $^3J$ = 8.0 Hz) (signals from two NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 26.5 (2C), 26.6 (2C), 29.1 (2C), 30.6 (2C), 41.6 (2C), 44.2 (2C), 68.7 (2C), 69.3 (2C), 70.8 (2C), 71.0 (2C), 108.3 (2C), 116.4 (2C), 124.6 (2C), 128.8 (2C), 131.4 (2C), 144.7 (2C). Mass spectrum: *m*/*z* 624.3209 $[M]^+$. $C_{32}H_{50}Cl_2N_4O_4$. Calculated: *M* 624.3165.

**Cyclic oligomers IXk (*n* > 2)** were isolated as a mixture of by-products in the synthesis of compound **VIId**. Eluent $CH_2Cl_2$–MeOH, 50:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.60–1.69 m (2*n*H), 1.83 quint (*n*H, $^3J$ = 5.8 Hz), 1.89 quint (*n*H, $^3J$ = 6.3 Hz), 2.95 q (*n*H, $^3J$ = 5.3 Hz), 3.19 br.s (*n*H), 3.43 br.s (2*n*H), 3.47–3.57 m (2*n*H), 4.75 br.s (*n*H), 6.44–6.50 m (*n*H), 6.64 d (*n*H, $^3J$ = 8.0 Hz), 6.84 t (*n*H, $^3J$ = 8.0) (signals from *n* NH protons could not be assigned unambiguously).

**Cyclic dimers IXa, IXb, IXd, IXj, and IXk (*general procedure*).** A mixture of 1.25 mmol (283 mg) of 2-bromo-1,3-dichlorobenzene (**VI**), 0.02 mmol (12 mg) of $Pd(dba)_2$, 0.023 mol (14 mg) of BINAP, 5 ml of anhydrous dioxane, 0.5 mmol of diamine **IIa**, **IIb**, **IId**, **IIj**, or **IIk**, and 1.5 mmol (144 mg) of sodium *tert*-butoxide was heated for 6 h under reflux in an argon atmosphere. The mixture was cooled, a sample containing *N*,*N*′-diaryl derivative **VIIIa**, **VIIIb**, **VIId**, **VIIIj**, or **VIIIk** was withdrawn to record NMR and MALDI-TOF mass spectra, 7 ml of anhydrous dioxane, 0.08 mmol (46 mg) of $Pd(dba)_2$, 0.09 mol (56 mg) of BINAP, 0.5 mmol of the corresponding amine **II**, and 1.5 mmol (144 mg) of sodium *tert*-butoxide were added, and the mixture was heated for 24–30 h under reflux. After cooling, the solution was separated by decanting, the precipitate was washed with a small amount of methylene chloride, the washings were combined with the organic phase and evaporated, and the solid residue was subjected to chromatography on silica gel using the following solvent systems as eluents (in succession): $CH_2Cl_2$; $CH_2Cl_2$–MeOH, 200:1 to 3:1; $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:1 to 10:4:1. The yields are given in Table 2.

***N*$^1$-{3-[2-(3-Aminopropylamino)ethylamino]-propyl}-3-chloro-*N*$^2$-(3-{2-[3-(2,6-dichlorophenylamino)propylamino]ethylamino}propyl)benzene-1,2-diamine (XIa)** was obtained from compound **VIIIa**. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.67–1.85 m (8H), 2.63–2.78 m (14H), 2.89 br.s (4H), 3.05–3.16 m (4H), 3.34 t (2H, $^3J$ = 6.0 Hz), 3.60 br.s (3H), 6.38 d (1H, $^3J$ = 8.1 Hz), 6.60 d (1H, $^3J$ = 6.6 Hz), 6.69 t (1H, $^3J$ = 8.0 Hz), 6.80 t (1H, $^3J$ = 7.8 Hz), 7.15 d (2H, $^3J$ = 8.0 Hz) (signals from six NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 28.4 (1C), 29.5 (1C), 30.5 (2C), 42.0 (1C), 42.2 (2C), 45.0 (1C), 47.6 (4C), 48.2 (1C), 48.3 (1C), 49.0 (2C), 108.4 (1C), 116.3 (1C), 121.3 (1C), 124.5 (1C), 125.9 (2C), 128.6 (3C), 131.2 (1C), 142.5 (1C), 144.4 (1C). Mass spectrum: *m*/*z* 600.18 $[M]^+$.

