Palladium-Catalyzed Amination of 3,5-Dihalopyridines – a Convenient Route to New Polyazamacrocycles

by **Alexei D. Averin***[a]), **Olesya A. Ulanovskaya**[a]), **Ilya A. Fedotenko**[a]), **Anatolii A. Borisenko**[a]), **Marina V. Serebryakova**[b]), and **Irina P. Beletskaya***[a])

[a]) Department of Chemistry, Lomonosov Moscow State University, Leninskie Gory, Moscow, 119992, Russia (phone/fax: 7(095)9393618; e-mail: beletska@org.chem.msu.su)

[b]) V. N. Orekhovich Institute of Biomedical Chemistry, Pogodinskaya st., 10, Moscow, 119992, Russia (phone: 7(095)2461641; e-mail: mserebr@mail.ru)

Dedicated to Professor *Rolf Huisgen* on the occasion of his 85th birthday

Pd-Catalyzed amination of 3,5-dibromo- and 3,5-dichloropyridine (**1a** and **1b**, resp.) with linear polyamines **2** leads to the formation of a new family of pyridine-containing macrocycles **3** with an '*exo*'-oriented pyridine N-atom (*Schemes 1* and *2*). The dependence of the macrocycle yield on the nature of the halogen atom, the length of the polyamine chain and C/N atom ratio, and the composition of the catalytic system is studied. The synthesis of mono- and bis(5-halopyridin-3-yl)-substituted polyamines **4**, **5**, **8**, **9**, and of 3,5-bis(polyamino)-substituted pyridines **6** is described (*Schemes 3* and *4*), and the use of these compounds as intermediates on the way to the macrocycles **7**, **16**, and **18** with larger cavity ('cyclodimers' and 'cyclotrimers') is demonstrated (*Schemes 5–10*).

Introduction. – In the last 15 years, substantial interest was evoked by the synthesis and coordination properties of different polyazamacrocycles which possess a pyridine moiety in the macrocyclic ring [1–13]. This pyridine fragment strongly influences the thermodynamic properties and the complexation kinetics by increasing the conformational rigidity of the ligand and by changing its basicity. Thus, the basicity was shown to decrease in such macrocycles as compared to corresponding saturated molecules like tetraazacycloalkanes. The metal complexes of the pyridine-containing macrocycles are usually less stable than those of tetraazacycloalkanes while the first demonstrate higher formation rates. In all such macrocycles incorporating pyridine, N-atoms are linked to the aromatic ring *via* one CH_2 or CH group. To date, only one macrocycle containing N-atoms directly linked to the pyridine ring has been reported [14]. This compound was obtained by the reduction of the corresponding diamide formed in the reaction of pyridine-2,6-diamine with diacyl dichloride under high-dilution conditions. Macrocycles of this type containing a 3,5-disubstituted pyridine moiety are yet unknown. In our recent work, we have proposed a simple one-pot approach to polyazamacrocycles with an '*endo*'-position[1]) of the pyridine N-atom derived from 2,6-dibromopyridine by using Pd-mediated amination with linear polyamines [15]. Therefore, it is of importance to elaborate a simple way to their isomers with an '*exo*'-oriented[1]) pyridine N-atom. These compounds may possess different complexing properties due to

[1]) The terms '*endo*'/'*exo*' are used to describe the orientation of an N-atom towards the interior/exterior of the macrocyclic skeleton.

spatially isolated donor sites: the pyridine N-atom and the secondary-amino groups of the polyamine-chain moiety.

Since the beginning of the era of the metal-catalyzed amination, the problem of the introduction of hetaryl halides in this process attracted the attention of researchers. Among such halides 3(5)-halopyridines have been frequently investigated. *Buchwald* in 1996 was the first to obtain pyridin-3-amines *via* a catalytic process by using his famous [$Pd(dba)_2$]/binap system[2]) [16]. This work was followed by the investigations of 3-bromopyridine amination in which ligands other than binap were tried: dppfOMe[2]) [17], $^tBu_3P$ [18], dppf[2]) [19], imidazolinium salts [20]. The 3-chloropyridine proved to be substantially less reactive than 2-chloropyridine [21][22], and excellent selectivity was observed in the case of the competition of I- and Cl-substitution for amino group in chloroiodo-substituted pyridines, as has been shown in recent reports [23–25]. Ni-Catalyzed reactions were efficient for 3-chloropyridine amination [26–29], and the possibility of the synthesis of 3,5-diamino-substituted pyridine was reported by *Fort* [26]. For our purpose, we chose the thoroughly explored and highly efficient [$Pd(dba)_2$]/binap system [30].

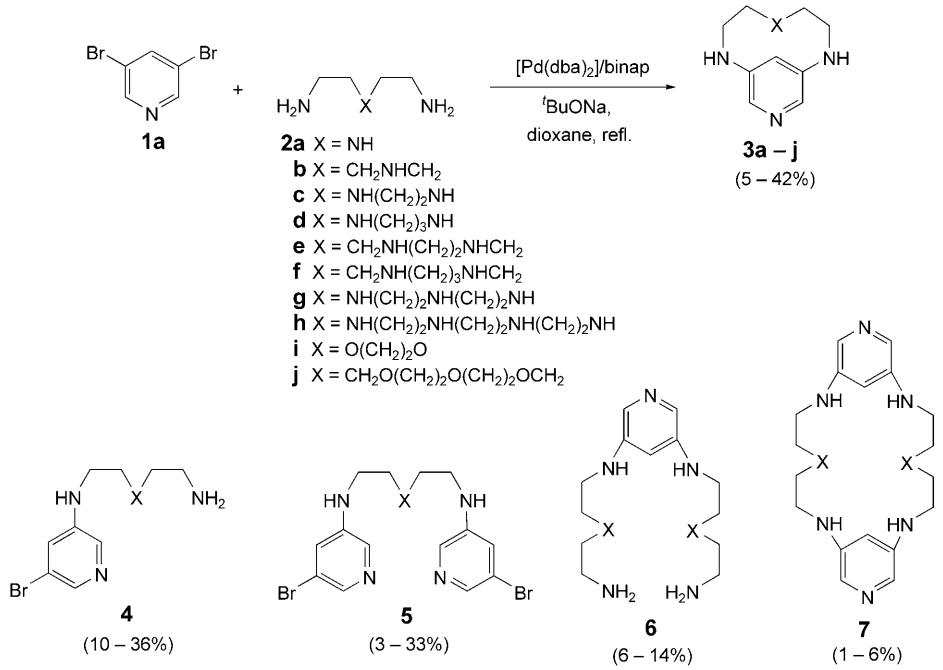
2. Results and Discussion. – 2.1. *Macrocycles Incorporating the 3,5-Disubstituted Pyridine Moiety.* In the beginning of our investigations, we employed 3,5-dibromopyridine (**1a**) in the reactions with a variety of triamines **2a**,**b**, tetramines **2c**–**f**, pentamine **2g**, hexamine **2h**, dioxadiamine **2i**, and trioxadiamine **2j** (*Scheme 1*). Reagents were taken in equimolar ratios, the reactions were run in boiling dioxane, and low concentrations (0.02M) were used to suppress the formation of linear oligomers. Under standard conditions, we took 8 mol-% of the catalyst precursor [$Pd(dba)_2$] and 9 mol-% of the binap ligand (4 and 4.5 mol-%, resp. for the substitution of one Br-atom). ^{t}BuONa, which proved to be efficient in the catalytic amination reactions, was employed as a base. The main data concerning the reaction conditions, product yields, and by-products formation are collected in *Table 1*. The product-mixture composition was analyzed by means of ^{1}H-NMR spectra by integrating nonoverlapping protons of binap and pyridine-ring protons of the reaction products.

All polyamines **2a**–**j** gave corresponding macrocycles **3a**–**j** together with by-products **4-7** but the yields of target compounds **3** were dramatically different (*Scheme 1* and *Table 1*). With polyamines **2b**,**d**–**f** and diamines **2i**,**j**, yields of the macrocycles ranged from 18 to 42% (*Table 1*, *Entries 2*, *5*, *8–12*, *16*, and *17*), whereas with polyamines **2a**,**c**,**g**,**h**, the yields did not exceed 5–6% (*Table 1*, *Entries 1*, *3*, *4*, and *13–15*). This is possibly due to the fact that the latter polyamines comprise only ethanediamine fragments, whereas other polyamines either do not have such fragments at all (like diamines **2i**,**j**) or contain both ethanediamine and propanediamine moieties. The Pd^0 atom of the catalytic complex may form more-stable five-membered chelates with ethanediamine fragments than six-membered chelates with propanediamine moieties, thus being eliminated from the catalytic cycle. It is to be noted that generally, the Pd-complexes with a diphosphine (binap) are more stable than Pd-complexes with

---

[2]) Abbreviations: dba = dibenzylideneacetone = 1,5-diphenylpent-1,4-dien-3-one; binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene = [1,1′-binaphthalene]-2,2′-diylbis[diphenylphosphine]; dppfOMe = 1-(diphenylphosphino)-2-(1-methoxyethyl)ferrocene; dppf = 1,1′-bis(diphenylphospino)ferrocene.

Scheme 1



a diamine, but in the case of a substantial polyamine excess over binap the chelates with the polyamine could play a significant role in decreasing the yields of the target macrocycles. Polyamines **2a**,**c**,**g**,**h** afforded the monoaminated pyridines **4** and **5** in rather high yields, thus establishing that the substitution of the second Br-atom by the amino group proceeds at a lower rate.

Conversion of the starting 3,5-dibromopyridine (**1a**) was found to be quantitative after 4–6 h of reflux, and prolonged heating did not lead to a notable change in the product-mixture composition. The decrease in the catalyst loading from 8 to 6 mol-% demanded longer heating (10 h, *Table 1*, *Entry 11*) to achieve full consumption of **1a** and gave higher yields of linear pyridinyl-sybstituted tetramines **4e** and **5e**. The change in the reagent ratio led to the increase of the yields of noncyclic products. A polyamine excess gave rise to bis(polyamino)-substituted pyridine **6e** as the main product (*Table 1*, *Entry 8*), but the yield of the macrocycle **3e** changed insignificantly. Excess of 3,5-dibromopyridine (**1a**) led to the preferential formation of a bis(pyridinyl)-substituted polyamine (*cf. Sect. 2.2*). In general, the larger the deviation from the stoichiometric ratio of starting compounds, the smaller was the yield of the desired macrocycle **3**, but simultaneously, there was less formation of unidentified linear oligomeric by-products. Thus, the stoichiometric ratio of the starting compounds is a crucial condition to maximize the yield of the macrocycles **3**. In many cases, we also observed the formation in small amounts of cyclodimers **7** among the by-products (*Table 1*, *Entries 6*, *7*, *9*, *10*, *12*, and *17*) (*cf. Sect. 2.3*). In contrast to the amination of 2,6-dibromopyridine [15], the amination of **1a** afforded lower yields of the macrocycles **3**

Table 1. *Synthesis of Macrocycles* **3a**–**j**

Entry	Dihalo-pyridine	Amine	Ratio **1/2**	Conc. [M]	[Pd(dba)$_2$]/L [mol-%]	Time [h]	Yield of **3** [%][a])	Yield of by-products [%][a])
1	**1a**	**2a**	1:1	0.02	8:9[b])	5	**3a** 5(3)	**4a** 27(13) **5a** (3)
2	**1a**	**2b**	1:1	0.02	8:9[b])	5.5	**3b** 42(33)	**5b** (23)
3	**1a**	**2c**	1:1	0.02	8:9[b])	4	**3c** 5(4)	**4c** + **5c** 60 **4c** (24) **5c** (33)
4	**1a**	**2c**	1:1	0.02	8:9[b])	8	**3c** 4(3)	**4c** (36) **5c** (22)
5	**1a**	**2d**	1:1	0.02	8:9[b])	6	**3d** 29(17)	
6	**1a**	**2e**	1:1.4	0.1	8:9[b])	6	**3e** 11	**6e** 19 **7e** 2
7	**1a**	**2e**	1:1	0.05	8:9[b])	5	**3e** 7(2)[c])	**6e** 8 **7e** 1.3
8	**1a**	**2e**	1:4	0.05	8:9[b])	4	**3e** 22(5)[c])	**6e** 77
9	**1a**	**2e**	1:1	0.02	8:9[b])	6	**3e** 36(10)[d])	**6e** 10 **7e** 6
10	**1a**	**2e**	1:1	0.02	8:9[b])	4	**3e** 19(17)	**6e** 7 **7e** 46
11	**1a**	**2e**	1:1	0.02	6:6.5[b])	10	**3e** 30(17)	**4e** + **5e** 56 **4e** (23) **5e** (33) **6e** 14
12	**1a**	**2f**	1:1	0.02	8:9[b])	5	**3f** 18(15)	**6f** 10 **7f** 3
13	**1a**	**2g**	1:1	0.02	8:9[b])	4.5	**3g** –(5)	**4g** (10) **5g** (27)
14	**1a**	**2h**	1:1	0.02	8:9[b])	4.5	**3h** –(4)	**4h** + **5h** 32 **4h** (14)
15	**1a**	**2h**	1:1	0.014	8:9[b])	8	**3h** 6	**4h** + **5h** 32 **4h** (25)
16	**1a**	**2i**	1:1	0.02	8:9[b])	6	**3i** 22(20)	**6i** 6
17	**1a**	**2j**	1:1	0.02	8:9[b])	5.5	**3j** –(27)	**5j** + **7j** 32
18	**1b**	**2e**	1:1	0.02	8:9[b])	8	**3e** 9(8)	**8e** + **9e** 85 **8e** (26) **9e** (40)
19	**1b**	**2e**	1:1	0.02	8:9[b])	69	**3e** 17	**8e** + **9e** 51 **6e** 9 **7e** 2 **8e** (36) **9e** (15)
20	**1b**	**2e**	1:1	0.02	8:20[e])	48	**3e** 13(11)	**8e** 15 **6e** 6 **7e** 7
21	**1b**	**2e**	1:1	0.02	8:20[f])	48	**3e** 0	**8e** + **9e** 31 **9e** (6)
22	**1b**	**2e**	1:1	0.02	8:20[g])	48	**3e** 3(2)	**8e** + **9e** 35 **9e** (28)

[a]) Yields by ^{1}H-NMR (yields after chromatography in parentheses). [b]) L = binap. [c]) Yield after the treatment of the reaction mixture with H_2O/CH_2Cl_2. [d]) Yield after the treatment of the reaction mixture with H_2O/CH_2Cl_2 and chromatography. [e]) L = di(*tert*-butyl)([1,1′-biphenyl]-2-yl)phosphine. [f]) L = dicyclohexyl([1,1′-biphenyl]-2-yl)phosphine. [g]) L = 2′-(dicyclohexylphosphino)-*N*,*N*-dimethyl-1,1′-biphenyl]-2-amine.

