Pd-CATALYZED AMINATION OF 2,6-DIHALOPYRIDINES WITH POLYAMINES

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Dedicated to Dr Karel Mach on the occasion of his 70th birthday in recognition of his outstanding contributions to the area of organometallic synthesis and catalysis.

The Pd-catalyzed amination of 2,6-dibromopyridine with various linear polyamines and oxapolyamines was studied. In this way polyazamacrocycles **3** containing one pyridine and one polyamine moiety were synthesized using equimolar amounts of starting compounds. Two alternative approaches were elaborated and compared for synthesis of macrocycles **11** comprising two pyridine and two polyamine fragments: via intermediate formation of N^{α},N^{ω}-bis(6-halopyridin-2-yl)polyamines **7**, **8** or via 2,6-bis(polyamino)-substituted pyridines **10**. A series of *N*-(6-*tert*-butoxypyridin-2-yl)-substituted polyamines **12** and N^{α},N^{ω}bis(6-*tert*-butoxypyridin-2-yl)-substituted polyamines **13** were obtained by similar procedures, and the possibilities of *N*,*N*-dihetarylation of such compounds using 2-bromopyridine and 2-bromo-6-*tert*-butoxypyridine were studied. The yields of linear and cyclic products were shown to be strongly dependent on the nature of starting polyamines and of the halogen atom.

Keywords: Aminations; Hartwig–Buchwald reaction; Palladium catalysis; Macrocycles; Azacrown compounds; Pyridines; Amines.

Macrocycles containing polyamine and pyridine fragments have attracted constant interest of researchers in recent decade, and various groups studied synthesis of the compounds with an *endo*-oriented pyridine atom[1]. Introduction of the pyridine moiety strongly influences thermodynamic properties and complexation kinetics by increasing the conformational rigidity of the ligand and by changing its basicity. In almost all known macrocycles of such type, nitrogen atoms of the polyamine chain and pyridine ring are separated by methylene, methyne or carbonyl groups: a single compound with C(sp^2)–N bond was obtained by reduction of the corre-

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sponding diamide formed from 2,6-diaminopyridine and bis(acyl chloride)[2]. Recently, synthesis of a number of pyridine-containing macrocycles by reaction of dimethyl pyridine-2,6-dicarboxylates has been reported[3]. We have shown that Pd-catalyzed amination of various dihaloarenes with polyamines is a powerful tool for the synthesis of a wide range of nitrogen and oxygen-containing macrocycles[4]. Such ligands containing nitrogen atoms directly bonded to an arene moiety may show original complexing properties and serve as new metal photosensors; in the last case, direct link between the macrocycle and arene through nitrogen should increase the measurable response of the ligand to complexation.

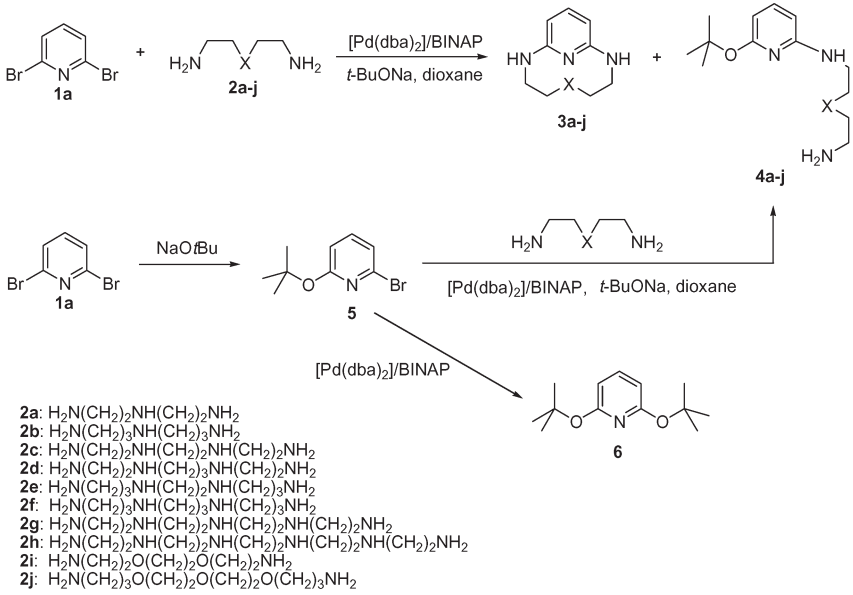
Taking the above mentioned facts into consideration, we decided to apply Pd-catalyzed amination reaction with linear polyamines to 2,6-dihalopyridines. It is to be noted that 2-bromopyridine was successfully aminated by Buchwald in 1996, just at the beginning of his studies on Pd-catalyzed amination[5]. Since that time, many examples of the catalytic amination of halopyridines involving either palladium[6] or nickel complexes[7] have been reported. Catalytic diamination of 2,6-dibromopyridine was employed in recent years to produce 2.6-bis(pyrazol-1-yl)pyridines[8], which found application as ligands in transition metal complexation[9] and for the synthesis of imidazolyl derivatives – useful bis(carbene)pyridine complexes[10]. It should be noted that in many cases bis(pyrazolyl)- and bis(triazolyl)pyridines were synthesized via non-catalytic aromatic nucleophilic substition using harsh conditions[11]. There are also several examples of the palladium-mediated synthesis of oligo-α-aminopyridines[12] and azacalixarenepyridines[13] which use 2,6-dibromopyridine, and also a successful diamination with *N*,*N*′,*N*″-tris(*tert*-butoxycarbonyl)cyclene giving a pyridine-based bis(tetraazamacrocyclic) compound has been reported[14]. Our own contribution to this field has been restricted to two preliminary publications[15], and here we report in details the results of the amination of 2,6-dibromopyridine using various linear polyamines.

RESULTS AND DISCUSSION

Synthesis of Macrocycles Containing One Pyridine and One Polyamine Moiety

First we investigated the reactions of 2,6-dibromopyridine (**1a**) with a number of polyamines **2a**–**2h** and oxapolyamines **2i**, **2j** taken in equimolar amounts in order to obtain corresponding macrocycles **3** containing one pyridine and one polyamine moiety. The reactions were run using

$Pd(dba)_2$/BINAP catalytic system (4–8/6–12 mole %) which is well documented in literature[16] and which we have found to be the most convenient for arylation of polyamines[17]. Sodium *tert*-butoxide was employed as a base, amination was carried out in dilute dioxane solutions (0.01–0.02 mol/l diamines) to prevent undesirable formation of linear oligomers, and the reactions ran to completion in 5–15 h depending on concentration (Scheme 1). The data concerning reaction conditions and yields of the products are presented in Table I. NMR yields in the reaction mixtures were measured after standard work-up prior to column chromatography on silica (see Experimental) by comparison of the signals intensities of pyridine ring (H-3 and H-5) and those of BINAP (H-5, H-5′, H-8 and H-8′ in binaphthyl).



SCHEME 1

The yields of target macrocycles **3** were found to be strongly dependent on the nature of polyamines **2a**–**2j**. While the reactions with tetraamines **2d**–**2f** afforded 21–32% yields of macrocycles **3d**–**3f** (Table I, entries 5, 6, 8, 9, 14), short triamines **2a**, **2b**, polyamines with repeating ethylenediamine unit **2c**, **2g**, **2h**, and oxadiamines **2i**, **2j** provided low yields of corresponding macrocycles. The efficiency of column chromatography on silica was also different in the isolation of various macrocycles: it failed with relatively small cycles **3a**, **3b** (entries 1, 2) and in case of hexaamine-containing

TABLE I
Synthesis of macrocycles **3a**–**3j**

Entry	Amine	c, mol/l	Pd/BINAP mole %	Yield of **3** %[a]	Yield of **4** %[a]	Notes
1	**2a**	0.01	8/12	11(0)	12(5)	
2	**2b**	0.01	8/12	14(0)	51(14)	
3	**2c**	0.02	4/6	7(4)	49(34)	
4	**2c**	0.02	8/12	13	28	
5	**2d**	0.02	4/6	21(17)	18(10)	
6	**2d**	0.02	8/12	20	26	
7	**2d**	0.02	2/3	10(5)	20(17)	
8	**2e**	0.02	4/6	24(13)	30[b]	
9	**2e**	0.01	8/12	22(14)	40[b]	
10	**2e**	0.005	8/12	7	32	30 h reflux
11	**2e**	0.02	4/6	4	0	40 equiv. K_2CO_3 30 h reflux
12	**2e**	0.02	4/6	4(2)	0	**1b** instead of **1a**, 28% yield of **8e**
13	**2e**	0.1	4/4.5	21(16)[c]	18[b]	
14	**2f**	0.02	4/6	32(30)	44(6)	
15	**2g**	0.02	4/6	7(3)	19(17)	
16	**2g**	0.01	8/12	11	14(1.5)	
17	**2h**	0.02	4/6	10(0)	21(2)	
18	**2h**	0.01	8/12	13	8	
19	**2i**	0.01	8/12	9(8)	26(9)	Yield of **11i** 9 %
20	**2j**	0.01	8/12	7(2)	33(12)	Yield of **11j** 8 %

[a] NMR yield after standard treatment of the reaction mixture with H_2O/CH_2Cl_2, yield after chromatography in parentheses. [b] **4e** was not isolated in pure state. [c] NMR yield of **3e** in the reaction mixture before standard treatment 27%.

