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

Alexei A. Yakushev 1,2, Nataliya M. Chernichenko 1, Maxim V. Anokhin 1, Alexei D. Averin 1,2,*, Alexei K. Buryak 2, Franck Denat 3 and Irina P. Beletskaya 1,2

1 Department of Chemistry, Lomonosov Moscow State University, Leninskie Gory, 1–3, Moscow 119991, Russia; E-Mails: longhauler@yandex.ru (A.A.Y.); natashachernichenko@mail.ru (N.M.C.); anokhinmv@gmail.com (M.V.A.); beletska@org.chem.msu.ru (I.P.B.)
2 A.N. Frumkin Institute of Physical Chemistry and Electrochemistry, 31 Leninskii prosp., Moscow 119991, Russia; E-Mail: akburyak@mail.ru
3 Institut de Chimie Moléculaire de l’Université de Bourgogne (ICMUB), UMR CNRS 6302, 9 avenue A. Savary, Dijon Cedex 21078, France; E-Mail: fdenat@u-bourgogne.fr

* Author to whom correspondence should be addressed; E-Mail: alexaveron@yandex.ru; Tel.: +7-495-939-1139; Fax: +7-495-939-3618.

Received: 5 December 2013; in revised form: 26 December 2013 / Accepted: 27 December 2013 / Published: 15 January 2014

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 oxadiamines 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 oxadiamines 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], benzo- and triazacryptands 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 polymacroyclic 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 polymacroyclic structures based on azas- 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 $^7\text{Li}$ and $^6\text{Li}$ 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$_2$CO$_3$ 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$_2$CO$_3$ 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 oxadiamines 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 oxadiamines 10a–k used in the synthesis of macrobicycles.

Macrocycles 4 and 5 were introduced in the Pd-catalyzed amination reactions with oxadiamines 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                      | 10h       | 11h, 13%                | mixture, 42%              |
| 2     | 4                      | 10j       | 11j, 31%                | mixture, 37%              |
| 3     | 4                      | 10k       | 11k, 19%                | 13k, 23%                  |
| 4     | 5                      | 10h       | 12h, 30%                | 14e, 27%                  |
| 5     | 5                      | 10j       | 12j, 20%                |                           |
| 6     | 5                      | 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 macrobicycle 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                      | (10a)     | 8/9                       | 15a, 19%              | 19a, 19%           |
| 2     | 6                      | (10b)     | 8/9                       | 15b, 12%              | 19b, 21%           |
| 3     | 6                      | (10c)     | 8/9                       | 15c, 25%              | 19c, 15%           |
| 4     | 6                      | (10d)     | 8/9                       | 15d, 36%              | 19d, 9%            |
| 5     | 6                      | (10e)     | 8/9                       | 15e, 28%              |                    |
| 6     | 6                      | (10f)     | 8/9                       | 15f, 33%              |                    |
| 7     | 6                      | (10g)     | 8/9                       | 15g, 24%              |                    |
| 8     | 6                      | (10h)     | 8/9                       | 15h, 20%              | 19h, 10%           |
| 9     | 6                      | (10i)     | 8/9                       | 15i, 37%              |                    |
| 10    | 6                      | (10k)     | 8/9                       | 15k, 38%              | 19k, 24%           |
| 11    | 7                      | (10k)     | 8/9                       | 16k, 5%               | 20k, 10%           |
| 12    | 7                      | (10k)     | 8/9                       | 16k, 4%               | 20k, 10%           |
| 13    | 7                      | (10k)     | 16/18                     | 16k, 10%              | 20k, 19%           |
| 14    | 7                      | (10i)     | 16/18                     | 16i, 10%              | 20i, 10%           |
| 15    | 7                      | (10h)     | 16/18                     | 16h, 18%              | 20h, 31%           |
| 16    | 8                      | (10d)     | 8/9                       | 17d, 25%              | 21d, 6%            |
| 17    | 8                      | (10f)     | 8/9                       | 17f, 10%              | 21f, 5%            |
| 18    | 8                      | (10h)     | 8/9                       | 17h, 57%              |                    |
| 19    | 8                      | (10i)     | 8/9                       | 17i, 28%              |                    |
| 20    | 8                      | (10k)     | 8/9                       | 17k, 35%              | 21k, 17%           |
| 21    | 9                      | (10h)     | 16/18                     | 18h, 25%              | 22h, 10%           |
| 22    | 9                      | (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 oxadiamines 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 trioxadiamine 10k afforded only 5% yield of the desired macrobicycle 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 Pd(dba)$_2$/BINAP was helpful (entry 13) though the yield remained low. Only the reaction with dioxadiamine 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, oxadiamine 10i,k provided average 25%–35% yields of the macrocyclization products 17d,i,k (entries 16, 19, 20), the reaction with dioxadiamine 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, macrotricyclicdimers 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 Pd(dba)$_2$/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 oxadiamines 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 trioxadiamine 10k and of 26 with dioxadiamine 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                    | (10h)     | DavePhos | 27h, 22%                |
| 2     | 23                    | (10i)     | DavePhos | 27i, 11%                |
| 3     | 23                    | (10k)     | DavePhos | 27k, 9%                 |
| 4     | 24                    | (10h)     | DavePhos | 28h, 5%                 |
| 5     | 24                    | (10k)     | DavePhos | 28k, 24%                |
| 6     | 25                    | (10k)     | BINAP    | 29k, 12%                |
| 7     | 26                    | (10h)     | BINAP    | 30h, 9%                 |
| 8     | 26                    | (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 \(N,N'-\text{bis}(3\text{-bromobenzyl})\) substituted diazacrown ethers 6 and 8, and the formation of valuable
macrotetracyclic 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 $^1$H 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, oxadiamines and polyamines, BINAP and DavePhos ligands, sodium tert-butoxide were purchased from Sigma-Aldrich (St. Louis, MO, USA) and used without further purification, Pd(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 (Br$_2$/CCl$_4$/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$_2$Cl$_2$, and the combined organic fractions were evaporated $\text{in vacuo}$, dissolved in CH$_2$Cl$_2$ (5–20 mL), washed three times with equal volumes of distilled water, dried over 4 Å molecular sieves, and the CH$_2$Cl$_2$ was evaporated $\text{in vacuo}$ 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-dioxa-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$_2$CO$_3$ (4.3 mmol, 530 mg) in MeCN (3 mL). Yield 419 mg (95%), as a yellowish viscous oil. $^1$H-NMR (CDCl$_3$) $\delta$ 2.73 (d, $^3$J = 4.6 Hz, 8H, CH$_2$N), 3.58 (t, $^3$J = 4.6 Hz, 8H, CH$_2$O), 3.63 (s, 4H, PhCH$_2$N), 7.17 (t, $^3$J = 7.8 Hz, 2H, H5(Ph)), 7.30–7.37 (m, 4H, 4H, PhCH$_2$N), 7.43 (X part of A'XX' system, 4H, H2(Ph)), 7.58 (s, 2H, H2(Ph)). $^{13}$C-NMR (CDCl$_3$) $\delta$ 55.0 (4C, CH$_2$N), 60.3 (2C, PhCH$_2$N), 69.4 (4C, CH$_2$O), 122.3 (2C, C3(Ph)), 127.3 (2C, CH(Ph)), 129.7 (2C, CH(Ph)), 129.9 (2C, CH(Ph)), 131.7 (2C, CH(Ph)), 142.2 (2C, C1(Ph)). HRMS (MALDI-TOF): C$_{22}$H$_{25}$Br$_2$N$_2$O$_2$ (M+H)$^+$ calcd.; 511.0596 observed; 511.0632.

