

Article

Pd-Catalyzed Amination in the Synthesis of a New Family of Macropolycyclic Compounds Comprising Diazacrown Ether Moieties

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Abstract: *N,N'*-bis(bromobenzyl) and *N,N'*-bis(halopyridinyl) derivatives of diaza-12-crown-4, diaza-15-crown-5 and diaza-18-crown-6 ethers were synthesized in high yields. The Pd-catalyzed macrocyclization reactions of these compounds were carried out using a variety of polyamines and oxadiazines were carried out to give novel macrobicyclic and macrotricyclic compounds of the cryptand type. The dependence of the yields of macropolycycles on the nature of the starting diazacrown derivatives and polyamines was established. Generally *N,N'*-bis(3-bromobenzyl)-substituted diazacrown ethers and oxadiazines provided better yields of the target products. The highest yield of the macrobicyclic products reached 57%.

Keywords: diazacrown ethers; polyamines; Pd catalysis; amination; macropolycycles

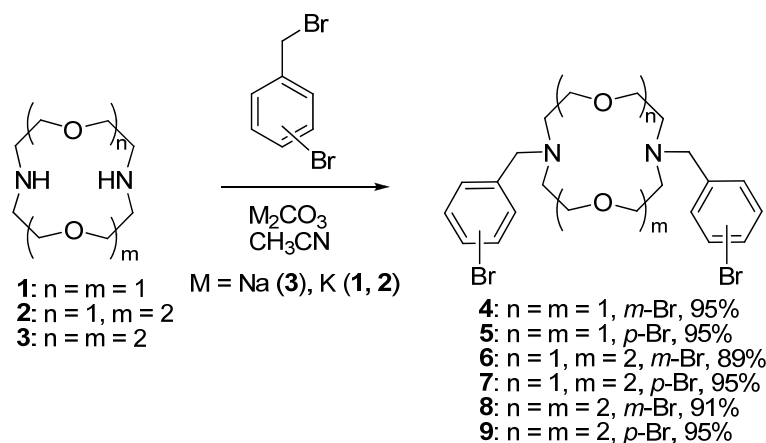
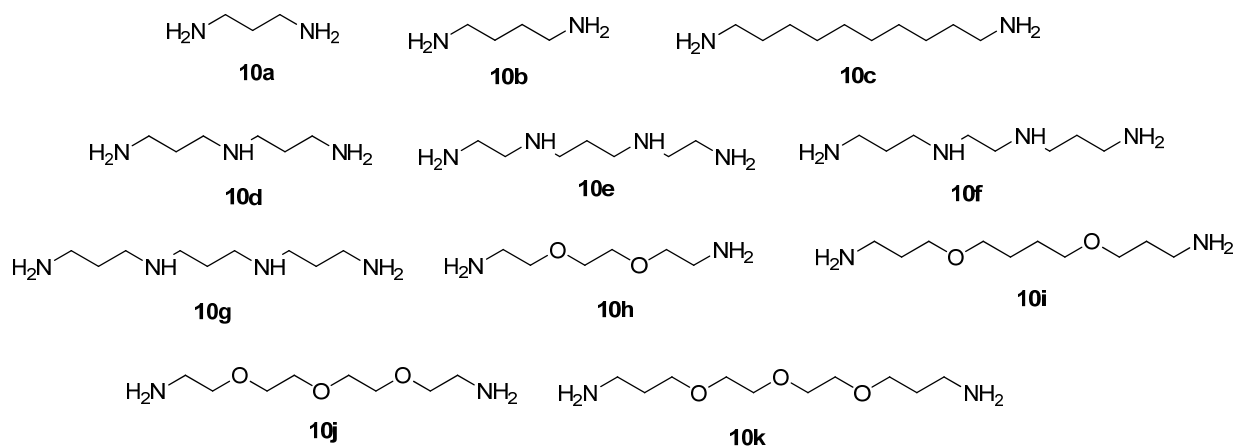
1. Introduction

Macropolycyclic compounds (cryptands) attract the continued interest of researchers due to their unique selective ion binding properties. Macrobicycles of the cryptand type derived from azacrown ethers were among the first reported molecules of this type, e.g., di- and triazapolyoxacryptands [1,2], benzocryptands possessing 1,2-, 1,3-, and 1,4-disubstituted benzene [3,4], and 2,6-disubstituted pyridine fragments [5]. Compounds with two diazacrown ethers combined in macrotricyclic systems via aliphatic or benzyl linkers were also described [6,7]. So-called cross-bridged polycyclic compounds comprising diazacrown ethers constitute another class of cryptands called supercryptands [8]. Krakowiak and coauthors elaborated convenient and versatile synthetic approaches to various macropolycycles in 1990s based on simple nucleophilic substitution reactions [9–11]. Our interest in this field arises from the possibilities of the application of the catalytic Buchwald-Hartwig amination in the construction of the polymacrocyclic systems capable of selective metal cations coordination. We have already successfully used this approach for the synthesis of macrobicycles comprising tetraazamacrocyclic [12–14] moieties and made the first steps in the formation of polymacrocyclic structures based on aza- and diazacrown ethers [15,16].

2. Results and Discussion

Initially we attempted to synthesize a series of macrobicycles possessing diaza-12-crown-4 moieties because these compounds are of interest for selective coordination of Li ions. The search for efficient macrocyclic chelators of this ion is important for the sequestration of ^7Li and ^6Li isotopes. It is well known that a partial change of oxygen for nitrogen atoms in 12-member macrocycles and introduction of podands to these nitrogen atoms increases the stability constants of the lithium complexes by 2–3 orders of magnitude [17,18], thus we might expect that the macrobicycles with additional donor atoms will also form more stable complexes with Li cations. At the first step we synthesized *N,N'*-bis(bromobenzyl) derivatives of diaza-12-crown-4 by reacting 1 equiv. of compound **1** with 2 equiv. of 3- and 4-bromobenzyl bromides in boiling acetonitrile using K_2CO_3 as a base. As a result, the corresponding derivatives **4** and **5** were obtained in almost quantitative yields (Scheme 1). The same method was applied for the modification of diaza-15-crown-5 (**2**) and diaza-18-crown-6 (**3**), and corresponding *N,N'*-bis(bromobenzyl) derivatives **6–9** were obtained in 89%–95% yields (Scheme 1). Na_2CO_3 was used as a base in the case of diaza-18-crown-6.

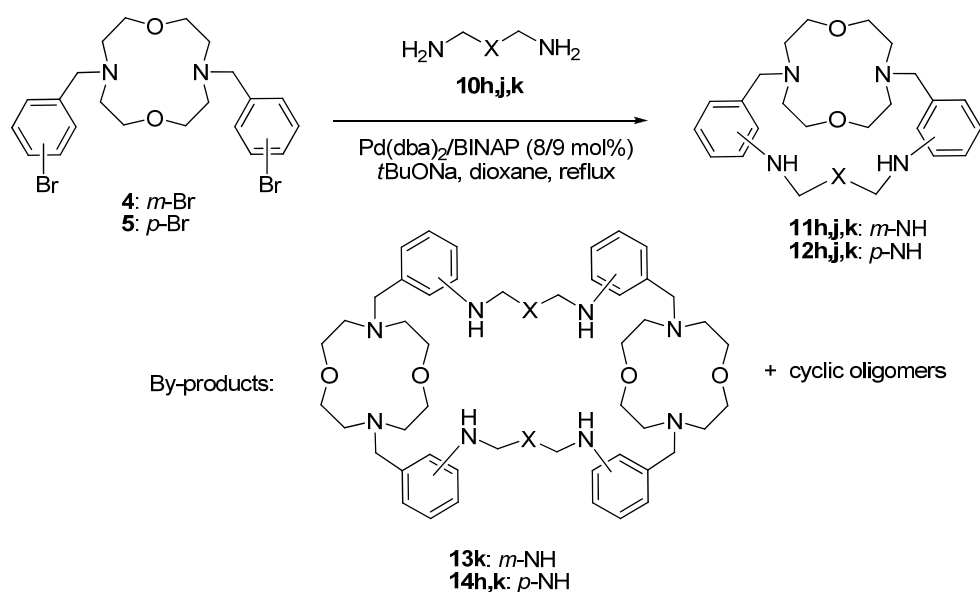
The macrocyclization reactions of compounds **4–9** were carried out using a series of di-, tri-, tetraamines, and oxadiazines **10a–k** differing in the chain length and the number of N and O atoms (Figure 1). The investigation of the extended set of polyamines was necessary for elucidation of the scope and limitations of the proposed method and for the construction of macrobicycles with various macrocyclic cavities what would be useful for tuning their coordination properties towards different metal cations.

Scheme 1. Synthesis of *N,N'*-bis(bromobenzyl) derivatives of diazacrown ethers **4–9**.**Figure 1.** Polyamines and oxadiazines **10a–k** used in the synthesis of macrobicycles.

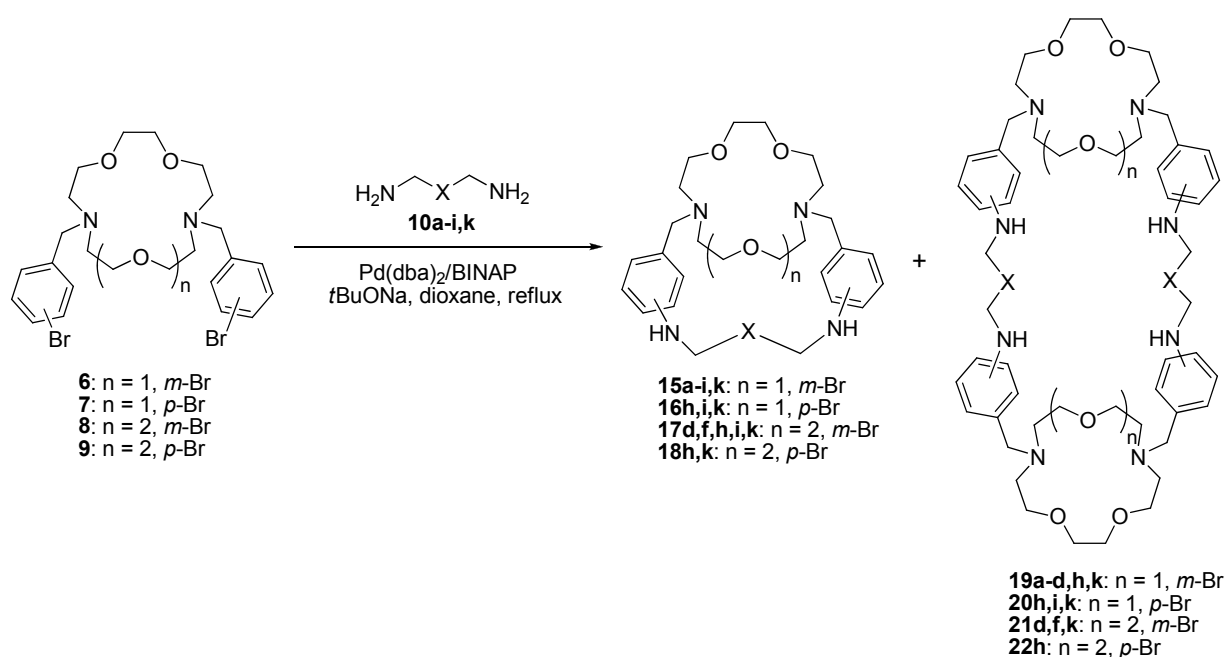
Macrocycles **4** and **5** were introduced in the Pd-catalyzed amination reactions with oxadiazines **10h,j,k** using 8 mol% Pd(dba)₂/BINAP catalytic system (dba—dibenzylideneacetone, BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene) which previously was shown to be optimal in the majority of the amination reactions of aryl halides, and especially in the macrocyclization processes involving polyamines. The syntheses were carried out in boiling dioxane ($c = 0.02$ M) using sodium *tert*-butoxide as a base (Scheme 2). Macrobicycles **11** and **12** were isolated by column chromatography on silica gel. The yields are given in Table 1.

We did not observe any correlation between the structures of the starting compounds and the yields of the macrobicycles, which ranged from 13% to 31%. In some cases macrotricyclic cyclodimers **13** and **14** were isolated, in yields comparable to those of the target compounds (Table 1, entries 3, 4, 6). In two cases mixtures of cyclic oligomers were obtained in yields *ca* 40% (entries 1, 2). These facts imply that in some cases the intramolecular diamination is hindered, probably due to unfavorable mutual orientation of two bromine atoms.

Further investigations were carried out using *N,N'*-bis(3-bromobenzyl) derivative of diaza-15-crown-5 **6** and a wide range of polyamines to study the process in details and to find out scope and limitations of the proposed approach. The reactions were conducted under the same conditions using 8 mol% catalyst (Scheme 3), the results are presented in Table 2.

Scheme 2. Synthesis of macrobicycles **11** and **12**.**Table 1.** Synthesis of macrobicycles **11** and **12**.

Entry	Diazacrown derivative	Polyamine	Yields of macrobicycles	Yields of cyclic oligomers
1	4	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10h	11h , 13%	mixture, 42%
2	4	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10j	11j , 31%	mixture, 37%
3	4	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10k	11k , 19%	13k , 23%
4	5	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10h	12h , 30%	14e , 27%
5	5	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10j	12j , 20%	
6	5	H ₂ NCH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ OCH ₂ CH ₂ NH ₂ 10k	12k , 15%	14k , 17%

Scheme 3. Synthesis of macrobicycles **15–18**.

In the majority of cases we obtained rather good yields of the target macrobicycles **15** ranging from 20% to 38%. The reactions with the shortest propane-1,3-diamine (**10a**) and butane-1,4-diamine (**10b**) gave poorer results (Table 2, entries 1, 2) due to the higher steric demands of these diamines for the mutual orientation of two bromine atoms in the starting compound **6**. For the rest of di- and polyamines we did not observe any clear dependence of the product yields on the chain length and on the number of the nitrogen and oxygen atoms. In many cases we managed to isolate macrotricyclic by-products **19**, and in the reaction with **10b** the yield of **19b** was twice as much as of the corresponding macrobicycycle **15b**. In all cases we also obtained complex mixtures of cyclic oligomers but their composition cannot be unambiguously established by NMR and mass spectroscopies because they possess almost the same structural fragments.

Table 2. Synthesis of macrobicycles **15**–**18**.

Entry	Diazacrown derivative	Polyamine	Pd(dba) ₂ /L, mol% ^a	Yields of macrobicycles	Yields of cyclodimers
1	6	H ₂ N—CH ₂ CH ₂ —NH ₂ (10a)	8/9	15a , 19%	19a , 19%
2	6	H ₂ N—CH ₂ CH ₂ CH ₂ —NH ₂ (10b)	8/9	15b , 12%	19b , 21%
3	6	H ₂ N—CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ —NH ₂ (10c)	8/9	15c , 25%	19c , 15%
4	6	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10d)	8/9	15d , 36%	19d , 9%
5	6	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10e)	8/9	15e , 28%	
6	6	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10f)	8/9	15f , 33%	
7	6	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10g)	8/9	15g , 24%	
8	6	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10h)	8/9	15h , 20%	19h , 10%
9	6	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10i)	8/9	15i , 37%	
10	6	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	8/9	15k , 38%	19k , 24%
11	7	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	8/9	16k , 5%	20k , 10%
12	7	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	8/9	16k , 4%	20k , 10%
13	7	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	16/18	16k , 10%	20k , 19%
14	7	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10i)	16/18	16i , 10%	20i , 10%
15	7	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10h)	16/18	16h , 18%	20h , 31%
16	8	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10d)	8/9	17d , 25%	21d , 6%
17	8	H ₂ N—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH—CH ₂ CH ₂ —NH ₂ (10f)	8/9	17f , 10%	21f , 5%
18	8	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10h)	8/9	17h , 57%	
19	8	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10i)	8/9	17i , 28%	
20	8	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	8/9	17k , 35%	21k , 17%
21	9	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10h)	16/18	18h , 25%	22h , 10%
22	9	H ₂ N—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —O—CH ₂ CH ₂ —NH ₂ (10k)	16/18	18k , 36%	

^a L = BINAP in all entries, except 12; in entry 12 L = DavePhos.