macrocycle **3h** (entry 17); macrocycle **3j** was isolated in a very small amount (entry 20). Thus macrocycles **3a**, **3b**, **3h** could be analyzed only in the reaction mixtures. The major by-products observed in all cases were *N*-(6-*tert*-butoxypyridin-2-yl)polyamines **4** whose formation proceeded via intermediate 2-bromo-6-*tert*-butoxypyridine **5** (Scheme 1). In all cases compounds **4** were isolated from the reaction mixtures by column chromatography. Special investigation revealed that 2-*tert*-butoxypyridine was formed by a non-catalytic substititon of one bromine atom by *tert*-butoxy group by the action of sodium *tert*-butoxide. The substitution is complete in 5 h under standard reaction conditions provided no catalyst is added. Previously, non-catalytic alkoxylation of 2-bromopyridine was documented in literature, but it required harsh conditions[18]. The other bromine atom in compound **5** can be smoothly substituted with sodium *tert*-butoxide under standard catalytic conditions to form **6** in quantitative yield. In case of oxadiamines **2i**, **2j**, corresponding cyclodimers **11i** and **11j** (vide infra) were isolated in 9 and 8% yields; they contain two polyamine and two oxadiamine groups. It is notable that such cyclodimers were not identified in case of short triamines **2a**, **2b**, for which they could be expected. We tried several alternative procedures for isolation of macrocycles **3**, like extraction with ether, treatment with CH_2Cl_2/HCl followed by KOH treatment, but they could only improve the **3**:**4** ratio in the mixture but did not afford pure compound **3**.

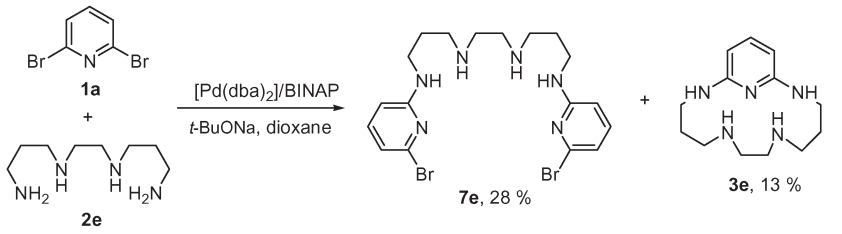
As the yields of macrocycles **3** were rather low, we tried several approaches to improve them. The application of a greater amount of the catalyst (8 instead of 4 mole %) and dilution of the reaction (0.01 instead of 0.02 mol/l) increased to some extent the yield of the target product in the reaction mixture (entries 4, 16, 18) with simultaneous decrease in the yields of **4**, but in other cases no effect was noted (entries 6, 9). Further dilution of the reaction to 0.005 mol/l resulted in a dramatic decrease in the macrocycle formation (entry 10). On the other hand, even at 0.1 mol/l the yield of **3e** was quite comparable to that at 0.01–0.02 mol/l (entries 8, 9, 13). Application of 4–8 mole % of the catalyst proved to be optimal, as the use of 2 mole % catalyst decreased the yield twofold (entry 7). Attempts to employ donor phosphane ligands[19] like 2-(dicyclohexylphosphanyl)biphenyl, 2-(di-*tert*-butylphosphanyl)biphenyl and 2-(dicyclohexylphosphanyl)-2′-(dimethylamino)biphenyl or carbene-based ligands[6] were totally unsuccesful. We also tried to avoid the formation of by-products **4** by using cesium or potassium carbonates instead of sodium *tert*-butoxide, but even after 30 h reflux the yield of the macrocycle **3e** was only 4% (entry 11). The same low yield was observed when using 2,6-dichloropyridine (**1b**) instead

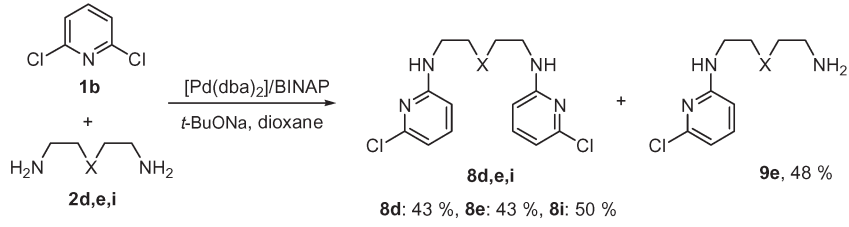
of 2,6-dibromopyridine (entry 12), though no formation of **4e** was noticed in this case. In this case N^{α},N^{ω}-bis(6-chloropyridin-2-yl)substituted tetraamine **8e** was rather formed and isolated in 28% yield. It must be stressed that in the latter cases the conversion of starting dihalopyridine was very low, but when using 2,6-dibromopyridine and Pd/BINAP system, no traces of residual dibromopyridine were observed in the reaction mixture. Low yields of the macrocycles might be explained by the formation of some oligomeric compounds which could not be either isolated or identified in the reaction mixtures. However, we have established earlier that sesondary NH groups of polyamines were inert in the amination reactions under conditions employed for the synthesis of macrocycles, hence we cannot consider this side reactions as a reason for low yields of target macrocycles **4**. Indeed, the results with di- and trioxadiamines **2i**, **2j** correlate with this fact.

Synthesis of Cyclodimers

To synthesize macrocycles containing two pyridine and two polyamine fragments (i.e. cyclodimers), we have elaborated two alternative methods. According to the method (*A*), polyamines are first hetarylated with 2 equiv. of 2,6-dihalopyridines to form N^{α},N^{ω}-bis(6-halopyridin-2-yl)polyamines which further react with the second equiv. of polyamines giving the desired cyclodimers. In the method (*B*), the intermediate 2,6-bis(polyamine)pyridines are formed by the reaction of 2,6-dibromopyridine (**1a**) with excess of polyamines **2**, and corresponding cyclodimers are formed by their reaction with the second molecule of 2,6-dibromopyridine. In accordance with the method (*A*), the reaction of tetraamine **2e** with 3 equiv. of 2,6-dibromopyridine **1a** in boiling dioxane (0.1 mol/l of **2e**) for ca. 5 h, in the presence of $Pd(dba)_2$ (8 mole %)/BINAP (9 mole %) catalyst and sodium *tert*-butoxide provided a mixture of the target bis(bromopyridinyl)-substituted tetraamine **7e** and macrocycle **3e** which were isolated by column chromatography in 28 and 13% yields, respectively (Scheme 2). The use of 2,6-dichloropyridine (**2b**) (3 equiv.) in this reaction led to a higher yield (43%) of the desired product **8e** and no macrocycle **3e** was observed. Monohetarylated compound **9e** was isolated in 48% yield as a by-product. Another tetraamine **2d** and dioxadiamine **2i** were also employed in this reaction to produce the corresponding bis(chloropyridinyl)-substituted polyamines **8e**, **8i** in 40 and 50% yields, respectively (Scheme 2).

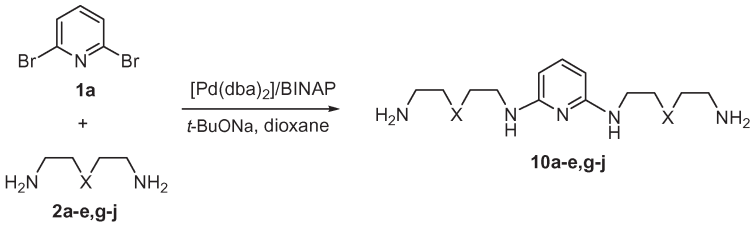
According to the second method (*B*), 2,6-dibromopyridine (**1a**) was treated with several equiv. of polyamines **2** to give the corresponding bis(polyamine)-substituted pyridines **10** (Scheme 3).





d: X = $NH(CH_2)_3NH$
e: X = $CH_2NH(CH_2)_2NHCH_2$
i: X = $O(CH_2)_2O$

SCHEME 2



a: X = NH
b: X = CH_2NHCH_2
c: X = $NH(CH_2)_2NH$
d: X = $NH(CH_2)_3NH$
e: X = $CH_2NH(CH_2)_2NHCH_2$
g: X = $NH(CH_2)_2NH(CH_2)_2NH$
h: X = $NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH$
i: X = $O(CH_2)_2O$
j: X = $CH_2O(CH_2)_2O(CH_2)_2OCH_2$

SCHEME 3

This process provided not only desired intermediates **10**, but also gave interesting and to some extent unexpected results; hence we studied it thoroughly. Data are collected in Table II. First, the amination of 2,6-dibromopyridine (**1a**) was carried out with 4 equiv. of polyamines **2** using 0.04 mol/l concentrations of **1a** and 8 mole % of the catalyst (Table II, entries 1, 3, 5, 6, 12, 18, 19, 20, 22). The target compounds **10a**–**10e**, **10g**–**10j** were formed in yields from moderate to high (42–72%), and in all cases

TABLE II
Synthesis of 2,6-bis(polyamine)-substituted polyamines **10a**–**10e**, **10g**–**10j**