4,10-Bis(4-bromobenzyl)-1,7-dioxa-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$_2$CO$_3$ (4.3 mmol, 530 mg) in MeCN (3 mL). Yield 421 mg (95%), of a beige crystalline powder, m.p. 88–90 °C. $^1$H-NMR (CDCl$_3$) $\delta$ 2.70 (t, $^3$J = 4.7 Hz, 8H, CH$_2$N), 3.56 (t, $^3$J = 4.7 Hz, 8H, CH$_2$O), 3.58 (s, 4H, PhCH$_2$N), 7.28 (A part of AA'XX' system, 4H, H2(Ph)), 7.42 (X part of AA'XX' system,
4H, H3(Ph)). $^{13}$C-NMR (CDCl3) δ 54.9 (4C, CH2N), 60.2 (2C, PhCH2N), 69.4 (4C, CH2O), 120.5 (2C, C4(Ph)), 130.4 (4C, CH(Ph)), 131.2 (4C, CH(Ph)), 138.8 (2C, C1(Ph)). HRMS (MALDI-TOF): C22H29Br2N2O2 (M+H)$^+$ calecd.; 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 K2CO3 (11.6 mmol, 1.6 g) in MeCN (8 mL). Yield 1.057 g (98%), of a yellow glassy compound. $^1$H-NMR (CDCl3) δ 2.71 (t, $^3$J = 5.0 Hz, 4H, CH2N), 2.75 (t, $^3$J = 5.8 Hz, 4H, CH2N), 3.52–3.57 (m, 8H, CH2O), 3.58 (s, 4H, CH2O or PyCH2N), 3.62 (s, 4H, PyCH2N or CH2O), 7.24 (d, $^3$J = 8.1 Hz, 2H, H5-Py), 7.71 (dd, $^3$J = 8.1 Hz, $^4$J = 1.4 Hz, 2H, H6-Py), 8.29 (br.s, 2H, H2-Py). $^{13}$C-NMR (CDCl3) δ 54.3 (2C, CH2N), 54.4 (2C, CH2N), 57.0 (2C, PyCH2N), 69.3 (2C, CH2O), 70.1 (2C, CH2O), 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): C22H31Cl2N4O3 (M+H)$^+$ calecd.; 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 K2CO3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 504 mg (98%), of a yellow glassy compound. $^1$H-NMR (CDCl3) δ 2.75 (t, $^3$J = 5.6 Hz, 8H, CH2N), 3.54 (s, 8H, CH2O), 3.56 (t, $^3$J = 5.6 Hz, 8H, CH2O), 3.65 (s, 4H, PyCH2N), 7.22 (d, $^3$J = 8.0 Hz, 2H, H5-Py), 7.67 (d, $^3$J = 8.0 Hz, 2H, H6-Py), 8.27 (br.s, 2H, H2-Py). $^{13}$C-NMR (CDCl3) δ 53.7 (4C, CH2N), 56.2 (2C, CH2NPy), 69.7 (4C, CH2O), 70.6 (4C, CH2O), 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): C24H35Cl2N4O4 (M+H)$^+$ calecd.; 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 K2CO3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 474 mg (85%), of a yellow glassy compound. $^1$H-NMR (CDCl3) δ 2.67–2.77 (m, 8H, CH2N), 3.46-3.52 (m, 8H, CH2O), 3.53 (s, 4H, CH2O or PyCH2N), 3.72 (br.s, 2H, PyCH2N or CH2O), 7.24 (br.s, 2H, H2-Py), 7.53 (br.s, 2H, H-Py). $^{13}$C-NMR (CDCl3) δ 54.4 (2C, CH2N), 54.9 (2C, CH2N), 57.0 (2C, PyCH2N), 61.4 (2C, PyCH2N), 68.6 (4C, CH2O), 69.6 br (2C, CH2O), 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): C22H31Br2N4O3 (M+H)$^+$ calecd.; 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 K2CO3 (5 mmol, 690 mg) in MeCN (3 mL). Yield 530 mg (88%) of a yellow crystalline powder, m.p. 131–133 °C. $^1$H-NMR (CDCl3) δ 2.39 (br.s, 8H, CH2N), 3.29–3.33 (m, 8H, CH2O), 3.34 (br.s, 12H, CH2O, PyCH2N), 7.00 (d, $^3$J = 7.8 Hz, 2H, H6-Py), 7.08 (d, $^3$J = 7.8 Hz, 2H, H4-Py), 7.36 (t, $^3$J = 7.7 Hz, 2H, H5-Py). $^{13}$C-NMR (CDCl3) δ 54.5 (4C, CH2N), 59.4 (2C, PyCH2N), 67.4 (4C, CH2O), 70.1 (4C, CH2O), 123.0 (2C, C6-Py), 126.4 (2C, C4-Py), 139.4 (2C, C5-Py), 141.3
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[22.5.5.13,7.118,22]hexatriaconta-3(36),4,6,18(35),19,21-hexaene (11h). Obtained from compound 4 (0.2 mmol, 102 mg), dioxadiamine 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, CH 2N), 3.32 (t, 3J = 4.9 Hz, 4H, CH 2NPh), 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, CH 2NPh), 55.3 (4C, CH 2N), 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): C28H43N4O4 (M+H)¹ calcd.; 499.3284 observed; 499.3251.

11,14,17,30,35-Pentaoxa-1,8,20,27-tetraazatetracyclo[25.5.5.13,7.121,25]nonatriaconta-3(39),4,6,21hexaene (11j). Obtained from compound 4 (0.2 mmol, 102 mg), trioxadiamine 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): C30H47N4O5 (M+H)¹ calcd.; 543.3546 observed; 543.3598.
12,15,18,32,37-Pentaoxa-1,8,22,29-tetraazatetracyclo[27.5.5.13,7.1.23,7]hentetraconta-3(41),4,6,23 (40),24,26-hexaene (11k). Obtained from compound 4 (0.2 mmol, 102 mg), trioxadiamine 10k (0.2 mmol, 44 mg) in the presence of Pd(dba)$_2$ (9 mg, 8 mol%), BINAP (11 mg, 9 mol%), NaO$_{t-Bu}$ (0.6 mmol, 57 mg) in abs. dioxygen (10 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:2. Yield 22 mg (19%), yellowish viscous oil. $^1$H-NMR (CDCl$_3$) $\delta$ 1.84 (quintet, $J = 6.0$ Hz, 4H, CH$_2$CH$_2$CH$_2$), 2.74 (br.s, 8H, CH$_2$N), 3.23 (t, $J = 6.4$ Hz, 4H, CH$_2$NPh), 3.51–3.63 (m, 16H, CH$_2$O, PhCH$_2$N), 3.64–3.69 (m, 4H, CH$_2$O), 6.48 (d, $J = 8.1$ Hz, 2H, H4(Ph) or H6(Ph)), 6.58 (d, $J = 7.2$ Hz, 2H, H6(Ph) or H4(Ph)), 6.90 (s, 2H, H2(Ph)), 7.07 (t, $J = 7.6$ Hz, 2H, H5(Ph)), two NH protons were not assigned. $^{13}$C-NMR (CDCl$_3$) $\delta$ 29.0 (2C, CH$_2$C$_2$H$_2$CH$_2$), 41.7 (2C, CH$_2$NPh), 54.9 (4C, CH$_2$N), 61.1 (2C, PhCH$_2$N), 69.6 (4C, CH$_2$O), 69.7 (2C, CH$_2$O), 70.2 (2C, CH$_2$O), 70.6 (2C, CH$_2$O), 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): C$_{32}$H$_{51}$N$_4$O$_5$ (M+H)$^+$ calcd.; 571.3859 observed; 571.3832.