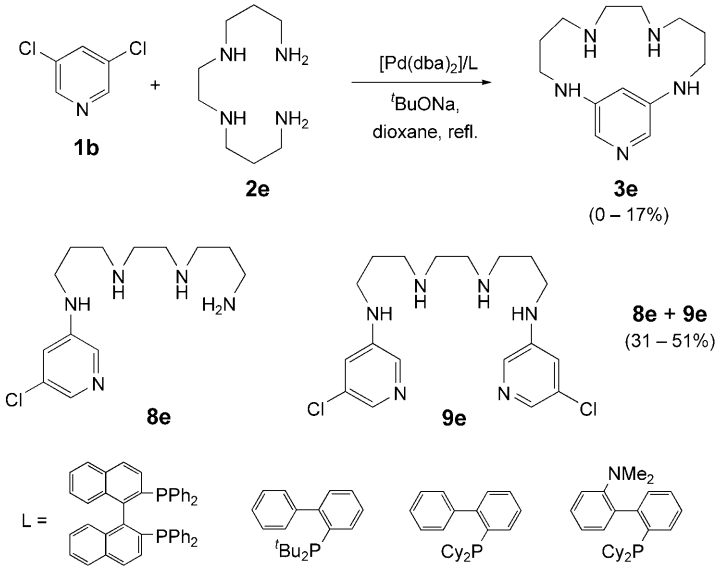
when the reaction mixtures were more concentrated. Moreover, as compounds **3** are more soluble in H_2O, the standard treatment of evaporated reaction mixture with CH_2Cl_2/H_2O prior to column chromatography reduced the isolated yields. The isolated macrocycles **3** were analyzed by ^{1}H- and ^{13}C-NMR, IR, UV, and MALDI-TOF mass spectroscopy.

The ^{1}H-NMR spectra of **3** exhibit the signals of H–C(2) and H–C(6) of the pyridine moiety at δ 7.25–7.35 (pyridine-ring numbering). The signal of H–C(4) of the pyridine moiety strongly depends on the size of the macrocycle. For the molecules with the longest linking polyamine-chain moiety like **3e**–**h**,**j**, the signal of H–C(4) is shifted upfield to δ 6.40–6.58, whereas for the molecules with a shorter linking chain moiety like **3a**,**b**,**h**, this signal is shifted downfield to δ 7.12-7.82. This fact may be due to through-space interactions between this H–C(4) and the N- or O-atoms of the polyamine-chain moiety which are rather close to the pyridine ring in such macrocycles. This explanation is supported by upfield shifts of the H–C(4) signal in the larger cyclodimeric macrocycles *J*(δ 6.14) and in open-chain bis(polyamino)-substituted derivatives **6** (δ 6.06). The protons CH_2N-Py of **3** are shifted downfield to δ 3.30–3.35 as compared to the corresponding protons of the cyclic and acyclic derivatives **4**–**7**.

We also investigated the possibility to use 3,5-dichloropyridine (**1b**) for the synthesis of macrocycles **3**. The amination reaction with model tetramine **2e** was found

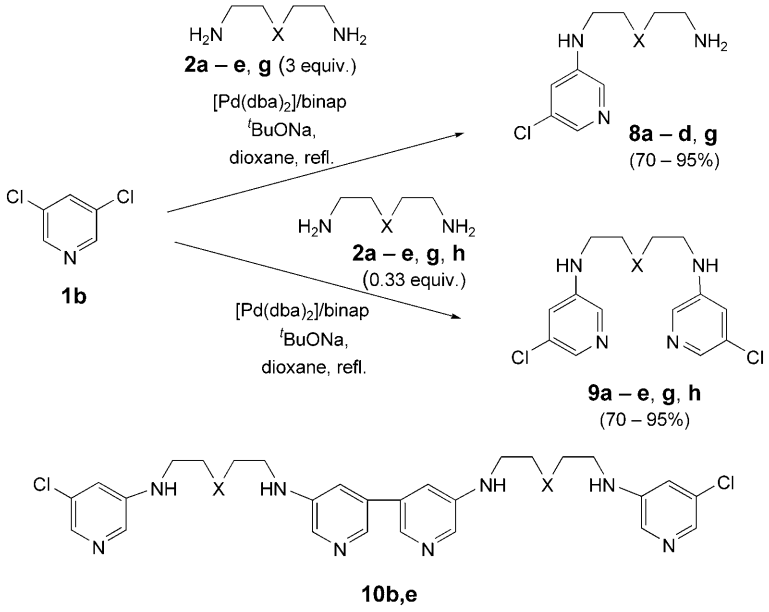
to proceed substantially slower than with dibromopyridine **1a**. After 8 h of reflux, the substitution of the first Cl-atom was complete, whereas the second amination step had proceeded insignificantly (*Table 1*, *Entry 18*). The reaction mixture contained mainly a mixture of mono- and diarylated polyamines **8e** and **9e** (*Scheme 2*). Only a long reflux period (69 h) provided 17% yield of the target macrocycle **3e** (*Table 1*, *Entry 19*), but the main products were still acyclic **8e** and **9e**. We tried some donor phosphine ligands such as di(*tert*-butyl)([1,1′-biphenyl]-2-yl)phosphine, dicyclohexyl([1,1′-biphenyl]-2-yl)phosphine, and 2′-(dicyclohexylphosphino)-*N*,*N*-dimethyl[1,1′-biphenyl]-2-amine which proved to be efficient in the amination of aryl chlorides [31]. In our case, the *tert*-butyl-substituted phosphine ligand was of the same efficiency as binap (*Table 1*, *Entry 20*), and the two other phosphine ligands were ineffective (*Entries 21* and *23*). In all cases, the main products were again **8e** and **9e**. It is of interest that these donor ligands were totally inefficient in the amination of 2,6-dihalopyridines [15].

Scheme 2



2.2. *Synthesis of Linear Pyridinyl-Substituted Polyamines.* As 3,5-dichloropyridine (**1b**) proved to be enough inert towards diamination, it was a convenient starting material for an easy synthesis of a series of mono- and dipyridinyl-substituted polyamines **8** and **9** by changing slightly the macrocyclization reaction conditions (*Scheme 3*). Thus, the same catalyst system $[Pd(dba)_2]$/binap was used, but the concentrations of the reaction mixtures were increased (0.1 – 0.2M), and the reactions were run for 5 – 8 h. A three-fold excess of polyamine was employed for the synthesis of **8**, and diarylation of the polyamine to **9** occurred with 3 equiv. of dichloropyridine **1b**. Data are collected in *Table 2*. Compounds **8** and **9** were obtained in 70 – 95% yields, in some cases by-products **10** were formed as a result of homocoupling of chloropyridines. This type of reaction was reported by *Fort* to occur often during amination reactions of chloropyridines [11]. It is to be noted that macrocycles **3** were never found among the

Scheme 3[a])



[a]) For **a**–**e**,**g**,**h**, see *Scheme 1*

Table 2. *Synthesis of Mono- and Dipyridinyl-Substituted Polyamines* **4**, **5**, **8**, *and* **9**

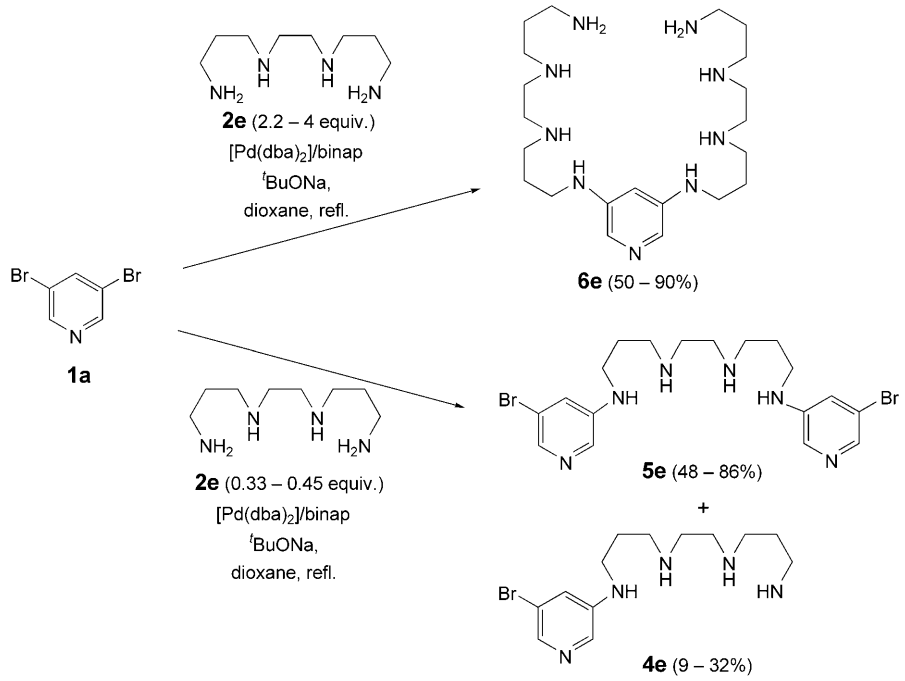
Entry	Dihalo-pyridine	Amine	Ratio **1**/**2**	Conc. [M]	[Pd(dba)$_2$]/ binap [mol-%]	Time [h]	Yield of **8** or **4** [%][a])	Yield of **9** or **5** [%][a])	Yield of other compounds [%]
1	**1b**	**2a**	3 : 1	0.1	8 : 9	7	**8a** 10	**9a** 85	Conversion 95%
2	**1b**	**2a**	1 : 3	0.1	8 : 9	7	**8a** 70	**9a** 23	
3	**1b**	**2b**	3 : 1	0.1	8 : 9	8.5		**9b** 80	**10b** 20
4	**1b**	**2b**	1 : 3	0.1	8 : 9	8.5	**8b** 70		**6b** 30
5	**1b**	**2c**	3 : 1	0.1	8 : 9	6	**8c** 30	**9c** 70	
6	**1b**	**2c**	1 : 3	0.1	8 : 9	6	**8c** 95		
7	**1b**	**2d**	3 : 1	0.1	8 : 9	5.5		**9d** 92(36)	
8	**1b**	**2d**	1 : 3	0.1	8 : 9	5	**8d** 77		**6d** 23
9	**1b**	**2e**	3 : 1	0.1	8 : 9	7		**9e** 80(45)	**10e** 20(18)
10	**1b**	**2e**	1 : 4	0.1	8 : 9	7	**8e** (82)	**9e** (13)	
11	**1a**	**2e**	3 : 1	0.2	4 : 4.5	6	**4e** 32(30)	**5e** 48(39)	Conversion 80%
12	**1a**	**2e**	2.5 : 1	0.1	8 : 9	8	**4e** 10	**5e** 90	
13	**1a**	**2e**	2.2 : 1	0.2	6 : 6.5	11.5	**4e** 9	**5e** 86	Conversion 95%
14	**1a**	**2e**	1 : 2.2	0.2	6 : 6.5	9.5			Conversion 95% **3e** 9, **6e** 50
15	**1a**	**2e**	1 : 4	0.1	8 : 9	8			**6e** 90
16	**1b**	**2g**	3 : 1	0.1	8 : 9	5.5		**9g** 80(55)	
17	**1b**	**2g**	1 : 3	0.1	8 : 9	5	**8g** 86		**6g** 14
18	**1b**	**2h**	3 : 1	0.1	8 : 9	5.5		**9h** 90(35)	
19	**1b**	**2i**	2.2 : 1	0.1	8 : 9	4.5		**5i** 50	Conversion 95%
20	**1b**	**2j**	2.2 : 1	0.1	8 : 9	6		**5j** 81	**3j** 5, **6j** 9

[a]) Yields by ^{1}H-NMR (yields after chromatography in parentheses).

by-products. Except for tetramine **2c** (*Table 2*, *Entries 5* and *6*), disubstituted polyamines **9** were formed in better yields than monosubstituted polyamines **8**.

We succeeded also to synthesize dipyridinyl-substituted polyamines **5** using dibromopyridine **1a** and tetramine **2e** under conditions similar to those described above for the synthesis of **9** (*Scheme 4*, *Table 2*, *Entries 11–13*). The ratio **1a**/**2e** could even be reduced to 2.2:1 (*Table 2*, *Entry 13*). The reaction of **1a** with an excess of polyamine **2e** (**1a**/**2e** 1:2.2 to 1:4) provided the 3,5-bis(polyamino)-substituted pyridine **6e** (*Scheme 4*, *Table 2*, *Entries 14* and *15*). The greater the excess of polyamine **2e**, the higher was the yield of **6e** (*Table 2*, *Entry 15*). The decrease in the catalyst loading from 8 to 4 mol-% (*Table 2*, *Entry 11*) led to lower yield of **5e** due to a lower degree of conversion (80% instead of 100%). The minimal amount of the catalytic system was found to be 6 mol-% with the proviso that prolonged heating was applied (*Table 2*, *Entries 13* and *14*).