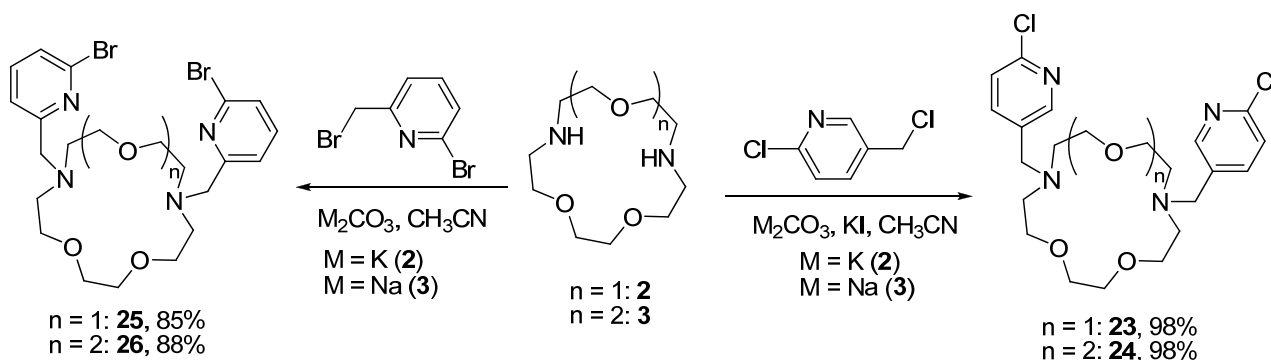
Other derivatives of diazacrown ethers **7**–**9** were tested mainly in the cyclization reactions with oxadiazines to establish the dependence of the product yields on the ring size and substitution patterns. The reactions of the isomeric diazacrown derivative **7** containing 4-bromobenzyl substituents provided substantially lower yields of the cryptands **16** (entries 11–15). Indeed, the use of the standard catalytic system in the macrocyclization reaction with trioxadiazine **10k** afforded only 5% yield of the desired macrobicycycle **16k** (entry 11). The application of another ligand DavePhos (2-(dimethylamino)-2'-(dicyclohexylphosphino)biphenyl) was not successful either (entry 12),

however, 16 mol% of the catalytic system $\text{Pd}(\text{dba})_2/\text{BINAP}$ was helpful (entry 13) though the yield remained low. Only the reaction with dioxadiazine **10h** proceeded better and produced the cryptand **16h** in 18% yield (entry 15). In all cases the yields of cyclic dimers **20** exceeded those of macrobicycles **16**.

The macrocyclization reactions with the derivative of diaza-18-crown-6 **8** bearing two 3-bromobenzyl substituents were quite successful (entries 16–20) at 8 mol% catalyst loadings. While the use of triamine **10d**, oxadiazine **10i,k** provided average 25%–35% yields of the macrocyclization products **17d,i,k** (entries 16, 19, 20), the reaction with dioxadiazine **10h** resulted in 57% yield of the target cryptand **17h** (entry 18), what is the best result ever observed among yields in the Pd-catalyzed macrocyclization reactions. On the other hand, macrotricyclic dimers **21** were isolated in certain cases in much lower yields. The reactions with isomeric derivative **9** were run using a 16 mol% catalytic system (entries 21, 22) and the yields of the target cryptands **18** were quite reasonable. It means that of four tested N,N' -bis(bromobenzyl) substituted diazacrowns, only compound **7** was recalcitrant in the intramolecular diamination processes.

The incorporation of the pyridine moiety in the structure of macrocyclic compounds can be useful as it increases the number of donor sites of the molecule what is favorable for the complexation of the cations with high coordination numbers. We synthesized N,N' -bis(halopyridinyl) derivatives of diazacrown ethers **23–26** differing in the nature of the halogen atom and the position of the nitrogen atom (Scheme 4). The reactions were conducted in boiling acetonitrile using sodium or potassium carbonates as bases, and the yields of the target compounds were excellent.

Scheme 4. Synthesis of N,N' -bis(halopyridinyl) derivatives of diazacrown ethers **23–26**.



All our attempts to induce the macrocyclization of compound **23** using the $\text{Pd}(\text{dba})_2/\text{BINAP}$ catalytic system failed, however the application of DavePhos instead of BINAP was helpful (Scheme 5, Table 3). The same situation was observed with the derivative **24**, however, the yields of the target macrobicycles **27**, **28** were reasonable only in some cases (entries 1, 5). The analysis of the reaction mixtures and fractions after chromatography revealed the formation of complex mixtures of oligomers and other unidentified products which could arise from the side reactions other than catalytic amination. This is supported by the fact that the conversion of starting N,N' -bis(chloropyridinyl) derivatives **23** and **24** was complete whereas only half of the oxadiazines was consumed. Unfortunately, the efficiency of the bromosubstituted derivatives **25** and **26** to form macrobicycles was even poorer than that of compounds **23** and **24**. Only in the reactions of **25** with trioxadiazine **10k** and of **26** with dioxadiazine **10h** did yields exceed 10% (entries 6, 8), in other cases they were negligible

and are not given in Table 3. A possible explanation is that bromine-containing derivatives **25** and **26** are more active than their chlorine-containing analogues **23** and **24** and participate in various side reactions. It is worth noting that both BINAP and DavePhos ligands can be used with limited success in the amination of compounds **25** and **26**.

Scheme 5. Synthesis of macrobicycles **27–30**.

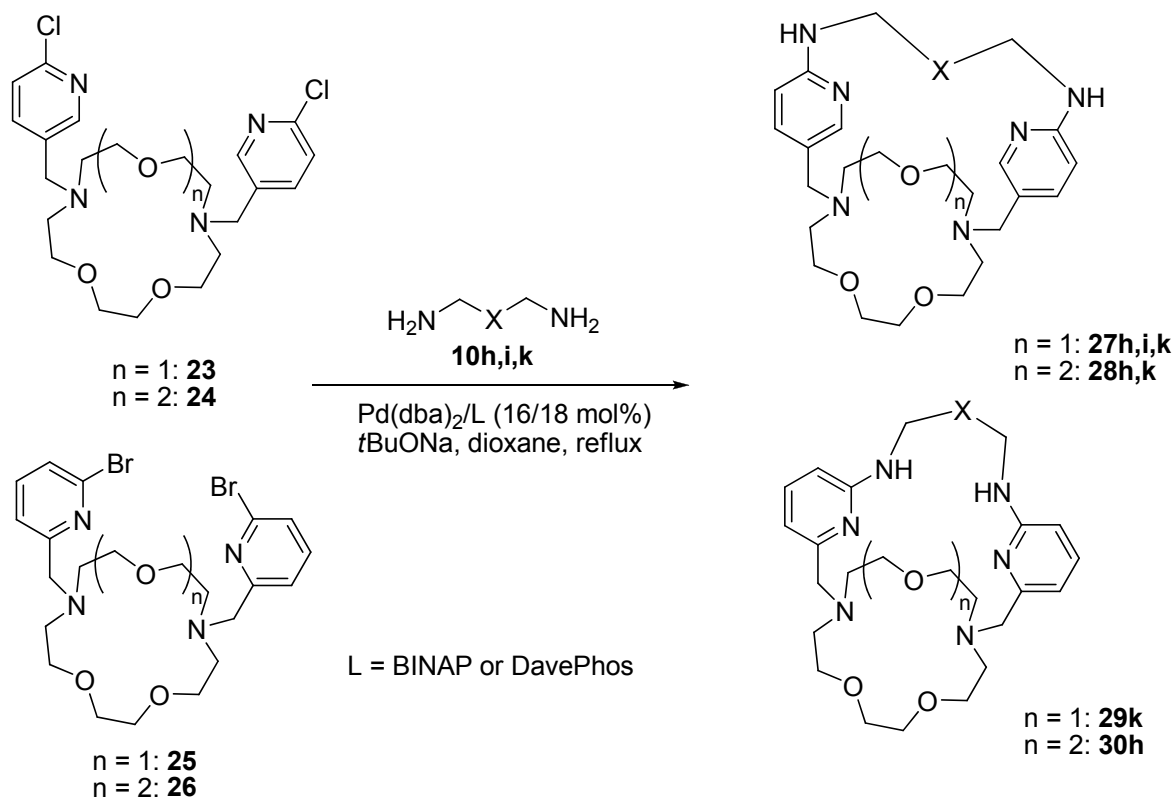


Table 3. Synthesis of macrobicycles **27–30**.

Entry	Diazacrown derivative	Polyamine	Ligand L	Yields of macrobicycles
1	23	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10h)	DavePhos	27h , 22%
2	23	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10i)	DavePhos	27i , 11%
3	23	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10k)	DavePhos	27k , 9%
4	24	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10h)	DavePhos	28h , 5%
5	24	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10k)	DavePhos	28k , 24%
6	25	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10k)	BINAP	29k , 12%
7	26	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10h)	BINAP	30h , 9%
8	26	$\text{H}_2\text{N}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{NH}_2$ (10h)	DavePhos	30h , 16%

To summarize, we have conducted an extended investigation of the scope of Pd-catalyzed amination in the synthesis of macrobicycles based on diazacrown ether moieties, and determined the dependence of the yields of the target cryptands on the nature of halogen-containing substituents in the starting compounds. The macrocyclization processes were shown to proceed more efficiently with *N,N'*-bis(3-bromobenzyl) substituted diazacrown ethers **6** and **8**, and the formation of valuable

macrotricyclic compounds was demonstrated. The studies of the coordination properties of novel macrobicycles towards different metal cations are underway now.

3. Experimental

3.1. General Information

NMR spectra were registered using a Bruker Avance 400 spectrometer (operating at 400 MHz for ^1H and 100.6 MHz for ^{13}C), MALDI-TOF spectra were obtained with a Bruker Ultraflex spectrometer using 1,8,9-trihydroxyanthracene as matrix and PEGs as internal standards. ESI-TOF spectra were recorded with a Bruker microQ-TOF spectrometer in methanol. Diazacrown ethers, 3- and 4-bromobenzyl bromides, 2-chloro-5-(chloromethyl)pyridine, 2-bromo-6-methylpyridine, oxadiazines and polyamines, BINAP and DavePhos ligands, sodium *tert*-butoxide were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used without further purification, $\text{Pd}(\text{dba})_2$ was synthesized from PdCl_2 according to the known procedure [19]. 2-Bromo-6-(bromomethyl)pyridine was synthesized from 2-bromo-6-methylpyridine using a standard bromination procedure ($\text{Br}_2/\text{CCl}_4/\text{NBS}$). Dioxane was distilled over NaOH, followed by distillation over sodium under argon, while acetonitrile, dichloromethane and methanol were used freshly distilled.

3.2. General Method for the Synthesis of *N,N'*-bis(haloaryl)substituted Diazacrown Ethers

A one-neck flask equipped with a magnetic stirrer and reflux condenser was charged with diazacrown ether (0.86–2.3 mmol), aryl halide halogenomethyl derivative (1.7–4.6 mmol), dry acetonitrile (3–8 mL) and sodium or potassium carbonate (3.4–11.2 mmol). The reaction mixture was stirred under reflux for several hours, the residue was filtered off, washed with CH_2Cl_2 , and the combined organic fractions were evaporated *in vacuo*, dissolved in CH_2Cl_2 (5–20 mL), washed three times with equal volumes of distilled water, dried over 4 Å molecular sieves, and the CH_2Cl_2 was evaporated *in vacuo* to give the pure target product. We have previously reported the synthesis and spectral data of compounds **6–9** [15].

4,10-Bis(3-bromobenzyl)-1,7-dioxo-4,10-diazacyclododecane (4). Obtained from diazacrown **1** (0.86 mmol, 150 mg), 3-bromobenzyl bromide (1.7 mmol, 431 mg) in the presence of K_2CO_3 (4.3 mmol, 530 mg) in MeCN (3 mL). Yield 419 mg (95%), as a yellowish viscous oil. ^1H -NMR (CDCl_3) δ 2.73 (d, $^3J = 4.6$ Hz, 8H, CH_2N), 3.58 (t, $^3J = 4.6$ Hz, 8H, CH_2O), 3.63 (s, 4H, PhCH_2N), 7.17 (t, $^3J = 7.8$ Hz, 2H, $\text{H}_5(\text{Ph})$), 7.30–7.37 (m, 4H, $\text{H}_4(\text{Ph})$, $\text{H}_6(\text{Ph})$), 7.58 (s, 2H, $\text{H}_2(\text{Ph})$). ^{13}C -NMR (CDCl_3) δ 55.0 (4C, CH_2N), 60.3 (2C, PhCH_2N), 69.4 (4C, CH_2O), 122.3 (2C, $\text{C}_3(\text{Ph})$), 127.3 (2C, $\text{CH}(\text{Ph})$), 129.7 (2C, $\text{CH}(\text{Ph})$), 129.9 (2C, $\text{CH}(\text{Ph})$), 131.7 (2C, $\text{CH}(\text{Ph})$), 142.2 (2C, $\text{C}_1(\text{Ph})$). HRMS (MALDI-TOF): $\text{C}_{22}\text{H}_{29}\text{Br}_2\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ calcd.; 511.0596 observed; 511.0632.

4,10-Bis(4-bromobenzyl)-1,7-dioxo-4,10-diazacyclododecane (5). Obtained from diazacrown **1** (0.86 mmol, 150 mg), 4-bromobenzyl bromide (1.7 mmol, 431 mg) in the presence of K_2CO_3 (4.3 mmol, 530 mg) in MeCN (3 mL). Yield 421 mg (95%), of a beige crystalline powder, m.p. 88–90 °C. ^1H -NMR (CDCl_3) δ 2.70 (t, $^3J = 4.7$ Hz, 8H, CH_2N), 3.56 (t, $^3J = 4.7$ Hz, 8H, CH_2O), 3.58 (s, 4H, PhCH_2N), 7.28 (A part of AA'XX' system, 4H, $\text{H}_2(\text{Ph})$), 7.42 (X part of AA'XX' system,

4H, H3(Ph)). ^{13}C -NMR (CDCl_3) δ 54.9 (4C, CH_2N), 60.2 (2C, PhCH_2N), 69.4 (4C, CH_2O), 120.5 (2C, C4(Ph)), 130.4 (4C, $\text{CH}(\text{Ph})$), 131.2 (4C, $\text{CH}(\text{Ph})$), 138.8 (2C, C1(Ph)). HRMS (MALDI-TOF): $\text{C}_{22}\text{H}_{29}\text{Br}_2\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$ calcd.; 511.0596 observed; 511.0557.