Entry	Amine	Ratio **1a**/**2**	c, mol/l	Pd/BINAP mole %	Yield of **10** %[a]	Yield of **3** %[a]	Yield of **4** %[a]
1	**2a**	1:4	0.04	8/9	72(0)	15(5)	13(3)
2	**2a**	1:4	0.1	4/4.5	60(20)[b]		10[c]
3	**2b**	1:4	0.04	8/9	70(9)	21	7
4	**2b**	1:4	0.1	4/4.5	82(25)[b]	9	9
5	**2c**	1:4	0.04	8/9	42	19	10
6	**2d**	1:4	0.04	8/9	54(6)	29(16)	
7	**2d**	1:4	0.1	4/4.5	70	17	
8	**2e**	1:1.5	0.04	4/4.5	4	23[17][d]	
9	**2e**	1:2	0.1	4/4.5	24(7)	18(14)	
10	**2e**	1:2	0.04	4/4.5	5(3)	22(10)[16][d]	
11	**2e**	1:4	0.04	4/6	(31)	(23)[14][d]	
12	**2e**	1:4	0.04	8/9	66(0)	33(20)	
13	**2e**	1:6	0.1	4/6	85[24][d]	12	3
14	**2e**	1:6	0.1	4/6	(21)	(13)[10][d]	
15	**2e**	1:6	0.2	4/4.5	90	10	
16	**2e**	1:6	0.2	4/4.5	91[22][d]	9	
17	**2e**	1:4	0.2	2/2.5	88	12	
18	**2g**	1:4	0.04	8/9	46	23	20
19	**2h**	1:4	0.04	8/9	50	27	12
20	**2i**	1:4	0.04	8/9	63(42)[e,f]		10(9)
21	**2i**	1:3	0.2	4/4.5	80		
22	**2j**	1:4	0.04	8/9	62(38)	24(16)[g]	8(4)
23	**2j**	1:4	0.1	4/6	64	19	

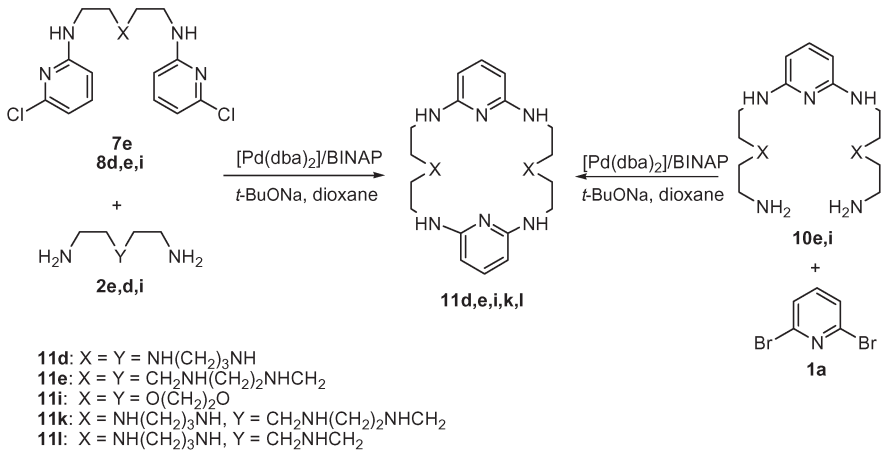
[a] NMR yields before standard treatment with CH_2Cl_2/H_2O, yields after standard treatment are given in parentheses. [b] NMR yields after treatment with CH_2Cl_2/aqHCl. [c] *N*-(6-bromopyridin-2-yl)-substituted triamine was obtained in 11% yield. [d] Yields after column chromatography. [e] Data for a mixture of **10i** with **3i**. [f] Cyclodimer **11i** was obtained in 22% yield in the reaction mixture before treatment, in 17% yield after treatment. [g] Cyclodimer **11j** was obtained in 14% yield in the reaction mixture before treatment, in 10% yield after treatment.

formation of substantial amounts of corresponding macrocycles **3** was observed. In most cases, their yields in the reaction mixtures were considerably higher than in the reactions with equimolar amounts of polyamines, which were conducted in more dilute solutions. The use of more concentrated (0.1 mol/l of **1a**) reaction mixtures with the same dibromopyridine/polyamine ratio 1:4 resulted in most cases in an increase in formation of compound **10** (entries 4, 7, 21), though the catalyst loading was diminished to 4 mole %. Several experiments were conducted with tetraamine **3e** to follow more precisely the regularities of the **10e** formation. When employing dibromopyridine-to-tetraamine ratio 1:1.5 or 1:2 at 0.04 mol/l of dibromide, bis(polyamine) derivative **10e** was formed in 4–5% while macrocycle **3e** was formed in 22–23% yield (entries 8, 10). Higher concentration (0.1 mol/l, entry 9) led to a notable increase in the **10e** formation, and the yield of **3e** slightly decreased. An increase in the dibromide-to-tetraamine ratio from 1:2 to 1:4 resulted in further increase in the **10e** yield (entry 11) without effect on the **3e** yield, and the use of twofold catalyst loading gave another increment of the yield of bis(polyamine)-substituted tetraamine (entry 12). The best yields of **10e** (up to 90%) were achieved by the use of 6-fold excess of tetraamine **2e** and concentrated solutions (0.1–0.2 mol/l), in these cases 4 or even 2 mole % of the catalyst can be used (entries 13, 15–18). The yield of macrocycle **3e** in these cases was substantially lower and did not exceed 12%. Remarkable is such a stable yield of macrocycle **3e** under different reaction conditions: from the 1:1 reagent ratio in 0.01 mol/l solution, to the 1:2 ratio in 0.1 mol/l solution or 1:4 ratio in 0.04 mol/l solution. The yield of the macrocycle after column chromatography ranged between 14 and 20%. An interesting feature of ^{1}H NMR spectra of compounds **10** is that the signals of aliphatic protons are quite broad while the signals of pyridine protons are sharp; often, instead of one doublet (for H3 and H3′ protons) and one triplet (for H4 protons), a set of several close doublets and triplets with the same coupling constants but different intensities was observed. This fact may be explained by the formation of sufficiently stable conformers due to intra- and intermolecular hydrogen bonds. The addition of an excess of corresponding polyamine to a solution of **10** either simplified the multiplet pattern or slightly broadened the normal doublet and triplet.

The problem of isolation and purification of bis(polyamine)-substituted tetraamines **10** was found to be quite serious. Standard treatment of the reaction mixture with CH_2Cl_2/H_2O to remove unreacted polyamine did not help, as most of the product **10** was taken with water (entries 9–12, 14). The

treatment with CH_2Cl_2/H_2O–HCl followed by KOH treatment of the water phase and its extraction with CH_2Cl_2 was also unsuccessful because the resulting compound **10** recovered from dichloromethane phase contained tetraamine **2e** (entries 2, 4). We attempted column chromatography of the reaction mixture without prior treatment, and the product **10e** was isolated in 22–24% yield, but it also contained tetraamine **2e** in the 1:1 to 1:2 mole ratio. Thus we decided to use compounds **10** in the synthesis of cyclodimers without any purification, producing them from 1 equiv. of dibromide and 3–4 equiv. of polyamine to minimize possible excess of polyamines which would lead to macrocycles and not to cyclodimers.

Following the method (*A*), cyclodimers **11d**, **11e**, **11i**, **11k**, **11l** were synthesized by the reaction of bis(halopyridinyl)-substituted polyamines **7e** and **8d**, **8e**, **8i** with polyamines **2b**, **2d**, **2e**, **2i** (Scheme 4).



11d: X = Y = $NH(CH_2)_3NH$
11e: X = Y = $CH_2NH(CH_2)_2NHCH_2$
11i: X = Y = $O(CH_2)_2O$
11k: X = $NH(CH_2)_3NH$, Y = $CH_2NH(CH_2)_2NHCH_2$
11l: X = $NH(CH_2)_3NH$, Y = CH_2NHCH_2

SCHEME 4

Reaction conditions and product yields are presented in Table III. The syntheses were conducted in boiling dioxane (reaction time ca. 10 h), under dilute conditions (0.01–0.05 mol/l). We have found that the use of the dibromo derivative **7e** provided the corresponding cyclodimer **11e** in a poorer yield than dichloro derivative **8e** (Table III, entries 2, 3). Bromoarenes are usually more active in amination reactions: in this case the lower yield could be due to excessive formation of linear oligomers. For the synthesis of two other symmetrical cyclodimers **11d**, **11i**, the corresponding bis(chloropyridinyl)polyamines **8d**, **8i** were used (entries 1, 4). The same procedure was successful for the synthesis of macrocycles **11k**, **11l** containing two different polyamine chains (entries 5 and 6). Cyclodimers **11d**, **11e**,

11i, **11k**, **11l** were isolated by column chromatography on silica gel. The reactions with tetraamine **2e** and dioxadiamine **2i** proved to be most successful (38–39% yield, entry 4). Lower catalyst loadings (entries 1, 5, 6) in the reactions with tri- and tetraamines and their derivatives provided poorer yields od corresponding cyclodimers. ^{1}H NMR spectra of compounds **11d**, **11e**, **11k**, **11l** the signals are notably broadened; in both ^{1}H and ^{13}C NMR spectra the two pyridine fragments are identical, and the two polyamine chains which are symmetrical are also identical. For macrocycle **11i**, on the contrary, the signals are sharp, but the two pyridine and two dioxadiamine chains are different and unsymmetrical. The same picture is observed in ^{1}H and ^{13}C NMR spectra of cyclodimer **11j** which was isolated as a by-product in the synthesis of macrocycle **3j**. This fact might be explained by the difference in the conformational rigidity of these macrocycles and by the intramolecular hydrogen bond formation in the case of cyclodimers containing tri- and tetraamine chains (**11d**, **11e**, **11k**, **11l**). It is interesting that the method provided the two macrocycles (**11e** and **11i**) in very good yields which are substantially higher than the yields of the corresponding macrocycles **3e** and **3i** containing one pyridine and one polyamine fragment.