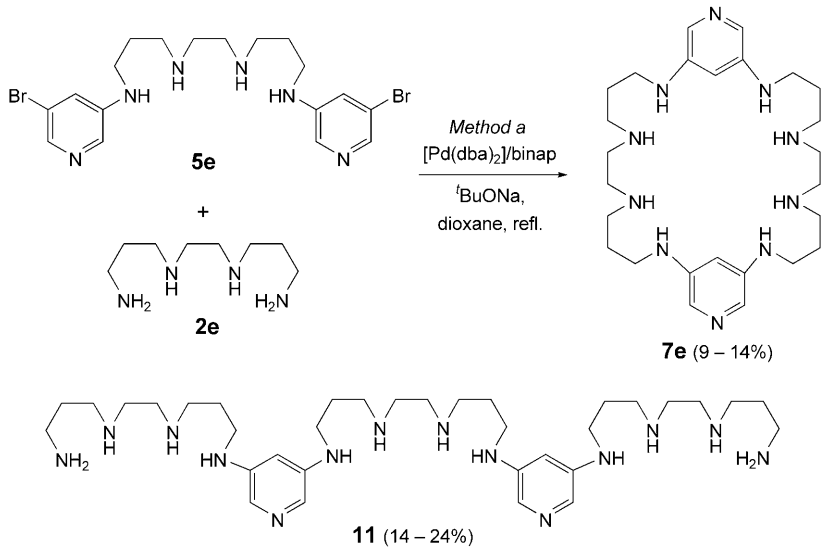
Scheme 4



2.3. *Synthesis of Cyclic Dimers.* Cyclodimers **7** were mentioned in *Sect. 2.1* as by-products formed in the course of the diamination of 3,5-dibromopyridine (**1a**). These compounds which posses a large cavity are of special interest as ligands since they are able to furnish bimetallic complexes. Therefore, we developed two alternative synthetic routes to such molecules starting from dipyridinyl-substituted polyamines **5** and **9** or bis(polyamino)-substituted pyridines **6**. *Method a* included the already described synthesis of dipyridinyl substituted polyamine **5e** (see *Sect. 2.2*) followed by its reaction with a second equiv. of tetramine **2e**. As the synthesis of **5e** required only 10% excess of

3,5-dibromopyridine (**1a**), and its yield was high (86%), **5e** was used for the cyclization reaction *in situ* without purification (*Scheme 5*). The reaction was run with [Pd(dba)$_2$]/binap 8:9 in dilute solution ($c = 0.02$M) and provided cyclodimer **7e** in 14% yield after 6 h of reflux (*Table 3*, *Entry 1*). Longer heating and increased catalyst loading did not improve the yield of **7e** (*Table 3*, *Entries 2* and *3*). The main by-products in this reaction were oligomer **11** and macrocycle **3e** which was formed by the reaction of an excess of **5e** with **2e**.

Scheme 5



Method b included the already described synthesis of bis(polyamino)-substituted pyridine **6e** (see *Sect. 2.2*) followed by the reaction with the second equiv. of 3,5-dibromopyridine (**1a**) (*Scheme 6*). Thus, cyclodimer **7e** was obtained in 9–12% yield (*Table 3*, *Entries 4* and *5*). As the formation of **6e** demanded an excess of tetramine **2e**, which was not consumed completely, macrocycle **3e** proved to be the main by-product (yields up to 24%). Oligomer **12** was formed in substantial amounts due to the easy diarylation reaction which led to this product even under the conditions of high dilution. Use of more-concentrated solutions decreased the yield of cyclodimer **7e** and increased the yield of oligomer **12** (*Table 3*, *Entries 6* and *7*).

Also 3,5-dichloropyridine (**1b**) could be used for the synthesis of cyclodimers according to *Method a*, *via* intermediate dipyridinyl-substituted polyamine **9e** (instead of **5e**). In this case, [Pd(dba)$_2$] with 2-di(*tert*-butyl)([1,1′-biphenyl]-2-yl)phosphine was employed as the catalytic system. This reaction demanded longer reflux and provided somewhat lower yields of **7e** (*Table 3*, *Entries 8–10*).

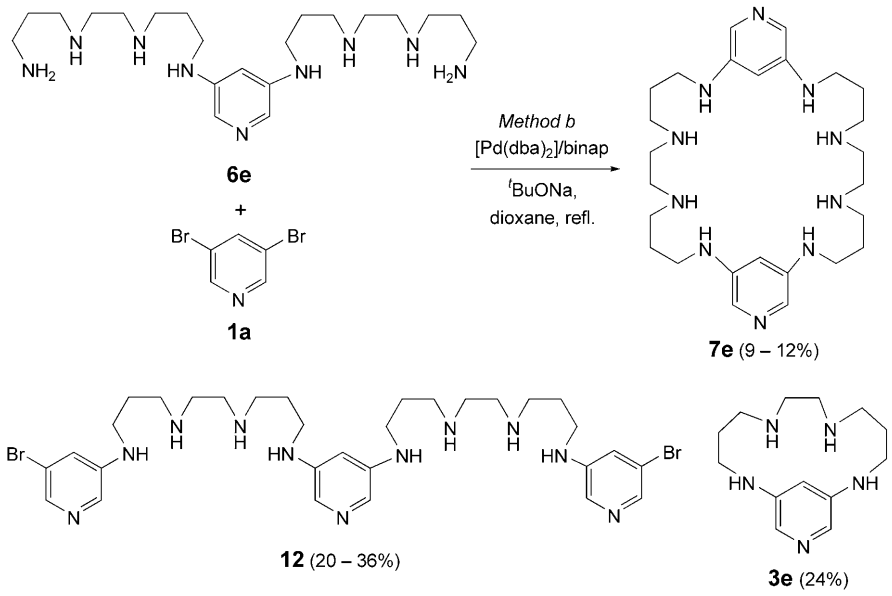
Method a was also used for the synthesis of cyclodimer **7b** (*Scheme 7*). The target macrocycle was isolated in 12% yield (*Table 3*, *Entry 11*), together with by-product **13** which is an intermediate on the way to **7b**. The cyclization reaction, in this case, did not

Table 3. *Synthesis of Cyclodimers* **7** *and* **16** *and of Cyclotrimer* **18**

Entry	Amine	Halo-pyridine	Conc. [M]	[Pd(dba)$_2$]/ L [mol-%][a])	Time [h]	Yield of cyclodimer [%][b])	Yields of other products [%][b])
1	**2e**	**5e**	0.02	8 : 9[c])	6	**7e** 14	**11** 14
2	**2e**	**5e**	0.02	11.5 : 12[c])	7.5	**7e** 14[e])	**3e** 14, **11** 34
3	**2e**	**5e**	0.02	16 : 18[c])	10.5	**7e** 9[f])	**3e** 24, **12** 24
4	**6e**	**1a**	0.02	10.5 : 11.5[c])	9	**7e** 9[e])	**3e** 16, **12** 20
5	**6e**	**1a**	0.02	16 : 18[c])	10.5	**7e** 12[f])	**3e** 24, **12** 36
6	**6e**	**1a**	0.1	16 : 18[c])	7	**7e** 0	**12** (25)
7	**2e**	**5e**	0.1	12 : 13[c])	7	**7e** 5	**3e** 10(6), **12e** 36(13)
8	**2e**	**9e**	0.04	8 : 16[d])	6	**7e** 6	**3e** 5
9	**2e**	**9e**	0.02	8 : 16[d])	10	**7e** 10	**3e** 9(8), **11** 10
10	**2e**	**9e**	0.03	8 : 20[d])	20	**7e** 7	**11** 3
11	**2b**	**5b**	0.05	16 : 18[c])	13.5	**7b** (12)	Conversion 93% **13** (9)
12	**2e**	**5b**	0.05	16 : 18[c])	13.5	**14** 0	**15** 25(15)
13	**6b**	**1c**	0.05	16 : 18[c])	13.5	**16** 24(16)	**17** 15
14	**2j**	**5j**	0.02	10 : 11	6	**7j** 15	
15	**2i**	**5i**	0.01	16 : 18	6	**7i** 0	
16	**6e**	**5e**	0.02	8 : 9	11	**18** 0	**3e** (23), **7e** (13)
17	**2e**	**12**	0.02	10 : 11	5	**18** 0	**3e** (43)
18	**11**	**1a**	0.02	10 : 11	5	**18** + **7e** (20)	**3e** (21)

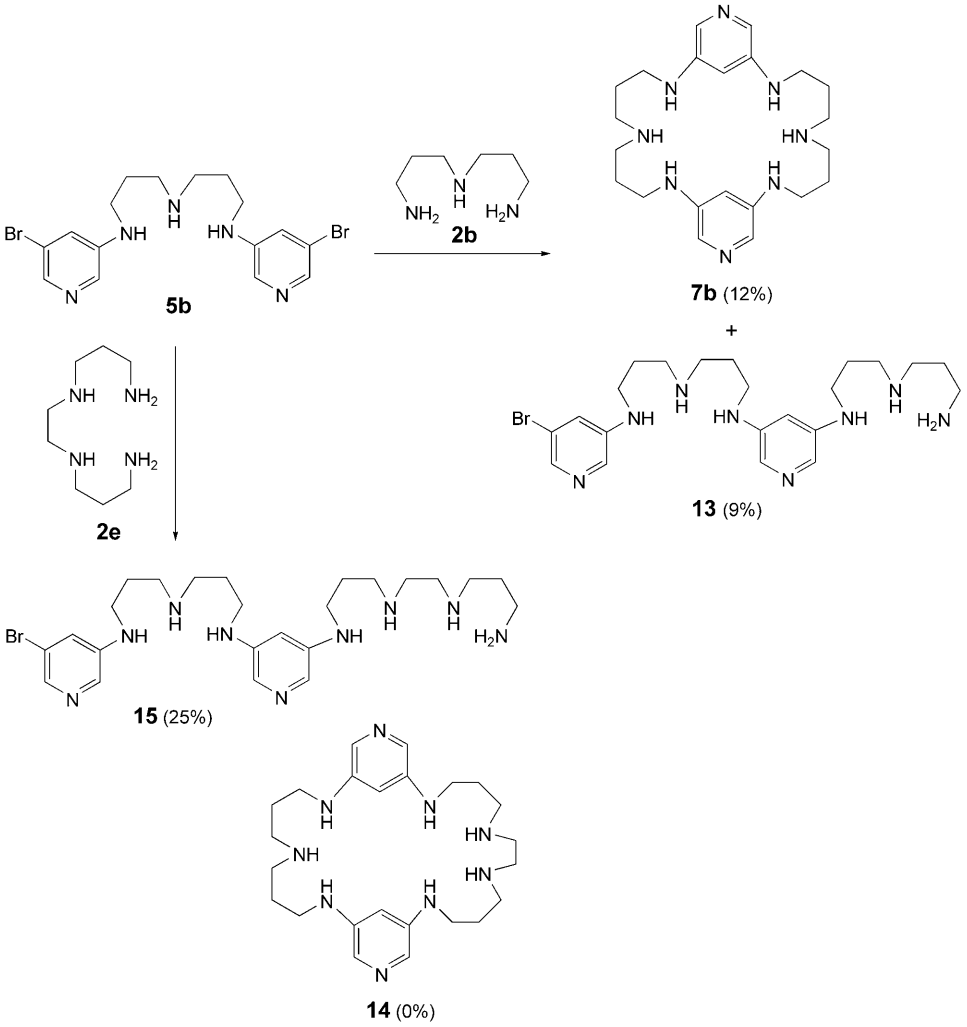
[a]) Calculated for 1 mol of cyclodimer. [b]) Yield by ^{1}H-NMR (yield after chromatography in parentheses). [c]) L = binap. [d]) L = di(*tert*-butyl)([1,1′-biphenyl]-2-yl)phosphine. [e]) Chromatography of the product of the two steps provided 11% of **7e**. [f]) Chromatography of the product of the two steps provided 10% of **7e**.

Scheme 6



run to completion, as 7% of starting dipyridinyl-substituted polyamine **5b** was recovered. An attempt to obtain 'unsymmetric' cyclodimer **14**, which would contain two different polyamine-chain moieties, *via* the reaction of **5b** with tetramine **2e** in more-concentrated solution ($c = 0.2$M), failed, and only linear compound **15** was formed in 15% yield, **5b** being recovered in 9% yield (*Table 3*, *Entry 12*).

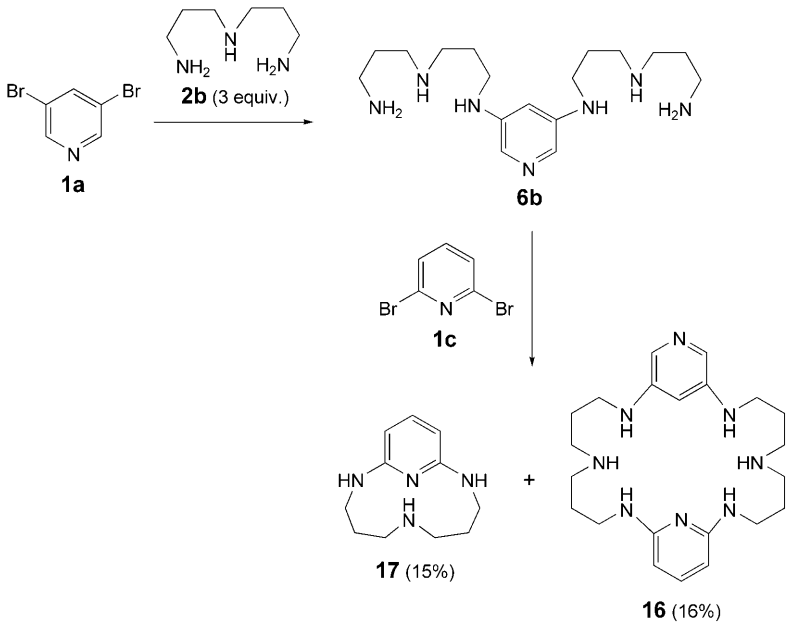
Scheme 7



The synthesis of an 'unsymmetric' cyclodimer **16**, comprising 3,5- and 2,6-disubstituted pyridines, was successful. According to *Method b*, **6b** was obtained *in situ* and treated with 2,6-dibromopyridine (**1c**) providing the target compound **1b** in 16% yield (*Scheme 8*; *Table 3*, *Entry 13*). The main by-product was macrocycle **17**

isolated in 15% yield, which was formed from the excess of triamine **2b** and 2,6-dibromopyridine (**1c**).