7,13-Bis[(6-chloropyridin-3-yl)methyl]-1,4,10-trioxa-7,13-diazacyclopentadecane (23). Obtained from diazacrown ether **2** (2.3 mmol, 500 mg), 2-chloro-5-(chloromethyl)pyridine (4.6 mmol, 745 mg) in the presence of K_2CO_3 (11.6 mmol, 1.6 g) in MeCN (8 mL). Yield 1.057 g (98%), of a yellow glassy compound. ^1H -NMR (CDCl_3) δ 2.71 (t, $^3J = 5.0$ Hz, 4H, CH_2N), 2.75 (t, $^3J = 5.8$ Hz, 4H, CH_2N), 3.52–3.57 (m, 8H, CH_2O), 3.58 (s, 4H, CH_2O or PyCH_2N), 3.62 (s, 4H, PyCH_2N or CH_2O), 7.24 (d, $^3J = 8.1$ Hz, 2H, H5-Py), 7.71 (dd, $^3J = 8.1$ Hz, $^4J = 1.4$ Hz, 2H, H6-Py), 8.29 (br.s, 2H, H2-Py). ^{13}C -NMR (CDCl_3) δ 54.3 (2C, CH_2N), 54.4 (2C, CH_2N), 57.0 (2C, PyCH_2N), 69.3 (2C, CH_2O), 70.1 (2C, CH_2O), 70.6 (2C, CH_2O), 123.9 (2C, C5-Py), 134.2 (2C, C1-Py), 139.4 (2C, C6-Py), 149.7 (2C, C2-Py), 150.0 (2C, C4-Py). HRMS (MALDI-TOF): $\text{C}_{22}\text{H}_{31}\text{Cl}_2\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$ calcd.; 469.1773 observed; 469.1742.

1,16-Bis[(6-chloropyridin-3-yl)methyl]-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (24). Obtained from diazacrown **3** (1 mmol, 262 mg), 2-chloro-5-(chloromethyl)pyridine (2 mmol, 324 mg) in the presence of K_2CO_3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 504 mg (98%), of a yellow glassy compound. ^1H -NMR (CDCl_3) δ 2.75 (t, $^3J = 5.6$ Hz, 8H, CH_2N), 3.54 (s, 8H, CH_2O), 3.56 (t, $^3J = 5.6$ Hz, 8H, CH_2O), 3.65 (s, 4H, PyCH_2N), 7.22 (d, $^3J = 8.0$ Hz, 2H, H5-Py), 7.67 (d, $^3J = 8.0$ Hz, 2H, H6-Py), 8.27 (br.s, 2H, H2-Py). ^{13}C -NMR (CDCl_3) δ 53.7 (4C, CH_2N), 56.2 (2C, CH_2NPy), 69.7 (4C, CH_2O), 70.6 (4C, CH_2O), 123.8 (2C, C5-Py), 134.3 (2C, C1-Py), 139.3 (2C, C6-Py), 149.6 (2C, C2-Py), 149.8 (2C, C4-Py). HRMS (MALDI-TOF): $\text{C}_{24}\text{H}_{35}\text{Cl}_2\text{N}_4\text{O}_4$ ($\text{M}+\text{H}$) $^+$ calcd.; 513.2035 observed; 513.2052.

4,13-Bis[(6-bromopyridin-2-yl)methyl]-1,7,10-trioxa-4,13-diazacyclohexadecane (25). Obtained from diazacrown ether **2** (1 mmol, 218 mg), 2-bromo-6-(bromomethyl)pyridine (2 mmol, 502 mg) in the presence of K_2CO_3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 474 mg (85%), of a yellow glassy compound. ^1H -NMR (CDCl_3) δ 2.67–2.77 (m, 8H, CH_2N), 3.46–3.52 (m, 8H, CH_2O), 3.53 (s, 4H, CH_2O or PyCH_2N), 3.72 (br.s, 4H, PyCH_2N or CH_2O), 7.24 (br.s, 2H, H-Py), 7.42 (br.s, 2H, H-Py), 7.53 (br.s, 2H, H-Py). ^{13}C -NMR (CDCl_3) δ 54.4 (2C, CH_2N), 54.9 (2C, CH_2N), 61.4 (2C, PyCH_2N), 68.6 (4C, CH_2O), 69.6 br (2C, CH_2O), 122.3 br (2C, H6-Py), 126.3 (2C, H4-Py), 139.2 (2C, H5-Py), 141.2 (2C, C3-Py), 159.5 (2C, C1-Py). HRMS (MALDI-TOF): $\text{C}_{22}\text{H}_{31}\text{Br}_2\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$ calcd.; 557.0763 observed; 557.0722.

7,16-Bis[(6-bromopyridin-2-yl)methyl]-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (26). Obtained from diazacrown ether **3** (1 mmol, 262 mg) 2-bromo-6-(bromomethyl)pyridine (2 mmol, 502 mg) in the presence of K_2CO_3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 530 mg (88%) of a yellow crystalline powder, m.p. 131–133 °C. ^1H -NMR (CDCl_3) δ 2.39 (br.s, 8H, CH_2N), 3.29–3.33 (m, 8H, CH_2O), 3.34 (br.s, 12H, CH_2O , PyCH_2N), 7.00 (d, $^3J = 7.8$ Hz, 2H, H6-Py), 7.08 (d, $^3J = 7.8$ Hz, 2H, H4-Py), 7.36 (t, $^3J = 7.7$ Hz, 2H, H5-Py). ^{13}C -NMR (CDCl_3) δ 54.5 (4C, CH_2N), 59.4 (2C, PyCH_2N), 67.4 (4C, CH_2O), 70.1 (4C, CH_2O), 123.0 (2C, C6-Py), 126.4 (2C, C4-Py), 139.4 (2C, C5-Py), 141.3

(2C, C3-Py), 159.4 (2C, C1-Py). HRMS (MALDI-TOF): $C_{24}H_{35}Br_2N_4O_4$ (M+H)⁺ calcd.; 601.1025 observed; 601.9973.

3.3. General Method for Palladium-Catalyzed Macrocyclizations

A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with diazacrown derivative **4–9** (0.2–0.25 mmol), Pd(dba)₂ (8–16 mol%), BINAP or DavePhos ligand (9–18 mol%), absolute dioxane (10–12 mL), the reaction mixture was stirred for several minutes, then the corresponding polyamine (0.2–0.25 mmol) and NaOt-Bu (0.6–0.75 mmol) were added, and the reaction mixture was stirred at reflux for 24 h. After cooling down to room temperature the residue was filtered off, washed with CH₂Cl₂ (5–10 mL), the combined organic fractions were evaporated *in vacuo*, the residue was dissolved in CH₂Cl₂ (10 mL), washed with distilled water (3 × 10 mL), dried over 4Å molecular sieves, and the solvent was evaporated *in vacuo*. The solid residue was chromatographed on silica gel (40–60 µm) using a sequence of eluents: CH₂Cl₂, CH₂Cl₂–MeOH 100:1–3:1, CH₂Cl₂–MeOH–NH₃(aq) 100:20:1–10:4:1.

11,14,27,32-Tetraoxa-1,8,17,24-tetraazatetracyclo[22.5.5.1^{3,7}.1^{18,22}]hexatriaconta-3(36),4,6,18(35),19,21-hexaene (11h). Obtained from compound **4** (0.2 mmol, 102 mg), dioxadamine **10h** (0.2 mmol, 30 mg) in the presence of Pd(dba)₂ (18 mg, 16 mol%), BINAP (22 mg, 18 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 13 mg (13%), of a yellowish viscous oil. ¹H-NMR (CDCl₃) δ 2.76 (br.s, 8H, CH₂N), 3.32 (t, ³J = 4.9 Hz, 4H, CH₂NPh), 3.58 (br.s, 12H, CH₂O, PhCH₂N), 3.66 (s, 4H, CH₂O), 3.72 (t, ³J = 4.9 Hz, 4H, CH₂O), 4.17 (br.s, 2H, NH), 6.46–6.54 (m, 4H, H4(Ph), H6(Ph)), 6.98 (s, 2H, H2(Ph)), 7.06 (t, ³J = 7.7 Hz, 2H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 43.8 (2C, CH₂NPh), 55.3 (4C, CH₂N), 62.0 (2C, PhCH₂N), 69.5 (4C, CH₂O), 69.7 (2C, CH₂O), 70.4 (2C, CH₂O), 111.3 (2C, CH(Ph)), 114.5 (2C, CH(Ph)), 118.2 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 139.8 (2C, C1(Ph)), 148.7 (2C, C3(Ph)). HRMS (MALDI-TOF): $C_{28}H_{43}N_4O_4$ (M+H)⁺ calcd.; 499.3284 observed; 499.3251.

11,14,17,30,35-Pentaoxa-1,8,20,27-tetraazatetracyclo[25.5.5.1^{3,7}.1^{21,25}]nonatriaconta-3(39),4,6,21(38),22,24-hexaene (11j). Obtained from compound **4** (0.2 mmol, 102 mg), trioxadamine **10j** (0.2 mmol, 38 mg) in the presence of Pd(dba)₂ (9 mg, 8 mol%), BINAP (11 mg, 9 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1. Yield 34 mg (31%), yellowish viscous oil. ¹H-NMR (CDCl₃) δ 2.86 (br.s, 8H, CH₂N), 3.32 (t, ³J = 3.9 Hz, 4H, CH₂NPh), 3.61 (br.s, 8H, CH₂O), 3.66 (s, 8H, CH₂O), 3.70 (t, ³J = 3.9 Hz, 4H, CH₂O), 6.48–6.56 (m, 4H, H4(Ph), H6(Ph)), 7.07 (t, ³J = 7.6 Hz, 2H, H5(Ph)), 7.12 (br.s, 2H, H2(Ph)), two NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 43.7 (2C, CH₂NPh), 54.6 (4C, CH₂N), 60.4 (2C, PhCH₂N), 68.7 (4C, CH₂O), 69.5 (2C, CH₂O), 70.3 (2C, CH₂O), 70.8 (2C, CH₂O), 111.6 (2C, CH(Ph)), 114.6 (2C, CH(Ph)), 117.8 (2C, CH(Ph)), 128.9 (2C, C5(Ph)), 149.2 (2C, C3(Ph)), two quaternary carbon atoms C1(Ph) were not assigned. HRMS (MALDI-TOF): $C_{30}H_{47}N_4O_5$ (M+H)⁺ calcd.; 543.3546 observed; 543.3598.

12,15,18,32,37-Pentaoxa-1,8,22,29-tetraazatetracyclo[27.5.5.1^{3,7}.1^{23,27}]hentetraconta-3(41),4,6,23(40),24,26-hexaene (11k). Obtained from compound **4** (0.2 mmol, 102 mg), trioxadiazine **10k** (0.2 mmol, 44 mg) in the presence of Pd(dba)₂ (9 mg, 8 mol%), BINAP (11 mg, 9 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 22 mg (19%), yellowish viscous oil. ¹H-NMR (CDCl₃) δ 1.84 (quintet, ³J = 6.0 Hz, 4H, CH₂CH₂CH₂), 2.74 (br.s, 8H, CH₂N), 3.23 (t, ³J = 6.4 Hz, 4H, CH₂NPh), 3.51–3.63 (m, 16H, CH₂O, PhCH₂N), 3.64–3.69 (m, 4H, CH₂O), 6.48 (d, ³J = 8.1 Hz, 2H, H4(Ph) or H6(Ph)), 6.58 (d, ³J = 7.2 Hz, 2H, H6(Ph) or H4(Ph)), 6.90 (s, 2H, H2(Ph)), 7.07 (t, ³J = 7.6 Hz, 2H, H5(Ph)), two NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 29.0 (2C, CH₂CH₂CH₂), 41.7 (2C, CH₂NPh), 54.9 (4C, CH₂N), 61.1 (2C, PhCH₂N), 69.6 (4C, CH₂O), 69.7 (2C, CH₂O), 70.2 (2C, CH₂O), 70.6 (2C, CH₂O), 111.0 (2C, CH(Ph)), 113.5 (2C, CH(Ph)), 117.3 (2C, CH(Ph)), 128.7 (2C, C5(Ph)), 140.5 (2C, C1(Ph)), 148.9 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₂H₅₁N₄O₅ (M+H)⁺ calcd.; 571.3859 observed; 571.3832.

Cyclodimer 13k. Obtained as the second product in the synthesis of macrobicycle **11k**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 27 mg (23%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.84 (quintet, ³J = 6.0 Hz, 8H, CH₂CH₂CH₂), 2.73 (br.s, 16H, CH₂N), 3.20 (t, ³J = 6.3 Hz, 8H, CH₂NPh), 3.50–3.70 (m, 48H, CH₂O, PhCH₂N), 6.43–6.46 (m, 8H, H4(Ph), H6(Ph)), 6.63 (s, 4H, H2(Ph)), 7.07 (t, ³J = 7.6 Hz, 4H, H5(Ph)), four NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 29.1 (4C, CH₂CH₂CH₂), 41.6 (4C, CH₂NPh), 57.7 (8C, CH₂N), 61.2 (4C, PhCH₂N), 69.4 (4C, CH₂O), 69.6 (8C, CH₂O), 70.2 (4C, CH₂O), 70.6 (4C, CH₂O), 111.1 (4C, CH(Ph)), 113.5 (4C, CH(Ph)), 117.8 (4C, CH(Ph)), 128.9 (4C, C5(Ph)), 140.3 (4C, C1(Ph)), 148.5 (4C, C3(Ph)). MS (MALDI-TOF): C₆₄H₁₀₁N₈O₁₀ (M+H)⁺ calcd.; 1141.76 observed; 1141.74.

10,13,25,30-Tetraoxa-1,7,16,22-tetraazatetracyclo[20.5.5.2^{3,6}.2^{17,20}]hexatriaconta-3,5,17,19,33,35-hexaene (12h). Obtained from compound **5** (0.2 mmol, 102 mg), dioxadiazine **10h** (0.2 mmol, 30 mg) in the presence of Pd(dba)₂ (18 mg, 16 mol%), BINAP (22 mg, 18 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 30 mg (30%), of a yellowish viscous oil. ¹H-NMR (CDCl₃) δ 2.73 (br.s, 8H, CH₂N), 3.30 (t, ³J = 5.1 Hz, 4H, CH₂NPh), 3.52 (s, 4H, PhCH₂N), 3.58 (br.s, 8H, CH₂O), 3.66 (s, 4H, CH₂O), 3.73 (t, ³J = 5.1 Hz, 4H, CH₂O), 4.07 (br.s, 2H, NH), 6.58 (d, ³J_{obs} = 8.3 Hz, 4H, H3(Ph)), 7.24 (d, ³J_{obs} = 8.3 Hz, 4H, H2(Ph)). ¹³C-NMR (CDCl₃) δ 43.9 (2C, CH₂NPh), 55.3 (4C, CH₂N), 60.1 (2C, PhCH₂N), 69.3 (2C, CH₂O), 70.1 (6C, CH₂O), 113.1 (4C, C3(Ph)), 129.7 (4C, C2(Ph)), 132.1 (2C, C1(Ph)), 147.2 (2C, C4(Ph)). HRMS (MALDI-TOF): C₂₈H₄₃N₄O₄ (M+H)⁺ calcd.; 499.3284 observed; 499.3318.

Cyclodimer 14h. Obtained as the second product in the synthesis of macrobicycle **12h**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 27 mg (27%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 2.71 (br.s, 16H, CH₂N), 3.28 (t, ³J = 4.4 Hz, 8H, CH₂NPh), 3.51–3.61 (m, 24H, CH₂O, PhCH₂N), 3.64 (s, 8H, CH₂O), 3.70 (t, ³J = 4.4 Hz, 8H, CH₂O), 4.06 (br.s, 4H, NH), 6.56 (d, ³J_{obs} = 8.2 Hz, 8H, H3(Ph)), 7.16 (d, ³J_{obs} = 8.2 Hz, 8H, H2(Ph)). ¹³C-NMR (CDCl₃) δ 43.5 (4C, CH₂NPh), 54.7 (8C, CH₂N), 60.5 (4C, PhCH₂N), 69.3 (8C, CH₂O), 69.7 (4C, CH₂O), 70.2 (4C, CH₂O), 112.8 (8C, C3

(Ph)), 130.1 (8C, C2(Ph)), 131.9 (4C, C1(Ph)), 147.1 (4C, C4(Ph)). MS (MALDI-TOF): $C_{56}H_{85}N_8O_8$ (M+H)⁺ calcd.; 997.65 observed; 997.66.