Cyclodimer 13k. Obtained as the second product in the synthesis of macrobicycle 11k. Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:2. Yield 27 mg (23%) of a yellowish glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 1.84 (quintet, $J = 6.0$ Hz, 8H, CH$_2$CH$_2$CH$_2$), 2.73 (br.s, 16H, CH$_2$N), 3.20 (t, $J = 6.3$ Hz, 8H, CH$_2$NPh), 3.50–3.70 (m, 48H, CH$_2$O, PhCH$_2$N), 6.43–6.46 (m, 8H, H4(Ph), H6(Ph)), 6.63 (s, 4H, H2(Ph)), 7.07 (t, $J = 7.6$ Hz, 4H, H5(Ph)), four NH protons were not assigned. $^{13}$C-NMR (CDCl$_3$) $\delta$ 29.1 (4C, CH$_2$C$_2$H$_2$CH$_2$), 41.6 (4C, CH$_2$NPh), 57.7 (8C, CH$_2$N), 61.2 (4C, PhCH$_2$N), 69.4 (4C, CH$_2$O), 69.6 (8C, CH$_2$O), 70.2 (4C, CH$_2$O), 70.6 (4C, CH$_2$O), 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): C$_{64}$H$_{101}$N$_8$O$_{10}$ (M+H)$^+$ calcd.; 1141.76 observed; 1141.74.

10,13,25,30-Tetraoxa-1,7,16,22-tetraazatetracyclo[20.5.5.23,6.217,20]hexatriaconta-3,5,17,19,33,35-hexaene (12h). Obtained from compound 5 (0.2 mmol, 102 mg), dioxadiamine 10h (0.2 mmol, 30 mg) in the presence of Pd(dba)$_2$ (18 mg, 16 mol%), BINAP (22 mg, 18 mol%), NaO$_{t-Bu}$ (0.6 mmol, 57 mg) in abs. dioxygen (10 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:2. Yield 30 mg (30%), of a yellowish viscous oil. $^1$H-NMR (CDCl$_3$) $\delta$ 2.73 (br.s, 8H, CH$_2$N), 3.30 (t, $J = 5.1$ Hz, 4H, CH$_2$NPh), 3.50–3.70 (m, 48H, CH$_2$O, PhCH$_2$N), 6.43–6.46 (m, 8H, H4(Ph), H6(Ph)), 6.63 (s, 4H, H2(Ph)), 7.24 (d, $J_{obs} = 8.3$ Hz, 4H, H3(Ph)). 13C-NMR (CDCl$_3$) $\delta$ 43.9 (2C, CH$_2$NPh), 55.3 (4C, CH$_2$N), 60.1 (2C, PhCH$_2$N), 69.3 (2C, CH$_2$O), 70.1 (6C, CH$_2$O), 113.1 (4C, C3(Ph)), 129.7 (4C, C2(Ph)), 132.1 (2C, C1(Ph)), 147.2 (2C, C4(Ph)). HRMS (MALDI-TOF): C$_{28}$H$_{43}$N$_4$O$_4$ (M+H)$^+$ calcd.; 499.3284 observed; 499.3318.

Cyclodimer 14h. Obtained as the second product in the synthesis of macrobicycle 12h. Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:2. Yield 27 mg (27%) of a yellowish glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 2.71 (br.s, 16H, CH$_2$N), 3.28 (t, $J = 4.4$ Hz, 8H, CH$_2$NPh), 3.51–3.61 (m, 24H, CH$_2$O, PhCH$_2$N), 3.64 (s, 8H, CH$_2$O), 3.70 (t, $J = 4.4$ Hz, 8H, CH$_2$O), 4.06 (br.s, 4H, NH), 6.56 (d, $J_{obs} = 8.2$ Hz, 8H, H3(Ph)), 7.16 (d, $J_{obs} = 8.2$ Hz, 8H, H2(Ph)). 13C-NMR (CDCl$_3$) $\delta$ 43.5 (4C, CH$_2$NPh), 54.7 (8C, CH$_2$N), 60.5 (4C, PhCH$_2$N), 69.3 (8C, CH$_2$O), 69.7 (4C, CH$_2$O), 70.2 (4C, CH$_2$O), 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_{8}O_{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 (12). Obtained from compound 5 (0.2 mmol, 102 mg), trioxadiamine 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, 3JObs = 8.3 Hz, 4H, H₃(Ph)), 7.30 (d, 3JObs = 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), 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_{4}O_{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), trioxadiamine 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) = 100:20:3. 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 = 6.3 Hz, 4H, CH₂NPh), 3.19 (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), 4.24 (br.s, 2H, NH), 6.57 (d, 3JObs = 8.3 Hz, 4H, H₃(Ph)), 7.24 (d, 3JObs = 8.3 Hz, 4H, H₂(Ph)). ¹³C-NMR (CDCl₃) δ 29.1 (4C, CH₂C_H₂CH₂), 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_{4}O_{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), 3.63–3.72 (m, 8H, CH₂O), 3.85 (br.s, 4H, NH), 6.53 (d, 3JObs = 8.3 Hz, 8H, H₃(Ph)), 7.11 (d, 3JObs = 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_{8}O_{10} (M+H)^+ calcd.; 1141.76 observed; 1141.78.

22,25,30-Triaoxa-1,8,12,19-tetraazatetracyclo[17.8.5.1^{3,7}.1^{13,17}]tetraatriaconta-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%), tBuONa (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
Molecules 2014, 19

(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, 3Jabs = 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)). 13C-NMR (CDCl 3) δ 28.9 (1C, CH2C6H2CH2), 41.7 (2C, CH2NPh), 53.2 (2C, CH2N), 54.7 (2C, CH2N), 60.7 (2C, PhCH2N), 70.2 (2C, CH2O), 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 CH2O carbon atoms give a very broad signal in the region 68–70 ppm). HRMS (MALDI-TOF): C27H41N4O3 (M+H)+ calcd.; 469.3178 observed; 469.3143.

1,8,12,19,28,35,39,46-Octaazaheptacyclo[44.8.5.519,28.13,7.113,17.130,34.140,44]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 macrobicycle 15a. Eluent CH2Cl2–MeOH = 3:1. Yield 22 mg (19%) of a yellowish glassy compound. 1H-NMR (CDCl3) δ 1.84 (br.s, 4H, CH2C6H2), 2.71–2.96 (m, 16H, CH2N), 3.29 (t, 3J = 5.4 Hz, 8H, CH2O, PhCH2N), 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. 13C-NMR (CDCl3) δ 27.3 (2C, CCH2CH2C), 42.9 (4C, CH2NPh), 53.2 (4C, CH2N), 54.7 (4C, CH2N), 61.9 (4C, PhCH2N), 67.7 (4C, CH2O), 69.4 (4C, CH2O), 110.7 (4C, CH(Ph)), 115.6 (4C, CH(Ph)), 128.5 (4C, C5(Ph)), 137.7 (4C, C1(Ph)), 149.6 (4C, C3(Ph)). HRMS (MALDI-TOF): C54H81N8O8 (M+H)+ calcd.; 937.6279 observed; 937.6385.