**Cyclic dimer (IXb)** was obtained from 0.5 mmol (110 mg) of triamine **IIb**. Eluent $CH_2Cl_2$–MeOH, 50:1 to 20:1. Light yellow oily substance. The NMR and mass spectra of **IXb** are given above.

**1,17-Dichloro-5,6,7,8,9,10,11,12,13,18,19,20,-21,22,23,24,25,26-octadecahydrodibenzo[*b*,*m*]-[1,4,8,12,15,19]hexaazacyclodocosine (IXd)** was synthesized from 0.5 mmol (66 mg) of triamine **IId**. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:2. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.87 quint (4H, $^3J$ = 6.9 Hz), 1.91 quint (4H, $^3J$ = 6.1 Hz), 2.84 t (4H, $^3J$ = 6.7 Hz), 2.87 t (4H, $^3J$ = 6.8 Hz), 2.97 t (4H, $^3J$ = 6.7 Hz), 3.20 t (4H, $^3J$ = 6.2 Hz), 5.28 br.s (2H), 6.43 d (2H, $^3J$ = 7.8 Hz), 6.65 d.d (2H, $^3J$ = 8.1 Hz, $^4J$ = 1.0 Hz), 6.85 t (2H, $^3J$ = 8.0 Hz) (signals from four NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 30.3 (2C), 30.6 (2C), 42.5 (2C), 44.7 (2C), 47.6 (2C), 48.3 (2C), 108.4 (2C), 116.6 (2C), 124.8 (2C), 128.8 (2C), 131.2 (2C), 144.8 (2C). Mass spectrum: *m*/*z* 478.2477 $[M]^+$. $C_{24}H_{36}Cl_2N_6$. Calculated: *M* 478.2379.

***N*$^1$-[3-(3-Aminopropylamino)propyl]-3-chloro-*N*$^2$-{3-[3-(2,6-dichlorophenylamino)propylamino]-**

**propyl}benzene-1,2-diamine (XId)** was isolated as the second product. Eluent $CH_2Cl_2$–MeOH–aq. $NH_3$, 100:20:3. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 1.69 quint (2H, $^3J$ = 6.8 Hz), 1.73–1.87 m (6H), 2.69–2.78 m (8H), 2.81 t (2H, $^3J$ = 6.1 Hz), 2.92 t (2H, $^3J$ = 6.2 Hz), 3.14 t (2H, $^3J$ = 5.8 Hz), 3.37 t (2H, $^3J$ = 6.7 Hz), 4.02 br.s (3H), 6.43 d (1H, $^3J$ = 7.6 Hz), 6.63 d (1H, $^3J$ = 8.0 Hz), 6.73 t (1H, $^3J$ = 8.0 Hz), 6.83 t (1H, $^3J$ = 8.0 Hz), 7.18 d (2H, $^3J$ = 8.0 Hz) (signals from four NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 28.9 (1C), 30.3 (2C), 31.0 (1C), 40.2 (1C), 42.0 (2C), 45.2 (1C), 47.5 (1C), 47.6 (1C), 47.7 (1C), 47.8 (1C), 108.6 (1C), 116.7 (1C), 121.5 (1C), 124.7 (1C), 126.1 (2C), 128.7 (3C), 131.3 (1C), 142.7 (1C), 144.5 (1C). Mass spectrum: *m*/*z* 514.24 $[M]^+$.

***N*,*N*′-[2,2′-(Ethane-1,2-diylbisoxy)bis(ethane-2,1-diyl)]bis(2,6-dichloroaniline) (VIIIj)** was synthesized from 1.25 mmol (283 mg) of 2-bromo-1,3-dichlorobenzene (**VI**) and 0.5 mmol (74 mg) of diamine **IIj**. Yield 85% (in the reaction mixture). Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 3.51 q (4H, $^3J$ = 5.5 Hz), 3.60 t (4H, $^3J$ = 5.0 Hz), 3.63 s (4H), 4.51 t (2H, $^3J$ = 6.0 Hz), 6.74 t (2H, $^3J$ = 8.0 Hz), 7.19 d (4H, $^3J$ = 8.0 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 46.9 (2C), 70.4 (2C), 70.5 (2C), 121.6 (2C), 126.2 (2C), 128.8 (2C), 142.7 (2C).