10,13,16,28,33-Pentaoxa-1,7,19,25-tetraazatetracyclo[23.5.5.2^{3,6}.2^{20,23}]nonatriaconta-3,5,20,22,36,38-hexaene (12j). Obtained from compound **5** (0.2 mmol, 102 mg), trioxadiazine **10j** (0.2 mmol, 38 mg) in the presence of Pd(dba)₂ (9 mg, 8 mol%), BINAP (11 mg, 9 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 26 mg (20%), of a yellowish viscous oil. ¹H-NMR (CDCl₃) δ 2.71 (t, ³J = 4.0 Hz, 8H, CH₂N), 3.31 (t, ³J = 5.1 Hz, 4H, CH₂NPh), 3.50 (s, 4H, PhCH₂N), 3.60 (t, ³J = 4.0 Hz, 8H, CH₂O), 3.67 (s, 8H, CH₂O), 3.72 (t, ³J = 5.1 Hz, 4H, CH₂O), 6.63 (d, ³J_{obs} = 8.3 Hz, 4H, H3(Ph)), 7.30 (d, ³J_{obs} = 8.3 Hz, 4H, H2(Ph)), two NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 43.7 (2C, CH₂NPh), 55.2 (4C, CH₂N), 60.0 (2C, PhCH₂N), 69.6 (2C, CH₂O), 70.1 (4C, CH₂O), 70.4 (2C, CH₂O), 70.8 (2C, CH₂O), 112.9 (4C, C3(Ph)), 129.0 (2C, C1(Ph)), 129.6 (4C, C2(Ph)), 147.1 (2C, C4(Ph)). HRMS (MALDI-TOF): $C_{30}H_{47}N_4O_5$ (M+H)⁺ calcd.; 543.3546 observed; 543.3511.

11,14,17,30,35-Pentaoxa-1,7,21,27-tetraazatetracyclo[25.5.5.2^{3,6}.2^{22,25}]hentetraconta-3,5,22,24,38,40-hexaene (12k). Obtained from compound **5** (0.2 mmol, 102 mg), trioxadiazine **10k** (0.2 mmol, 44 mg) in the presence of Pd(dba)₂ (9 mg, 8 mol%), BINAP (11 mg, 9 mol%), NaOt-Bu (0.6 mmol, 57 mg) in abs. dioxane (10 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 18 mg (15%), of a yellowish viscous oil. ¹H-NMR (CDCl₃) δ 1.89 (quintet, ³J = 5.9 Hz, 4H, CH₂CH₂CH₂), 2.71 (t, ³J = 4.0 Hz, 8H, CH₂N), 3.25 (t, ³J = 6.3 Hz, 4H, CH₂NPh), 3.51 (s, 4H, PhCH₂N), 3.57 (t, ³J = 4.0 Hz, 8H, CH₂O), 3.60–3.65 (m, 4H, CH₂O), 3.62 (t, ³J = 5.2 Hz, 4H, CH₂O), 3.68–3.72 (m, 4H, CH₂O), 4.24 (br.s, 2H, NH), 6.57 (d, ³J_{obs} = 8.3 Hz, 4H, H3(Ph)), 7.24 (d, ³J_{obs} = 8.3 Hz, 4H, H2(Ph)). ¹³C-NMR (CDCl₃) δ 28.9 (2C, CH₂CH₂CH₂), 42.3 (2C, CH₂NPh), 55.1 (4C, CH₂N), 60.5 (2C, PhCH₂N), 69.8 (4C, CH₂O), 70.1 (2C, CH₂O), 70.3 (2C, CH₂O), 70.6 (2C, CH₂O), 112.4 (4C, C3(Ph)), 130.0 (4C, C2(Ph)), 132.0 (2C, C1(Ph)), 147.6 (2C, C4(Ph)). HRMS (MALDI-TOF): $C_{32}H_{51}N_4O_5$ (M+H)⁺ calcd.; 571.3859 observed; 571.3890.

Cyclodimer 14k. Obtained as the second product in the synthesis of macrobicycle **12k**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:3. Yield 20 mg (17%), of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.86 (quintet, ³J = 5.3 Hz, 8H, CH₂CH₂CH₂), 2.70 (br.s, 16H, CH₂N), 3.19 (t, ³J = 5.7 Hz, 8H, CH₂NPh), 3.50–3.61 (m, 40H, CH₂O, PhCH₂N), 3.63–3.67 (m, 8H, CH₂O), 3.85 (br.s, 4H, NH), 6.53 (d, ³J_{obs} = 8.3 Hz, 8H, H3(Ph)), 7.11 (d, ³J_{obs} = 8.3 Hz, 8H, H2(Ph)). ¹³C-NMR (CDCl₃) δ 29.1 (4C, CH₂CH₂CH₂), 41.8 (4C, CH₂NPh), 54.4 (8C, CH₂N), 60.6 (4C, PhCH₂N), 69.4 (8C, CH₂O), 69.7 (4C, CH₂O), 70.2 (4C, CH₂O), 70.6 (4C, CH₂O), 112.4 (8C, C3(Ph)), 130.2 (8C, C2(Ph)), 130.4 (4C, C1(Ph)), 147.5 (4C, C4(Ph)). MS (MALDI-TOF): $C_{64}H_{101}N_8O_{10}$ (M+H)⁺ calcd.; 1141.76 observed; 1141.78.

22,25,30-Trioxa-1,8,12,19-tetraazatetracyclo[17.8.5.1^{3,7}.1^{13,17}]tetratriaconta-3(34),4,6,13(33),14,16-hexaene (15a). Obtained from compound **6** (0.25 mmol, 139 mg), diamine **10a** (0.25 mmol, 19 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), *t*BuONa (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 3:1. Yield 22 mg (19%), of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.75 (br.s, 1H, CH₂CH₂CH₂), 2.06 (br.s, 1H, CH₂CH₂CH₂), 2.17

(d, $^2J = 13.3$ Hz, 2H), 2.38 (dd, $^2J = 12.1$ Hz, 2H), 2.72–2.96 (m, 4H), 3.18–3.25 (m, 2H), 3.26–3.32 (m, 4H), 3.35–3.41 (m, 2H), 3.47–3.78 (m, 8H), 3.91 (d, $^3J = 11.6$ Hz, 2H), 4.02 (t, $^3J = 9.0$ Hz, 2H), 4.10 (br.s, 2H, NH), 6.35 (d, $^3J_{obs} = 6.9$ Hz, 2H, H4(Ph) or H6(Ph)), 6.47 (d, $^3J = 7.8$ Hz, 2H, H6(Ph) or H4(Ph)), 7.01 (t, $^3J = 7.8$ Hz, 2H, H5(Ph)), 7.43 (br.s, 2H, H2(Ph)). ^{13}C -NMR (CDCl_3) δ 28.9 (1C, $\text{CH}_2\text{CH}_2\text{CH}_2$), 41.7 (2C, CH_2NPh), 53.2 (2C, CH_2N), 54.7 (2C, CH_2N), 60.7 (2C, PhCH_2N), 70.2 (2C, CH_2O), 111.8 br (2C, CH(Ph)), 113.9 br (2C, CH(Ph)), 118.8 br (2C, CH(Ph)), 129.1 (2C, C5(Ph)), 148.7 (2C, C3(Ph)), two quaternary atoms C1(Ph) were not assigned due to a broad signal line; four CH_2O carbon atoms give a very broad signal in the region 68–70 ppm). HRMS (MALDI-TOF): $\text{C}_{27}\text{H}_{41}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$ calcd.; 469.3178 observed; 469.3143.

1,8,12,19,28,35,39,46-Octaazaheptacyclo[44.8.5.5^{19,28}.1^{3,7}.1^{13,17}.1^{30,34}.1^{40,44}]octahexaconta-3(68),4,6,13(67),14,16,30(61),31,33,40(60),41,43-dodecaene (19a). Obtained as the second product in the synthesis of macrobicyclic compound **15a**. Eluent CH_2Cl_2 –MeOH = 3:1. Yield 22 mg (19%) of a yellowish glassy compound. ^1H -NMR (CDCl_3) δ 1.84 (br.s, 4H CCH_2C), 2.71–2.96 (m, 16H, CH_2N), 3.29 (t, $^3J = 5.4$ Hz, 8H, CH_2NPh), 3.48–3.79 (m, 32H, CH_2O , PhCH_2N), 6.49 (br.s, 4H, H4(Ph) or H6(Ph)), 6.55 (br.s, 4H, H6(Ph) or H4(Ph)), 7.02–7.08 (m, 8H, H2(Ph), H5(Ph)), NH protons were not assigned. ^{13}C -NMR (CDCl_3) δ 27.3 (2C, CCH_2C), 42.9 (4C, CH_2NPh), 53.2 (4C, CH_2N), 54.7 (4C, CH_2N), 61.9 (4C, PhCH_2N), 67.3 (4C, CH_2O), 67.7 (4C, CH_2O), 69.4 (4C, CH_2O), 110.7 (4C, CH(Ph)), 115.6 (4C, CH(Ph)), 118.2 (4C, CH(Ph)), 128.5 (4C, C5(Ph)), 137.7 (4C, C1(Ph)), 149.6 (4C, C3(Ph)). HRMS (MALDI-TOF): $\text{C}_{54}\text{H}_{81}\text{N}_8\text{O}_8$ ($\text{M}+\text{H}$) $^+$ calcd.; 937.6279 observed; 937.6385.

23,26,3,-Trioxa-1,8,13,20-tetraazatricyclo[18.8.5.1^{3,7}.1^{14,18}]pentatriaconta-3(35),4,6,14(34),15,17-hexaene (15b). Obtained from compound **6** (0.25 mmol, 139 mg), diamine **10b** (0.25 mmol, 22 mg) in the presence of Pd(dba)_2 (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH_2Cl_2 –MeOH = 3:1. Yield 14 mg (12%) of a yellowish glassy compound. ^1H -NMR (CDCl_3) δ 1.83 (br.s, 4H, $\text{CCH}_2\text{CH}_2\text{C}$), 2.85–3.08 (m, 4H, CH_2N), 3.15–3.22 (m, 4H, CH_2N), 3.40 (br.s, 4H, CH_2NPh), 3.53–3.88 (m, 16H, CH_2O , PhCH_2N), 3.97 (br.s, 2H, NH), 6.41 (br.s, 2H, H4(Ph) or H6(Ph)), 6.49 (br.s, 2H, H6(Ph) or H4(Ph)), 7.03 (t, $^3J = 7.6$ Hz, 2H, H5(Ph)), 7.39 (br.s, 2H, H2(Ph)). ^{13}C -NMR (CDCl_3) δ 26.6 (2C, $\text{CCH}_2\text{CH}_2\text{C}$), 43.5 br (2C, CH_2NAr), 53.2 (2C, CH_2N), 54.2 (2C, CH_2N), 61.3 (2C, PhCH_2N), 69.0 (2C, CH_2O), 70.0 (4C, CH_2O), 111.1 br (2C, CH(Ph)), 115.8 br (2C, CH(Ph)), 118.1 br (2C, CH(Ph)), 128.6 (2C, C5(Ph)), 148.8 (2C, C3(Ph)), two quaternary atoms C1(Ph) were not assigned due to a broad signal line. HRMS (MALDI-TOF): $\text{C}_{28}\text{H}_{43}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) $^+$ calcd.; 483.3335 observed; 483.3275.

22,25,50,53,58,65-Hexaoxa-1,7,12,19,28,35,40,47-octaazaheptacyclo-[45.8.5.5^{19,28}.2^{3,6}.1^{13,17}.1^{30,34}.1^{41,45}]octahexaconta-3,5,13(68),14,16,30(62),31,33,41(61),42,44,69-dodecaene (19b). Obtained as the second product in the synthesis of macrobicyclic compound **15b**. Eluent CH_2Cl_2 –MeOH = 3:1. Yield 25 mg (21%) of a yellowish glassy compound. ^1H -NMR (CDCl_3) δ 1.71 (br.s, 8H CCH_2C), 2.45–3.08 (m, 16H CH_2N), 3.18 (t, $^3J = 5.5$ Hz, 8H, CH_2NPh), 3.52–3.82 (m, 32H, CH_2O , PhCH_2N), 4.65 (br.s, 4H, NH), 6.48 (d, $^3J_{obs} = 7.2$ Hz, 4H, H(Ph) or H6(Ph)), 6.56 (br.s, 4H, H6(Ph) or H4(Ph)), 7.01 (br.s, 4H, H2(Ph)), 7.03 (t, $^3J = 7.6$ Hz, 4H, H5(Ph)). ^{13}C -NMR (CDCl_3) δ 26.6 (4C, $\text{CCH}_2\text{CH}_2\text{C}$), 43.1 (4C, CH_2NPh), 53.9 (4C, CH_2N), 54.9 (4C, CH_2N), 60.3 (4C, PhCH_2N), 67.2 (4C, CH_2O), 67.4 (4C,

CH₂O), 67.9 (4C, CH₂O), 112.6 (4C, CH(Ph)), 112.9 (4C, CH(Ph)), 118.1 (4C, CH(Ph)), 128.9 (4C, C5(Ph)), 137.5 (4C, C1(Ph)), 148.6 (4C, C3(Ph)). HRMS (MALDI-TOF): C₅₆H₈₅N₈O₆ (M+H)⁺ calcd.; 965.6592 observed; 965.6511.

29,32,37-Trioxa-1,8,19,26-tetraazatetracyclo[24.8.5.1^{3,7}.1^{20,24}]hentetraconta-3(41),4,6,20(40),21,23-hexaene (15c). Obtained from compound **6** (0.25 mmol, 139 mg), diamine **10c** (0.25 mmol, 43 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1. Yield 38 mg (27%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.10–1.37 (m, 12H, CCH₂C), 1.45–1.55 (m, 4H, CH₂CNPh) 2.60–3.21 (m, 12H, CH₂N, CH₂NPh), 3.58–3.83 (m, 16H, CH₂O, PhCH₂N), 4.22 (br.s, 2H, NH), 6.48 (d, ³J_{obs} = 6.7 Hz, 2H, H4(Ph)), 6.59 (d, ³J_{obs} = 5.7 Hz, 2H, H6(Ph)), 6.84 (br.s 2H, H2(Ph)), 7.05 (t, ³J = 7.7 Hz, 2H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 26.1 (2C, CCH₂C), 28.1 (2C, CCH₂C), 28.2 (2C, CCH₂C), 28.7 (2C, CCCH₂C), 43.5 (2C, CH₂NPh), 53.9 (2C, CH₂N), 54.3 (2C, CH₂N), 60.2 (2C, PhCH₂N), 67.3 (2C, CH₂O), 67.5 (2C, CH₂O), 70.0 (2C, CH₂O), 112.0 (2C, CH(Ph)), 114.0 (2C, CH(Ph)), 117.8 (2C, CH(Ph)), 129.2 (2C, C5(Ph)), 137.4 (2C, C1(Ph)), 148.9 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₄H₅₅N₄O₃ (M+H)⁺ calcd.; 567.4274 observed; 567.4225.