23,26,3,-Trioxa-1,8,13,20-tetraazatricyclo[18.8.5.13,7.114,18]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 2Cl2–MeOH = 3:1. Yield 14 mg (12%) of a yellowish glassy compound. 1H-NMR (CDCl3) δ 1.83 (br.s, 4H, CH2C6H2), 2.85–3.08 (m, 4H, CH2N), 3.15–3.22 (m, 4H, CH2N), 3.40 (br.s, 4H, CH2NPh), 3.53–3.88 (m, 16H, CH2O, PhCH2N), 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)). 13C-NMR (CDCl3) δ 26.6 (2C, CCH2CH2C), 43.5 br (2C, CH2NAr), 53.2 (2C, CH2N), 54.2 (2C, CH2N), 61.3 (2C, PhCH2N), 69.4 (2C, CH2O), 70.0 (4C, CH2O), 111.1 br (2C, CH(Ph)), 115.8 (2C, CH(Ph)), 128.5 (4C, C5(Ph)), 137.7 (4C, C1(Ph)), 149.6 (4C, C3(Ph)). HRMS (MALDI-TOF): C28H43N4O3 (M+H)+ calcd.; 483.3335 observed; 483.3275.

22,25,50,53,58,65-Hexaoxa-1,7,12,19,28,35,40,47-octaazaheptacyclo-[45.8.5.519,28.36.113,17.130,34.141,45]octahexaconta-3(68),4,6,13(67),14,16,30(61),31,33,40(60),41,43-dodecaene (19b). Obtained as the second product in the synthesis of macrobicycle 15b. Eluent CH2Cl2–MeOH = 3:1. Yield 25 mg (21%) of a yellowish glassy compound. 1H-NMR (CDCl3) δ 1.71 (br.s, 8H, CCH2CH2C), 2.45–3.08 (m, 16H, CH2N), 3.18 (t, 3J = 5.5 Hz, 8H, CH2NPh), 3.52–3.82 (m, 32H, CH2O, PhCH2N), 4.65 (br.s, 4H, NH), 6.48 (d, 3Jabs = 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)). 13C-NMR (CDCl3) δ 26.6 (4C, CCH2CH2C), 43.1 (4C, CH2NPh), 53.9 (4C, CH2N), 54.9 (4C, CH2N), 60.3 (4C, PhCH2N), 67.2 (4C, CH2O), 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, C(Ph)), 148.6 (4C, C(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%), NaO-t-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, 12 Н, CCH₂C), 1.45–1.55 (m, 4H, CH₂CNPh) 2.60–3.21 (m, 12 Н, CH₂N, CH₂NPh), 3.58–3.83 (m, 16 Н, CH₂O, PhCH₂N), 4.22 (br.s, 2 Н, NH), 6.48 (d, 3J = 6.7 Hz, 2H, H₄(Ph)), 6.59 (d, 3J = 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, C(Ph)), 137.4 (2C, C(Ph)), 148.9 (2C, C(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-
[58.8.5.5.26,35.13,7.120,24.137,41.154,58]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, 24 Н, CCH₂C), 1.50–1.59 (m, 8H, CH₂CNAr), 2.67–2.92 (m, 16 Н, CH₂N), 3.02 (br.s, 8 Н, CH₂NPh), 3.50–3.75 (m, 32 Н, CH₂O, PhCH₂N), 4.38 (br.s, 4 Н, 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, C(Ph)), 129.0 (4C, C(Ph)), 148.8 (4C, C(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[21.8.5.1.3.7.1.20,24]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%), NaO-t-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, 4 Н, CCH₂C), 2.65–2.75 (m, 8H, CH₂N), 3.02 (br.s, 8H, CH₂NPh), 3.50–3.75 (m, 32H, CH₂N, 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 26.4 (2C, CCH₂C), 41.6 (2C, CH₂NPh), 46.3 (2C, CH₂NHC₅H₅), 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.; 567.4275 observed; 567.4225.
26,29,57,60,65,72-Hexaaza-1,8,12,16,23,32,39,43,47,54-decaazaheptacyclo-[52.8.5.23.32.14.7.34.38.148.52]-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, 8Н, CH₂CH₂), 2.60–2.82 (m, 24Н, CH₂N), 3.14 (br.s, 8Н, 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, 4Н, 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[23.8.5.13,7.119,23]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, CH₂CH₂), 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, CH₂NCH₂), 54.9 (2C, CH₂), 55.3 (2C, CH₂), 60.5 (2C, PhCH₂N), 69.3 (2C, CH₂O), 69.6 (2C, CH₂O), 70.1 (2C, CH₂O), 110.8 (2C, CH₂), 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-hexatetracyclo[24.8.5.13,7.120,24]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, 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 47mg (33%) of a yellow glassy compound. ¹H-NMR (CDCl₃) δ 1.74 (quintet, 3J = 7.3 Hz, 2H, H₄(Ph) or H₆(Ph)), 2.55–2.81 (m, 16Н, 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, CH₂NCH₂), 48.3 (2C, CH₂NCH₂), 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-Trioxy-1,8,12,16,20,27-hexatetraconta[25.8.5.13,7.121,25]dodecactetaconta-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,
CCH(C), 1.78 (quintet, \(^3J = 5.3\) Hz, 4H, CCH(C)), 2.67–2.76 (m, 12H, CH\(_2\)N, CH\(_2\)NHCH\(_2\)), 2.79 (t, \(^3J = 5.6\) Hz, 4H, CH\(_2\)N), 3.12 (t, \(^3J = 6.3\) Hz, 4H, CH\(_2\)NPh), 3.53–3.65 (m, 16H, CH\(_2\)O, PhCH\(_2\)N), 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. \(^13\)C-NMR (CDCl\(_3\)) \(\delta\) 27.5 (1C, CCH\(_2\)C), 28.4 (2C, CCH\(_2\)C), 42.4 (2C, CH\(_2\)NPh), 47.9 (2C, CH\(_2\)NHCH\(_2\)), 49.2 (2C, CH\(_2\)NHCH\(_2\)), 54.7 (2C, CH\(_2\)N), 55.0 (2C, CH\(_2\)N), 60.5 (2C, PhCH\(_2\)N), 69.5 (4C, CH\(_2\)O), 70.2 (2C, CH\(_2\)O), 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): C\(_{33}\)H\(_{55}\)N\(_6\)O\(_3\) (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\(^1\),18.22]nonatriaconta-3(39),4,6,18(38),19,21-hexaene (15h). Obtained from compound 6 (0.25 mmol, 139 mg), dioxadiamine 10h (0.25 mmol, 37 mg) in the presence of Pd(db)\(_2\) (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH\(_2\)Cl\(_2\)–MeOH = 10:1. Yield 27 mg (20%) of a yellowish glassy compound. 1H-NMR (CDCl\(_3\)) \(\delta\) 2.61–3.15 (m, 8H, CH\(_2\)N), 3.30 (br.s, 4H, CH\(_2\)NPh), 3.50–3.75 (m, 24H, CH\(_2\)O, PhCH\(_2\)N), 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. \(^13\)C-NMR (CDCl\(_3\)) \(\delta\) 43.9 (2C CH\(_2\)NPh), 53.4 (2C, CH\(_2\)N), 54.7 (2C, CH\(_2\)N), 61.0 (2C, PhCH\(_2\)N), 67.4 (2C, CH\(_2\)O), 67.8 (2C, CH\(_2\)O), 69.3 (4C, CH\(_2\)O), 70.2 (2C, CH\(_2\)O), 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): C\(_{30}\)H\(_{47}\)N\(_4\)O\(_5\) (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-[53.8.5.5.5.32,32.23,6.117,21.134,38.149,53]-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 CH\(_2\)Cl\(_2\)–MeOH = 3:1. Yield 14 mg (10%) of a yellowish glassy compound. 1H-NMR (DMSO-d\(_6\), 363K) \(\delta\) 2.84 (br.s, 16H, CH\(_2\)N), 3.21 (t, \(^3J = 5.6\) Hz, 8H, CH\(_2\)NPh), 3.52–3.68 (m, 48H, CH\(_2\)O, PhCH\(_2\)N), 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. \(^13\)C-NMR (DMSO-d\(_6\), 363K) \(\delta\) 42.7 (4C, CH\(_2\)NPh), 53.5 (4C, CH\(_2\)N), 53.9 (4C, CH\(_2\)N), 59.6 (4C, PhCH\(_2\)N), 67.5 (4C, CH\(_2\)O), 68.0 (4C, CH\(_2\)O), 68.9 (4C, CH\(_2\)O), 69.5 (8C, CH\(_2\)O), 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): C\(_{60}\)H\(_{93}\)N\(_8\)O\(_{10}\) (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), dioxadiamine 10i (0.25 mmol, 51 mg) in the presence of Pd(db)\(_2\) (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOt-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH\(_2\)Cl\(_2\)–MeOH = 10:1. Yield 56 mg (37%) as a yellowish glassy compound. 1H-NMR (CDCl\(_3\)) \(\delta\) 1.57–1.67 (m, 4H, CCH\(_2\)C), 1.80 (quintet, \(^3J = 5.3\) Hz, 4H, NCCH\(_2\)CN), 2.57–3.16 (m, 12H, CH\(_2\)N), 3.36–3.43 (m, 4H, CH\(_2\)O), 3.47 (t, \(^3J = 4.7\) Hz, 4H, CH\(_2\)O), 3.54–3.75 (m, 16H, CH\(_2\)O, PhCH\(_2\)N), 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. \(^13\)C-NMR
Molecules 2014, 19, 956