TABLE III
Synthesis of cyclodimers **11d**, **11e**, **11i**, **11k**, **11l**

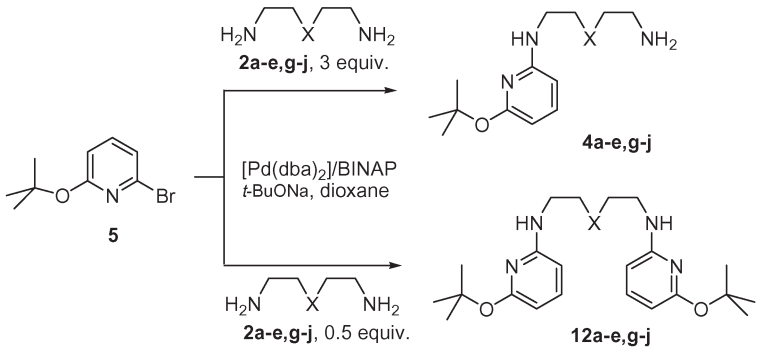
Entry	Amine	Hetaryl halide	$[Pd(dba)_2]$/BINAP	*c*, mol/l	Yield after chromatography %
1	**2d**	**8d**	7/7.5	0.05	**11d**, 14
2	**2e**	**7e**	10/14.5	0.01	**11e**, 16
3	**2e**	**8e**	18/18	0.017	**11e**, 38
4	**2i**	**8i**	8/9	0.025	**11i**, 39
5	**2e**	**8d**	7/7.5	0.05	**11k**, 19
6	**2b**	**8d**	7/7.5	0.05	**11l**, 11
7	**10e**	**1a**	13/14	0.025	**11e**, 49[a]
8	**10i**	**1a**	13/14	0.025	**11i**, 0[b]

[a] **3e** isolated in 17% yield. [b] **3i** isolated in 20% yield.

According to approach (*B*), we attempted an alternative synthesis of macrocycles **11**. Macrocycles **11e**, **11i** were chosen as target compounds for this synthetic route as they were obtained in higher yields by method (*A*). Compounds **10e**, **10i** obtained in situ and 2,6-dibromopyridine (**1a**) were reacted in equimolar amounts (Scheme 4) using the $Pd(dba)_2$ (13 mole %)/ BINAP (14 mole %) catalytic system, in boiling dioxane (0.025 mol/l); reflux was continued for several hours. The results of method (*B*) were different from those of method (*A*): while **11e** was isolated in 49% yield (Table III, entry 7), cyclodimer **11i** was recorded in small amounts only in the reaction mixture and could not be isolated by column chromatography. It should be noted that corresponding macrocycles **3e**, **3i** were isolated in 17 and 20% yields, respectively, from the reaction of 2,6-dibromopyridine with excess of polyamines **2e**, **2i** which was used for the synthesis of intermediates **10e**, **10i**.

Synthesis of Mono-, Di-, and Polyhetarylated Polyamines

We have specially studied the hetarylation of polyamines **2** with 2-bromo-6-*tert*-butoxypyridine (**5**) because the resulting hetarylated polyamines are of interest as polydentate ligands for metal ions. Compound **5** was reacted with 3 equiv. of corresponding amines **2a**–**2e**, **2g**–**2j** using 4 mole % of the catalytic system $Pd(dba)_2$/BINAP; in all cases the major product was **4a**–**4e**, **4g**–**4j** (Scheme 5).



a: X = NH
b: X = CH_2NHCH_2
c: X = $NH(CH_2)_2NH$
d: X = $NH(CH_2)_3NH$
e: X = $CH_2NH(CH_2)_2NHCH_2$
g: X = $NH(CH_2)_2NH(CH_2)_2NH$
h: X = $NH(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH$
i: X = $O(CH_2)_2O$
j: X = $CH_2O(CH_2)_2O(CH_2)_2OCH_2$

SCHEME 5

The reaction conditions and yields of the products are given in Table IV. When using a threefold excess of polyamine, the formation of dihetarylated by-products **12** is well supressed, only in the case of hexaamine derivative **4h** the ratio **4h**:**12h** is substantially higher due to better solubility of the desired product in water (entry 7; the yields given in Table IV after the standard H_2O/CH_2Cl_2 treatment to separate products **4** from the excess of polyamines). When using equimolar quantities of the starting compounds, almost equimolar amounts of **4e** and **12e** were isolated (entry 5). To ensure the synthesis of N^{α},N^{ω}-bis(6-*tert*-butoxypyridin-2-yl)-substituted polyamines **12** in good yields, we used 2–2.2 equiv. of **5** (Scheme 5). The data concerning the yields of target products are collected in Table V. In most cases, the yields of compounds **12** were high (Table V, entries 1–7, 8). In some cases the formation of trihetarylated products **13** in notable amounts was observed (entries 1, 3, 4, 6, 8). The hetarylation of only terminal pyridinyl-substituted nitrogen atom was observed in all these cases, even in the presence of other secondary amino groups like in compounds **13a**, **13c**, **13d**, **13g**. Trihetarylated compounds are easily distinguished by characteristic signals of methylene protons (δ_H 4.2–4.3 ppm) and pyridine protons (δ_H 6.2, 6.6, and 7.3 ppm) in the CH_2NPy_2 fragment, and also by the signals in MALDI-TOF spectra. While compound **12e** was formed in a high amount (entry 5), it could be isolated only in 25% yield after column chromatography. As for compound **12j**, it was also isolated in low yield (entry 9); the formation of 2,6-di-*tert*-butoxypyridine (**6**) in 43% suggests

TABLE IV
Synthesis of *N*-(6-*tert*-butoxypyridin-2-yl)-substituted polyamines **4a**–**4e**, **4g**–**4j** ($Pd(dba)_2$/BINAP 4/4.5 mole %, **1a**:**2** mole ratio 1:3)

Entry	Amine	Yield of **4**, %	Yield of **12**, %
1	**2a**	85	13
2	**2b**	83	17
3	**2c**	80	20
4	**2d**	83	17
5	**2e**[a]	(31)[b]	(29)
6	**2g**	76	13
7	**2h**	34	17
8	**2i**	(57)	
9	**2j**	(41)	(15)

[a] **1a**:**2e** mole ratio 1:1.1. [b] Yields after column chromatography are given in parentheses.

that trioxadiamine was either not enough stable or not enough reactive under these conditions.

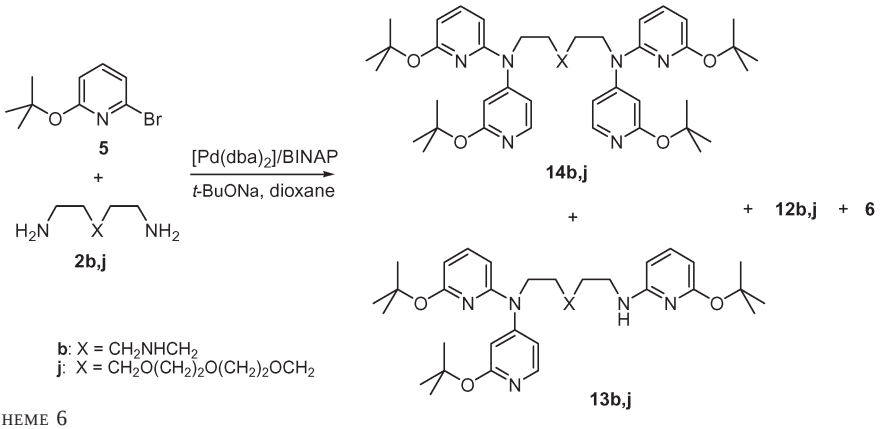
To investigate the scope and limitations of polyhetarylation of polyamines with bromopyridines, we have performed the synthesis of tetrahetaryl derivatives **14** using polyamines **2b**, **2j** and 4–6 equiv. of 2-bromo-6-*tert*-butoxypyridine (**5**) in the presenece of 4–6 mole % of the $Pd(dba)_2$/BINAP catalyst (Scheme 6). Under these conditions target tetrahetaryl compounds **14b**, **14j** were obtained in 10 and 16% yields, whereas trihetaryl derivatives **13b**, **13j** were obtained in 25 and 29% yields, and dihetaryl polyamines **12b**, **12j** in 31 and 16% yields, respectively. In both cases 2,6-di-*tert*-butoxypyridine (**6**) was obtained in substantial yields (54 and 45%).