29,32,63,66,71,78-Hexaoxa-1,8,19,26,35,42,53,60-octaazaheptacyclo-[58.8.5.5^{26,35}.1^{3,7}.1^{20,24}.1^{37,41}.1^{54,58}]dooctaconta-3(82),4,6,20(81),21,23,37(75),38,40,54(74),55,57-dodecaene (19c). Obtained as the second product in the synthesis of macrobicycle **15c**. Eluent CH₂Cl₂–MeOH = 3:1. Yield 21 mg (15%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.15–1.37 (m, 24H, CCH₂C), 1.50–1.59 (m, 8H, CH₂CNAr), 2.67–2.92 (m, 16H, CH₂N), 3.02 (br.s, 8H, CH₂NPh), 3.50–3.75 (m, 32H, CH₂O, PhCH₂N), 4.38 (br.s, 4H, NH), 6.46 (d, ³J = 8.1 Hz, 4H, H4(Ph)), 6.56 (br.s, 4H, H6(Ph)), 6.72 (br.s, 4H, H2(Ph)), 7.05 (t, ³J = 7.7 Hz, 4H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 27.1 (4C, CCH₂C), 29.4 (12C, CCH₂C), 43.9 (4C, CH₂NPh), 53.3 (4C, CH₂N), 53.9 (4C, CH₂N), 60.2 (4C, PhCH₂N), 67.0–70.0 (m, 12C, CH₂O), 111.1 (4C, CH(Ph)), 114.2 (4C, CH(Ph)), 118.0 (4C, CH(Ph)), 129.0 (4C, C5(Ph)), 148.8 (4C, C3(Ph)), four quaternary C1(Ph) atoms were not assigned. HRMS (MALDI-TOF): C₆₈H₁₀₉N₈O₆ (M+H)⁺ calcd.; 1133.8470 observed; 1133.8562.

26,29,34-Trioxa-1,8,12,16,23-pentaazatetracyclo[21.8.5.1^{3,7}.1^{17,21}]octatriaconta-3(38),4,6,17(37),18,20-hexaene (15d). Obtained from compound **6** (0.25 mmol, 139 mg), triamine **10d** (0.25 mmol, 33 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:3. Yield 47 mg (36%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.92 (br.s, 4H, CCH₂C), 2.65–2.75 (m, 8H, CH₂N), 2.88 (br.s, 4H, CH₂NHCH₂), 3.21 (t, ³J = 5.4 Hz, 4H, CH₂NPh), 3.53 (s, 4H, PhCH₂N), 3.55–3.65 (m, 12H, CH₂O), 5.10 (br.s, 2H, PhNH), 6.43 (br.s, 2H, H4(Ph) or H6(Ph)), 6.50 (d, ³J_{obs} = 6.7 Hz, 2H, H6(Ph) or H4(Ph)), 6.90 (br.s, 2H, H2(Ph)), 7.03 (t, ³J = 7.7 Hz, 2H, H5(Ph)), one NH proton was not assigned. ¹³C-NMR (CDCl₃) δ 26.4 (2C, CCH₂C), 41.6 (2C, CH₂NPh), 46.3 (2C, CH₂NHCH₂), 54.2 (2C, CH₂N), 54.9 (2C, CH₂N), 60.4 (2C, PhCH₂N), 69.2 (4C, CH₂O), 70.0 (2C, CH₂O), 110.7 (2C, CH(Ph)), 113.6 (2C, CH(Ph)), 117.5 (2C, CH(Ph)), 128.9 (2C, C5(Ph)), 140.4 (2C, C1(Ph)), 148.2 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₀H₄₈N₅O₃ (M+H)⁺ calcd.; 526.3757 observed; 526.3798.

26,29,57,60,65,72-Hexaoxa-1,8,12,16,23,32,39,43,47,54-decaazaheptacyclo-[52.8.5.5^{23,32}.1^{3,7}.1^{17,21}.1^{34,38}.1^{48,52}]-hexaheptaconta-3(76),4,6,17(75),18,20,34(69),35,37,48(68),49,51-dodecaene (**19d**). Obtained as the second product in the synthesis of macrobicycle **15d**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 12 mg (9%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.80 (br.s, 8H, CCH₂C), 2.60–2.82 (m, 24H, CH₂N), 3.14 (br.s, 8H, CH₂NPh), 3.48–3.68 (m, 32H, CH₂O, PhCH₂N), 6.44 (br.s, 4H, H4(Ph) or H6(Ph)), 6.55 (br.s 4H, H6(Ph) or H4(Ph)), 6.79 (br.s, 4H, H2(Ph)), 7.05 (br.s, 4H, H5(Ph)), NH protons were not assigned. MS (MALDI-TOF): C₆₀H₉₅N₁₀O₆ (M+H)⁺ calcd.; 1051.74 observed; 1051.72.

28,31,36-Trioxa-1,8,11,15,18,25-hexatetracyclo[23.8.5.1^{3,7}.1^{19,23}]tetraconta-3(40),4,6,19(39),20,22-hexaene (**15e**). Obtained from compound **6** (0.25 mmol, 139 mg), tetraamine **10e** (0.25 mmol, 40 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 39 mg (28%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.78 (quintet, ³J = 5.5 Hz, 2H, CCH₂C), 2.70 (t, ³J = 5.5 Hz, 8H, CH₂NHCH₂), 2.82 (t, ³J = 5.7 Hz, 4H, CH₂N), 2.87 (t, ³J = 5.2 Hz, 4H, CH₂N), 3.31 (t, ³J = 4.7 Hz, 4H, CH₂NPh), 3.53 (s, 4H, PhCH₂N), 3.56–3.66 (m, 12H, CH₂O), 4.79 (br.s, 2H, PhNH), 6.51 (d, ³J = 7.7 Hz, 2H, H4(Ph) or H6(Ph)), 6.54 (dd, ³J = 7.8 Hz, ⁴J = 1.5 Hz, 2H, H6(Ph) or H4(Ph)), 6.96 (br.s, 2H, H2(Ph)), 7.03 (t, ³J = 7.8 Hz, 2H, H5(Ph)), two NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 25.9 (1C, CCH₂C), 42.5 (2C, CH₂NPh), 47.7 (2C, CH₂NHCH₂), 48.8 (2C, CH₂NHCH₂), 54.9 (2C, CH₂N), 55.3 (2C, CH₂N), 60.5 (2C, PhCH₂N), 69.3 (2C, CH₂O), 69.6 (2C, CH₂O), 70.1 (2C, CH₂O), 110.8 (2C, CH(Ph)), 113.7 (2C, CH(Ph)), 117.6 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 140.9 (2C, C1(Ph)), 148.3 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₁H₅₁N₆O₃ (M+H)⁺ calcd.; 555.4022 observed; 555.3979.

29,32,37-Trioxa-1,8,12,15,19,26-hexaazatetracyclo[24.8.5.1^{3,7}.1^{20,24}]hentetraconta-3(41),4,6,20(40),21,23-hexaene (**15f**). Obtained from compound **6** (0.25 mmol, 139 mg), tetraamine **10f** (0.25 mmol, 44 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 47mg (33%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.74 (quintet, ³J = 6.3 Hz, 4H, CCH₂C), 2.55–2.81 (m, 16H, CH₂N), 3.15 (t, ³J = 6.3 Hz, 4H, CH₂NPh), 3.51–3.66 (m, 16H, CH₂O, PhCH₂N), 6.43 (d, ³J = 7.8 Hz, 2H, H4(Ph) or H6(Ph)), 6.54 (d, ³J = 7.3 Hz, 2H, H6(Ph) or H4(Ph)), 6.90 (br.s, 2H, H2(Ph)), 7.04 (t, ³J = 7.7 Hz, 2H, H5(Ph)) NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 28.8 (2C, CCH₂C), 42.5 (2C, CH₂NPh), 47.7 (2C, CH₂NHCH₂), 48.3 (2C, CH₂NHCH₂), 54.5 (2C, CH₂N), 54.9 (2C, CH₂N), 60.4 (2C, PhCH₂N), 64.9 (4C, CH₂O), 70.1 (2C, CH₂O), 110.4 (2C, CH(Ph)), 113.9 (2C, CH(Ph)), 117.3 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 140.5 (2C, C1(Ph)), 148.7 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₂H₅₃N₆O₃ (M+H)⁺ calcd.; 569.4179 observed; 569.4142.

30,33,38-Trioxa-1,8,12,16,20,27-hexaazatetracyclo[25.8.5.1^{3,7}.1^{21,25}]dodecatetraconta-3(42),4,6,21(41),22,24-hexaene (**15g**). Obtained from compound **6** (0.25 mmol, 139 mg), tetraamine **10g** (0.25 mmol, 47 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 34 mg (24%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.74 (quintet, ³J = 7.3 Hz, 2H,

CCH₂C), 1.78 (quintet, $^3J = 5.3$ Hz, 4H, CCH₂C), 2.67–2.76 (m, 12H, CH₂N, CH₂NHCH₂), 2.79 (t, $^3J = 5.6$ Hz, 4H, CH₂N), 3.12 (t, $^3J = 6.3$ Hz, 4H, CH₂NPh), 3.53–3.65 (m, 16H, CH₂O, PhCH₂N), 4.27 (br.s, 2H, PhNH), 6.46 (dd, $^3J = 7.7$ Hz, $^4J = 1.8$ Hz, 2H, H4(Ph) or H6(Ph)), 6.58 (d, $^3J = 7.7$ Hz, 2H, H6(Ph) or H4(Ph)), 6.89 (br.s, 2H, H2(Ph)), 7.05 (t, $^3J = 7.7$ Hz, 2H, H5(Ph)), two NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 27.5 (1C, CCH₂C), 28.4 (2C, CCH₂C), 42.4 (2C, CH₂NPh), 47.9 (2C, CH₂NHCH₂), 49.2 (2C, CH₂NHCH₂), 54.7 (2C, CH₂N), 55.0 (2C, CH₂N), 60.5 (2C, PhCH₂N), 69.5 (4C, CH₂O), 70.2 (2C, CH₂O), 110.7 (2C, CH(Ph)), 113.6 (2C, CH(Ph)), 117.5 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 140.9 (2C, C1(Ph)), 148.7 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₃H₅₅N₆O₃ (M+H)⁺ calcd.; 583.4335 observed; 583.4390.

11,14,27,30,35-Pentaoxa-1,8,17,24-tetraazatetracyclo[22.8.5.1^{3,7}.1^{18,22}]nonatriaconta-3(39),4,6,18(38),19,21-hexaene (15h). Obtained from compound **6** (0.25 mmol, 139 mg), dioxadamine **10h** (0.25 mmol, 37 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1. Yield 27 mg (20%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 2.61–3.15 (m, 8H, CH₂N), 3.30 (br.s, 4H, CH₂NPh), 3.50–3.75 (m, 24H, CH₂O, PhCH₂N), 6.53 (dd, $^3J = 8.1$ Hz, $^4J = 1.6$ Hz, 2H, H4(Ph) or H6(Ph)), 6.58 (br.s, 2H, H6(Ph) or H4(Ph)), 7.06 (t, $^3J = 7.8$ Hz, 2H, H5(Ph)), 7.19 (br.s, 2H, H2(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 43.9 (2C CH₂NPh), 53.4 (2C, CH₂N), 54.7 (2C, CH₂N), 61.0 (2C, PhCH₂N), 67.4 (2C, CH₂O), 67.8 (2C, CH₂O), 69.3 (4C, CH₂O), 70.2 (2C, CH₂O), 111.1 (2C, CH(Ph)), 116.3 (2C, CH(Ph)), 118.9 (2C, CH(Ph)), 128.9 (2C, C5(Ph)), 137.8 (2C, C1(Ph)), 149.1 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₀H₄₇N₄O₅ (M+H)⁺ calcd.; 543.3543 observed; 543.3588.

10,13,26,29,42,45,58,61,66,73-Decaoxa-1,7,16,23,32,39,48,55-octaazaheptacyclo-[53.8.5.5.5.^{32,32}.2^{3,6}.1^{17,21}.1^{34,38}.1^{49,53}]ocatheptaconta-3,5,17(76),18,20,34(70),35,37,49(69),50,52,77-dodecaene (19h). Obtained as the second product in the synthesis of macrobicycle **15h**. Eluent CH₂Cl₂–MeOH = 3:1. Yield 14 mg (10%) of a yellowish glassy compound. ¹H-NMR (DMSO-*d*₆, 363K) δ 2.84 (br.s, 16H, CH₂N), 3.21 (t, $^3J = 5.6$ Hz, 8H, CH₂NPh), 3.52–3.68 (m, 48H, CH₂O, PhCH₂N), 6.50 (d, $^3J = 8.1$ Hz, 4H, H4(Ph) or H6(Ph)), 6.52 (d, $^3J = 8.3$ Hz, 4H, H6(Ph) or H4(Ph)), 6.72 (br.s, 4H, H2(Ph)), 6.99 (t, $^3J = 7.8$ Hz, 4H, H5(Ph)), NH protons were not assigned. ¹³C-NMR (DMSO-*d*₆, 363K) δ 42.7 (4C, CH₂NPh), 53.5 (4C, CH₂N), 53.9 (4C, CH₂N), 59.6 (4C, PhCH₂N), 67.5 (4C, CH₂O), 68.0 (4C, CH₂O), 68.9 (4C, CH₂O), 69.5 (8C, CH₂O), 111.7 (4C, CH(Ph)), 112.2 (4C, CH(Ph)), 116.5 (4C, CH(Ph)), 128.1 (4C, C5(Ph)), 148.3 (4C, C3(Ph)), four quaternary C1(Ph) atoms were not assigned. HRMS (MALDI-TOF): C₆₀H₉₃N₈O₁₀ (M+H)⁺ calcd.; 1085.7014 observed; 1085.7086.

11,16,29,32,37-Pentaoxa-1,8,19,26-tetraazatetracyclo[24.8.5.1^{3,7}.1^{20,24}]hentetraconta-3(41),4,6,20(40),21,23-hexaene (15i). Obtained from compound **6** (0.25 mmol, 139 mg), dioxadamine **10i** (0.25 mmol, 51 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1. Yield 56 mg (37%) as a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.57–1.67 (m, 4H, CCH₂CH₂C), 1.80 (quintet, $^3J = 5.3$ Hz, 4H, NCCH₂CN), 2.57–3.16 (m, 12H, CH₂N), 3.36–3.43 (m, 4H, CH₂O), 3.47 (t, $^3J = 4.7$ Hz, 4H, CH₂O), 3.54–3.75 (m, 16H, CH₂O, PhCH₂N), 6.47 (d, $^3J_{obs} = 7.1$ Hz, 4H, H4(Ph), H6(Ph)), 6.96 (br.s, 2H, H2(Ph)), 7.05 (t, $^3J = 7.7$ Hz, 2H, H5(Ph)), NH protons were not assigned. ¹³C-NMR

(CDCl₃) δ 26.4 (2C, CCH₂CH₂C), 29.1 (2C, NCCH₂N), 41.7 (2C, CH₂NPh), 53.0 (2C, CH₂N), 54.3 (2C, CH₂N), 60.2 (2C, PhCH₂N), 67.2 (2C, CH₂O), 67.5 (2C, CH₂O), 69.0 (2C, CH₂O), 69.2 (2C, CH₂O), 70.5 (2C, CH₂O), 110.1 (2C, CH(Ph)), 115.3 (2C, CH(Ph)), 118.2 (2C, CH(Ph)), 128.9 (2C, C5(Ph)), 137.4 (2C, C1(Ph)), 149.3 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₄H₅₅N₄O₅ (M+H)⁺ calcd.; 599.4172 observed; 599.4130.