(CDCl3) δ 26.4 (2C, CCH2CH2C), 29.1 (2C, NCCCH2N), 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)+ calcld.; 599.4172 observed; 599.4130.

12,15,18,32,35,40-Hexaoxa-1,8,22,29-tetraazatetracyclo[27.8.5.3.1.23.27]tetratetraconta-3(44),4,6,23(43),24,26-hexaene (15k). Obtained from compound 6 (0.25 mmol, 139 mg), trioxadiamine 10k (0.25 mmol, 51 mg) in the presence of Pd(dba)2 (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaO-t-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, CH2CH2CH2), 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)+ calcld.; 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-[64.8.5.529,38.13,7.123,27.140,44.160,64]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, CH2CH2CH2C), 2.75 (t, 3J = 4.8 Hz, 8H, CH2CH2N), 2.77 (t, 3J = 4.8 Hz, 8H, CH2CH2N), 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), 52.8 (8C, CH2N), 60.3 (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)+ calcld.; 1229.82 observed; 1229.84.

10,13,25,28,33-Pentaaxo-1,7,16,22-tetraazatetracyclo[20.8.5.23.6.17.20]nonatriaconta-3,5,17,19,36,38-hexaene (16h). Obtained from compound 7 (0.5 mmol, 278 mg), dioxadiamine 10h (0.5 mmol, 74 mg) in the presence of Pd(dba)2 (46 mg, 16 mol%), BINAP (56 mg, 18 mol%), NaO-t-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 = 7.0 Hz, 4H, H3(Ph), H3'(Ph)), 7.09 (d, 3J = 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)),
Molecules 2014, 19

131.4 (4C, C2(Ph), C2'(Ph)), 148.3 (2C, C4(Ph)). HRMS (MALDI-TOF): C30H47N4O5 (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-[50.8.5.22,31,23,6.217,20.233,36,247,50]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) = 100:20:3–100:20:1. 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, PhCH2N or CH2O), 3.74 (t, 3J = 5.0 Hz, 8H, CH2O), 4.04 (br.s, 4H, NH), 6.51 (d, 3Jabs = 8.1 Hz, 8H, H3(Ph), H3'(Ph)), 7.16 (d, 3Jobs = 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): C60H93N8O10 (M+H)+ calcd.; 1085.7014 observed; 1085.6952.

11,16,29,32,37-Pentaoxa-1,7,20,26-tetraazatetracyclo[24.8.5.23,6.221,24]tritetraconta-3,5,21,23,42-hexaene (16i). Obtained from compound 7 (0.25 mmol, 139 mg), dioxadiamine 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, 3Jobs = 8.1 Hz, 4H, H3(Ph), H3'(Ph)), 7.21 (d, 3Jabs = 8.1 Hz, 4H, H2(Ph), H2'(Ph)), NH protons were not assigned. 13C-NMR (CDCl3) δ 26.5 (2C, CCH2CH2C), 29.6 (4C, CCH2C), 42.6 (2C, CH2NPh), 53.2 (2C, CH2N), 54.0 (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): C34H55N4O5 (M+H)+ calcd.; 599.4172 observed; 599.4131.

11,16,29,32,45,50,63,66,71,80-Decaoxa-1,7,20,26,tetraazaheptacyclo-[58.8.5.26,35.22,31,24]heptaconta-3,5,21,23,42-hexaene (16k). Obtained from compound 7 (0.25 mmol, 139 mg), trioxadiamine 10k (0.25 mmol, 51 mg) in the presence of Pd(dba)2 (23 mg, 16 mol%), BINALP (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 1.66 (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), 4.45 (br.s, 8H, NH), 6.57 (d, 3Jobs = 8.0 Hz, 8H, H3(Ph), H3'(Ph)), 7.23 (d, 3Jabs = 8.0 Hz, 8H, H2(Ph), H2'(Ph)). 13C-NMR (CDCl3) δ 26.7 (4C, CCH2CH2C), 29.6 (4C, CH2C), 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): C68H109N8O10 (M+H)+ calcd.; 1197.8266 observed; 1197.8215.

11,14,17,30,33,38-Hexaoxa-1,7,21,27-tetraazatetracyclo[25.8.5.23,6.22,25]tetratetraconta-3,5,22,24,41,43-hexaene (16k). Obtained from compound 7 (0.25 mmol, 139 mg), trioxadiamine 10k
Molecules 2014, 19 958

(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, 3Jobs = 7.9 Hz, 4H, H3(Ph), H3'(Ph)), 7.16 (d, 3Jobs = 7.9 Hz, 4H, H2(Ph), H2'(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), C3'(Ph)), 127.5 (2C, C1(Ph)), 131.8 (4C, C2(Ph), C2'(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-[61.8.5.527.36.23.622.25.238.41.157.61]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, NH), 6.56 (d, 3Jobs = 7.8 Hz, 8H, H3(Ph), H3'(Ph)), 7.21 (d, 3Jobs = 7.8 Hz, 8H, H2(Ph), H2'(Ph)). 13C-NMR (CDCl3) δ 29.0 (4C, CCH2C), 42.1 (4C, CH2NPh), 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), C3'(Ph)), 125.1 (4C, C1(Ph)), 131.4 (8C, C2(Ph), C2'(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[21.8.8.13,7.117,21]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 (br.s, 8H, CCH2C), 2.73 (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), 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), C3'(Ph)), 125.1 (4C, C1(Ph)), 131.4 (8C, C2(Ph), C2'(Ph)), 148.0 (4C, C4(Ph)). HRMS (MALDI-TOF): C32H52N5O4 (M+H)+ calcd.; 570.4019 observed; 530.3976.

26,29,34,37-Tetraoxa-1,8,12,16,23-pentaazatetracyclo[21.8.8.13,7.117,21]hentetraconta-3(41),4,6,17(40),18,20-hexaene (17d). 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,
$^{3}J_{obs} = 6.3$ Hz, 4H, H4(Ph) or H6(Ph)), 6.67 (br.s, 4H, H2(Ph)), 7.05 (t, $^{3}J = 7.6$ Hz, 4H, H5(Ph)), NH protons were not assigned. $^{13}$C-NMR (CDCl3) δ 29.6 (4C, CH2C), 42.7 (4C, CH2NPh), 48.3 (4C, CH2NHCH2), 53.8 (8C, CH2N), 60.2 (4C, PhCH2N), 70.1 (8C, CH2O), 70.7 (8C, CH2O), 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): C64H103N10O8 (M+H)$^{+}$ calcd.; 1139.80 observed; 1139.79.