This result can be explained by the fact that the catalytic substitution of the rest bromine atom with *tert*-butoxy group in compound **5** proceeds faster than the introduction of the second pyridyl substitutent at the nitrogen atom. Though it is known that BINAP generally suppresses *N*,*N*-dihetarylation process in monoamines unlike tris(*o*-tolyl)phosphane, the reactions of polyamines nevertheless require the use of BINAP as a ligand, and it was this ligand that promoted successful polyhetarylation of diamines using simple bromoarenes[17]. Possibly a further increase in the catalyst loading and use of greater excess of compound **5** helps to improve the result.

TABLE V
Synthesis of N^{α},N^{ω}-bis(6-*tert*-butoxypyridin-2-yl)-substituted polyamines **12a**–**12e**, **12g**–**12j** ($Pd(dba)_2$/BINAP 4/4.5 mole %, **1a**:**2** mole ratio 2:1)

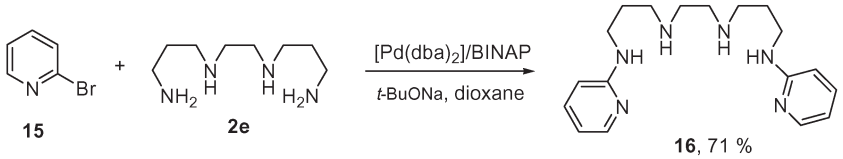
Entry	Amine	Yield of **12**, %	Yield of **13**, %
1	**2a**	90	10
2	**2b**	95(85)[a]	
3	**2c**	86	14
4	**2d**	85	4
5	**2e**	80(25)	
6	**2g**	80	20
7	**2h**	55	
8	**2i**	90(79)	10
9	**2j**	(22)	(3)[b]

[a] Yields after column chromatography are given in parentheses. [b] **6** was isolated in 43% yield, **14j** was isolated in 2% yield.



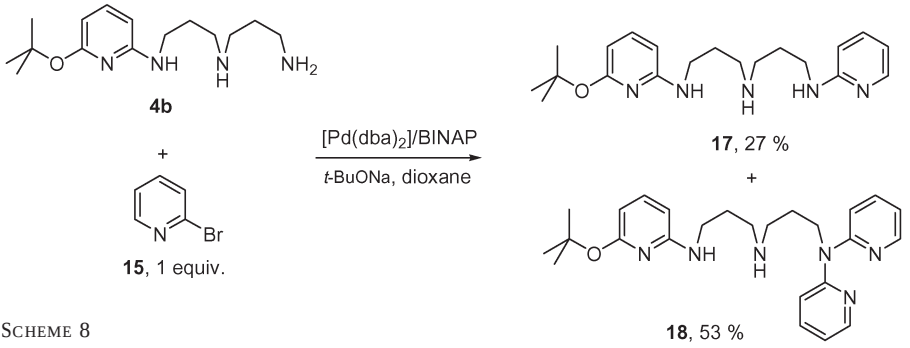
SCHEME 6

The reactivity of 2-bromo-6-*tert*-butoxypyridine (**5**) was low to provide polyamines tetrahetarylation, presumably due to unfavorable steric factor (*tert*-butoxy group). We decided to investigate the activity of sterically non-hindered 2-bromopyridine (**15**) in these reactions and to compare the results. The reaction of selected tetraamine **2e** with 2 equiv. of **15** proceeds smoothly to give the dihetarylated product **16** in 71% yield (Scheme 7).



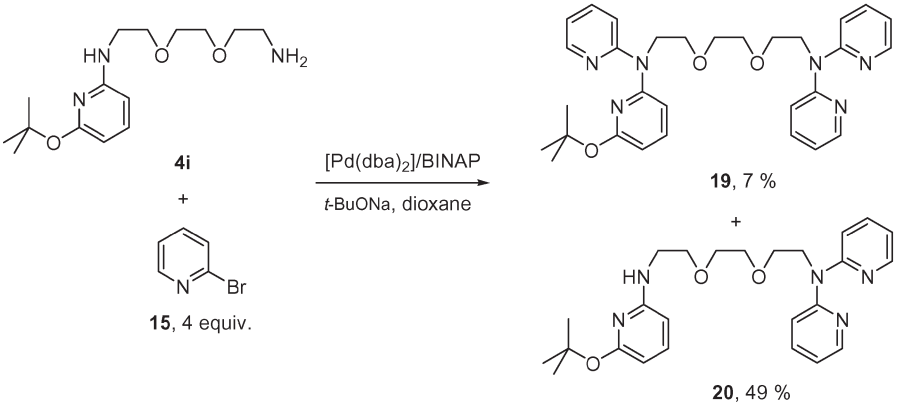
SCHEME 7

The result of the reaction of equimolar amounts of 2-bromopyridine (**15**) and monohetarylated triamine **4b** was more curious: while the target unsymmetrical N^1,N^3-dihetarylated derivative **17** was obtained in 27% yield, trihetarylated product **18** was isolated in 53% yield (Scheme 8).



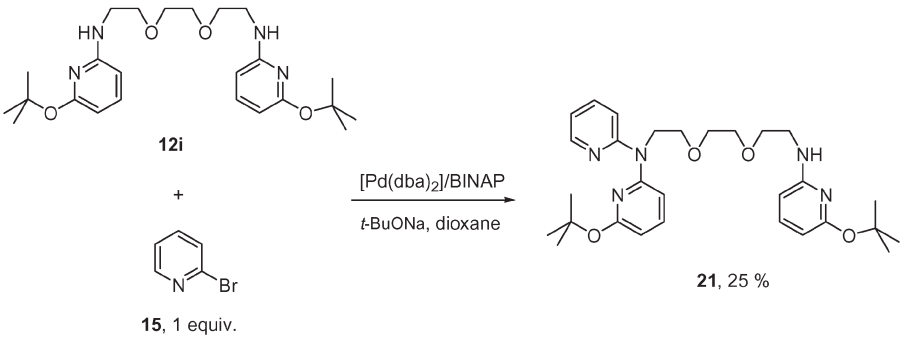
SCHEME 8

It is of importance that the second equiv. of **15** attacked only *N*-pyridyl and not *N*-(6-*tert*-butoxypyridyl) moiety. The experiment with the four-fold excess of 2-bromopyridine (**15**) showed that in this case trihetaryl derivative **20** was again the main product (49% yield), while tetrahetaryl dioxadiamine **19** was isolated only in 7% yield (Scheme 9).



SCHEME 9

The difficulty in obtaining compound **19** is due to steric hindrance caused by 6-*tert*-butoxypyridin-2-yl group. Trihetaryl derivative **21** (25% yield) was also obtained in the reaction of N^1,N^2-bis(6-*tert*-butoxypyridin-2-yl)-substituted dioxadiamine **12i** with 2-bromopyroidine (**15**) when the reagents were taken in equimolar amounts (Scheme 10).



SCHEME 10

However, the same reaction with the triamine and tetraamine dipyridyl derivatives **12b**–**12d** were unsuccessful, even with the use of excess **15**. This implies that the presence of both *tert*-butoxypyridinyl substituent and secondary amino groups of the CH_2NHCH_2 type in the reagents substan-

tially hinders the arylation reaction. Another conclusion can be derived that *N*,*N*-dihetarylation proceeds successfully only with a low conversion, and then it is seriously retarded. This explains both the fact that trihetarylated products were formed as by-products in the synthesis of N^{α},N^{ω}-dihetaryl species and that tetrahetaryl compounds were obtained in low yields even if an excess of bromopyridines **5** and **15** was used.

To sum up, we proposed a convenient one-pot catalytic method for the synthesis of pyridinyl-containing macrocycles, elaborated two alternative two-step approaches to cyclodimers containing two pyridine and two polyamine fragments, showed the possibilities of obtaining linear mono-, di- and polyhetaryl polyamines, found limitations of these reactions and studied the dependence of the yields of cyclic and linear products on the nature of starting polyamines.

EXPERIMENTAL

Starting compounds: 2,6-dibromopyridine (**1a**), 2,6-dichloropyridine (**1b**), 2-bromopyridine (**15**), polyamines **2a**–**2f**, **2i**, **2j**, sodium *tert*-butoxide, BINAP and other ligands mentioned in the text were purchased from Aldrich or Acros and used without additional purification. Pentaamine **2g** and hexaamine **2h** were purchased from Acros and purified by successive crystallizations of their monohydrates from toluene until their purity reached ca. 90%. Dioxane and ether were distilled over sodium hydroxide and sodium, dichloromethane and methanol were used freshly distilled. $[Pd(dba)_2]$ was synthesized from $PdCl_2$ according to a described procedure[20]. ^1H and ^{13}C NMR spectra were registered on a Bruker Avance-400 and Varian VXR-400 spectrometers in $CDCl_3$ (400 and 100.6 MHz, respectively), chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. MALDI-TOF mass spectra in the positive mode were taken with Bruker Reflex and Autoflex devices with 1,8,9-trihydroxyanthracene, 2,4,6-trihydroxyacetophenone and 3,5-dihydroxybenzoic acid as matrices. Mass spectra of positive ions obtained by electron impact (EI, 70 eV) were measured on a Kratos MS-30 instrument. IR spectra in KBr were recorded with an Ikar spectrometer, UV/VIS spectra in MeOH with a Hewlett–Packard HP 1524 spectrometer. Column chromatography was carried out using silica (Fluka, 40–60 mesh).