Scheme 8

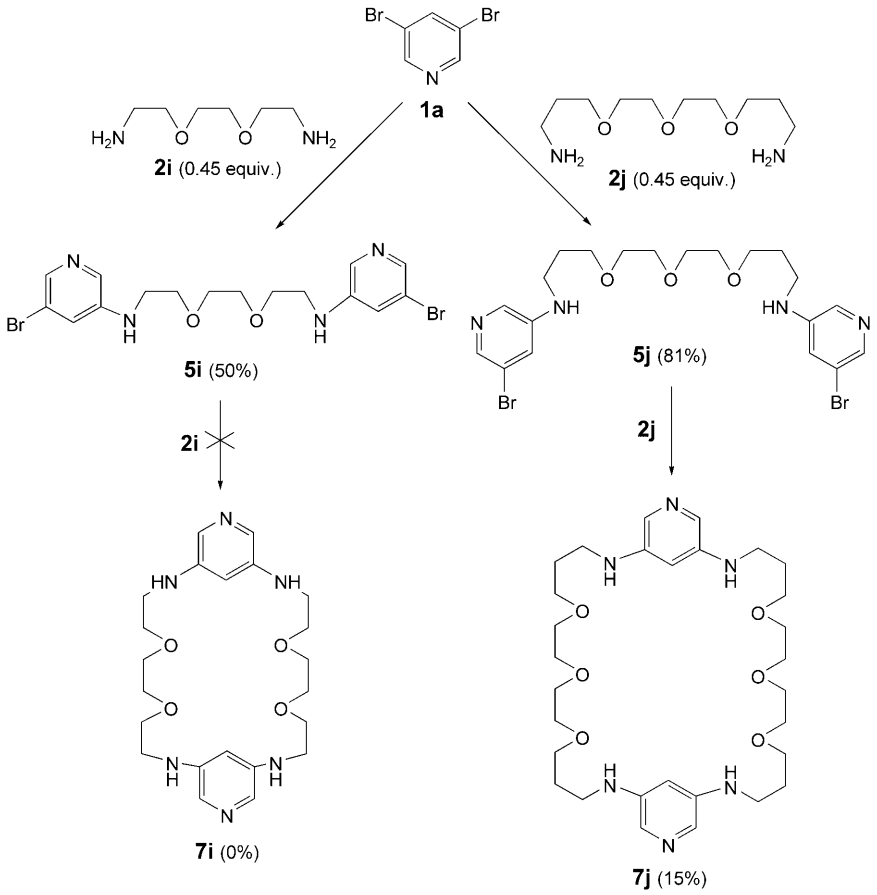


We also submitted dioxadiamine **2i** and trioxadiamine **2j** to the macrocyclization conditions. *Method a* gave dipyridinyl-substituted dioxadiamine **5i** in 50% yield, while **5j** was obtained in 81% yield. Further transformation of the latter with the second molecule of diamine **2j** provided the corresponding cyclodimer **7j** in 15% yield, while the corresponding reaction to give **7i** was unsuccessful (*Table 3*, *Entries 14* and *15*; *Scheme 9*).

At last, cyclotrimer **18** was synthesized according to three alternative schemes. *Method c* involved the reaction of **5e** with **6e**, *Method d* the reaction of oligomer **11** with 3,5-dibromopyridine (**1a**), and *Method e* the reaction of another oligomer, **12**, with tetramine **2e** (*Scheme 10*). Compounds **11** and **12** were obtained *in situ* and thus were mixed with an excess of tetramine **2e** or 3,5-dibromopyridine (**1a**), respectively. *Methods c* and *e* were inefficient, the cyclotrimer **18** being detected in the reaction mixtures in only trace amounts, whereas *Method d* provided 20% yield of a mixture of desired cyclotrimer **18** and cyclodimer **7e** (*Table 3*, *Entries 16–18*). Unfortunately, column chromatography did not allow to cleanly separate these two cyclic oligomers. All the methods yielded in substantial amounts also macrocycles **3e** and **7e**, which were isolated by chromatography (*Table 3*, *Entries 16–18*).

3. Conclusions. – We developed a simple and convenient approach to polyaza- and polyoxapolyazamacrocycles containing one or more 3,5-disubstituted pyridine moieties *via* a palladium-catalyzed amination reaction and demonstrated scope and limitation of

Scheme 9



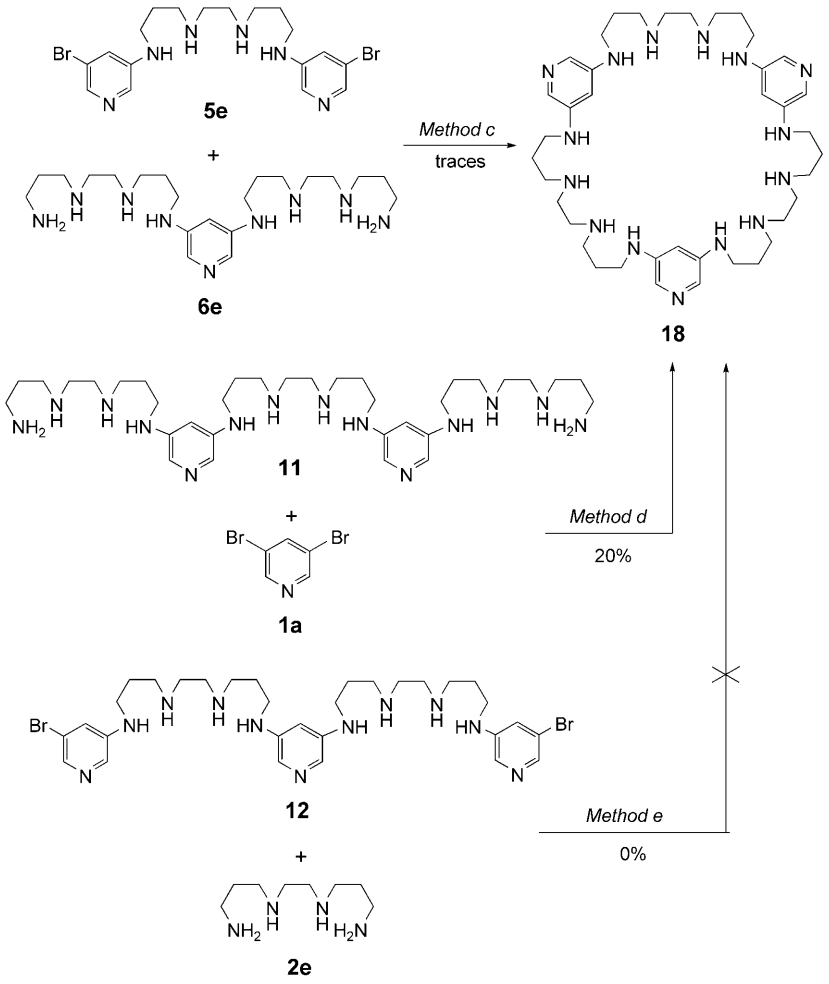
the application of the involved 3,5-dihalopyridines and polyamines. The synthesis of mono- and dipyridinyl-substituted polyamines and 3,5-bis(polyamino)-substituted pyridines was also worked out. These compounds were employed in the synthesis of cyclodimers possessing large cavities of the macrocyclic ring. Macrocycles of these types are promising ligands for metal-ion coordination.

This work was supported by *RFBR* grants N 02-03-33331, 03-03-32627, 03-03-22001, and *PICS* grant N 2105.

Experimental Part

General. All reactions were run under Ar in abs. dioxane. [Pd(dba)$_2$] was synthesized according to [31]. The binap, ^{t}BuONa, starting dihalopyridines **1** and polyamines **2a**–**f**,**i**,**j** were purchased from *Aldrich* and *Acros* and used without further purification. Pentamine **2h** and hexamine **2g** of technical quality were purified by successive crystallization of their monohydrates from toluene. Column chromatography (CC): silica gel (40–60 mcm) from *Merck*, its amount being estimated from the standard proportion 8–10 ml/1 mmol of the reaction mixture. UV/VIS spectra: *Hewlett-Packard HP-8256* spectrometer; λ_{max} (ε) in nm. IR Spectra: *Ikar* devices: in

Scheme 10



cm^{-1}. NMR Spectra: *Varian VXR-400* and *Bruker DPX-300* spectrometers, δ in ppm, J in Hz; not all NH protons were assigned for some compounds. MALDI-TOF-MS *Bruker Daltonics-Proflex-III* spectrometer; in *m/z* (rel. %).

General Procedure for **3a**–**j**. A mixture of 3,5-dibromopyridine (**1a**; 0.5 mmol, 119 mg), [Pd(dba)$_2$] (8 mol-%, 23 mg), binap (9 mol-%, 27 mg), abs. dioxane (25 ml), polyamine **2** (0.5 mmol), and ^{t}BuONa (1.5 mmol, 150 mg) was refluxed for 4–6 h. After cooling to r.t., a drop of H_2O was added, the org. soln. filtered off and evaporated, and the residue subjected to CC (silica gel, CH_2Cl_2, CH_2Cl_2/MeOH 50:1 → 3:1, CH_2Cl_2/MeOH/aq. NH_3 soln. 100:20:1 → 10:3:1): **3** and by-products **4** and **5** (for **6** and **7**, see below).

2,5,8,11-Tetraazabicyclo[7.3.1]trideca-1(13),9,11-triene (**3a**). From **1a** (0.5 mmol, 119 mg), *N*-(2-aminoethyl)ethane-1,2-diamine (**2a**; 0.5 mmol, 52 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5 h reflux. **3a** (3 mg, 3%), **4a** (17 mg, 13%), and **5a** (6 mg, 3%).

Data of **3a**: ^{1}H-NMR ($CDCl_3$): 2.92 (*t*, *J* = 6.7, 4 H); 3.41 (*t*, *J* = 6.7, 4 H); 4.50 (br. *s*, 2 H); 7.12 (*t*, *J* = 2.3, 1 H); 8.05 (*d*, *J* = 2.3, 2 H). MALDI-TOF-MS: 179.0 ($[M+H]^+$).

Data of N-*(2-Aminoethyl)*-N′-*(5-bromopyridin-3-yl)ethane-1,2-diamine* (**4a**): ^{1}H-NMR ($CDCl_3$): 1.58 (br. *s*, 3 H); 2.67 (*dd*, *J* = 6.3, 5.1, 2 H); 2.81 (*m*, 2 H); 2.91 (*m*, 2 H); 3.15 (*q*, *J* = 5.1, 2 H); 4.51 (*s*, 1 H); 7.00 (*t*, *J* = 2.2, 1 H); 7.92 (*d*, *J* = 2.4, 1 H); 7.96 (*d*, *J* = 2.0, 1 H). ^{13}C-NMR ($CDCl_3$): 41.6 (1 C); 42.8 (1 C); 47.9 (1 C); 51.9 (1 C); 120.5 (1 C); 121.1 (1 C); 134.5 (1 C); 138.9 (1 C); 145.4 (1 C). MALDI-TOF-MS: 259.0 (M^+).

Data of N-*(5-Bromopyridin-3-yl)*-N′-*{2-[(5-bromopyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**5a**): ^{1}H-NMR ($CDCl_3$): 2.99 (*t*, *J* = 5.6, 4 H); 3.28 (br. *s*, 4 H); 4.72 (br. *s*, 2 H); 7.01 (*t*, *J* = 2.1, 2 H); 7.94 (*d*, *J* = 2.1, 2 H); 7.95 (*d*, *J* = 2.1, 2 H).

2,6,10,13-Tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (**3b**) From dibromopyridine **1a** (0.5 mmol, 119 mg), *N*-(3-aminopropyl)propane-1,3-diamine (**2b**; 0.5 mmol, 66 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5 h reflux: **3b** (34 mg, 33%). UV/VIS: 316 (1500). ^{1}H-NMR ($CDCl_3$): 1.58 (*q*, *J* = 5.2, 4 H); 2.60 (br. *s*, 4 H); 3.36 (br. *s*, 4 H); 4.34 (br. *s*, 2 H); 7.34 (br. *s*, 2 H); 7.82 (br. *s*, 1 H). ^{13}C-NMR ($CDCl_3$): 30.2 (2 C); 39.5 (2 C); 45.9 (2 C); 102.7 (1 C); 123.9 (2 C); 145.8 (2 C). MALDI-TOF-MS: 206.0 (M^+).

N,N′-*bis{3-[(3-aminopropyl)amino]propyl}pyridine-3,5-diamine* (**6b**). Reaction of **1a** with a 3-fold excess of **2b** provided **6b** in 90% yield. ^{1}H-NMR ($CDCl_3$): 1.58 (*q*, *J* = 5.7, 4 H); 1.76 (*q*, *J* = 6.2, 4 H); 2.60 (*t*, *J* = 5.3, 4 H); 2.71 (*t*, *J* = 6.0, 4 H); 2.72 (*t*, *J* = 6.0, 4 H); 3.20 (*t*, *J* = 6.2, 4 H); 6.08 (*t*, *J* = 2.3, 1 H); 7.42 (*d*, *J* = 2.3, 2 H). ^{13}C-NMR ($CDCl_3$): 28.4 (2 C); 32.9 (2 C); 39.6 (2 C); 41.4 (2 C); 47.1 (2 C); 47.5 (2 C); 100.5 (1 C); 124.3 (2 C); 144.9 (2 C). MALDI-TOF-MS: 338.9 ($[M+H]^+$).

2,5,8,11,14-Pentaazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**3c**). From **1a** (0.5 mmol, 119 mg), *N,N′*-bis(2-aminoethyl)ethane-1,2-diamine (**2c**; 0.5 mmol, 73 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 8 h reflux: **3c** (3 mg, 3%), **4c** (55 mg, 36%), and **5c** (25 mg, 22%).

Data of **3c**: ^{1}H-NMR ($CDCl_3$): 2.02 (br. *s*, 2 H); 2.78 (*s*, 4 H); 2.83 (*t*, *J* = 5.5, 4 H); 3.31 (*t*, *J* = 5.5, 4 H); 4.51 (br. *s*, 2 H); 6.88 (*t*, *J* = 2.2, 1 H); 7.35 (*d*, *J* = 2.2, 2 H). MALDI-TOF-MS: 222.1 ($[M+H]^+$).

Data of N-*(2-Aminoethyl)*-N′-*{2-[(5-bromopyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**4c**): UV/VIS (MeOH): 256 (13200), 320 (4700). IR (KBr): 3274, 3049, 2928, 2848, 1661, 1582, 1516, 1448, 1326, 1232, 1123, 1001, 843, 699. ^{1}H-NMR ($CDCl_3$): 1.94 (br. *s*, 4 H); 2.66 (*t*, *J* = 5.8, 2 H); 2.73 (*s*, 4 H); 2.80 (*t*, *J* = 5.8, 2 H); 2.88 (*t*, *J* = 5.8, 2 H); 3.15 (br. *s*, 2 H); 4.69 (br. *s*, 1 H); 7.00 (*t*, *J* = 2.2, 1 H); 7.92 (*d*, *J* = 2.1, 1 H); 7.93 (*d*, *J* = 2.3, 1 H). ^{13}C-NMR ($CDCl_3$): 41.5 (1 C); 42.6 (1 C); 47.9 (1 C); 48.9 (1 C); 49.0 (1 C); 52.1 (1 C); 120.4 (1 C); 121.0 (1 C); 134.4 (1 C); 138.6 (1 C); 145.5 (1 C). MALDI-TOF-MS: 302.0 ($[M+H]^+$).