29,32,37,40-Tetraoxa-1,8,12,15,19,26-hexaazatetracyclo[24.8.8.13,7.120,24]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%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:35:6. Yield 15 mg (10%) of a yellow glassy compound. $^{1}$H-NMR (CDCl3) δ 1.77 (quintet, $^{3}J = 5.7$ Hz, 4H, CCH2C), 2.58–2.85 (m, 16H, CH$_2$N), 3.15 (t, $^{3}J = 5.9$ Hz, 4H, CH$_2$NPh), 3.45-3.70 (m, 20H, CH$_2$O, PhCH$_2$N), 6.44 (d, $^{3}J = 7.9$ Hz, 2H, H6(Ph) or H4(Ph)), 6.56 (d, $^{3}J = 7.2$ Hz, 2H, H4(Ph) or H6(Ph)), 6.82 (br.s, 2H, H2(Ph)), 7.05 (t, $^{3}J = 7.7$ Hz, 2H, H5(Ph)), NH protons were not assigned. 13C-NMR (CDCl3) δ 28.8 (2C, CCH$_2$C), 42.7 (2C, CH$_2$NPh), 47.9 (2C, CH$_2$NHCH2), 48.2 (2C, CH$_2$NHCH2), 54.5 (4C, CH$_2$N), 60.0 (2C, PhCH$_2$N), 69.8 (4C, CH2O), 70.6 (4C, CH$_2$O), 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): C$_{34}$H$_{57}$N$_{6}$O$_{4}$ (M+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-[58.8.8.826,35.13,7.120,24.137,41.154,58]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 CH$_2$Cl$_2$–MeOH = 10:1–3:1. Yield 8 mg (5%) of a yellow glassy compound. $^{1}$H-NMR (CDCl3) δ 1.76 (br.s, 8H, CCH$_2$C), 2.68–2.81 (m, 32H, CH$_2$N), 3.15 (br.s, 8H, CH$_2$NPh), 3.50–3.63 (m, 40H, CH$_2$O, PhCH$_2$N), 6.43 (d, $^{3}J = 7.2$ Hz, 4H, H6(Ph) or H4(Ph)), 6.60 (br.s, 4H, H2(Ph)), 7.05 (t, $^{3}J = 7.5$ Hz, 4H, H5(Ph)), NH protons were not assigned. MS (MALDI-TOF): C$_{68}$H$_{113}$N$_{12}$O$_{8}$ (M+H)$^{+}$ calcd.; 1225.88 observed; 1125.90.

11,14,17,31,34,40-Hexaoxa-1,8,21,28-tetraazatetracyclo[26.8.8.13,7.122,26]hexatetraconta-3(46),4,6,22 (45),23,25-hexaene (17h). Obtained from compound 8 (0.25 mmol, 150 mg), dioxadiamine 10h (0.25 mmol, 37 mg) in the presence of Pd(dba)$_2$ (12 mg, 8 mol%), BINAP (14 mg, 9 mol%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH = 10:1–3:1. Yield 83 mg (57%) of a yellowish glassy compound. $^{1}$H-NMR (CDCl3) δ 1.76 (br.s, 8H, CCH$_2$C), 2.68–2.81 (m, 32H, CH$_2$N), 3.15 (br.s, 8H, CH$_2$NPh), 3.50–3.63 (m, 40H, CH$_2$O, PhCH$_2$N), 6.43 (d, $^{3}J = 7.2$ Hz, 4H, H6(Ph) or H4(Ph)), 6.60 (br.s, 4H, H2(Ph)), 6.62 (d, $^{3}J = 8.0$ Hz, 4H, H4(Ph) or H6(Ph)), 7.05 (t, $^{3}J = 7.5$ Hz, 4H, H5(Ph)), NH protons were not assigned. 13C-NMR (CDCl3) δ 43.6 (2C, CH$_2$NPh), 52.8 (4C, CH$_2$N), 59.6 (2C, PhCH$_2$N), 67.3 (4C, CH$_2$O), 68.3 (4C, CH$_2$O), 70.2 (2C, CH$_2$O), 110.9 (2C, CH(Ph)), 115.8 (2C, CH(Ph)), 129.3 (2C, C5(Ph)), 138.1 (2C, C1(Ph)), 149.0 (2C, C3(Ph)). HRMS (ESI-TOF): C$_{32}$H$_{51}$N$_{4}$O$_{6}$ (M+H)$^{+}$ calcd.; 587.3809 observed; 587.3815.

12,17,31,34,39,42-Hexaaza-1,8,21,28-tetraazatetracyclo[26.8.8.13,7.122,26]hexatetraconta-3(46),4,6,22 (45),23,25-hexaene (17i). Obtained from compound 8 (0.25 mmol, 150 mg), dioxadiamine 10i (0.25 mmol,
51 mg) in the presence of Pd(db2)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, 3Jobs = 7.0 Hz, 2H, H4(Ph) or H6(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-Heptaoxa-1,8,22,29-tetraazatetracyclo[27.8.8.13,7.123,27]heptatetraconta-3(47),4,6,23(46),24,26-hexaene (17k). Obtained from compound 8 (0.25 mmol, 150 mg), trioxadiamine 10k (0.25 mmol, 55 mg) in the presence of Pd(db2)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, 2H, NH), 4.18 (br.s, 2H, H2(Ph)), 6.48 (d, 3Jobs = 7.2 Hz, 2H, H4(Ph) or H6(Ph)), 6.61 (d, 3Jobs = 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), 67.3 (4C, CH2O), 68.5 (4C, CH2O), 69.5 (2C, CH2O), 70.1 (2C, CH2O), 70.5 (2C, CH2O), 70.7 (2C, CH2O), 110.8 (2C, CH(Ph)), 111.5 (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.

12,15,18,32,35,49,52,55,59,69,72,77,80,87,90-Tetradecaoxa-1,8,22,29,38,45,59,66-octaazaheptacyclo-[64.8.8.829,38.13,7.123,27.140,44.160,64]tetranonaconta-3(94),4,6,23(93),24,26,40(84),41,43,60(83),61,63-dodecaene (21k). Obtained from compound 9 (0.25 mmol, 150 mg), dioxadiamine 10h (0.25 mmol, 37 mg) in the presence of Pd(db2)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 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, 3Jobs = 7.0 Hz, 4H, H6(Ph) or H4(Ph)), 6.73 (s, 4H, H2(Ph)), 7.05 (t, 3J = 7.5 Hz, 4H, H5(Ph)). MS (MALDI-TOF): C72H117N8O14 (M+H)+ calcd.; 659.4384 observed; 659.4389.

10,13,25,28,33,36-Hexaaza-1,7,16,22-tetraazatetracyclo[20.8.8.23,6.217,20]dotetraconta-3,5,17,19,39,41-hexaene (18h). Obtained from compound 9 (0.25 mmol, 150 mg), dioxadiamine 10h (0.25 mmol, 37 mg) in the presence of Pd(db2)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, $^3J_{abs} = 8.5$ Hz, 4H, H3(Ph), H3'(Ph)), 7.17 (d, $^3J_{abs} = 8.5$ Hz, 4H, H2(Ph), H2'(Ph)), NH protons were not assigned.

$^{13}$C-NMR (CDCl3) $\delta$ 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), C3'(Ph)), 128.8 (2C, C1(Ph)), 129.8 (4C, C2(Ph), C2'(Ph)), 147.2 (2C, C4(Ph)). HRMS (ESI-TOF): C32H51N4O6 (M+H)$^+$ calcd.; 587.3809 observed; 587.3829.