Typical Procedure for the Synthesis of Macrocycles **3a**–**3j**

A two-neck flask flushed with dry argon equipped with a magnetic stirrer and condenser was charged with absolute dioxane (in an amount to obtain 0.01–0.02 mol/l concentration of the reagents), appropriate amounts of $[Pd(dba)_2]$ (4–8 mole %), BINAP (6–12 mole %) and 1 equiv. of 2,6-dibromopyridine (**1a**), the mixture was stirred for several minutes, then 1 equiv. of polyamine **2** was added, followed by 3 equiv. of sodium *tert*-butoxide, and the reaction mixture was refluxed for 5–7 h (at 0.02 mol/l) or for 15 h (at 0.01 mol/l). Then the reaction mixture was cooled down to ambient temperature, one drop of water is added to neutralize excess of sodium *tert*-butoxide; the solution was filtered, evaporated in vacuum, and the residue was dissolved in 20 ml of dichloromethane. The solution was washed with 10 ml of water, and then aqueous phase was washed with dichloromethane (2 × 20 ml).

Combined organic layers were dried over anhydrous sodium sulfate, dichloromethane was evaporated in vacuum, and, after recording NMR spectra of the crude mixture, the residue was chromatographed on silica using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1.

2,5,8,13-Tetraazabicyclo[7.3.1]trideca-1(13),9,11-triene (**3a**). This compound was obtained from 2,6-dibromopyridine **1a** (0.5 mmol, 119 mg), triamine **2a** (0.5 mmol, 52 mg), in the presence of [Pd(dba)$_2$] (23 mg, 8 mole %) and BINAP (42 mg, 12 mole %), sodium *tert*-butoxide (1.5 mmol, 150 mg) in dioxane (50 ml). According to ^{1}H NMR spectrum of the reaction mixture, it contained 11% of the target macrocycle **3a**. ^{1}H NMR: 2.86 t, 4 H, J = 6.0; 3.32 t, 4 H, J = 6.0; 5.67 d, 2 H, J = 7.4; 7.05 t, 1 H, J = 7.4. (NH protons were not unambiguously assigned.) HRMS MALDI-TOF (*m/z*) for $C_9H_{14}N_4$ calculated: 179.1296 [M^+ + H]; found: 179.1301.

2,6,10,15-Tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene (**3b**). This compound was obtained from 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), triamine **2b** (0.5 mmol, 66 mg), in the presence of [Pd(dba)$_2$] (23 mg, 8 mole %) and BINAP (42 mg, 12 mole %), sodium *tert*-butoxide (1.5 mmol, 150 mg) in dioxane (50 ml). According to ^{1}H NMR spectrum of the reaction mixture, it contained 14% of the target macrocycle **3b**. ^{1}H NMR: 1.76 quintet, 4 H, J = 6.9; 2.77 t, 4 H, J = 6.9; 3.32 br s, 4 H; 5.67 d, 2 H, J = 7.4; 7.02 t, 1 H, J = 7.4. (NH protons were not unambiguously assigned.) ^{13}C NMR: 31.2, 2 C; 40.1, 2 C; 45.5, 2 C; 93.9, 2 C; 137.4, 1 C; 158.1, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{11}H_{18}N_4$ calculated: 207.1609 [M^+ + H]; found: 207.1610.

2,5,8,11,16-Pentaazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**3c**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1 mmol, 237 mg), tetraamine **2c** (1 mmol, 146 mg), in the presence of [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (42 mg, 6 mole %), sodium *tert*-butoxide (4 mmol, 400 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 9 mg (4%), yellowish oil. ^{1}H NMR: 2.39 br s, 2 H; 2.84 t, 4 H, J = 5.6; 2.85 s, 4 H; 3.53 q, 4 H, J = 5.3; 4.47 t, 2 H, J = 5.9; 5.65 d, 2 H, J = 7.9; 7.05 t, 1 H, J = 7.9. ^{13}C NMR: 39.8, 2 C; 50.7, 2 C; 52.7, 2 C; 96.2, 2 C; 136.5, 1 C; 158.2, 2 C. MS MALDI-TOF (*m/z*): 221.1 [M^+].

2,5,9,12,17-Pentaazabicyclo[11.3.1]heptadeca-1(17),13,15-triene (**3d**). This compound was obtained from 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), triamine **2d** (0.5 mmol, 80 mg), in the presence of [Pd(dba)$_2$] (12 mg, 4 mole %) and BINAP (21 mg, 6 mole %), sodium *tert*-butoxide (1.5 mmol, 150 mg) in dioxane (25 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 20 mg (17%), yellowish oil. ^{1}H NMR: 1.71 quintet, 2 H, J = 5.9; 2.77 t, 4 H, J = 5.6; 2.83 t, 4 H, J = 5.6; 3.61 t, 4 H, J = 5.8; 4.76 t, 2 H, J = 6.2; 5.67 d, 2 H, J = 7.9; 7.06 t, 1 H, J = 7.9. (2 NH protons were not unambiguously assigned.) ^{13}C NMR: 29.1, 1 C; 40.8, 2 C; 49.5, 2 C; 50.1, 2 C; 96.5, 2 C; 138.5, 1 C; 158.0, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{12}H_{21}N_5$ calculated: 236.1875 [M^+ + H]; found: 236.1850.

2,6,9,13,18-Pentaazabicyclo[12.3.1]octadeca-1(18),14,16-triene (**3e**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1 mmol, 237 mg), tetraamine **2e** (1 mmol, 174 mg), in the presence of [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (42 mg, 6 mole %), sodium *tert*-butoxide (4 mmol, 400 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 32 mg (13%), pale-yellow crystals, m.p. 71–73 °C. ^{1}H NMR: 1.71 quintet, 4 H, J = 5.4; 2.63 t, 4 H, J = 5.3; 2.68 s, 4 H; 3.37 q, 4 H, J = 5.2; 5.57 d, 2 H, J = 7.9; 7.14 t, 1 H, 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 30.2, 2 C; 40.5, 2 C; 47.4, 2 C; 49.3, 2 C; 94.0, 2 C; 138.7, 1 C; 158.8, 2 C. MS EI, *m/z* (rel.%): 249 (100) [M^+], 162 (63), 148 (33), 136 (85), 123 (50). IR: 3254, 2937, 2879, 1604, 1521, 1459, 1361, 1340, 1261, 1240,

1143, 1106, 775, 724, 700. UV/VIS: 252 (11 600), 320 (10 400). HRMS MALDI-TOF (*m/z*) for $C_{13}H_{23}N_5$ calculated: 250.2031 [M^+ + H]; found: 250.2029.

2,6,10,14,19-Pentaazabicyclo[13.3.1]nonadeca-1(19),15,17-triene (**3f**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1 mmol, 237 mg), tetraamine **2f** (1 mmol, 188 mg), in the presence of [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (42 mg, 6 mole %), sodium *tert*-butoxide (4 mmol, 400 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 78 mg (30%), pale-yellow crystals, m.p. 99–101 °C. ^{1}H NMR: 1.67 quintet, 2 H, *J* = 6.1; 1.74 quintet, 4 H, *J* = 5.9; 2.16 br s, 2 H; 2.72 t, 4 H, *J* = 5.6; 2.74 t, 4 H, *J* = 6.0; 3.37 t, 4 H, *J* = 6.7; 5.39 br s, 2 H; 5.59 d, 2 H, *J* = 7.8; 7.13 t, 1 H, *J* = 7.8. ^{13}C NMR: 29.1, 2 C; 29.3, 1 C; 40.5, 2 C; 47.9, 2 C; 48.0, 2 C; 94.5, 2 C; 138.5, 1 C; 158.3, 2 C. MS EI, *m/z* (rel.%): 263 (100) [M^+], 176 (34), 162 (59), 150 (76), 148 (67), 136 (84), 123 (57). IR: 3296, 2929, 2858, 1602, 1517, 1429, 1384, 1240, 1143, 775, 724.

2,5,8,11,14,19-Hexaazabicyclo[13.3.1]nonadeca-1(19),15,17-triene (**3g**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1 mmol, 237 mg), pentaamine **2g** (1 mmol, 189 mg), in the presence of [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (42 mg, 6 mole %), sodium *tert*-butoxide (4 mmol, 400 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 8 mg (3%), yellowish oil. ^{1}H NMR: 2.28 br s, 3 H; 2.70 br s, 4 H; 2.77 t, 4 H, *J* = 5.7; 2.83 t, 4 H, *J* = 6.6; 3.35 q, 4 H, *J* = 6.2; 4.69 t, 2 H, *J* = 5.4; 5.67 d, 2 H, *J* = 7.7; 7.13 t, 1 H, *J* = 7.7. ^{13}C NMR: 41.1, 2 C; 48.2, 2 C; 48.4, 2 C; 50.0, 2 C; 95.5, 2 C; 138.8, 1 C; 158.2, 2 C. MS MALDI-TOF (*m/z*): 265.3 [M^+ + H].

2,5,8,11,14,17,22-Heptaazabicyclo[16.3.1]docosa-1(22),18,20-triene (**3h**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1 mmol, 237 mg), hexaamine **2h** (1 mmol, 232 mg), in the presence of [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (42 mg, 6 mole %), sodium *tert*-butoxide (4 mmol, 400 mg) in dioxane (50 ml). According to ^{1}H NMR spectrum of the reaction mixture, it contained 10% of the product. ^{1}H NMR: 2.28 br s, 4 H; 2.64–2.84 m, 12 H; 2.37 br s, 4 H; 3.37 t, 4 H, *J* = 5.5; 4.62 br s, 2 H; 5.67 d, 2 H, *J* = 8.0; 7.14 t, 1 H, *J* = 8.0.