12,15,18,32,35,40-Hexaoxa-1,8,22,29-tetraazatetracyclo[27.8.5.1^{3,7}.1^{23,27}]tetratetraconta-3(44),4,6,23(43),24,26-hexaene (15k). Obtained from compound **6** (0.25 mmol, 139 mg), trioxadiazine **10k** (0.25 mmol, 51 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1. Yield 58 mg (38%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.82 (quintet, ³J = 6.1 Hz, 4H, CCH₂C), 2.74 (t, ³J = 4.7 Hz, 4H, CH₂N), 2.77 (t, ³J = 4.7 Hz, 4H, CH₂N), 3.18 (t, ³J = 6.3 Hz, 4H, CH₂NPh), 3.57 (t, ³J = 5.8 Hz, 4H, CH₂O), 3.57–3.67 (m, 24H, CH₂O, PhCH₂N), 4.10 (br.s, 2H, NH), 6.45 (d, ³J = 7.7 Hz, 2H, H4(Ph) or H6(Ph)), 6.55 (d, ³J = 7.3 Hz, 2H, H6(Ph) or H4(Ph)), 6.83 (br.s, 2H, H2(Ph)), 7.04 (t, ³J = 7.8 Hz, 2H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 28.9 (2C, CCH₂C), 41.5 (2C, CH₂NPh), 53.0 (2C, CH₂N), 54.4 (2C, CH₂N), 60.3 (2C, PhCH₂N), 67.2 (2C, CH₂O), 67.6 (2C, CH₂O), 69.0 (2C, CH₂O), 69.6 (2C, CH₂O), 70.0 (2C, CH₂O), 70.4 (2C, CH₂O), 110.4 (2C, CH(Ph)), 115.2 (2C, CH(Ph)), 118.3 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 137.3 (2C, C1(Ph)), 149.4 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₄H₅₅N₄O₆ (M+H)⁺ calcd.; 615.4121 observed; 615.4157.

12,15,18,32,35,49,52,55,69,72,77,84-Dodecaoxa-1,8,22,29,38,45,59,66-octaazaheptacyclo-[64.8.5.5^{29,38}.1^{3,7}.1^{23,27}.1^{40,44}.1^{60,64}]octaoctaconta-3(88),4,6,23(87),24,26,40(81),41,43,60(80),61,63-dodeca-ene (19k). Obtained as the second product in the synthesis of macrobicycle **15k**. Eluent CH₂Cl₂–MeOH = 3:1. Yield 37 mg (24%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.84 (quintet, ³J = 5.8 Hz, 8H, CCH₂C), 2.75 (t, ³J = 4.8 Hz, 8H, CH₂N), 2.78 (t, ³J = 4.8 Hz, 8H, CH₂N), 3.18 (t, ³J = 5.9 Hz, 8H, CH₂NPh), 3.53–3.68 (m, 56H, CH₂O, PhCH₂N), 4.06 (br.s, 4H, NH), 6.44 (d, ³J = 7.6 Hz, 4H, H4(Ph) or H6(Ph)), 6.59 (d, ³J = 7.2 Hz, 4H, H6(Ph) or H4(Ph)), 6.69 (br.s, 4H, H2(Ph)), 7.05 (t, ³J = 7.7 Hz, 4H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 29.0 (4C, CCH₂C), 41.4 (4C, CH₂NPh), 54.2 (8C, CH₂N), 60.5 (4C, PhCH₂N), 69.3 (4C, CH₂O), 69.4 (4C, CH₂O), 69.9 (4C, CH₂O), 70.0 (4C, CH₂O), 70.2 (4C, CH₂O), 70.4 (4C, CH₂O), 110.6 (4C, CH(Ph)), 113.2 (4C, CH(Ph)), 117.2 (4C, CH(Ph)), 128.7 (4C, C5(Ph)), 140.3 (4C, C1(Ph)), 148.5 (4C, C3(Ph)). MS (MALDI-TOF): C₆₈H₁₀₉N₈O₆ (M+H)⁺ calcd.; 1229.82 observed; 1229.84.

10,13,25,28,33-Pentaoxa-1,7,16,22-tetraazatetracyclo[20.8.5.2^{3,6}.2^{17,20}]nonatriaconta-3,5,17,19,36,38-hexaene (16h). Obtained from compound **7** (0.5 mmol, 278 mg), dioxadiazine **10h** (0.5 mmol, 74 mg) in the presence of Pd(dba)₂ (46 mg, 16 mol%), BINAP (56 mg, 18 mol%), NaOt-Bu (1.5 mmol, 144 mg) in abs. Dioxane (25 mL). Eluent CH₂Cl₂–MeOH = 5:1, CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1. Yield 49 mg (18%) as a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.69–2.86 (m, 8H, CH₂N), 3.27 (t, ³J = 4.5 Hz, 4H, CH₂NPh), 3.51–3.70 (m, 24H, CH₂O, PhCH₂N), 6.54 (d, ³J_{obs} = 7.0 Hz, 4H, H3(Ph), H3'(Ph)), 7.09 (d, ³J_{obs} = 7.5 Hz, 4H, H2(Ph), H2'(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 43.4 (2C, CH₂NPh), 52.8 (2C, CH₂N), 54.8 (2C, CH₂N), 60.1 (2C, PhCH₂N), 67.0 (2C, CH₂O), 69.0–69.9 (m, 8C, CH₂O), 113.0 (4C, C3(Ph), C3'(Ph)), 126.0 (2C, C1(Ph)),

131.4 (4C, C2(Ph), C2'(Ph)), 148.3 (2C, C4(Ph)). HRMS (MALDI-TOF): $C_{30}H_{47}N_4O_5$ (M+H)⁺ calcd.; 543.3546 observed; 543.3577.

10,13,25,40,43,55,58,63,72-Decaoxa-1,7,16,22,31,37,46,52-octaazaheptacyclo-[50.8.5.5^{22,31}.2^{3,6}.2^{17,20}.2^{33,36}.2^{47,50}]octaheptaconta-3,5,17,19,33,35,47,49,66,68,75,77-dodecaene (20h). Obtained as the second product in the synthesis of macrobicycle **16h**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1–100:20:3. Yield 85 mg (31%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.59 (t, ³J = 5.0 Hz, 8H, CH₂N), 2.67 (t, ³J = 4.6 Hz, 8H, CH₂N), 3.27 (t, ³J = 4.5 Hz, 8H, CH₂NPh), 3.47 (br.s, 8H, CH₂O), 3.51–3.64 (m, 16H, CH₂O), 3.66 (s, 8H, CH₂O or PhCH₂N), 3.68 (s, 8H, PhCH₂N or CH₂O), 3.74 (t, ³J = 5.0 Hz, 8H, CH₂O), 4.04 (br.s, 4H, NH), 6.51 (d, ³J_{obs} = 8.1 Hz, 8H, H3(Ph), H3'(Ph)), 7.16 (d, ³J_{obs} = 8.1 Hz, 8H, H2(Ph), H2'(Ph)). ¹³C-NMR (CDCl₃) δ 43.6 (4C, CH₂NPh), 52.2 (4C, CH₂N), 55.3 (4C, CH₂N), 61.2 (4C, PhCH₂N), 67.0–69.9 (m, 20C), 113.3 (8C, C3(Ph), C3'(Ph)), 125.0 (4C, C1(Ph)), 131.4 (8C, C2(Ph), C2'(Ph)), 147.6 (4C, C4(Ph)). HRMS (MALDI-TOF): $C_{60}H_{93}N_8O_{10}$ (M+H)⁺ calcd.; 1085.7014 observed; 1085.6952.

11,16,29,32,37-Pentaoxa-1,7,20,26-tetraazatetracyclo[24.8.5.2^{3,6}.2^{21,24}]tritetraconta-3,5,21,23,42-hexaene (16i). Obtained from compound **7** (0.25 mmol, 139 mg), dioxadamine **10i** (0.25 mmol, 51 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 5:1. Yield 15 mg (10%) as a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.65 (br.s, 4H, CCH₂CH₂C), 1.86 (quintet, ³J = 5.7 Hz, 4H, NCCH₂CN), 2.58–3.10 (m, 8H, CH₂N), 3.20 (t, ³J = 5.7 Hz, 4H, CH₂NPh), 3.37–3.45 (m, 4H, CH₂O), 3.47–3.72 (m, 16H, CH₂O, PhCH₂N), 3.78–3.93 (m, 4H, CH₂O), 6.51 (d, ³J_{obs} = 8.1 Hz, 4H, H3(Ph), H3'(Ph)), 7.21 (d, ³J_{obs} = 8.1 Hz, 4H, H2(Ph), H2'(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 26.5 (2C, CCH₂CH₂C), 29.3 (2C, CCH₂C), 42.6 (2C, CH₂NPh), 53.2 (2C, CH₂N), 54.0 (2C, CH₂N), 60.1 (2C, PhCH₂N), 67.6 (2C, CH₂O), 69.5 (2C, CH₂O), 70.7 (2C, CH₂O), 71.0 (4C, CH₂O), 112.3 (4C, C3(Ph), C3'(Ph)), 127.5 (2C, C1(Ph)), 131.6 (4C, C2(Ph), C2'(Ph)), 148.8 (2C, C4(Ph)). HRMS (MALDI-TOF): $C_{34}H_{55}N_4O_5$ (M+H)⁺ calcd.; 599.4172 observed; 599.4131.

11,16,29,32,45,50,63,66,71,80-Decaoxa-1,7,20,26,35,41,54,60-ocatazaheptacyclo-[58.8.5.5^{26,35}.2^{3,6}.2^{21,24}.2^{37,40}.1^{55,58}]hexaoctaconta-3,5,21,23,37,39,55,57,74,76,83,85-dodecaene (20i). Obtained as the second product in the synthesis of macrobicycle **16i**. Eluent CH₂Cl₂–MeOH = 5:1. Yield 15 mg (10%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.66 (br.s, 8H, CCH₂CH₂C), 1.86 (quintet, ³J = 5.7 Hz, 8H, NCCH₂CN), 2.47 (br.s, 8H, CH₂N), 3.06 (br.s, 8H, CH₂N), 3.19 (t, ³J = 5.3 Hz, 8H, CH₂NPh), 3.37–3.45 (m, 8H, CH₂O), 3.47–3.72 (m, 32H, CH₂O, PhCH₂N), 3.88 (br.s, 8H, CH₂O), 4.45 (br.s, 4H, NH), 6.57 (d, ³J_{obs} = 8.0 Hz, 8H, H3(Ph), H3'(Ph)), 7.23 (d, ³J_{obs} = 8.0 Hz, 8H, H2(Ph), H2'(Ph)). ¹³C-NMR (CDCl₃) δ 26.7 (4C, CCH₂CH₂C), 29.6 (4C, CCH₂C), 42.3 (4C, CH₂NPh), 51.9 (4C, CH₂N), 54.9 (4C, CH₂N), 60.1 (4C, PhCH₂N), 67.2 (8C, CH₂O), 69.1 (4C, CH₂O), 69.4 (4C, CH₂O), 70.0 (4C, CH₂O), 112.5 (8C, C3(Ph), C3'(Ph)), 125.2 (4C, C1(Ph)), 131.4 (8C, C2(Ph), C2'(Ph)), 148.1 (4C, C4(Ph)). HRMS (MALDI-TOF): $C_{68}H_{109}N_8O_{10}$ (M+H)⁺ calcd.; 1197.8266 observed; 1197.8215.

11,14,17,30,33,38-Hexaoxa-1,7,21,27-tetraazatetracyclo[25.8.5.2^{3,6}.2^{22,25}]tetratetraconta-3,5,22,24,41,43-hexaene (16k). Obtained from compound **7** (0.25 mmol, 139 mg), trioxadamine **10k**

(0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 5:1. Yield 15 mg (10%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.85 (quintet, ³J = 5.3 Hz, 4H, CCH₂C), 2.90–3.12 (m, 8H, CH₂N), 3.21 (t, ³J = 5.5 Hz, 4H, CH₂NPh), 3.52–3.73 (m, 24H, CH₂O, PhCH₂N), 3.82–3.94 (m, 4H, CH₂O), 6.46 (d, ³J_{obs} = 7.9 Hz, 4H, H₃(Ph), H_{3'}(Ph)), 7.16 (d, ³J_{obs} = 7.9 Hz, 4H, H₂(Ph), H_{2'}(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 28.6 (2C, CCH₂C), 41.7 (2C, CH₂NPh), 52.8 (2C, CH₂N), 54.1 (2C, CH₂N), 59.9 (2C, PhCH₂N), 69.7 (2C, CH₂O), 69.9 (2C, CH₂O), 70.2 (4C, CH₂O), 70.6 (4C, CH₂O), 112.3 (4C, C₃(Ph), C_{3'}(Ph)), 127.5 (2C, C₁(Ph)), 131.8 (4C, C₂(Ph), C_{2'}(Ph)), 148.8 (2C, C₄(Ph)). HRMS (MALDI-TOF): C₃₄H₅₅N₄O₆ (M+H)⁺ calcd.; 615.4121 observed; 615.4063.

11,14,17,30,33,46,49,52,66,69,74,82-Dodecaoxa-1,7,21,27,36,42,56,63-octaazaheptacyclo-[61.8.5.5^{27,36}.2^{3,6}.2^{22,25}.2^{38,41}.1^{57,61}]octaoctaconta-3,5,22,24,38,40,57(77),58,60,78,85,87-dodecaene (20k). Obtained as the second product in the synthesis of macrobicycle **16k**. Eluent CH₂Cl₂–MeOH = 5:1. Yield 29 mg (19%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.86 (quintet, ³J = 5.8 Hz, 8H, CCH₂C), 2.45 (br.s, 8H, CH₂N), 3.04 (br.s, 8H, CH₂N), 3.18 (t, ³J = 6.3 Hz, 8H, CH₂NPh), 3.38–3.72 (m, 48H, CH₂O, PhCH₂N), 3.89 (br.s, 8H, CH₂O), 4.49 (br.s, 4H, NH), 6.56 (d, ³J_{obs} = 7.8 Hz, 8H, H₃(Ph), H_{3'}(Ph)), 7.21 (d, ³J_{obs} = 7.8 Hz, 8H, H₂(Ph), H_{2'}(Ph)). ¹³C-NMR (CDCl₃) δ 29.0 (4C, CCH₂C), 42.1 (4C, CH₂NPh), 52.0 (4C, CH₂N), 54.9 (4C, CH₂N), 60.2 (4C, PhCH₂N), 67.2 (4C, CH₂O), 67.6 (4C, CH₂O), 69.0 (4C, CH₂O), 70.0 (4C, CH₂O), 70.1 (4C, CH₂O), 70.4 (4C, CH₂O), 112.5 (8C, C₃(Ph), C_{3'}(Ph)), 125.1 (4C, C₁(Ph)), 131.4 (8C, C₂(Ph), C_{2'}(Ph)), 148.0 (4C, C₄(Ph)). MS (MALDI-TOF): C₆₈H₁₀₉N₈O₁₂ (M+H)⁺ calcd.; 1229.82 observed; 1229.83.

26,29,34,37-Tetraoxa-1,8,12,16,23-pentaazatetracyclo[21.8.8.1^{3,7}.1^{17,21}]hentetraconta-3(41),4,6,17(40),18,20-hexaene (17d). Obtained from compound **8** (0.25 mmol, 150 mg), triamine **10d** (0.25 mmol, 33 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 35 mg (25%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.78 (quintet, ³J = 6.3 Hz, 4H, CCH₂C), 2.75 (t, ³J = 6.4 Hz, 4H, CH₂NHCH₂), 2.76 (t, ³J = 5.6 Hz, 8H, CH₂N), 3.21 (t, ³J = 6.4 Hz, 4H, CH₂NPh), 3.56–3.62 (m, 20H, CH₂O, PhCH₂N), 6.43 (dd, ³J = 7.8 Hz, ⁴J = 1.9 Hz, 2H, H₆(Ph) or H₄(Ph)), 6.51 (d, ³J = 7.3 Hz, 2H, H₄(Ph) or H₆(Ph)), 6.88 (br.s, 2H, H₂(Ph)), 7.06 (t, ³J = 7.7 Hz, 2H, H₅(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 24.2 (2C, CCH₂C), 42.9 (2C, CH₂NPh), 48.2 (2C, CH₂NHCH₂), 54.6 (4C, CH₂N), 60.0 (2C, PhCH₂N), 70.0 (4C, CH₂O), 70.6 (4C, CH₂O), 110.2 (2C, CH(Ph)), 113.7 (2C, CH(Ph)), 117.1 (2C, CH(Ph)), 128.8 (2C, C₅(Ph)), 140.9 (2C, C₁(Ph)), 148.7 (2C, C₃(Ph)). HRMS (MALDI-TOF): C₃₂H₅₂N₅O₄ (M+H)⁺ calcd.; 570.4019 observed; 570.3976.