10,13,25,28,40,43,55,58,66,75,78-dodecaoxa-1,7,16,22,31,37,46,52-octaazaheptacyclo-[50.8.8.8$^{22,23}$.$^{23,24}$]$^{22,23}$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) $\delta$ 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), H3'(Ph)), 7.09 (d, $^3J_{obs} = 8.2$ Hz, 8H, H2(Ph), H2'(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[25.8.8.23,6.222,25]heptatetraconta-3,5,22,24,44,46-hexaene (18k). Obtained from compound 9 (0.25 mmol, 150 mg), trioxadiamine 10k (0.25 mmol, 55 mg) in the presence of Pd(dba)2 (24 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaO$t$-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) $\delta$ 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), H3'(Ph)), 6.79 (d, $^3J_{obs} = 8.1$ Hz, 4H, H2(Ph), H2'(Ph)), NH protons were not assigned. 13C-NMR (CDCl3) $\delta$ 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), C3'(Ph)), 124.5 (2C, C1(Ph)), 130.5 (4C, C2(Ph), C2'(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[20.8.5.23,6.219,22]hentetraconta-3,5,17,19,36,38-hexaene (27h). Obtained from compound 23 (0.5 mmol, 235 mg), dioxadiamine 10h (0.5 mmol, 74 mg) in the presence of Pd(dba)2 (24 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaO$t$-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH2Cl2–MeOH–NH3(aq) = 100:20:2. Yield 60 mg (22%) of a yellowish glassy compound. 1H-NMR (CDCl3) $\delta$ 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)). $^{13}$C-NMR (CDCl3) $\delta$ 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): C38H59N4O7 (M+H)$^+$ calcd.; 569.4384 observed; 569.4375.

10,15,27,30,35-Pentaoxa-1,5,7,18,20,24-hexaazatetracyclo[22.8.5.23,6.219,22]hentetraconta-3,5,19,21,38,40-hexaene (27i). Obtained from compound 23 (0.25 mmol, 117 mg), dioxadiamine 10i (0.25 mmol,
51 mg) in the presence of Pd(dba)$_2$ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:1–100:20:3. Yield 17 mg (11%) of a yellow glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 1.63–1.70 (m, 4H, CCH$_2$CH$_2$C), 1.87 (quintet, $^3J$ = 5.5 Hz, 4H, CCH$_2$C), 2.71 (br.s, 8H, CH$_2$N), 3.39 (t, $^3J$ = 5.2 Hz, 4H, CH$_2$NPy), 3.42–3.48 (m, 4H, CH$_2$O), 3.50–3.64 (m, 20H, CH$_2$O, PyCH$_2$N), 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)). $^{13}$C-NMR (CDCl$_3$) $\delta$ 26.8 (2C, CCH$_2$CH$_2$C), 29.3 (2C, CCH$_2$C), 40.7 (2C, CH$_2$NPy), 54.4 (2C, CH$_2$N), 54.5 (2C, CH$_2$N), 57.4 (2C, PyCH$_2$N), 69.0 (2C, CH$_2$O), 69.5 (4C, CH$_2$O), 70.6 (2C, CH$_2$O), 71.0 (2C, CH$_2$O), 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): C$_{32}$H$_{53}$N$_{6}$O$_{5}$ (M+H)$^+$ calcd.; 601.4077 observed; 601.4043.

11,14,17,30,33,38-Hexaoxa-1,5,7,21,23,27-hexaoazatetracyclo[25.8.5.23,6.222,25]tetratetraconta-3,5,22,24,41,43-hexaene (27k). Obtained from compound 23 (0.25 mmol, 117 mg), trioxadiamine 10k (0.25 mmol, 55 mg) in the presence of Pd(dba)$_2$ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH = 5:1, CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:1–100:20:3. Yield 14 mg (9%) of a yellow glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 1.87 (quintet, $^3J$ = 5.9 Hz, 4H, CCH$_2$C), 2.71 (t, $^3J$ = 5.3 Hz, 4H, CH$_2$N), 2.77 (t, $^3J$ = 4.7 Hz, 4H, CH$_2$N), 3.39 (br.s, 4H, CH$_2$NPy), 3.51-3.70 (m, 28H, CH$_2$O, PyCH$_2$N), 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)). $^{13}$C-NMR (CDCl$_3$) $\delta$ 29.0 (2C, CCH$_2$C), 40.0 (2C, CH$_2$NPy), 54.1 (2C, CH$_2$N), 54.3 (2C, CH$_2$N), 57.2 (2C, PyCH$_2$N), 68.7 (2C, CH$_2$O), 69.2 (2C, CH$_2$O), 70.1 (2C, CH$_2$O), 70.5 (2C, CH$_2$O), 70.6 (2C, CH$_2$O), 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): C$_{32}$H$_{53}$N$_{6}$O$_{6}$ (M+H)$^+$ calcd.; 617.4027 observed; 617.3967.

10,13,25,28,33,36-Hexaoxa-1,5,7,16,18,22-hexaoazatetracyclo[20.8.8.23,6.217,20]dotetraconta-3,5,17,19,39,41-hexaene (28h). Obtained from compound 24 (0.25 mmol, 128 mg), dioxadiamine 10h (0.25 mmol, 37 mg) in the presence of Pd(dba)$_2$ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:1–100:20:2. Yield 37 mg (5%) as a yellow glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 1.87 (quintet, $^3J$ = 5.9 Hz, 4H, CCH$_2$C), 2.71 (t, $^3J$ = 5.3 Hz, 4H, CH$_2$N), 2.77 (t, $^3J$ = 4.7 Hz, 4H, CH$_2$N), 3.39 (br.s, 4H, CH$_2$NPy), 3.51-3.70 (m, 28H, CH$_2$O, PyCH$_2$N), 6.32 (d, $^3J$ = 8.2 Hz, 2H, H5(Py)), 7.54 (d, $^3J$ = 8.2 Hz, 2H, H6(Py)), 7.90 (br.s, 2H, H2(Py)). $^{13}$C-NMR (CDCl$_3$) $\delta$ 29.0 (2C, CCH$_2$C), 40.0 (2C, CH$_2$NPy), 54.1 (2C, CH$_2$N), 54.3 (2C, CH$_2$N), 57.2 (2C, PyCH$_2$N), 68.7 (2C, CH$_2$O), 69.2 (2C, CH$_2$O), 69.4 (2C, CH$_2$O), 70.1 (2C, CH$_2$O), 70.5 (2C, CH$_2$O), 70.6 (2C, CH$_2$O), 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 (ESI-TOF): C$_{30}$H$_{49}$N$_{6}$O$_{6}$ (M+H)$^+$ calcd.; 589.3713 observed; 589.3715.