Data of N^1,N^2-*Bis{2-[(5-bromopyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**5c**): UV/VIS (MeOH): 256 (19900), 320 (7200). IR (KBr): 3275, 2924, 2850, 1661, 1581, 1448, 1353, 1223, 1096, 1001, 844, 699. ^{1}H-NMR ($CDCl_3$): 2.36 (br. *s*, 2 H); 2.75 (*s*, 4 H); 2.88 (*t*, *J* = 5.5, 4 H); 3.16 (*t*, *J* = 5.5, 4 H); 4.57 (br. *s*, 2 H); 7.00 (*t*, *J* = 2.3, 2 H); 7.93 (*d*, *J* = 2.6, 2 H); 7.95 (*d*, *J* = 2.0; 2 H). ^{13}C-NMR ($CDCl_3$): 42.5 (2 C); 47.8 (2 C); 48.5 (2 C); 120.6 (2 C); 121.1 (2 C); 134.3 (2 C); 138.8 (2 C); 145.3 (2 C). MALDI-TOF-MS: 456.9 (M^+).

2,5,9,12,15-Pentaazabicyclo[11.3.1]heptadeca-1(17),13,15-triene (**3d**). From **1a** (0.5 mmol, 119 mg), *N,N′-bis(2-aminoethyl)propane-1,3-diyl* (**2d**; 0.5 mmol, 80 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 6 h reflux. **3d** (34 mg, 29%). UV/VIS (MeOH): 246 (9000), 322 (4000). IR (KBr): 3245, 2923, 2852, 1658, 1591, 1481, 1306, 1224, 1166, 1117, 1010, 908, 818, 708. ^{1}H-NMR ($CDCl_3$): 1.58 (*q*, *J* = 5.6, 2 H); 1.94 (br. *s*, 2 H); 2.73 (*t*, *J* = 5.8, 4 H); 2.77 (*t*, *J* = 5.8, 4 H); 3.37 (*t*, *J* = 5.7, 4 H); 4.00 (br. *s*, 2 H); 6.71 (*t*, *J* = 2.2, 1 H); 7.35 (*d*, *J* = 2.2, 2 H). ^{13}C-NMR ($CDCl_3$): 29.7 (1 C); 43.5 (2 C); 49.3 (2 C); 49.8 (2 C); 101.0 (1 C); 126.5 (2 C); 145.0 (2 C). MALDI-TOF-MS: 236.2 ($[M+H]^+$).

2,6,9,13,16-Pentaazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**3e**). From **1a** (0.5 mmol, 119 mg), *N*-{2-[(3-aminopropyl)amino]ethyl}propane-1,3-diamine (**2e**; 0.5 mmol, 87 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 4 h reflux: **3e** (21 mg, 17%). UV/VIS (MeOH): 246 (sh), 326 (4000). IR (KBr): 3277, 2924, 2851, 1653, 1587, 1525, 1472, 1317, 1219, 1165, 821, 708. ^{1}H-NMR ($CDCl_3$): 1.69 (*q*, *J* = 5.7, 4 H); 2.66 (*t*, *J* = 5.3, 4 H); 2.69 (*s*, 4 H); 3.36 (*t*, *J* = 6.3, 4 H); 6.59 (*t*, *J* = 2.3, 1 H); 7.30 (*d*, *J* = 2.3, 2 H). ^{13}C-NMR ($CDCl_3$): 31.8 (2 C); 40.6 (2 C); 45.7 (2 C); 49.4 (2 C); 99.0 (1 C); 126.2 (2 C); 146.0 (2 C). MALDI-TOF-MS: 250.1 ($[M+H]^+$).

In the case of the treatment of the crude product (after evaporation) with CH_2Cl_2/H_2O prior to CC, the yield of **3e** was 12 mg (10%).

From **1a** (4 mmol, 952 mg), **2e** (4 mmol, 696 mg), dioxane (200 ml), [Pd(dba)$_2$] (138 mg, 6 mol-%), binap (162 mg, 6.5 mol-%), and ^{t}BuONa (12 mmol, 1.2 g), after 10 h reflux, the yield of **3e** was 168 mg (17%).

N-*{2-[(3-Aminopropyl)amino]ethyl}*-N′-*(5-bromopyridin-3-yl)propane-1,3-diamine* (**4e**). From **1a** (4 mmol, 952 mg) and **2e** (4 mmol, 696 mg), according to above-mentioned procedure: **4e** (300 mg, 23%). ^{1}H-NMR ((D$_6$)DMSO): 1.51 (*q*, *J* = 6.5, 2 H); 1.64 (*q*, *J* = 6.7, 2 H); 2.55 (*t*, *J* = 7.7, 2 H); 2.56 (br. *s*, 4 H); 2.62

(*m*, 4 H); 3.04 (*q*, *J* = 5.0, 2 H); 6.33 (br. *s*, 1 H); 7.06 (*t*, *J* = 1.9, 1 H); 7.74 (*d*, *J* = 1.6, 1 H); 7.91 (*d*, *J* = 2.2, 1 H). MALDI-TOF-MS: 330.1 ($[M+H]^+$).

N-*(5-Bromopyridin-3-yl)*-N-*{2-{[3-[(5-bromopyridin-3-yl)amino]propyl}amino}ethyl]propane-1,3-diamine* (**5e**). From **1a** (4 mmol, 952 mg) and **2e** (4 mmol, 696 mg), according to above mentioned procedure: **5e** (320 mg, 33%).

From **1a** (1.5 mmol, 356 mg), **2e** (0.5 mmol, 87 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 4 h reflux: **5e** (208 mg, 86%). ^{1}H-NMR ($CDCl_3$): 1.75 (*q*, *J* = 6.5, 4 H); 2.69 (*s*, 4 H); 2.72 (*t*, *J* = 6.1, 4 H); 3.13 (*t*, *J* = 6.6, 4 H); 6.94 (*t*, *J* = 2.2, 2 H); 7.87 (*d*, *J* = 2.4, 2 H); 7.89 (*d*, *J* = 2.0, 2 H). ^{13}C-NMR ($CDCl_3$): 28.5 (2 C); 42.1 (2 C); 47.9 (2 C); 49.1 (2 C); 119.6 (2 C); 120.9 (2 C); 134.0 (2 C); 137.8 (2 C); 145.4 (2 C). MALDI-TOF-MS: 485.0 ($[M+H]^+$).

N^3,N^5-*Bis{3-{[2-[(3-aminopropyl)amino]ethyl}amino}propy}pyridine-3,5-diamine* (**6e**). From **1a** (0.5 mmol, 119 mg), **2e** (1.1 – 2 mmol, 191 – 348 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 4 h reflux: **6e** (50 – 90%). ^{1}H-NMR ($CDCl_3$): 1.59 (*q*, *J* = 6.8, 4 H); 1.74 (*q*, *J* = 6.6, 4 H); 2.62 (*t*, *J* = 6.6, 4 H); 2.67 (*m*, 12 H); 2.70 (*t*, *J* = 6.5, 4 H); 3.12 (*t*, *J* = 6.5, 4 H); 6.08 (*s*, 1 H); 7.34 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 28.5 (2 C); 32.9 (2 C); 29.6 (2 C); 41.3 (2 C); 46.9 (2 C); 47.1 (2 C); 48.6 (4 C); 100.4 (1 C); 124.3 (2 C); 144.5 (2 C). MALDI-TOF-MS: 424.4 ($[M+H]^+$).

2,6,10,14,17-Pentaazabicyclo[13.3.1]nonadeca-1(19),15,17-triene (**3f**). From **1a** (0.5 mmol, 119 mg), **2f** (0.5 mmol, 94 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5 h reflux: **3f** (20 mg, 15%). UV/VIS (MeOH): 250 (12600), 324 (6300). ^{1}H-NMR ($CDCl_3$): 1.66 (*q*, *J* = 6.5, 2 H); 1.69 (*q*, *J* = 6.5, 4 H); 2.69 (*t*, *J* = 7.5, 4 H); 2.70 (*t*, *J* = 4 H, 5.6); 3.29 (*t*, *J* = 7.2, 4 H); 4.50 (br. *s*, 2 H); 6.40 (*t*, *J* = 2.5, 1 H); 7.32 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 29.5 (2 C); 29.7 (2 C); 42.0 (2 C); 47.5 (2 C); 49.3 (2 C); 121.1 (1 C); 125.9 (2 C); 145.3 (2 C). MALDI-TOF-MS: 264.2 ($[M+H]^+$).

2,5,8,11,14,17-Hexaazabicyclo[13.3.1]nonadeca-1(19),15,17-triene (**3g**). From **1a** (0.5 mmol, 119 mg), *N*-(2-aminoethyl)-*N′*-{2-[(2-aminoethyl)amino]ethyl}ethane-1,2-diamine (**2g**; 0.5 mmol, 95 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 4.5 h reflux: **3g** (7 mg, 5%). ^{1}H-NMR ($CDCl_3$): 2.05 (br. *s*, 3 H); 2.74 (*s*, 8 H); 2.88 (*t*, *J* = 6.0, 4 H); 3.36 (*q*, *J* = 5.7, 4 H); 4.00 (br. *s*, 2 H); 6.57 (*t*, *J* = 2.2, 1 H); 7.36 (*d*, *J* = 2.2, 2 H). MALDI-TOF-MS: 265.2 ($[M+H]^+$).

N-*(2-Aminoethyl)*-N-*{2-{[2-[(5-bromopyridin-3-yl)amino]ethyl}amino}ethyl}ethane-1,2-diamine* (**4g**). Yield 17 mg (10%). ^{1}H-NMR ($CDCl_3$): 2.14 (br. *s*, 5 H); 2.65 (*t*, *J* = 5.9, 2 H); 2.71 (*s*, 4 H); 2.72 (*s*, 4 H); 2.78 (*J* = 5.9, 2 H); 2.87 (*m*, 2 H); 3.14 (*q*, *J* = 4.8, 2 H); 4.73 (br. *s*, 1 H); 6.99 (*t*, *J* = 2.3, 1 H); 7.91 (*d*, *J* = 2.5, 1 H); 7.92 (*d*, *J* = 2.2, 1 H). ^{13}C-NMR ($CDCl_3$): 41.6 (1 C); 42.7 (1 C); 47.9 (1 C); 48.9 (1 C); 49.1 (1 C); 49.2 (1 C); 49.3 (1 C); 52.2 (1 C); 120.4 (1 C); 121.0 (1 C); 134.4 (1 C); 138.6 (1 C); 145.5 (1 C). MALDI-TOF-MS: 345.1 ($[M+H]^+$).

N-*{2-[(5-Bromopyridin-3-yl)amino]ethyl}*-N-*{2-{[2-[(5-bromopyridin-3-yl)amino]ethyl}amino}ethyl}-ethane-1,2-diamine* (**5g**). Yield 35 mg (27%). ^{1}H-NMR ($CDCl_3$): 2.75 (*s*, 8 H); 2.88 (*t*, *J* = 5.5, 4 H); 3.15 (*t*, *J* = 5.3, 4 H); 4.87 (br. *s*, 2 H); 6.98 (*t*, *J* = 2.1, 2 H); 7.91 (*d*, *J* = 1.9, 2 H); 7.92 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 42.4 (2 C); 47.7 (2 C); 48.3 (2 C); 48.6 (2 C); 53.2 (2 C); 120.4 (2 C); 121.0 (2 C); 134.4 (2 C); 138.6 (2 C); 145.4 (2 C). MALDI-TOF-MS: 500.0 ($[M+H]^+$).

2,5,8,11,14,17,20-Heptaazabicyclo[16.3.1]docosa-1(22),18,20-triene (**3h**). From **1a** (0.34 mmol, 80 mg), 3,6,9,12-tetraazatetradecane-1,14-diamine (**2h**; 0.34 mmol, 80 mg), dioxane (25 ml), [Pd(dba)$_2$] (16 mg, 8 mol-%), binap (18 mg, 9 mol-%), and ^{t}BuONa (1 mmol, 100 mg), after 8 h reflux: **3h** (4 mg, 4%). ^{1}H-NMR ($CDCl_3$): 2.71 (*s*, 4 H); 2.72 (*s*, 8 H); 2.83 (*t*, *J* = 5.6, 4 H); 3.25 (*t*, *J* = 5.7, 4 H); 6.45 (*t*, *J* = 2.2, *J* = 1 H); 7.39 (*d*, *J* = 2.2, 2 H). MALDI-TOF-MS: 330.2 ($[M+Na]^+$).

N-*(5-Bromopyridin-3-yl)-3,6,9,12-tetraazatetradecane-1,14-diamine* (**4h**). Yield 33 mg (25%). ^{1}H-NMR ($CDCl_3$): 2.02 (br. *s*, 6 H); 2.39 (*t*, *J* = 6.2, 2 H); 2.47 (*t*, *J* = 6.2, 2 H); 2.66 (*t*, *J* = 5.9, 2 H); 2.72 (*s*, 8 H); 2.78 (*t*, *J* = 5.9, 2 H); 2.86 (*m*, 2 H); 3.15 (br. *s*, 2 H); 7.00 (*t*, *J* = 2.0, 1 H); 7.93 (*d*, *J* = 2.0, 2 H). MALDI-TOF-MS: 410.1 ($[M+Na]^+$).

5,8-Dioxa-2,11,14-triazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**3i**). From **1a** (0.5 mmol, 119 mg), 2,2′-[ethane-1,2-diylbis(oxy)]bis[ethanamine] **2i** (0.5 mmol, 74 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 6 h reflux: **3i** (30 mg, 27%). UV/VIS (MeOH): 320 (5600) ^{1}H-NMR ($CDCl_3$): 3.38 (*t*, *J* = 4.5, 4 H); 3.59 (*s*, 4 H); 3.62 (*t*, *J* = 4.7, 4 H); 4.23 (br. *s*, 2 H); 7.38 (*d*, *J* = 2.3, 2 H); 7.42 (*t*, *J* = 2.3, 1 H). ^{13}C-NMR ($CDCl_3$): 44.7 (2 C); 70.3 (2 C); 72.8 (2 C); 104.7 (1 C); 126.5 (2 C); 145.2 (2 C). MALDI-TOF-MS: 223.0 ($[M^+]$).