**1,18-Dichloro-5,6,7,9,10,12,13,14,19,20,21,-23,24,-26,27,28-hexadecahydrodibenzo[*h*,*t*]-[1,4,13,16,7,10,19,22]tetraoxatetraazacyclotetracosine (IXj)** was synthesized from 0.5 mmol (74 mg) of diamine **IIj**. Eluent $CH_2Cl_2$–MeOH, 100:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 3.13 t (4H, $^3J$ = 5.1 Hz), 3.33 br.s (4H), 3.64 s (4H), 3.67 t (4H, $^3J$ = 5.0 Hz), 3.70 t (4H, $^3J$ = 5.6 Hz), 3.75 s (4H), 5.31 br.s (2H), 6.48 d (2H, $^3J$ = 8.0 Hz), 6.65 d (2H, $^3J$ = 7.7 Hz), 6.85 t (2H, $^3J$ = 8.0 Hz) (signals from two NH protons could not be assigned unambiguously). $^{13}$C NMR spectrum, $\delta_C$, ppm: 43.3 (2C), 46.8 (2C), 69.5 (2C), 70.4 (2C), 70.6 (2C), 71.3 (2C), 108.6 (2C), 116.7 (2C), 124.7 (2C), 129.1 (2C), 131.4 (2C), 144.6 (2C). Mass spectrum: *m*/*z* 512.25 $[M]^+$.

**2,6-Dichloro-*N*-(2-{2-[2-(2-chlorophenylamino)-ethoxy]ethoxy}ethyl)aniline (XIIj)**. Eluent $CH_2Cl_2$–MeOH, 500:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 3.26 t (2H, $^3J$ = 5.1 Hz), 3.52 t (2H, $^3J$ = 5.0 Hz), 3.62 t (2H, $^3J$ = 5.1 Hz), 3.66 s (4H), 3.69 t (2H, $^3J$ = 5.3 Hz), 4.66 br.s (2H), 6.63 t (1H, $^3J$ = 7.7 Hz), 6.66 d (1H, $^3J$ = 7.8 Hz), 6.76 t (1H, $^3J$ = 7.8 Hz), 7.12 t (1H, $^3J$ = 7.7 Hz), 7.21 d (2H, $^3J$ = 7.8 Hz), 7.24 d (1H, $^3J$ = 7.7 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 43.2 (1C), 46.9 (1C), 69.5 (1C), 70.4 (1C), 70.5 (2C), 111.4 (1C), 117.3 (1C), 119.5 (1C), 121.6 (1C), 126.2 (2C), 127.7 (1C), 128.8 (2C), 129.1 (1C), 142.7 (1C), 144.0 (1C). Mass spectrum: *m*/*z* 402.0694 $[M]^+$. $C_{18}H_{21}Cl_3N_2O_2$. Calculated: *M* 402.0669.

***N*,*N*′-{2,2′-[Ethane-1,2-diylbis(oxy)]bis(ethane-2,1-diyl)}bis(2-chloroaniline) (XIIIj).** Eluent $CH_2Cl_2$–MeOH, 500:1. Light yellow oily substance. $^1$H NMR spectrum, δ, ppm: 3.35 t (4H, $^3J$ = 5.2 Hz), 3.68 s (4H), 3.74 t (4H, $^3J$ = 5.4 Hz), 4.66 br.s (2H), 6.63 t (2H, $^3J$ = 7.7 Hz), 6.66 d (2H, $^3J$ = 7.8 Hz), 7.12 t.d (2H, $^3J$ = 7.7, $^4J$ = 0.9 Hz), 7.24 d.d (2H, $^3J$ = 7.7, $^4J$ = 0.8 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 43.2 (2C), 69.5 (2C), 70.5 (2C), 111.3 (2C), 117.3 (2C), 119.5 (2C), 127.7 (2C), 129.1 (2C), 144.0 (2C). Mass spectrum: *m*/*z* 368.1083 $[M]^+$. $C_{18}H_{22}Cl_2N_2O_2$. Calculated: *M* 368.1058.