11,14,17,30,33,38,41-Heptaoxa-1,5,7,21,23,27-hexaoazatetracyclo[25.8.8.23,6.222,25]heptatetraconta-3,5,22,24,44,46-hexaene (28k). Obtained from compound 24 (0.25 mmol, 128 mg), trioxadiamine 10k (0.25 mmol, 55 mg) in the presence of Pd(dba)$_2$ (23 mg, 16 mol%), DavePhos (18 mg, 18 mol%), NaOr-Bu (0.75 mmol, 72 mg) in abs. dioxane (12 mL). Eluent CH$_2$Cl$_2$–MeOH–NH$_3$(aq) = 100:20:1–100:20:2. Yield 40 mg (24%) of a yellow glassy compound. $^1$H-NMR (CDCl$_3$) $\delta$ 1.87 (quintet, $^3J$ = 5.5 Hz, 4H, CCH$_2$C), 2.69 (t, $^3J$ = 5.5 Hz, 4H, CH$_2$N), 2.79 (t, $^3J$ = 4.6 Hz, 4H, CH$_2$N), 3.38 (q, $^3J$ = 6.1 Hz, 4H, CH$_2$NPY), 3.52-3.69 (m, 32H, CH$_2$O, PyCH$_2$N), 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)). $^{13}$C-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[27.8.5.13,7.123,27]tetratetraconta-3(44),4,6,23(43),24,26-hexaene (29k). Obtained from compound 25 (0.25 mmol, 140 mg), trioxadiamine 10k (0.25 mmol, 55 mg) in the presence of Pd(dba)₂ (23 mg, 16 mol%), BINAP (28 mg, 18 mol%), NaO₄t-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[22.8.8.13,7.118,22]dotetraconta-3(42),4,6,18(41),19,21-hexaene (30h). Obtained from compound 26 (0.227 mmol, 137 mg), dioxadiamine 10h (0.23 mmol, 34 mg) in the presence of Pd(dba)₂ (21 mg, 16 mol%), DavePhos (16 mg, 18 mol%), NaO₄t-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, oxadiamine 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 oxadiamine linkers, while in the case of macrobicycles with pyridyl spacers, the yields are generally substantially lower and hardly surpass 20%. A number of compounds
Molecules 2014, 19

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

Acknowledgments

This work was carried out in the frame of the International Associated French–Russian Laboratory of Macrocycle Systems and Related Materials (LAMREM) of RAS and CNRS, the work was financially supported by the RFBR grants N 12-03-93107 and 13-03-00813, CNRS, and the Russian Academy of Sciences program Elaboration of the methods for the synthesis of chemical compounds and construction of new materials.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Bianchi, A.; Ciampolini, M.; Micheloni, M.; Chimichi, S.; Zanobini, F. Synthesis and characterization of the cage 12,17-dioxa-1,5,9- triazabicyclo [7.5.5] nonadecane. Its basicity and complexing properties. Gazz. Chim. Ital. 1987, 117, 499–502.
2. Bencini, A.; Bianchi, A.; Borselli, A.; Ciampolini, M.; Micheloni, M.; Paoli, P.; Valtancoli, B.; Dapporto, P.; Garcia-Espana, E.; Ramirez, J.A. Structural aspects of the protonation of small cages. Preparation of the new aza-cage 12,17-dimethyl-1,9,12,17-tetra-azabicyclo[7.5.5]nonadecane (L). Thermodynamic studies on solution equilibria. Crystal structures of [H2L][CoCl4] and [H2L1][CoCl4] salts. J. Chem. Soc. Perkin Trans. 1990, 1990, 209–214.
3. Bemtegen, J.M.; Springer, M.E.; Loyola, V.M.; Wilkins, R.G.; Taylor, R.W. Formation and dissociation kinetics of alkaline-earth ions with benzo-substituted cryptands. Inorg. Chem. 1984, 23, 3348–3353.
4. Chapoteau, E.; Czech, B.P.; Kumar, A.; Pose, A. Synthesis and complexing abilities of novel benzocryptands. J. Incl. Phenom. 1988, 6, 41–47.
5. Wehner, W.; Vögtle, F. Ligandstruktur und komplexierung, VIII: Pyridinophan-Kryptate. Tetrahedron Lett. 1976, 17, 2603–2606.
6. Arnaud-Neu, F.; Sanchez, M.; Yahya, R.; Schwing-Weill, M.-J.; Lehn, J.-M. Nature and stability of some metallic complexes of dinucleating cryptands in solution. I. A polyaza-polyoxa cylindrical macrotricycle and its monocyclic subunit. Helv. Chim. Acta 1985, 68, 456–464.
7. Boudon, C.; Gisselbrecht, J.P.; Gross, M.; Kotzyba-Hibert, F.; Lehn, J.-M. Electrochemical generation of mono- and dinuclear mercuric cryptates. J. Electroanal. Chem. 1986, 202, 191–201.
8. Graf, E.; Lehn, J.M. Cryptates sphériques. Synthèse et complexes d’Inclusion de ligands macroticycliques sphériques. Helv. Chim. Acta 1981, 64, 1040–1057.
9. Krakowiak, K.E.; Bradshaw, J.S.; Dalley, N.K.; Zhu, Ch.; Yi, G.; Curtis, J.C.; Li, D.; Izatt, R.M. Preparation and cation complexing properties of some macrocyclic ligands. J. Org. Chem. 1992, 57, 3166–3173.
10. Bradshaw, J.S.; Krakowiak, K.E.; An, H.; Wang, T.; Zhu, Ch.; Izatt, R.M. A novel two-step method to prepare new unsymmetrical cryptands. *Tetrahedron Lett.* **1992**, *33*, 4871–4874.

11. Krakowiak, K.E. Simple methods for the synthesis of cryptands and supercryptands. *J. Incl. Phen. Mol. Recogn.* **1997**, *29*, 283–288.

12. Averin, A.D.; Shukhaev, A.V.; Buryak, A.K.; Denat, F.; Guilard, R.; Beletskaya, I.P. Synthesis of a new family of bi- and polycyclic compounds via Pd-catalyzed amination of 1,7-di(3-bromobenzyl)cyclen. *Tetrahedron Lett.* **2008**, *49*, 3950–3954.

13. Kobelev, S.M.; Averin, A.D.; Buryak, A.K.; Denat, F.; Guilard, R.; Beletskaya, I.P. Synthesis of macrobi- and macrotricyclic compounds comprising pyrimidyl substituted cyclen and cyclam. *Heterocycles* **2011**, *82*, 1447–1476.

14. Kobelev, S.M.; Averin, A.D.; Buryak, A.K.; Denat, F.; Guilard, R.; Beletskaya, I.P. Pd-catalyzed amination in the synthesis of cyclen-based macrotricycles. *Tetrahedron Lett.* **2012**, *53*, 210–213.

15. Yakushev, A.A.; Anokhin, M.V.; Averin, A.D.; Maloshitskaya, O.A.; Beletskaya, I.P. Palladium-catalyzed amination in the synthesis of aza- and diazacrown trismacroyclic compounds. *Russ. Chem. Bull.* **2012**, *61*, 1474–1482.

16. Yakushev, A.A.; Anokhin, M.V.; Averin, A.D.; Maloshitskaya, O.A.; Savelyev, E.N.; Butov, G.M.; Orlinson, B.S.; Novakov, I.A.; Beletskaya, I.P. Synthesis of macropolycycles comprising diazacrown and adamantane moieties via Pd-catalyzed amination reaction. *Macrocycles* **2013**, *6*, 40–46.

17. Kataky, R.; Matthes, K.E.; Nicholson, P.E.; Parker, D.; Buschman, H.-J. Synthesis and binding properties of amide-functionalised polyaza macrocycles. *J. Chem. Soc. Perkin Trans.* **1990**, *1990*, 1425–1432.

18. Matthes, K.E.; Parker, D.; Buschmann, H.J.; Ferguson, G. Structure and complexation behaviour of calcium-selective [12]-N\textsubscript{2}O\textsubscript{2} macrocycles incorporating amide substituents. *Tetrhedron Lett.* **1987**, *28*, 5573–5576.

19. Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J.J.; Ibers, J.A. Chemistry of dibenzylideneacetone-palladium(0) complexes I. Novel tris(dibenzylideneacetone)-dipalladium(solvent) complexes and their reactions with quinines. *J. Organomet. Chem.* **1974**, *65*, 253–266.

*Sample Availability*: Not available.

© 2014 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/3.0/).