26,29,57,60,65,68,75,78-Octaoxa-1,8,12,16,23,32,39,43,47,54-decaazaheptacyclo-[52.8.8.8^{32,32}.1^{3,7}.1^{17,21}.1^{34,38}.1^{48,52}]doctaconta-3(82),4,6,17(81),18,20,34(72),35,37,48(71),49,51-dodecaene (21d). Obtained as the second product in the synthesis of macrobicycle **17d**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:35:6. Yield 9 mg (6%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.79 (br.s, 8H, CCH₂C), 2.73 (t, ³J = 6.3 Hz, 8H, CH₂NHCH₂), 2.76–2.82 (m, 16H, CH₂N), 3.16 (t, ³J = 6.1 Hz, 8H, CH₂NPh), 3.54–3.62 (m, 40H, CH₂O, PhCH₂N), 6.45 (d, ³J = 7.8 Hz, 4H, H₆(Ph) or H₄(Ph)), 6.60 (d,

$^3J_{obs} = 6.3$ Hz, 4H, H4(Ph) or H6(Ph)), 6.67 (br.s, 4H, H2(Ph)), 7.05 (t, $^3J = 7.6$ Hz, 4H, H5(Ph)), NH protons were not assigned. ^{13}C -NMR (CDCl_3) δ 29.6 (4C, CCH_2C), 42.7 (4C, CH_2NPh), 48.3 (4C, CH_2NHCH_2), 53.8 (8C, CH_2N), 60.2 (4C, PhCH_2N), 70.1 (8C, CH_2O), 70.7 (8C, CH_2O), 111.1 (4C, CH(Ph)), 113.3 (4C, CH(Ph)), 117.8 (4C, CH(Ph)), 129.0 (4C, C5(Ph)), 140.7 (4C, C1(Ph)), 148.6 (4C, C3(Ph)). MS (MALDI-TOF): $\text{C}_{64}\text{H}_{103}\text{N}_{10}\text{O}_8$ ($\text{M}+\text{H}$) $^+$ calcd.; 1139.80 observed; 1139.79.

29,32,37,40-Tetraoxa-1,8,12,15,19,26-hexaazatetracyclo[24.8.8.1^{3,7}.1^{20,24}]tetratetraconta-3(44),4,6,20(43),21,23-hexaene (17f). Obtained from compound **8** (0.25 mmol, 150 mg), tetraamine **10f** (0.25 mmol, 44 mg) in the presence of Pd(dba)_2 (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent $\text{CH}_2\text{Cl}_2\text{--MeOH--NH}_3(\text{aq}) = 100:25:5\text{--}100:35:6$. Yield 15 mg (10%) of a yellow glassy compound. ^1H -NMR (CDCl_3) δ 1.77 (quintet, $^3J = 5.7$ Hz, 4H, CCH_2C), 2.58–2.85 (m, 16H, CH_2N), 3.15 (t, $^3J = 5.9$ Hz, 4H, CH_2NPh), 3.45–3.70 (m, 20H, CH_2O , PhCH_2N), 6.44 (d, $^3J = 7.9$ Hz, 2H, H6(Ph) or H4(Ph)), 6.56 (d, $^3J = 7.2$ Hz, 2H, H4(Ph) or H6(Ph)), 6.82 (br.s, 2H, H2(Ph)), 7.05 (t, $^3J = 7.7$ Hz, 2H, H5(Ph)), NH protons were not assigned. ^{13}C -NMR (CDCl_3) δ 28.8 (2C, CCH_2C), 42.7 (2C, CH_2NPh), 47.9 (2C, CH_2NHCH_2), 48.2 (2C, CH_2NHCH_2), 54.5 (4C, CH_2N), 60.0 (2C, PhCH_2N), 69.8 (4C, CH_2O), 70.6 (4C, CH_2O), 110.5 (2C, CH(Ph)), 113.7 (2C, CH(Ph)), 117.4 (2C, CH(Ph)), 128.9 (2C, C5(Ph)), 139.5 (2C, C1(Ph)), 145.8 (2C, C3(Ph)). HRMS (MALDI-TOF): $\text{C}_{34}\text{H}_{57}\text{N}_6\text{O}_4$ ($\text{M}+\text{H}$) $^+$ calcd.; 613.4441 observed; 613.4412.

29,32,63,66,71,74,81,84-Octaoxa-1,8,12,15,19,26,35,42,46,49,53,60-dodecaazaheptacyclo-[58.8.8.8^{26,35}.1^{3,7}.1^{20,24}.1^{37,41}.1^{54,58}]octaoctaconta-3(88),4,6,20(87),21,23,37(78),38,40,54(77),55,57-dodecaene (21f). Obtained as the second product in the synthesis of macrobicycle **17d**. Eluent $\text{CH}_2\text{Cl}_2\text{--MeOH--NH}_3(\text{aq}) = 100:35:6$. Yield 8 mg (5%) of a yellow glassy compound. ^1H -NMR (CDCl_3) δ 1.76 (br.s, 8H, CCH_2C), 2.68–2.81 (m, 32H, CH_2N), 3.15 (br.s, 8H, CH_2NPh), 3.50–3.63 (m, 40H, CH_2O , PhCH_2N), 6.43 (d, $^3J_{obs} = 7.2$ Hz, 4H, H6(Ph) or H4(Ph)), 6.60 (br.s, 4H, H2(Ph)), 6.62 (d, $^3J = 8.0$ Hz, 4H, H4(Ph) or H6(Ph)), 7.05 (t, $^3J = 7.5$ Hz, 4H, H5(Ph)), NH protons were not assigned. MS (MALDI-TOF): $\text{C}_{68}\text{H}_{113}\text{N}_{12}\text{O}_8$ ($\text{M}+\text{H}$) $^+$ calcd.; 1225.88 observed; 1225.90.

11,14,17,31,34,40-Hexaoxa-1,8,21,28-tetraazatetracyclo[26.8.6.1^{3,7}.1^{22,26}]tetratetraconta-3(44),4,6,22(43),23,25-hexaene (17h). Obtained from compound **8** (0.25 mmol, 150 mg), dioxadamine **10h** (0.25 mmol, 37 mg) in the presence of Pd(dba)_2 (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent $\text{CH}_2\text{Cl}_2\text{--MeOH} = 10:1\text{--}3:1$. Yield 83 mg (57%) of a yellowish glassy compound. ^1H -NMR (CDCl_3) δ 2.73 (br.s, 8H, CH_2N), 3.23 (t, $^3J = 5.1$ Hz, 4H, CH_2NPh), 3.34 (br.s, 4H, CH_2O), 3.51 (br.s, 8H, CH_2O), 3.58 (t, $^3J = 4.9$ Hz, 8H, CH_2O), 3.62 (s, 4H, PhCH_2N), 3.68 (t, $^3J = 5.1$ Hz, 4H, CH_2O), 6.45 (br.s, 4H, H(Ph)), 6.47 (d, $^3J = 8.0$ Hz, 2H, H(Ph)), 7.07 (t, $^3J = 7.8$ Hz, 2H, H5(Ph)), NH protons were not assigned. ^{13}C -NMR (CDCl_3) δ 43.6 (2C, CH_2NPh), 52.8 (4C, CH_2N), 59.6 (2C, PhCH_2N), 67.3 (4C, CH_2O), 68.3 (4C, CH_2O), 69.4 (2C, CH_2O), 70.2 (2C, CH_2O), 110.9 (2C, CH(Ph)), 115.8 (2C, CH(Ph)), 118.0 (2C, CH(Ph)), 129.3 (2C, C5(Ph)), 138.1 (2C, C1(Ph)), 149.0 (2C, C3(Ph)). HRMS (ESI-TOF): $\text{C}_{32}\text{H}_{51}\text{N}_4\text{O}_6$ ($\text{M}+\text{H}$) $^+$ calcd.; 587.3809 observed; 587.3815.

12,17,31,34,39,42-Hexaoxa-1,8,21,28-tetraazatetracyclo[26.8.8.1^{3,7}.1^{22,26}]hexatetraconta-3(46),4,6,22(45),23,25-hexaene (17i). Obtained from compound **8** (0.25 mmol, 150 mg), dioxadamine **10i** (0.25 mmol,

51 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 3:1, CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1. Yield 45 mg (28%) as a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.65–1.71 (m, 4H, CCH₂CH₂C), 1.87 (quintet, ³J = 6.0 Hz, 4H, CCH₂C), 2.77 (t, ³J = 5.2 Hz, 8H, CH₂N), 3.21 (t, ³J = 6.3 Hz, 4H, CH₂NPh), 3.42–3.48 (m, 4H, CH₂O), 3.54 (t, ³J = 5.8 Hz, 4H, CH₂O), 3.56–3.64 (m, 20H, CH₂O, PhCH₂N), 6.44 (dd, ³J = 8.0 Hz, ⁴J = 1.8 Hz, 2H, H6(Ph) or H4(Ph)), 6.56 (d, ³J_{obs} = 7.0 Hz, 2H, H4(Ph) or H6(Ph)), 6.78 (br.s, 2H, H2(Ph)), 7.06 (t, ³J = 7.7 Hz, 2H, H5(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 26.7 (2C, CCH₂CH₂C), 29.3 (2C, CCH₂C), 42.0 (2C, CH₂NPh), 54.4 (4C, CH₂N), 60.1 (2C, PhCH₂N), 69.5 (2C, CH₂O), 70.0 (4C, CH₂O), 70.7 (2C, CH₂O), 70.8 (4C, CH₂O), 110.3 (2C, CH(Ph)), 113.6 (2C, CH(Ph)), 117.2 (2C, CH(Ph)), 128.8 (2C, C5(Ph)), 140.9 (2C, C1(Ph)), 148.8 (2C, C3(Ph)). HRMS (MALDI-TOF): C₃₆H₅₉N₄O₆ (M+H)⁺ calcd.; 643.4435 observed; 643.4479.

12,15,18,32,35,40,43-Hepta-1,8,22,29-tetraazatetracyclo[27.8.8.1^{3,7}.1^{23,27}]heptatetraconta-3(47), 4,6,23(46),24,26-hexaene (17k). Obtained from compound **8** (0.25 mmol, 150 mg), trioxadiazine **10k** (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1. Yield 57 mg (35%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.82 (quintet, ³J = 6.0 Hz, 4H, CCH₂C), 2.92 (br.s, 8H, CH₂N), 3.18 (t, ³J = 6.4 Hz, 4H, CH₂NPh), 3.54–3.60 (m, 12H, CH₂O), PhCH₂N), 3.62–3.67 (m, 12H, CH₂O), 3.76 (br.s, 4H, CH₂O), 4.18 (br.s, 2H, NH), 6.48 (d, ³J_{obs} = 7.2 Hz, 2H, H4(Ph) or H6(Ph)), 6.61 (d, ³J_{obs} = 7.2 Hz, 2H, H6(Ph) or H4(Ph)), 6.75 (br.s, 2H, H2(Ph)), 7.05 (t, ³J = 7.7 Hz, 2H, H5(Ph)). ¹³C-NMR (CDCl₃) δ 29.0 (2C, CCH₂C), 41.4 (2C, CH₂NPh), 52.9 (2C, CH₂N), 54.0 (2C, CH₂N), 59.8 (2C, PhCH₂N), 67.3 (4C, CH₂O), 68.5 (4C, CH₂O), 69.5 (2C, CH₂O), 70.1 (2C, CH₂O), 70.5 (2C, CH₂O), 110.8 (2C, CH(Ph)), 115.1 (2C, CH(Ph)), 117.4 (2C, CH(Ph)), 129.3 (2C, C5(Ph)), 138.2 (2C, C1(Ph)), 149.0 (2C, C3(Ph)). HRMS (ESI-TOF): C₃₆H₅₉N₄O₇ (M+H)⁺ calcd.; 659.4384 observed; 659.4389.

12,15,18,32,35,49,52,55,69,72,77,80,87,90-Tetradeca-1,8,22,29,38,45,59,66-octaazaheptacyclo-[64.8.8.8^{29,38}.1^{3,7}.1^{23,27}.1^{40,44}.1^{60,64}]tetranonaconta-3(94),4,6,23(93),24,26,40(84),41,43,60(83),61,63-dodecaene (21k). Obtained as the second product in the synthesis of macrobicycle **17k**. Eluent CH₂Cl₂–MeOH = 10:3. Yield 28 mg (17%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.83 (quintet, ³J = 5.7 Hz, 8H, CCH₂C), 2.81 (br.s, 16H, CH₂N), 3.18 (t, ³J = 6.3 Hz, 8H, CH₂NPh), 3.50–3.68 (m, 64H, CH₂O, PhCH₂N), 4.56 (br.s, 4H, NH), 6.46 (d, ³J = 7.8 Hz, 4H, H4(Ph) or H6(Ph)), 6.55 (d, ³J_{obs} = 7.0 Hz, 4H, H6(Ph) or H4(Ph)), 6.73 (s, 4H, H2(Ph)), 7.05 (t, ³J_{obs} = 7.5 Hz, 4H, H5(Ph)). MS (MALDI-TOF): C₇₂H₁₁₇N₈O₁₄ (M+H)⁺ calcd.; 1317.87 observed; 1317.84.

10,13,25,28,33,36-Hexa-1,7,16,22-tetraazatetracyclo[20.8.8.2^{3,6}.2^{17,20}]dotetraconta-3,5,17,19,39,41-hexaene (18h). Obtained from compound **9** (0.25 mmol, 150 mg), dioxadiazine **10h** (0.25 mmol, 37 mg) in the presence of Pd(dba)₂ (24 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 3:1, CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1–100:20:3. Yield 37 mg (25%) of a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 2.68 (t, ³J = 5.4 Hz, 8H, CH₂N), 3.27 (t, ³J = 4.8 Hz, 4H, CH₂NPh), 3.53 (s, 4H, CH₂O), 3.59 (t, ³J = 5.4 Hz, 8H, CH₂O), 3.62

(s, 8H, CH₂O), 3.65 (s, 4H, PhCH₂N), 3.73 (t, ³J = 4.8 Hz, 4H, CH₂O), 6.55 (d, ³J_{obs} = 8.5 Hz, 4H, H₃(Ph), H_{3'}(Ph)), 7.17 (d, ³J_{obs} = 8.5 Hz, 4H, H₂(Ph), H_{2'}(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 43.7 (2C, CH₂NPh), 54.9 (4C, CH₂N), 59.7 (2C, PhCH₂N), 69.4 (2C, CH₂O), 69.8 (4C, CH₂O), 70.0 (2C, CH₂O), 70.8 (4C, CH₂O), 113.1 (4C, C₃(Ph), C_{3'}(Ph)), 128.8 (2C, C₁(Ph)), 129.8 (4C, C₂(Ph), C_{2'}(Ph)), 147.2 (2C, C₄(Ph)). HRMS (ESI-TOF): C₃₂H₅₁N₄O₆ (M+H)⁺ calcd.; 587.3809 observed; 587.3829.