**Cyclic dimer (IXk)** was synthesized from 0.5 mmol (102 mg) of diamine **IIk**. Eluent $CH_2Cl_2$–MeOH, 100:1 to 50:1. Light yellow oily substance. The NMR and mass spectra are given above.

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## REFERENCES

1. Bradshaw, J.S., Krakowiak, K.E., and Izatt, R.M., *Aza-Crown Macrocycles*, New York: Wiley, 1993.
2. Burguette, M.I., Escuder, B., Garcia-Espana, E., Luis, S.V., and Miravet, J.F., *Tetrahedron*, 2002, vol. 58, p. 2839.
3. Militsopoulou, M., Tsiakopoulos, N., Chochos, C., and Magoulas, G., *Tetrahedron Lett*., 2002, vol. 43, p. 2593.
4. Favre-Reguillon, A., Segat-Dioury, F., Nait-Bouda, L., Cosma, C., Siaugue, J.-M., Foos, J., and Guy, A., *Synlett*, 2000, p. 868.
5. Ray, J.K., Haldar, M.K., Gupta, S., and Kar, G.K., *Tetrahedron*, 2000, vol. 56, p. 909.
6. De Wall, S.L., Meadows, E.S., Barbour, L.J., and Gokel, G.W., *Chem. Commun*., 1999, p. 1553.
7. Meadows, E.S., De Wall, S.L., Barbour, L.J., and Gokel, G.W., *Chem. Commun*., 1999, p. 1555.
8. Kubo, K., Yamamoto, E., and Sakurai, T., *Heterocycles*, 1998, vol. 48, p. 2133.
9. Koulov, A.V., Mahoney, J.M., and Smith, B.D., *Org. Biomol. Chem*., 2003, vol. 1, p. 1467.
10. Vetrichelvan, M., Lai, Y.-H., and Mok, K.F., *J. Chem. Soc., Dalton Trans*., 2003, p. 295.

11. Borisova, N.E., Reshetova, M.D., and Ustynyuk, Yu.A., *Chem. Rev*., 2007, vol. 107, p. 46.
12. Witulski, B., Weber, M., Bergstrasser, U., Desvergne, J.-P., Bassani, D.M., and Bouas-Laurent, H., *Org. Lett*., 2001, vol. 3, p. 1467.
13. Gouloumis, A., Lawson, R.G., Vasquez, P., Echegoyen, L., and Torres, T., *Tetrahedron*, 2002, vol. 58, p. 961.
14. Gunnlaugsson, T., Nieunwenhuyzen, M., Richard, M., and Thoss, V., *J. Chem. Soc., Perkin Trans. 2*, 2002, p. 141.
15. Beletskaya, I.P., Bessmertnykh, A.G., Averin, A.D., Denat, F., and Guilard, R., *Eur. J. Org. Chem*., 2005, p. 261.
16. Yang, B.H. and Buchwald, S.L., *J. Organomet. Chem*., 1999, vol. 576, p. 125.
17. Averin, A.D., Shukhaev, A.V., Golub, S.L., Buryak, A.K., and Beletskaya, I.P., *Synthesis*, 2007, p. 2995.
18. Averin, A.D., Ulanovskaya, O.A., Pleshkova, N.A., Borisenko, A.A., and Beletskaya, I.P., *Collect. Czech. Chem. Commun*., 2007, vol. 72, p. 785.
19. Averin, A.D., Ulanovskaya, O.A., Fedotenko, I.A., Borisenko, A.A., Serebryakova, M.V., and Beletskaya, I.P., *Helv. Chim. Acta*, 2005, vol. 88, p. 1983.
20. Beletskaya, I.P., Bessmertnykh, A.G., Averin, A.D., Denat, F., and Guilard, R., *Eur. J. Org. Chem*., 2005, p. 281.
21. Wolfe, J.P. and Buchwald, S.L., *J. Org. Chem*., 2000, vol. 65, p. 1144.
22. Ukai, T., Kawazura, H., Ishii, Y., Bonnet, J.J., and Ibers, J.A., *J. Organomet. Chem*., 1974, vol. 65, p. 253.