6,9,12-Trioxa-2,16,19-triazabicyclo[15.3.1]henicosa-1(21),17,19-triene (**3j**). From **1a** (0.5 mmol, 119 mg), 3,3′-[oxybis(ethane-2,1-diyloxy)]bis[propan-1-amine] (**2j**; 0.5 mmol, 110 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5.5 h reflux: **3j** (29 mg,

22%). UV/VIS (MeOH): 324 (5800). ^{1}H-NMR ($CDCl_3$): 1.81 (*q*, *J* = 5.7, 4 H); 3.29 (*t*, *J* = 6.1, 4 H); 3.55 (*t*, *J* = 5.3, 4 H); 3.58 (*m*, 4 H); 3.67 (*m*, 4 H); 4.35 (br. *s*, 2 H); 6.44 (*t*, *J* = 2.4, 1 H); 7.33 (*d*, *J* = 2.4, 2 H). ^{13}C-NMR ($CDCl_3$): 29.5 (2 C); 41.6 (2 C); 69.3 (2 C); 69.9 (2 C); 70.8 (2 C); 102.2 (1 C); 124.7 (2 C); 145.8 (2 C). MALDI-TOF-MS: 295.1 (M^+).

General Procedure for **8a**–**e**,**g**, **9a**–**e**,**g**,**h**, *and* **5b**,**i**,**j**. In an Ar-flushed flask, a mixture of an appropriate amount (0.5–1.5 mmol) of 3,5-dichloropyridine (**1b**) or 3,5-dibromopyridine (**1a**), [Pd(dba)$_2$] (8 mol-%), binap (9 mol-%), absolute dioxane (25 ml), an appropriate amount (0.5–1.5 mmol) of polyamine, and ^{t}BuONa (1.5 mmol) was refluxed for 4–6 h and then cooled to r.t. A drop of H_2O was added, the org. soln. filtered off and evaporated, and the residue subjected to CC (silica gel, CH_2Cl_2, CH_2Cl_2/MeOH 50 : 1 → 3 : 1, CH_2Cl_2/MeOH/aq. NH_3 soln. 100 : 20 : 1 → 10 : 3 : 1).

N-*(2-Aminoethyl)*-N-*(5-chloropyridin-3-yl)ethane-1,2-diamine* (**8a**) From **1b** (0.5 mmol, 74 mg), **2a** (1.5 mmol, 152 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 7 h reflux: **8a** (70%). ^{1}H-NMR ($CDCl_3$): 2.63 (*t*, *J* = 5.6, 2 H); 2.75 (*t*, *J* = 5.5, 2 H); 2.86 (*t*, *J* = 5.6, 2 H); 3.12 (*t*, *J* = 5.9, 2 H); 6.83 (*t*, *J* = 2.2, 1 H); 7.85 (*d*, *J* = 1.9, 1 H); 7.88 (*d*, *J* = 2.4, 1 H). ^{13}C-NMR ($CDCl_3$): 41.3 (1 C); 42.6 (1 C); 47.6 (1 C); 51.7 (1 C); 117.5 (1 C); 132.0 (1 C); 134.0 (1 C); 136.4 (1 C); 145.1 (1 C). MALDI-TOF-MS: 215.1 ($[M+H]^+$).

N-*(5-Chloropyridin-3-yl)*-N′-*{2-[(5-chloropyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**9a**). From **1b** (1.5 mmol, 222 mg), **2a** (0.5 mmol, 51 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 7 h reflux: **9a** (85%). ^{1}H-NMR ($CDCl_3$): 2.86 (*t*, *J* = 5.6, 4 H); 3.16 (*t*, *J* = 5.6, 4 H); 6.82 (*t*, *J* = 2.2, 2 H): 7.85 (*d*, *J* = 2.2, 4 H). ^{13}C-NMR ($CDCl_3$): 42.8 (2 C); 47.8 (2 C); 117.8 (2 C); 132.2 (2 C); 134.1 (2 C); 136.9 (2 C); 144.9 92 C). MALDI-TOF-MS: 335.1 (M^+).

N-*(5-Bromopyridin-3-yl)*-N′-*{3-[(5-bromopyridin-3-yl)amino]propyl}propane-1,3-diamine* (**5b**). From **1a** (2 mmol, 474 mg), **2b** (1 mmol, 131 mg), dioxane (5 ml), [Pd(dba)$_2$] (46 mg, 8 mol-%), binap (55 mg, 9 mol-%), and ^{t}BuONa (3 mmol, 300 mg), after 6 h reflux: **5b** (90%). ^{1}H-NMR ($CDCl_3$): 1.83 (*q*, *J* = 6.5, 4 H); 2.78 (*t*, *J* = 6.5, 4 H); 3.19 (*t*, *J* = 6.5, 4 H); 4.67 (br. *s*, 2 H); 6.97 (*t*, *J* = 2.3, 2 H); 7.89 (*d*, *J* = 2.5, 2 H); 7.94 (*d*, *J* = 2.0, 2 H). ^{13}C-NMR ($CDCl_3$): 28.7 (2 C); 42.1 (2 C); 47.9 (2 C); 120.2 (2 C); 121.1 (2 C); 134.3 (2 C); 138.7 (2 C); 145.3 (2 C).

N-*(3-Aminopropyl)*-N′-*(5-chloropyridin-3-yl)propane-1,3-diamine* (**8b**). From **1b** (0.5 mmol, 74 mg), **2b** (1.5 mmol, 197 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 8.5 h reflux: **8b** (70%). ^{1}H-NMR ($CDCl_3$): 1.36 (br. *s*, 3 H); 1.63 (*q*, *J* = 7.0, 2 H); 1.72 (*q*, *J* = 6.6, 2 H); 2.62 (*t*, *J* = 7.0, 2 H); 2.71 (*t*, *J* = 6.7, 2 H); 2.72 (*t*, *J* = 7.1, 2 H); 3.10 (*t*, *J* = 6.4, 2 H); 6.78 (*t*, *J* = 2.2, 1 H); 7.76 (*d*, *J* = 1.9, 1 H); 7.83 (*d*, *J* = 2.5, 1 H). ^{13}C-NMR ($CDCl_3$): 28.8 (1 C); 32.9 (1 C); 39.6 (1 C); 41.6 (1 C); 47.0 (1 C); 47.4 (1 C); 116.0 (1 C); 131.4 (1 C); 133.2 (1 C); 134.7 (1 C); 144.6 (1 C). MALDI-TOF-MS: 243.1 ($[M+H]^+$).

N-*(5-Chloropyridin-3-yl)*-N′-*{3-[(5-chloropyridin-3-yl)amino]propyl}propane-1,3-diamine* (**9b**). From **1b** (1.5 mmol, 222 mg), **2b** (0.5 mmol, 66 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 8.5 h reflux: **9b** (80%). ^{1}H-NMR ($CDCl_3$): 1.77 (*q*, *J* = 6.4, 4 H); 2.71 (*t*, *J* = 6.4, 4 H); 3.16 (*t*, *J* = 6.6, 4 H); 6.79 (*t*, *J* = 2.2, 2 H); 7.82 (*d*, *J* = 1.9, 2 H); 7.84 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 28.9 (2 C); 42.0 (2 C); 47.9 (2 C); 117.1 (2 C); 132.2 (2 C); 133.8 (2 C); 136.2 (2 C); 145.1 (2 C). MALDI-TOF-MS: 354.1 ($[M+H]^+$).

N^5,N$^{5'}$-*Bis{3-{[3-[(5-chloropyridin-3-yl)amino]propyl}amino]propyl}-[3,3′-bipyridine]-5,5′-diamine* (**10b**). Yield 20%. ^{1}H-NMR ($CDCl_3$): 1.77 (*q*, *J* = 6.0, 4 H); 1.78 (*q*, *J* = 6.0, 4 H); 2.63 (*t*, *J* = 5.5, 4 H); 2.71 (*t*, *J* = 6.4, 4 H); 3.19 (*t*, *J* = 6.6, 4 H); 3.84 (*t*, *J* = 7.0, 4 H); 6.79 (*t*, *J* = 2.2, 2 H); 7.34 (*t*, *J* = 2.3, 2 H); 7.82 (*d*, *J* = 1.9, 2 H); 7.84 (*d*, *J* = 2.5, 2 H); 8.20 (*d*, *J* = 1.8, 2 H); 8.29 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 29.2 (2 C); 29.9 (2 C); 41.7 (2 C); 46.3 (2 C); 47.6 (2 C); 49.8 (2 C); 117.1 (2 C); 127.2 (2 C); 132.2 (2 C); 133.8 (4 C); 136.2 (2 C); 140.6 (2 C); 142.0 (2 C); 143.4 (2 C); 145.1 (2 C). MALDI-TOF-MS: 636.1 (M^+).

N-*(2-Aminoethyl)*-N′-*{2-[(5-chloropyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**8c**). From **1b** (0.5 mmol, 74 mg), **2c** (1.5 mmol, 219 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 6 h reflux: **8c** (95%). ^{1}H-NMR ($CDCl_3$): 2.62 (*m*, 2 H); 2.69 (*s*, 4 H); 2.74 (*t*, *J* = 6.0, 2 H); 2.83 (*q*, *J* = 5.2, 2 H); 3.11 (*t*, *J* = 5.2, 2 H); 5.31 (br. *s*, 1 H); 6.81 (br. *s*, 1 H); 7.79 (br. *s*, 1 H); 7.87 (br. *s*, 1 H). ^{13}C-NMR ($CDCl_3$): 40.8 (1 C); 41.9 (1 C); 47.2 (1 C); 48.2 (1 C); 48.3 (1 C); 51.5 (1 C); 116.5 (1 C); 131.4 (1 C); 133.3 (1 C); 135.2 (1 C); 144.8 (1 C). MALDI-TOF-MS: 258.1 ($[M+H]^+$).

N,N′-*Bis{2-[(5-chloropyridin-3-yl)amino]ethyl}ethane-1,2-diamine* (**9c**). From **1b** (1.5 mmol, 222 mg), **2c** (0.5 mmol, 73 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 6 h reflux: **9c** (70%). ^{1}H-NMR ($CDCl_3$): 2.71 (*s*, 4 H); 2.86 (*t*, *J* = 5.6, 4 H); 3.13

(*t*, *J* = 5.6, 4 H); 6.82 (*t*, *J* = 2.3, 2 H); 7.84 (*d*, *J* = 1.9, 2 H); 7.88 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 42.5 (2 C); 47.8 (2 C); 48.7 (2 C); 117.4 (2 C); 132.0 (2 C); 133.9 (2 C); 133.9 (2 C); 136.3 (2 C); 145.1 (2 C).

N-*(2-Aminoethyl)*-N′-*{2-[(5-chloropyridin-3-yl)amino]ethyl}propane-1,3-diamine* (**8d**). From **1b** (0.5 mmol, 74 mg), **2d** (1.5 mmol, 240 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5 h reflux: **8d** (77%). ^{1}H-NMR ($CDCl_3$): 1.64 (*q*, *J* = 6.8, 2 H); 2.57–2.75 (*m*, 8 H); 2.80 (*t*, *J* = 5.5, 2 H); 3.11 (br. *s*, 2 H); 6.82 (*s*, 1 H); 7.78 (*s*, 1 H); 7.87 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$): 29.4 (1 C); 40.7 (1 C); 41.7 (1 C); 47.1 (1 C); 47.3 (1 C); 47.6 (1 C); 51.7 (1 C); 116.3 (1 C); 131.2 (1 C); 133.1 (1 C); 134.9 (1 C); 144.4 (1 C). MALDI-TOF-MS: 272.0 ($[M+H]^+$).

N^3,N^5-*Bis{2-{{3-[(2-aminoethyl)amino]propyl}amino}ethyl}pyridine-3,5-diamine* (**6d**). Yield 23%. ^{1}H-NMR ($CDCl_3$): 1.63 (*q*, *J* = 6.8, 4 H); 2.57–2.75 (*m*, 16 H); 2.80 (*t*, *J* = 5.5, 4 H); 3.12 (br. *s*, 4 H); 6.12 (*s*, 1 H); 7.38 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 29.4 (2 C); 40.7 (2 C); 42.1 (2 C); 47.0 (2 C); 47.3 (2 C); 51.7 (2 C); 100.8 (1 C); 124.5 (2 C); 144.7 (2 C). MALDI-TOF-MS: 396.2 ($[M+H]^+$).

N,N′-*Bis{2-[(5-chloropyridin-3-yl)amino]ethyl}propane-1,3-diamine* (**9d**). From **1b** (1.5 mmol, 222 mg), **2d** (0.5 mmol, 80 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5.5 h reflux: **9d** (69 mg, 36%). ^{1}H-NMR ($CDCl_3$): 1.66 (*q*, *J* = 6.8, 2 H); 2.68 (*t*, *J* = 6.9, 4 H); 2.86 (*t*, *J* = 5.7, 4 H); 3.14 (*t*, *J* = 5.7, 4 H); 4.81 (br. *s*, 2 H); 6.84 (*t*, *J* = 2.0, 2 H); 7.87 (*d*, *J* = 1.7, 2 H); 7.89 (*d*, *J* = 2.3, 2 H). ^{13}C-NMR ($CDCl_3$): 30.3 (1 C); 42.6 (2 C); 47.7 (2 C); 48.0 (2 C); 117.6 (2 C); 132.2 (2 C); 134.1 (2 C); 136.6 (2 C); 145.1 (2 C). MALDI-TOF-MS: 383.0 ($[M+H]^+$).

N-*{2-[(3-Aminopropyl)amino]ethyl}*-N′-*(5-chloropyridin-3-yl)propane-1,3-diamine* (**8e**). From **1b** (0.5 mmol, 74 mg), **2e** (0.5 mmol, 87 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 8 h reflux: **8e** (38 mg, 26%).

From **1b** (0.5 mmol, 74 mg), **2e** (2 mmol, 348 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 7 h reflux: **8e** (117 mg, 82%). ^{1}H-NMR ($CDCl_3$): 1.65 (*q*, *J* = 6.5, 2 H); 1.78 (*q*, *J* = 6.2, 2 H); 2.34 (br. *s*, 4 H); 2.63–2.80 (*m*, 10 H); 3.15 (*q*, *J* = 5.9, 2 H); 5.12 (br. *s*, 1 H); 6.80 (*t*, *J* = 2.2, 1 H); 7.80 (*d*, *J* = 2.1, 2 H); 7.85 (*d*, *J* = 2.7, 1 H). ^{13}C-NMR ($CDCl_3$): 28.5 (1 C); 33.0 (1 C); 40.4 (1 C); 42.4 (1 C); 47.8 (1 C); 48.1 (1 C); 49.2 (2 C); 117.2 (1 C); 132.2 (1 C); 134.0 (1 C); 136.2 (1 C); 145.4 (1 C). MALDI-TOF-MS: 286.2 ($[M+H]^+$).