*10,13,25,28,40,43,55,58,63,66,75,78-dodecaoxa-1,7,16,22,31,37,46,52-octaazaheptacyclo-[50.8.8.8.2^{22,31}.2^{3,6}.2^{17,20}.2^{33,36}.2^{47,50}]*tetraoctaconta-3,5,17,19,33,35,47,49,69,71,81,83-dodecaene (**22h**). Obtained as the second product in the synthesis of macrobicycle **18h**. Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:25:5. Yield 15 mg (10%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.77 (br.s, 16H, CH₂N), 3.26 (br.s, 8H, CH₂NPh), 3.58 (br.s, 40H, CH₂O), 3.63 (s, 8H, PhCH₂N), 3.68 (br.s, 8H, CH₂O), 3.95 (br.s, 4H, NH), 6.54 (d, ³J_{obs} = 8.2 Hz, 8H, H₃(Ph), H_{3'}(Ph)), 7.09 (d, ³J_{obs} = 8.2 Hz, 8H, H₂(Ph), H_{2'}(Ph)). HRMS (MALDI-TOF): C₆₄H₁₀₁N₈O₁₂ (M+H)⁺ calcd.; 1173.7538 observed; 1173.7472.

*11,14,17,30,33,38,41-Heptaoxa-1,7,21,27-tetraazatetracyclo[25.8.8.2^{3,6}.2^{22,25}]*heptatetraconta-3,5,22,24,44,46-hexaene (**18k**). Obtained from compound **9** (0.25 mmol, 150 mg), trioxadiazine **10k** (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (24 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 10:1, 3:1. Yield 59 mg (36%) as a yellowish glassy compound. ¹H-NMR (CDCl₃) δ 1.80 (br.s, 4H, CCH₂C), 2.70 (br.s, 8H, CH₂N), 3.13 (br.s, 4H, CH₂NPh), 3.34 (br.s, 4H, CH₂O), 3.50 (br.s, 8H, CH₂O), 3.58 (s, 8H, CH₂O), 3.63–3.69 (m, 12H, CH₂O, PhCH₂N), 6.50 (d, ³J_{obs} = 8.1 Hz, 4H, H₃(Ph), H_{3'}(Ph)), 6.79 (d, ³J_{obs} = 8.1 Hz, 4H, H₂(Ph), H_{2'}(Ph)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 28.9 (2C, CCH₂C), 41.8 (2C, CH₂NPh), 52.2 (4C, CH₂N), 58.6 (2C, PhCH₂N), 66.8 (4C, CH₂O), 68.5 (4C, CH₂O), 69.7 (2C, CH₂O), 70.2 (2C, CH₂O), 70.4 (2C, CH₂O), 112.7 (4C, C₃(Ph), C_{3'}(Ph)), 124.5 (2C, C₁(Ph)), 130.5 (4C, C₂(Ph), C_{2'}(Ph)), 148.4 (2C, C₄(Ph)). HRMS (ESI-TOF): C₃₆H₅₉N₄O₇ (M+H)⁺ calcd.; 659.4384 observed; 659.4375.

*10,13,25,28,33-Pentaoxa-1,5,7,16,18,22-hexaazatetracyclo[20.8.5.2^{3,6}.2^{17,20}]*nonatriaconta-3,5,17,19,36,38-hexaene (**27h**). Obtained from compound **23** (0.5 mmol, 235 mg), dioxadiazine **10h** (0.5 mmol, 74 mg) in the presence of Pd(dba)₂ (46 mg, 16 mol%), DavePhos (36 mg, 18 mol%), NaOt-Bu (1.5 mmol, 144 mg) in abs. Dioxane (25 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:2. Yield 60 mg (22%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.56 (t, ³J = 5.1 Hz, 4H, CH₂N), 2.66 (t, ³J = 4.6 Hz, 4H, CH₂N), 3.42 (br.s, 4H, CH₂NPy), 3.52 (t, ³J = 5.1 Hz, 4H, CH₂O), 3.55–3.62 (m, 8H, CH₂O), 3.66 (s, 4H, CH₂O or PyCH₂N), 3.67 (s, 4H, PyCH₂N or CH₂O), 3.72 (t, ³J = 5.1 Hz, 4H, CH₂O), 5.11 (br.s, NH), 6.30 (d, ³J = 8.5 Hz, 2H, H₅(Py)), 7.47 (d, ³J = 8.5 Hz, 2H, H₆(Py)), 7.94 (s, 2H, H₂(Py)). ¹³C-NMR (CDCl₃) δ 41.6 (2C, CH₂NPy), 54.7 (2C, CH₂N), 55.2 (2C, CH₂N), 57.4 (2C, PyCH₂N), 69.6 (4C, CH₂O), 69.7 (2C, CH₂O), 70.0 (2C, CH₂O), 70.8 (2C, CH₂O), 108.3 (2C, C₅(Py)), 123.9 (2C, C₁(Py)), 138.6 (2C, C₆(Py)), 147.4 (2C, C₂(Py)), 158.0 (2C, C₄(Py)). HRMS (MALDI-TOF): C₂₈H₄₅N₆O₅ (M+H)⁺ calcd.; 545.3451 observed; 545.3480.

*10,15,27,30,35-Pentaoxa-1,5,7,18,20,24-hexaazatetracyclo[22.8.5.2^{3,6}.2^{19,22}]*hentetraconta-3,5,19,21,38,40-hexaene (**27i**). Obtained from compound **23** (0.25 mmol, 117 mg), dioxadiazine **10i** (0.25 mmol,

51 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1–100:20:3. Yield 17 mg (11%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.63–1.70 (m, 4H, CCH₂CH₂C), 1.87 (quintet, ³J = 5.5 Hz, 4H, CCH₂C), 2.71 (br.s, 8H, CH₂N), 3.39 (t, ³J = 5.2 Hz, 4H, CH₂NPy), 3.42–3.48 (m, 4H, CH₂O), 3.50–3.64 (m, 20H, CH₂O, PyCH₂N), 5.26 (br.s, 2H, NH), 6.35 (d, ³J = 8.5 Hz, 2H, H5(Py)), 7.58 (d, ³J = 8.5 Hz, 2H, H6(Py)), 7.91 (br.s, 2H, H2(Py)). ¹³C-NMR (CDCl₃) δ 26.8 (2C, CCH₂CH₂C), 29.3 (2C, CCH₂C), 40.7 (2C, CH₂NPy), 54.4 (2C, CH₂N), 54.5 (2C, CH₂N), 57.4 (2C, PyCH₂N), 69.0 (2C, CH₂O), 69.5 (4C, CH₂O), 70.6 (2C, CH₂O), 71.0 (2C, CH₂O), 107.1 (2C, C5(Py)), 122.5 (2C, C1(Py)), 139.4 (2C, C6(Py)), 147.4 (2C, C2(Py)), 158.1 (2C, C4(Py)). HRMS (MALDI-TOF): C₃₂H₅₃N₆O₅ (M+H)⁺ calcd.; 601.4077 observed; 601.4043.

11,14,17,30,33,38-Hexaoxa-1,5,7,21,23,27-hexaazatetracyclo[25.8.5.2^{3,6}.2^{22,25}]tetraetraconta-3,5,22,24,41,43-hexaene (27k). Obtained from compound **23** (0.25 mmol, 117 mg), trioxadiazine **10k** (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1–100:20:3. Yield 14 mg (9%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.87 (quintet, ³J = 5.9 Hz, 4H, CCH₂C), 2.71 (t, ³J = 5.3 Hz, 4H, CH₂N), 2.77 (t, ³J = 4.7 Hz, 4H, CH₂N), 3.39 (br.s, 4H, CH₂NPy), 3.51–3.70 (m, 28H, CH₂O, PyCH₂N), 5.64 (br.s, 2H, NH), 6.32 (d, ³J = 8.6 Hz, 2H, H5(Py)), 7.54 (d, ³J = 8.6 Hz, 2H, H6(Py)), 7.90 (br.s, 2H, H2(Py)). ¹³C-NMR (CDCl₃) δ 29.0 (2C, CCH₂C), 40.0 (2C, CH₂NPy), 54.1 (2C, CH₂N), 54.3 (2C, CH₂N), 57.2 (2C, PyCH₂N), 68.7 (2C, CH₂O), 69.2 (2C, CH₂O), 69.4 (2C, CH₂O), 70.1 (2C, CH₂O), 70.5 (2C, CH₂O), 70.6 (2C, CH₂O), 107.5 (2C, C5(Py)), 123.0 (2C, C1(Py)), 139.9 (2C, C6(Py)), 146.6 (2C, C2(Py)), 157.7 (2C, C4(Py)). HRMS (MALDI-TOF): C₃₂H₅₃N₆O₆ (M+H)⁺ calcd.; 617.4027 observed; 617.3967.

10,13,25,28,33,36-Hexaoxa-1,5,7,16,18,22-hexaazatetracyclo[20.8.8.2^{3,6}.2^{17,20}]dotetraconta-3,5,17,19,39,41-hexaene (28h). Obtained from compound **24** (0.25 mmol, 128 mg), dioxadiazine **10h** (0.25 mmol, 37 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:3. Yield 7 mg (5%) as a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.70 (br.s, 8H, CH₂N), 3.47–3.54 (m, 8H, CH₂NPy, CH₂O), 3.55–3.61 (m, 16H, CH₂O), 3.67 (s, 4H, PyCH₂N), 3.73 (t, ³J = 4.7 Hz, 4H, CH₂O), 5.61 (br.s, 2H, NH), 6.37 (d, ³J = 8.2 Hz, 2H, H6(Py)), 7.52 (d, ³J = 8.2 Hz, 2H, H5(Py)), 7.97 (br.s, 2H, H2(Py)). HRMS (ESI-TOF): C₃₀H₄₉N₆O₆ (M+H)⁺ calcd.; 589.3713 observed; 589.3715.

11,14,17,30,33,38,41-Heptaoxa-1,5,7,21,23,27-hexaazatetracyclo[25.8.8.2^{3,6}.2^{22,25}]heptatetraconta-3,5,22,24,44,46-hexaene (28k). Obtained from compound **24** (0.25 mmol, 128 mg), trioxadiazine **10k** (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH–NH₃(aq) = 100:20:1–100:20:2. Yield 40 mg (24%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.87 (quintet, ³J = 6.0 Hz, 4H, CCH₂C), 2.69 (t, ³J = 5.5 Hz, 4H, CH₂N), 2.79 (t, ³J = 4.6 Hz, 4H, CH₂N), 3.38 (q, ³J = 6.1 Hz, 4H, CH₂NPy), 3.52–3.69 (m, 32H, CH₂O, PyCH₂N), 5.20 (br.s, 2H, NH), 6.32 (d, ³J = 8.6 Hz, 2H, H5(Py)), 7.47 (dd, ³J = 8.6 Hz, ⁴J = 2.0 Hz, 2H, H6(Py)), 7.89 (d, ⁴J = 2.0 Hz, 2H, H2(Py)). ¹³C-NMR

(CDCl₃) δ 29.1 (2C, CCH₂C), 39.8 (2C, CH₂NPy), 54.1 (4C, CH₂N), 56.8 (2C, PyCH₂N), 69.4 (2C, CH₂O), 69.9 (4C, CH₂O), 70.2 (4C, CH₂O), 70.5 (2C, CH₂O), 70.8 (2C, CH₂O), 107.1 (2C, C5(Py)), 123.1 (2C, C1(Py)), 138.8 (2C, C6(Py)), 147.7 (2C, C2(Py)), 158.2 (2C, C4(Py)). HRMS (ESI-TOF): C₃₄H₅₇N₆O₇ (M+H)⁺ calcd.; 661.4288 observed; 661.4241.

12,15,18,32,35,40-Hexaoxa-1,8,22,29,43,44-hexaazatetracyclo[27.8.5.1^{3,7}.1^{23,27}]tetratetraconta-3(44), 4,6,23(43),24,26-hexaene (29k). Obtained from compound **25** (0.25 mmol, 140 mg), trioxadiazine **10k** (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 3:1. Yield 21 mg (12%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.02 (br.s, 4H, CCH₂C), 2.60–2.88 (m, 8H, CH₂N), 3.15 (q, ³J = 5.6 Hz, 4H, CH₂NPy), 3.28 (t, ³J = 5.6 Hz, 4H, CH₂O), 3.31–3.38 (m, 4H, CH₂O), 3.40–3.65 (m, 20H, CH₂O, PyCH₂N), 5.82 (t, ³J = 4.8 Hz, 2H, NH), 6.41 (d, ³J = 8.5 Hz, 2H, H4(Py) or H6(Py)), 6.51 (d, ³J = 7.1 Hz, 2H, H6(Py) or H4(Py)), 7.45 (dd, ³J = 8.5 Hz, ³J = 7.1 Hz, 2H, H5(Py)). ¹³C-NMR (CDCl₃) δ 28.8 (2C, CCH₂C), 39.3 (2C, CH₂NPy), 53.8 (2C, CH₂N), 56.1 (2C, CH₂N), 61.9 (2C, PyCH₂N), 66.8 (2C, CH₂O), 66.9 (2C, CH₂O), 67.5 (2C, CH₂O), 69.0 (2C, CH₂O), 70.3 (2C, CH₂O), 70.6 (2C, CH₂O), 105.1 (2C, C4(Py) or C6(Py)), 112.5 (2C, C6(Py) or C4(Py)), 139.3 (2C, C5(Py)), 156.4 (2C, C1(Py)), 160.1 (2C, C3(Py)). HRMS (MALDI-TOF): C₃₂H₅₂N₆NaO₆ (M+Na)⁺ calcd.; 639.3846 observed; 639.3803.

11,14,27,30,35,38-Hexaoxa-1,8,17,24,41,42-hexaazatetracyclo[22.8.8.1^{3,7}.1^{18,22}]dotetraconta-3(42),4, 6,18(41),19,21-hexaene (30h). Obtained from compound **26** (0.227 mmol, 137 mg), dioxadiazine **10h** (0.23 mmol, 34 mg) in the presence of Pd(dba)₂ (21 mg, 16 mol%), DavePhos (16 mg, 18 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH₂Cl₂–MeOH = 3:1. Yield 21 mg (16%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 2.64 (br.s, 8H, CH₂N), 3.03 (br.s, 4H, CH₂NPy), 3.30 (s, 4H, CH₂O), 3.33–3.38 (m, 8H, CH₂O), 3.47 (t, ³J = 4.5 Hz, 4H, CH₂O), 3.50–3.68 (m, 12H, CH₂O, PyCH₂N), 6.42 (d, ³J = 8.5 Hz, 2H, H4(Py) or H6(Py)), 6.51 (d, ³J = 7.2 Hz, 2H, H6(Py) or H4(Py)), 7.46 (t, ³J = 7.8 Hz, 2H, H5(Py)), NH protons were not assigned. ¹³C-NMR (CDCl₃) δ 42.5 (2C, CH₂NPy), 52.3 (4C, CH₂N), 60.4 (2C, PyCH₂N), 67.1 (4C, CH₂O), 67.3 (4C, CH₂O), 68.4 (2C, CH₂O), 69.8 (2C, CH₂O), 105.4 (2C, C4(Py) or C6(Py)), 112.8 (2C, C6(Py) or C4(Py)), 138.8 (2C, C5(Py)), 158.2 (2C, C1(Py)), 161.7 (2C, C3(Py)). HRMS (MALDI-TOF): C₃₀H₄₉N₆O₆ (M+H)⁺ calcd.; 589.3714 observed; 589.3675.

4. Conclusions

We can conclude that as a result of this investigation, we have elaborated a convenient and versatile approach to a previously unknown family of macrobicycles based on diazacrown ethers possessing additional diamine, oxadiazine and tetraamine chains using Pd-catalyzed amination reactions. We established the dependence of the yields of target cryptands on the nature of the starting compounds and found out that in the case of macrobicycles possessing benzyl spacers, quite good yields of the products as high as 57% can be achieved, mainly with *meta*-aminobenzyl spacers, especially with triamine and oxadiazine linkers, while in the case of macrobicycles with pyridyl spacers, the yields are generally substantially lower and hardly surpass 20%. A number of compounds

synthesized in this work are now under investigation concerning their coordination properties towards various metal cations.

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Conflicts of Interest

The authors declare no conflict of interest.

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Sample Availability: Not available.

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