5,8-Dioxa-2,11,16-triazabicyclo[10.3.1]hexadeca-1(16),12,14-triene (**3i**). This compound was obtained from 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), dioxadiamine **2i** (0.5 mmol, 74 mg), in the presence of [Pd(dba)$_2$] (23 mg, 8 mole %) and BINAP (42 mg, 12 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH 10:1. Yield 9 mg (8%), yellowish oil. ^{1}H NMR: 3.51 br s, 4 H; 3.68 s, 4 H; 3.71 t, 4 H, *J* = 3.5; 4.41 br s, 2 H; 6.17 br s, 2 H; 7.11 t, 1 H, *J* = 7.9. ^{13}C NMR: 42.1, 2 C; 70.2, 2 C; 70.8, 2 C; 96.6, 2 C; 137.8, 1 C; 155.9, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{11}H_{17}N_3O_2$ calculated: 223.1321 [M^+]; found: 223.1327.

6,9,12-Trioxa-2,16,21-triazabicyclo[15.3.1]henicosa-1(21),17,19-triene (**3j**). This compound was obtained from 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), trioxadiamine **2j** (0.5 mmol, 110 mg), in the presence of [Pd(dba)$_2$] (23 mg, 8 mole %) and BINAP (42 mg, 12 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in dioxane (50 ml). Eluent CH_2Cl_2/MeOH 10:1. Yield 3 mg (2%), yellowish oil. ^{1}H NMR: 1.80 quintet, 4 H, *J* = 6.7; 3.44 q, 4 H, *J* = 6.7; 3.45–3.60 m, 12 H; 4.66 br s, 2 H; 5.62 d, 2 H, *J* = 7.9; 7.13 t, 1 H, *J* = 7.9. ^{13}C NMR: 29.0, 2 C; 38.7, 2 C; 68.6, 2 C; 69.0, 2 C; 70.0, 2 C; 93.5, 2 C; 137.3, 1 C; 157.5, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{15}H_{25}N_3O_3$ calculated: 295.1896 [M^+]; found: 295.1890.

2-Bromo-6-*tert*-butoxypyridine (**5**)

A two-neck flask flushed with dry argon, equipped with a condenser and magnetic stirrer, was charged with absolute dioxane (5 ml), 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), sodium *tert*-butoxide (1 mmol, 100 mg), and the reaction mixture was refluxed for 5 h. After cooling to ambient temperature, one drop of water was added, the solution was filtered and evaporated in vacuum. Yield 110 mg (96%), colorless liquid. ^{1}H NMR: 1.56 s, 9 H; 6.55 d, 1 H, *J* = 8.2; 6.95 d, 1 H, *J* = 7.4; 7.32 t, 1 H, *J* = 7.8. ^{13}C NMR: 28.4, 3 C; 80.8, 1 C; 111.4, 1 C; 119.4, 1 C; 137.6, 1 C; 139.5, 1 C; 162.9, 1 C. MS EI, *m/z* (rel.%): 231 (4) [M^+], 229 (4) [M^+], 216 (1), 214 (1), 176 (26), 175 (78), 174 (27), 173 (78), 158 (3), 156 (3), 147 (7), 145 (7), 94 (100).

2,6-Di-*tert*-butoxypyridine (**6**)

A two-neck flask flushed with dry argon, equipped with a condenser and magnetic stirrer, was charged with absolute dioxane (5 ml), 2,6-dibromopyridine (**1a**) (0.5 mmol, 119 mg), [Pd(dba)$_2$] (12 mg, 4 mole %), BINAP (20 mg, 6 mole %), sodium *tert*-butoxide (3 mmol, 300 mg), and the reaction mixture was refluxed for 7 h. After cooling to ambient temperature, one drop of water was added, the solution was filtered and evaporated in vacuum. Yield 105 mg (94%), colorless liquid. ^{1}H NMR: 1.55 s, 18 H; 6.24 d, 2 H, *J* = 7.9; 7.36 t, 1 H, *J* = 7.9. ^{13}C NMR: 28.8, 6 C; 78.7, 2 C; 105.4, 2 C; 140.0, 1 C; 162.0, 2 C. MS EI, *m/z* (rel.%): 223 (1) [M^+], 167 (3), 152 (3), 112 (9), 111 (100).

Typical Procedure for the Synthesis of *N*-(6-*tert*-Butoxypyridin-2-yl)-Substituted Polyamines **4a**–**4e**, **4g**–**4j**

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with absolute dioxane (taken in amount to obtain 0.1–0.2 mol/l concentration of the reagents), appropriate amounts of [Pd(dba)$_2$] (4 mole %), BINAP (4.5 mole %) and 1 equiv. of 2-bromo-6-*tert*-butoxypyridine (**5**), the mixture is stirred for several minutes, then 3 equiv. of polyamine **2** were added, followed by 1 equiv. of sodium *tert*-butoxide, and the reaction mixture was refluxed for 5–10 h. Then the reaction mixture was cooled down to ambient temperature, the solution was filtered, evaporated in vacuum, and the residue was dissolved in 20 ml of dichloromethane. The solution was washed with 10 ml of water, and then the water phase with dichloromethane (2 × 20 ml). Combined organic layers were dried over anhydrous sodium sulfate, dichloromethane was evaporated in vacuum and, after recording NMR spectra of the crude mixture, the residue was chromatographed on silica using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1. Alternatively, compounds **4** can be obtained as by-products in the synthesis of cyclodimers **3**.

N-(2-Aminoethyl)-N′-(6-tert-butoxypyridin-2-yl)ethane-1,2-diamine (**4a**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), triamine **2a** (3 mmol, 309 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 85%. Alternatively, it was obtained in the synthesis of **3a** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:1–100:20:2. Yield 6 mg (5%), yellowish oil. ^{1}H NMR: 1.53 s, 9 H; 2.00 br s, 3 H; 2.65 t, 2 H, *J* = 5.8; 2.76 t, 2 H, *J* = 5.7; 2.82 t, 2 H, *J* = 5.8; 3.35 br s, 2 H; 4.74 br s, 1 H; 5.91 d, 1 H, *J* = 8.1; 5.92 d, 1 H, *J* = 8.1; 7.23 t, 1 H. *J* = 8.1.

^{13}C NMR: 29.0, 3 C; 41.5, 1 C; 41.9, 1 C; 48.8, 1 C; 51.9, 1 C; 98.4, 1 C, 100.6, 1 C; 139.5, 1 C; 157.4, 1 C; 163.2, 1 C. MS MALDI-TOF (*m/z*): 253.1 [M^+ + H], 194.0 [$M^+ - C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{13}H_{24}N_4O$ calculated: 253.2028 [M^+ + H]; found: 253.1999.

N-(3-Aminopropyl)-N′-(6-tert-butoxypyridin-2-yl)propane-1,3-diamine (**4b**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), triamine **2b** (3 mmol, 393 mg), in the presence of $Pd(dba)_2$ (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 83%. Alternatively, it was obtained in the synthesis of **3b** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:2. Yield 19 mg (14%), yellowish oil. ^{1}H NMR: 1.54 s, 9 H; 1.62 quintet, 2 H, *J* = 7.0; 1.76 quintet, 2 H, *J* = 6.6; 2.66 t, 2 H, *J* = 6.8; 2.72 t, 2 H, *J* = 6.9; 2.75 t, 2 H, *J* = 6.9; 3.31 t, 2 H, *J* = 6.5; 4.82 br s, 1 H; 5.87 d, 1 H, *J* = 7.9; 5.92 d, 1 H, *J* = 7.8; 7.24 t, 1 H, *J* = 7.9. (3 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.6, 3 C; 29.3, 1 C; 33.2, 1 C; 40.1, 1 C; 40.6, 1 C; 47.5, 1 C; 47.9, 1 C; 78.2, 1 C; 97.8, 1 C; 99.8, 1 C; 140.0, 1 C; 157.2, 1 C; 162.8, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{15}H_{28}N_4O$ calculated: 280.2263 [M^+]; found: 280.2238.

N-(2-Aminoethyl)-N′-{2-[(6-tert-butoxypyridin-2-yl)amino]ethyl}ethane-1,2-diamine (**4c**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), tetraamine **2c** (3 mmol, 438 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 80%. Alternatively, it was obtained in the synthesis of **3c** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 100 mg (34%), yellowish oil. ^{1}H NMR: 1.53 s, 9 H; 1.88 br s, 4 H; 2.64 t, 2 H, *J* = 5.9; 2.72 s, 4 H; 2.77 t, 2 H, *J* = 5.8; 2.84 t, 2 H, *J* = 5.8; 3.35 t, 2 H, *J* = 4.7; 4.74 br s, 1 H; 5.91 d, 1 H, *J* = 7.6; 5.93 d, 1 H, *J* = 7.6; 7.23 t, 1 H, *J* = 7.6. ^{13}C NMR: 28.7, 3 C; 41.1, 1 C; 41.5, 1 C; 48.5, 1 C; 48.6, 1 C; 48.7, 1 C; 51.6, 1 C; 78.3, 1 C; 98.2, 1 C; 100.0, 1 C; 139.0, 1 C; 157.2, 1 C; 162.8, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{15}H_{29}N_5O$ calculated: 296.2450 [M^+ + H]; found: 296.2495.