N-*(5-Chloropyridin-3-yl)*-N′-*{2-{{3-[(5-chloropyridin-3-yl)amino]propyl}amino}ethyl}propane-1,3-diamine* (**9e**). Yield 40 mg (40%). From **1b** (1.5 mmol, 222 mg), **2e** (0.5 mmol, 87 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 7 h reflux: **9e** (89 mg, 45%). ^{1}H-NMR ($CDCl_3$): 1.81 (*q*, *J* = 6.3, 4 H); 2.17 (br. *s*, 2 H); 2.78 (*t*, *J* = 6.2, 4 H); 2.81 (*s*, 4 H); 3.13 (*t*, *J* = 6.2, 4 H); 4.52 (br. *s*, 2 H); 6.78 (*t*, *J* = 1.9, 2 H); 7.78 (*d*, *J* = 1.3, 2 H); 7.84 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 28.1 (2 C); 42.0 (2 C); 47.6 (2 C); 48.4 (2 C); 117.3 (2 C); 132.2 (2 C); 134.0 (2 C); 136.2 (2 C); 145.3 (2 C). UV/VIS: 256 (22500), 320 (7500). MALDI-TOF-MS: 397.1 ($[M+H]^+$).

N^5,N$^{5'}$-*Bis{3-{{2-{{3-[(5-chloropyridin-3-yl)amino]propyl}amino}ethyl}amino}propyl}[3,3′-bipyridine]-5,5′-diamine* (**10e**). Yield 32 mg (18%). ^{1}H-NMR ($CDCl_3$): 1.75 (*q*, *J* = 6.3, 4 H); 1.77 (*q*, *J* = 6.2, 4 H); 1.98 (br. *s*, 4 H); 2.63 (*t*, *J* = 6.4, 4 H); 2.71 (*s*, 8 H); 2.74 (*t*, *J* = 6.4, 4 H); 3.13 (*t*, *J* = 6.4, 4 H); 3.80 (*t*, *J* = 7.0, 4 H); 5.04 (br. *s*, 4 H); 6.76 (*t*, *J* = 2.3, 2 H); 7.36 (*t*, *J* = 2.2, 2 H); 7.78 (*d*, *J* = 2.0, 2 H); 7.82 (*d*, *J* = 2.5, 2 H); 8.17 (*d*, *J* = 2.0, 2 H); 8.22 (*d*, *J* = 1.9, 2 H). ^{13}C-NMR ($CDCl_3$): 27.5 (2 C); 28.6 (2 C); 42.3 (2 C); 46.4 (2 C); 48.0 (2 C); 49.1 (2 C); 49.3 (2 C); 49.9 (2 C); 117.1 (2 C); 127.3 (2 C); 132.2 (2 C); 133.9 (4 C); 136.0 (2 C); 140.6 (2 C); 142.0 (2 C); 143.4 (2 C); 145.3 (2 C).

N-*(2-Aminoethyl)*-N′-*{2-{{2-[(5-chloropyridin-3-yl)amino]ethyl}amino}ethyl}ethane-1,2-diamine* (**8g**). From **1b** (0.5 mmol, 74 mg), **2g** (1.5 mmol, 284 mg), dioxane (25 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5 h reflux: **8g** (86%). ^{1}H-NMR ($CDCl_3$): 2.47 (*t*, *J* = 6.0, 2 H); 2.69 (*s*, 8 H); 2.74 (*t*, *J* = 5.7, 2 H); 2.82 (*t*, *J* = 4.6, 2 H); 3.12 (*t*, *J* = 4.7, 2 H); 6.83 (*t*, *J* = 1.9, 1 H); 7.78 (*d*, *J* = 1.6, 1 H); 7.87 (*d*, *J* = 2.2, 1 H). ^{13}C-NMR ($CDCl_3$): 40.6 (1 C); 41.8 (1 C); 45.1 (1 C); 46.5 (1 C); 47.0 (1 C); 48.1 (1 C); 48.3 (1 C); 51.7 (1 C); 116.3 (1 C); 131.1 (1 C); 133.1 (1 C); 134.9 (1 C); 144.7 (1 C). MALDI-TOF-MS: 301.2 ($[M+H]^+$).

N-*{2-[(5-Chloropyridin-3-yl)amino]ethyl}*-N′-*{2-{[2-({2-[(5-chloropyridin-3-yl)amino]ethyl}amino)ethyl]-amino}ethyl}ethane-1,2-diamine* (**9g**). From **1b** (1.5 mmol, 222 mg), **2g** (0.5 mmol, 95 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5.5 h reflux: **9g** (114 mg, 55%). ^{1}H-NMR ($CDCl_3$): 2.82 (*s*, 8 H); 2.88 (*t*, *J* = 5.5, 4 H); 3.16 (br. *s*, 4 H); 4.00 (br. *s*, 3 H); 5.32 (br. *s*, 2 H); 6.80 (*t*, *J* = 2.3, 2 H); 7.75 (*d*, *J* = 2.0, 2 H); 7.92 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 42.6 (2 C); 47.8 (2 C); 48.7 (2 C); 49.1 (2 C); 117.6 (2 C); 132.1 (2 C); 134.1 (2 C); 136.5 (2 C); 145.2 (2 C). MALDI-TOF-MS: 412.1 ($[M+H]^+$).

N^{1},N^{14}-*Bis(5-chloropyridin-3-yl)-3,6,9,12-tetraazatetradecane-1,14-diamine* (**9h**). From **1b** (1.5 mmol, 222 mg), **2g** (0.5 mmol, 116 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 5.5 h reflux: **9h** (80 mg, 35%). ^{1}H-NMR ($CDCl_3$): 2.70 (*s*, 12 H); 2.86 (*t*, *J* = 5.3, 4 H); 3.13 (*t*, *J* = 5.4, 4 H); 6.83 (*s*, 2 H); 7.85 (*s*, 2 H); 7.89 (*s*, 2 H). ^{13}C-NMR ($CDCl_3$): 42.6 (2 C); 47.7 (2 C); 48.7 (2 C); 49.0 (4 C); 117.5 (1 C); 132.1 (2 C); 134.1 (2 C); 136.4 (2 C); 145.2 (2 C). MALDI-TOF-MS: 455.1 ($[M+H]^+$).

N,N′-*[Ethanediylbis(oxyethane-2,1-diyl)]bis[5-bromopyridin-3-amine]* (**5i**). From **1a** (1.1 mmol, 261 mg), **2i** (0.5 mmol, 74 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 4.5 h reflux: **5i** (50%). ^{1}H-NMR ($CDCl_3$): 3.26 (*q*, *J* = 5.3, 4 H); 3.67 (*t*, *J* = 5.2, 4 H); 3.68 (*s*, 4 H); 4.79 (br. *s*, 2 H); 7.00 (*t*, *J* = 2.5, 2 H); 7.91 (*d*, *J* = 2.5, 2 H); 7.96 (*d*, *J* = 2.5, 2 H). ^{13}C-NMR ($CDCl_3$): 42.9 (2 C); 69.3 (2 C); 70.3 (2 C); 120.8 (2 C); 121.0 (2 C); 134.5 (2 C); 139.2 (2 C); 145.1 (2 C).

N,N′-*[Oxybis(ethane-2,1-diyloxypropane-3,1-diyl]bis[5-bromopyridin-3-amine]* (**5j**). From **1a** (1.1 mmol, 261 mg), **2j** (0.5 mmol, 110 mg), dioxane (5 ml), [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg), after 6 h reflux: **5j** (89%). ^{1}H-NMR ($CDCl_3$): 1.86 (*q*, *J* = 5.9, 4 H); 3.17 (*q*, *J* = 6.1, 4 H); 3.59 (*m*, 4 H); 3.60 (*t*, *J* = 5.6, 4 H); 3.65 (*m*, 4 H); 4.84 (*t*, *J* = 5.3, 2 H); 6.95 (*t*, *J* = 2.2, 2 H); 7.88 (*d*, *J* = 2.5, 2 H); 7.89 (*d*, *J* = 1.9, 2 H). ^{13}C-NMR ($CDCl_3$): 28.3 (2 C); 41.5 (2 C); 66.9 (2 C); 70.0 (2 C); 119.7 (2 C); 121.0 (2 C); 134.3 (2 C); 138.0 (2 C); 145.6 (2 C).

2,6,9,13,16,19,23,26,30,33-Decaazatricyclo[29.3.1.1^{14,18}]hexatriaconta-1(35),14(36),15,17,31,33-hexaene (**7e**). *Method a*. In an Ar-flushed flask, a mixture of **1a** (2.2 mmol, 422 mg), **2e** (1 mmol, 174 mg), [Pd(dba)$_2$] (35 mg, 6 mol-%), binap (40 mg, 6.5 mol%), abs. dioxane (5 ml), and ^{t}BuONa (2 mmol, 300 mg), was refluxed for 11 h: **5e** (86%) and **4e** (9%). Then **2e** (0.9 mmol, 157 mg), [Pd(dba)$_2$] (30 mg, 5.5 mol-%), binap (35 mg, 5.5 mol-%), abs. dioxane (45 ml), and ^{t}BuONa (3 mmol, 300 mg) were added to the mixture, which was refluxed for additional 7.5 h: **7e** (14%).

Method b. In an Ar-flushed flask, a mixture of **1a** (1 mmol, 237 mg), **2e** (3 mmol, 522 mg), [Pd(dba)$_2$] (46 mg, 8 mmol-%), binap (55 mg, 9 mol-%), abs. dioxane (10 ml), and ^{t}BuONa (3 mmol, 300 mg) was refluxed for 8 h. The thus obtained **6e** (*ca.* 90% yield) was combined with **1a** (2 mmol, 474 mg), [Pd(dba)$_2$] (46 mg, 8 mmol-%), binap (55 mg, 9 mol-%), abs. dioxane (10 ml), and ^{t}BuONa (3 mmol, 300 mg), and the mixture was refluxed for 11.5 h: **7e** (12%). The combined reaction mixtures were subjected to CC (CH_2Cl_2/MeOH/aq. NH_3 soln. 100 : 20 : 1 → 10 : 3 : 1): **7e** (110 mg, 11%) and **3e** 129 mg, (13%) **7e**: ^{1}H-NMR ($CDCl_3$): 1.72 (*q*, *J* = 6.3, 8 H); 2.70 (br. *s*, 16 H); 3.14 (*t*, *J* = 6.8, 8 H); 6.14 (*t*, *J* = 2.2, 2 H); 7.37 (*d*, 2.2 H, 4 H). ^{1}H-NMR ((D_6)DMSO): 1.71 (*q*, *J* = 6.6, 8 H); 2.69 (*t*, *J* = 6.7, 8 H); 2.75 (*s*, 8 H); 3.04 (*t*, *J* = 6.7, 8 H); 6.11 (br. *s*, 2 H); 7.19 (*d*, *J* = 2.1, 4 H). ^{13}C-NMR ($CDCl_3$): 40.5 (4 C); 48.0 (4 C); 49.1 (4 C); 49.4 (4 C); 102.1 (2 C); 125.2 (4 C); 145.4 (4 C). MALDI-TOF-MS: 499.4 ($[M+H]^+$).

2,6,10,13,16,20,24,27-Octaazatricyclo[23.3.1.1^{11,15}]triaconta-1(29),11(30),12,14,25,27-hexaene (**7b**) *Method a*. From **5b** (0.9 mmol), synthesized by the above-mentioned procedure and used without purification, **2b** (1 mmol, 131 mg), [Pd(dba)$_2$] (46 mg, 8 mol-%), binap (55 mg, 9 mol-%), abs. dioxane (20 ml), and ^{t}BuONa (3 mmol, 300 mg) after 13.5 h reflux: **7b** (48 mg, 12%). ^{1}H-NMR ((D_6)DMSO): 1.66 (br. *s*, 8 H); 2.58 (br. *s*, 8 H); 3.00 (br. *s*, 8 H); 6.04 (*s*, 2 H); 7.19 (4 H). ^{13}C-NMR ((D_6)DMSO): 28.70 (4 C); 40.94 (4 C); 47.26 (4 C); 99.9 (4 C); 1213.7 (4 C); 145.4 (4 C). MALDI-TOF-MS: 413.2 ($[M+H]^+$).

N^3-{3-[(3-Aminopropyl)amino]propyl}-N^5-{3-{[3-[(5-bromopyridin-3-yl)amino]propyl}amino}propyl}-pyridine-3,5-diamine (**13**). Yield 44 mg (9%). ^{1}H-NMR ($CDCl_3$): 1.61 (br. *s*, 2 H); 1.72 (br. *s*, 6 H); 2.60 (br. *s*, 2 H); 2.67 (br. *s*, 8 H); 3.09 (br. *s*, 6 H); 6.04 (*s*, 1 H); 6.90 (*s*, 1 H); 7.33 (*s*, 2 H); 7.85 (br. *s*, 2 H). ^{13}C-NMR ($CDCl_3$): 28.4 (1 C); 28.7 (1 C); 29.0 (1 C); 29.1 (1 C); 41.9 (1 C); 42.0 (1 C); 42.1 (1 C); 42.2 (1 C); 47.8 (2 C); 47.9 (2 C); 101.7 (1 C); 119.8 (1 C); 121.0 (1 C); 125.1 (2 C); 134.2 (1 C); 138.0 (1 C); 145.1 (2 C); 145.6 (1 C).

N^3-{3-{[2-[(3-Aminopropyl)amino]ethyl}amino}propyl}-N^5-{3-{[3-[(5-bromopyridin-3-yl)amino]propyl}-amino}propyl}pyridine-3,5-diamine (**15**) Intermediate **5b** was obtained in ca. 90% according to the *Method a* described above and was used without purification. To the reaction mixture, **2e** (1 mmol, 174 mg), [Pd(dba)$_2$] (46 mg, 8 mol-%), binap (55 mg, 9 mol-%), and ^{t}BuONa (3 mmol, 300 mg) were added, and the mixture was refluxed for additional 4 h: **15** (80 mg, 15%). ^{1}H-NMR ((D_6)DMSO): 1.55 (br. *s*, 2 H); 1.65 (br. *s*, 6 H); 2.58 (br. *s*, 14 H); 3.02 (br. *s*, 6 H); 5.52 (br. *s*, 2 H); 6.04 (*s*, 1 H); 6.27 (br. *s*, 1 H); 7.06 (*s*, 1 H); 7.18 (*s*, 2 H); 7.75 (*s*, 1 H); 7.91 (*s*, 1 H). ^{13}C-NMR ((D_6)DMSO): 28.5 (1 C); 28.6 (1 C); 28.8 (1 C); 28.9 (1 C); 40.4 (1 C); 40.7 (1 C); 40.9 (2 C); 47.0 (2 C); 48.5 (2 C); 48.7 (1 C); 48.8 (1 C); 99.9 (1 C); 118.7 (1 C); 120.6 (1 C); 123.7 (2 C); 134.0 (1 C); 136.0 (1 C); 145.5 (2 C); 146.5 (1 C).

2,6,10,16,20,24,27,30-Octaazatricyclo[23.3.1.1^{11,15}]triaconta-1(29),11(30),12,14,25,27-hexaene (**16**) *Method b*. A mixture of **1a** (1 mmol, 237 mg), **2b** (3 mmol, 393 mg), [Pd(dba)$_2$] (46 mg, 8 mmol-%), binap (55 mg, 9 mol-%), abs. dioxane (5 ml), and ^{t}BuONa (3 mmol, 300 mg) was refluxed for 6 h. The thus obtained

6b (*ca.* 90% yield) was combined with **1c** (2 mmol, 474 mg), [Pd(dba)$_2$] (46 mg, 8 mmol-%), binap (55 mg, 9 mol-%), abs. dioxane (15 ml), ^{t}BuONa (3 mmol, 300 mg), and the mixture was refluxed for 13.5 h: **16** (62 mg, 15%). ^{1}H-NMR ((D$_6$)DMSO): 1.61 (br. *s*, 8 H); 2.55 (br. *s*, 8 H); 3.04 (br. *s*, 8 H); 5.51 (5.52) (*d*, *J* = 7.6 (7.8), 2 H); 6.02 (6.05) (*s*, 1 H); 6.92 (6.97) (*t*, *J* = 7.6 (7.8), 1 H); 7.15 (7.17) (*s*, 2 H); two close sets of signals of aromatic protons with equal intensities are present, the second set is given in parentheses. ^{13}C-NMR ((D$_6$)DMSO): 28.8 (1 C); 29.5 (1 C); 35.0 (1 C); 35.1 (1 C); 47.1 (1 C); 47.2 (1 C); 94.1 (2 C); 101.0 (1 C); 124.1 (2 C); 138.1 (1 C); 145.4 (2 C); 158.0 (2 C). MALDI-TOF-MS: 413.2 ([*M* + H]$^+$).

2,6,10,15-Tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (**17**). Yield 32 mg (16%). ^{1}H-NMR ((D$_6$)DMSO): 1.62 (*q*, *J* = 5.8, 4 H); 2.55 (*t*, *J* = 6.8, 4 H); 3.20 (br. *s*, 4 H); 5.58 (*d*, *J* = 7.8, 2 H); 6.37 (*t*, *J* = 6.4, 2 H); 6.97 (*t*, *J* = 7.8, 1 H). ^{13}C-NMR ((D$_6$)DMSO): 29.5 (2 C); 44.0 (2 C); 47.0 (2 C); 94.0 (2 C); 138.1 (1 C); 158.1 (2 C). MALDI-TOF-MS: 206.9 (*M*$^+$).

6,9,12,26,29,32-Hexaoxa-2,16,19,22,36,39-hexaazatricyclo[35.3.1.1^{17,21}]dotetraconta-1(41),17(42),18,20,37,39-hexaene (**7j**). From **5j** (0.4 mmol), synthesized by the above-mentioned procedure and used without purification, **2j** (0.3 mmol, 66 mg), [Pd(dba)$_2$] (23 mg, 10 mol-%), binap (27 mg, 11 mol-%), ^{t}BuONa (1.5 mmol, 150 mg), dioxane (25 ml), after 6 h reflux: **7j** (15%). ^{1}H-NMR (CDCl$_3$): 1.84 (*q*, *J* = 5.3, 8 H); 3.18 (*t*, *J* = 5.3, 8 H); 3.50 – 3.68 (*m*, 24 H); 6.07 (*t*, *J* = 2.2, 2 H); 7.38 (*d*, *J* = 2.2, 4 H). MALDI-TOF-MS: 591.1 ([*M* + H]$^+$).

N^3,N$^{3'}$-*[Ethane-1,2-diylbis(iminopropane-3,1-diyl)]bis[*N^5-*{3-{[2-[(3-aminopropyl)amino]ethyl}amino}propyl]pyridine-3,5-diamine]* (**11**). Tetramine **2e** (1 mmol, 174 mg) was treated with **5e** (0.45 mmol), which was synthesized by the above-mentioned procedure from **1a** (1.1 – 1.5 mmol, 261 – 356 mg) and **2e** (0.5 mmol, 87 mg), in the presence of [Pd(dba)$_2$] (35 – 46 mg, 12 – 16 mol-%), binap (41 – 54 mg, 13 – 18 mol-%), and ^{t}BuONa (1.5 – 2.25 mmol, 150 – 225 mg), in dioxane (5 ml) under reflux for 6 – 7 h: **11** (45 mg, 13%). ^{1}H-NMR ((D$_6$)DMSO): 1.61 (br. *s*, 12 H); 2.51 (*m*, 28 H); 2.95 (br. *s*, 8 H); 6.04 (*s*, 2 H); 7.16 (*s*, 4 H). ^{13}C-NMR ((D$_6$)DMSO): 29.1 (4 C); 33.4 (2 C); 39.9 (2 C); 41.0 (4 C); 47.3 (6 C); 49.2 (6 C); 100.0 (2 C); 123.7 (4 C); 145.6 (4 C). MALDI-TOF-MS: 673.2 ([*M* + H]$^+$).

N^3,N^5-*bis{3-{[2-{[3-[(5-bromopyridin-3-yl)amino]propyl}amino}ethyl]amino}propyl}pyridine-3,5-diamine* (**12**). Under reflux, **1a** (1.5 mmol, 356 mg) was treated with **6e** (0.45 mmol), which was synthesized by the above-mentioned procedure from **1a** (0.5 mmol, 119 mg) and **2e** (2 mmol, 348 mg), in the presence of [Pd(dba)$_2$] (46 mg, 16 mol-%), binap (54 mg, 18 mol-%), and ^{t}BuONa (3 mmol, 300 mg), in dioxane (5 ml) under reflux for 7 h: **12** (94 mg, 25%). ^{1}H-NMR ((D$_6$)DMSO): 1.73 (*q*, *J* = 6.1, 8 H); 2.71 (*t*, *J* = 6.8, 8 H); 2.79 (*s*, 8 H); 3.06 (*t*, *J* = 7.2, 8 H); 6.10 (*s*, 1 H); 6.37 (br. *s*, 2 H); 7.08 (*s*, 2 H); 7.21 (*s*, 2 H); 7.75 (*s*, 2 H); 7.93 (2 H). ^{13}C-NMR ((D$_6$)DMSO): 27.3 (4 C); 46.0 (2 C); 46.1 (2 C); 46.4 (2 C); 46.7 (2 C); 100.1 (1 C); 118.7 (2 C); 120.5 (2 C); 123.8 (2 C); 134.0 (2 C); 136.1 (2 C); 145.3 (2 C); 146.4 (2 C).

2,6,9,13,16,19,23,26,30,33,36,40,43,47,50-Pentadecaazatetracyclo[46.3.1.1^{14,18}.1^{31,35}]tetrapentaconta-1(52),14(54),15,17,31(53),32,34,48,50-nonaene (**18**). *Method c*. Compound **5e**, obtained *in situ* from **2e** (0.5 mmol, 87 mg) and **1a** (1.1 mmol, 261 mg), was treated with **6e**, obtained *in situ* from **1a** (0.5 mmol, 119 mg) and **2e** (1.1 mmol, 192 mg), in the presence of [Pd(dba)$_2$] (23 mg, 8 mol-%), binap (27 mg, 9 mol-%), and ^{t}BuONa (1.5 mmol, 150 mg) under reflux for 11 h in dioxane (25 ml). CC (CH$_2$Cl$_2$/MeOH/aq. NH$_3$ soln. 100 : 20 : 3 → 10 : 3 : 1) provided **3e** (29 mg, 23%) and **7e** (34 mg, 13%); no **18** was isolated.

Method d. Compound **11**, obtained *in situ* from **5e** (0.45 mmol) according to the above-mentioned procedure, was treated with **1a** (0.4 mmol, 95 mg), in the presence of [Pd(dba)$_2$] (23 mg, 10 mol-%), binap (27 mg, 11 mol-%), and ^{t}BuONa (1 mmol, 100 mg) under reflux for 5 h in dioxane (25 ml). CC (CH$_2$Cl$_2$/MeOH/aq. NH$_3$ soln. 100 : 20 : 2 → 10 : 3 : 1) provided **3e** (26 mg, 21%) and **18**/**7e** (60 mg, *ca.* 20%). **18**: ^{1}H-NMR (CDCl$_3$): 1.71 (br. *s*, 12 H); 2.69 (br. *s*, 24 H); 3.02 (br. *s*, 12 H); 6.09 (*s*, 3 H); 7.20 (*s*, 6 H). MALDI-TOF-MS: 749.3 ([*M* + H]$^+$).

Method e. Compound **12**, obtained *in situ* from compound **6e** (0.45 mmol) according to the above-mentioned procedure, was treated with **2e** (0.4 mmol, 70 mg) in the presence of [Pd(dba)$_2$] (23 mg, 10 mol%), binap (27 mg, 11 mol-%), and ^{t}BuONa (1 mmol, 100 mg) under reflux for 5 h in dioxane (25 ml). CC (CH$_2$Cl$_2$/MeOH/aq. NH$_3$ soln. 100 : 20 : 3) provided **3e** (54 mg, 43%); no **18** was isolated.

REFERENCES

[1] H. Stetter, W. Frannk, R. Mertens, *Tetrahedron* **1981**, *37*, 767.
[2] J. Costa, R. Delgado, *Inorg. Chem.* **1993**, *32*, 5257.
[3] R. Delgado, S. Quintino, M. Teixeira, A. Zhang, *J. Chem. Soc., Dalton Trans.* **1996**, 55.

[4] V. Felix, J. Costa, R. Delgado, M. G. B. Drew, M. T. Duarte, C. Resende, *J. Chem. Soc., Dalton Trans.* **2001**, 1462.
[5] W. D. Kim, D. C. Hrncir, G. E. Kiefer, A. D. Sherry, *Inorg. Chem.* **1995**, *34*, 222.
[6] S. Aime, M. Botta, S. G. Crich, G. B. Giovenzana, G. Jommi, R. Pagliarin, M. Sisti, *Inorg. Chem.* **1997**, *36*, 2992.
[7] A. Favre-Reguillon, F. Segat-Dioury, L. Nait-Bouda, C. Cosma, J.-M. Siaugue, J. Foos, A. Guy, *Synlett* **2000**, 868.
[8] J.-M. Siaugue, A. Favre-Reguillon, F. Dioury, G. Plancque, J. Foos, C. Madic, C. Moulin, A. Guy, *Eur. J. Inorg. Chem.* **2003**, 2834.
[9] A. M. Herrera, R. J. Staples, S. V. Kryatov, A. Y. Nazarenko, E. V. Rybak-Akimova, *Dalton Trans.* **2003**, 846.
[10] A. M. Herrera, G. V. Kalayda, J. S. Disch, J. P. Wilkstrom, I. V. Korendovych, R. J. Staples, C. F. Campana, A. Y. Nazarenko, T. E. Haas, E. V. Rybak-Akimova, *Dalton Trans.* **2003**, 4482.
[11] G. K. Pandey, S. Srivastava, O. P. Pandey, S. K. Sengupta, *Indian J. Chem., Sect. A* **1998**, 447.
[12] F. Denat, S. Lacour, S. Brandes, R. Guilard, *Tetrahedron Lett.* **1997**, *38*, 4417.
[13] S. Brandes, F. Denat, S. Lacour, F. Rabiet, F. Barbette, P. Pullumbi, R. Guilard, *Eur. J. Org. Chem.* **1998**, 2349.
[14] U. Luning, *Liebigs Ann. Chem.* **1987**, 949.
[15] I. P. Beletskaya, A. D. Averin, N. A. Pleshkova, A. A. Borisenko, M. V. Serebryakova, F. Denat, R. Guilard, *Synlett* **2005**, 87.
[16] S. Wagaw, S. L. Buchwald, *J. Org. Chem.* **1996**, *61*, 7240.
[17] J.-F. Marcoux, S. Wagaw, S. L. Buchwald, *J. Org. Chem.* **1997**, *62*, 1568.
[18] M. Nishiyama, T. Yamamoto, Y. Koie, *Tetrahedron Lett.* **1998**, *39*, 617.
[19] S. Jaime-Figuera, Y. Lin, J. M. Muchowski, D. G. Putman, *Tetrahedron Lett*. **1998**, *39*, 1313.
[20] J. Cheng, M. L. Trudell, *Org. Lett*. **2001**, *3*, 1371.
[21] T. H. Jonckers, B. W. Maes, G. L. Lemiere, G. Rombouts, *Tetrahedron* **2001**, *57*, 7027.
[22] B. U. W. Maes, K. T. J. Loones, T. H. M. Jonckers, G. L. F. Lemiere, R. A. Dommisse, A. Haemers, *Synlett* **2002**, 1995.
[23] T. H. Jonckers, B. W. Maes, G. L. Lemiere, G. Rombouts, *Synlett* **2003**, 615.
[24] C. Meyers, B. U. W. Maes, K. T. J. Loones, G. Bal, G. L. F. Lemiers, R. A. Dommisse, *J. Org. Chem.* **2004**, *69*, 6010.
[25] K. T. J. Loones, B. U. W. Maes, R. A. Dommisse, G. L. F. Lemiere, *Chem. Commun.* **2004**, 2466.
[26] T. Desmarets, R. Schneider, Y. Fort, *Tetrahedron Lett*. **2000**, *41*, 2875.
[27] T. Desmarets, R. Schneider, Y. Fort., *Tetrahedron* **2001**, *57*, 7657.
[28] T. Desmarets, R. Schneider, Y. Fort., *Tetrahedron Lett*. **2001**, *42*, 247.
[29] B. Gradel, E. Brenner, R. Schneider, Y. Fort, *Tetrahedron Lett*. **2001**, *42*, 5689.
[30] J. P. Wolfe, S. L. Buchwald, *J. Org. Chem.* **2000**, *65*, 1144.
[31] T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet, J. A. Ibers, *J. Organomet. Chem.* **1974**, *65*, 253.

Received March 4, 2005