N-(2-Aminoethyl)-N′-{2-[(6-tert-butoxypyridin-2-yl)amino]ethyl}propane-1,3-diamine (**4d**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), tetraamine **2d** (3 mmol, 480 mg), in the presence of [$Pd(dba)_2$**]** (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 83%. Alternatively, it was obtained in the synthesis of **3d** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 8 mg (10%), yellowish oil. ^{1}H NMR: 1.51 s, 9 H; 1.69 quintet, 2 H, *J* = 6.7; 2.31 br s, 4 H; 2.64 t, 2 H, *J* = 5.6; 2.68 t, 2 H, *J* = 6.6; 2.71 t, 2 H, *J* = 6.6; 2.77 t, 2 H, *J* = 5.8; 2.83 t, 2 H, *J* = 5.8; 3.36 q, 2 H, *J* = 6.3; 5.01 br s, 1 H; 5.90 d, 1 H, *J* = 7.8; 5.92 d, 1 H, *J* = 7.9; 7.21 t, 1 H, *J* = 7.9. ^{13}C NMR: 28.9, 3 C; 29.2, 1 C; 41.1, 1 C; 41.4, 1 C; 48.2, 2 C; 48.8, 1 C; 51.9, 1 C; 78.6, 1 C; 98.5, 1 C; 100.5, 1 C; 139.3, 1 C; 157.3, 1 C; 163.1, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{16}H_{31}N_5O$ calculated: 310.2607 [M^+ + H]; found: 310.2577.

N-{2-[(3-Aminopropyl)amino]ethyl}-N′-(6-tert-butoxypyridin-2-yl)propane-1,3-diamine (**4e**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (0.5 mmol, 117 mg), tetraamine **2e** (0.57 mmol, 100 mg), in the presence of [$Pd(dba)_2$] (12 mg, 4 mole %) and BINAP (18 mg, 5.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3, 10:3:1. Yield 50 mg (31%), yellowish oil. ^{1}H NMR: 1.53 s, 9 H; 1.63 quintet, 2 H, *J* = 6.7; 1.78 quintet, 2 H, *J* = 6.7; 2.11 br s, 4 H; 2.68 t, 2 H, *J* = 6.7; 2.72 s, 4 H; 2.73 t, 2 H, *J* = 6.7; 2.76 t, 2 H, *J* = 6.7; 3.31 t, *J* = 6.6; 4.75 br s, 1 H; 5.89 d, 1 H, *J* = 7.6; 5.91 d, 1 H, *J* = 7.6; 7.24 t, 1 H, *J* = 7.6. IR: 3290, 2929,

2844, 1591, 1488, 1453, 1449, 1357, 1326, 1237, 1151, 1140, 1036, 886, 783, 729. UV/VIS: 246 (8700), 302 (5300). HRMS MALDI-TOF (*m/z*) for $C_{17}H_{33}N_5O$ calculated: 324.2763 [M^+ + H]; found: 324.2780.

N-(3-Aminopropyl)-N′-(3-{[6-(1,1-dimethylethoxy)-2-pyridinyl]amino}propyl)-1,3-propanediamine (**4f**). This compound was obtained in the synthesis of **3f** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 20 mg (6%), yellowish oil. ^{1}H NMR: 1.53 s, 9 H; 1.68–1.80 m, 6 H; 2.66 t, 2 H, *J* = 7.0; 2.68–2.80 m, 8 H; 3.29 br s, 2 H; 5.87 d, 1 H, *J* = 8.2; 5.92 d, 1 H, *J* = 7.8; 7.23 t, 1 H, *J* = 8.0. (NH protons were not unambiguously assigned.) ^{13}C NMR: 29.1, 3 C; 29.2, 2 C; 29.6, 1 C; 40.5, 1 C; 47.9, 1 C; 48.0, 2 C; 48.1, 1 C; 48.5, 1 C; 78.5, 1 C; 98.0, 1 C; 100.2, 1 C; 139.4, 1 C; 158.2, 1 C.

N-(2-Aminoethyl)-N′-{2-[(2-{[6-(1,1-dimethylethoxy)pyridin-2-yl]amino}ethyl)amino]ethyl}-ethane-1,2-diamine (**4g**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), pentaamine **2g** (3 mmol, 567 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 76%. Alternatively, it was obtained in the synthesis of **3g** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 58 mg (17%), yellowish oil. ^{1}H NMR: 1.53 s, 9 H; 2.12 br s, 5 H; 2.48 t, 2 H, *J* = 5.8; 2.60–2.78 m, 10 H; 2.84 t, 2 H, *J* = 5.4; 3.36 t, 2 H, *J* = 5.6; 4.95 br s, 1 H; 5.93 d, 1 H, *J* = 7.6; 5.94 d, 1 H, *J* = 7.8; 7.24 t, 1 H, *J* = 7.7. ^{13}C NMR: 28.7, 3 C; 41.3, 1 C; 41.6, 1 C; 48.6, 1 C; 48.8, 1 C; 48.9, 1 C; 49.0, 2 C; 51.9, 1 C; 78.3, 1 C; 98.2, 1 C; 100.1, 1 C; 139.1, 1 C; 157.2, 1 C; 162.9, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{17}H_{34}N_6O$ calculated: 339.2872 [M^+ + H]; found: 339.2881.

N-(2-Aminoethyl)-N′-[2-({2-[(2-{[6-(1,1-dimethylethoxy)pyridin-2-yl]amino}ethyl)amino]ethyl}-amino)ethyl]ethane-1,2-diamine (**4h**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (1 mmol, 230 mg), hexaamine **2h** (3 mmol, 696 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 34%. Alternatively, it was obtained in the synthesis of **3g** as a by-product. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 5 mg (1.5%), yellowish oil. ^{1}H NMR: 1.52 s, 9 H; 2.07 br s, 6 H; 2.46 t, 2 H, *J* = 7.1; 2.61–2.79 m, 14 H; 2.83 t, 2 H, *J* = 7.2; 3.35 br s, 2 H; 4.84 br s, 1 H; 5.90 d, 1 H, *J* = 7.9; 5.92 d, 1 H, *J* = 7.8; 7.22 t, 1 H, *J* = 7.9. ^{13}C NMR: 28.7, 3 C; 41.1, 1 C; 41.5, 1 C; 48.5, 1 C; 48.6, 1 C; 48.7, 1 C; 48.8, 3 C; 48.9, 1 C; 52.9, 1 C; 78.3, 1 C; 98.2, 1 C; 100.1, 1 C; 139.0, 1 C; 157.2, 1 C; 162.8, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{19}H_{39}N_7O$ calculated: 382.3294 [M^+ + H]; found: 382.3297.

N-{2-[2-(2-Aminoethoxy)ethoxy]ethyl}-6-(1,1-dimethylethoxy)pyridin-2-amine (**4i**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (0.75 mmol, 173 mg), dioxadiamine **2i** (2.25 mmol, 333 mg), in the presence of [$Pd(dba)_2$] (18 mg, 4 mole %) and BINAP (21 mg, 4.5 mole %), sodium *tert*-butoxide (0.75 mmol, 73 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH 25:1, 10:1. Yield 126 mg (57%), yellowish oil. ^{1}H NMR: 1.52 s, 9 H; 2.39 br s, 2 H; 2.86 t, 2 H, *J* = 5.2; 3.46 t, 2 H, *J* = 5.2; 3.50 t, 2 H, *J* = 5.2; 3.61 s, 4 H; 3.66 t, 2 H, *J* = 5.3; 4.82 br s, 1 H; 5.92 d, 1 H, *J* = 7.8; 5.93 d, 1 H, *J* = 8.1; 7.23 t, 1 H, *J* = 8.0. ^{13}C NMR: 28.9, 3 C; 41.4, 1 C; 41.7, 1 C; 70.1, 1 C; 70.2, 1 C; 70.3, 1 C; 72.7, 1 C; 78.6, 1 C; 98.7, 1 C; 100.6, 1 C; 139.4, 1 C; 157.2, 1 C; 163.1, 1 C. MS MALDI-TOF (*m/z*): 298.0 [M^+ + H], 241.9 [$M^+ - C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{15}H_{27}N_3O_2$ calculated: 298.2130 [M^+ + H]; found: 298.2075.

N-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-6-(1,1-dimethylethoxy)pyridin-2-amine (**4j**). This compound was obtained from 2-bromo-6-*tert*-butoxypyridine (**5**) (0.75 mmol, 173 mg),

trioxadiamine **2j** (2.25 mmol, 495 mg), in the presence of [Pd(dba)$_2$] (18 mg, 4 mole %) and BINAP (21 mg, 4.5 mole %), sodium *tert*-butoxide (0.75 mmol, 73 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH 25:1, 10:1. Yield 113 mg (41%), yellowish oil. ^{1}H NMR: 1.50 s, 9 H; 1.74 quintet, 2 H, *J* = 6.3; 1.83 quintet, 2 H, *J* = 6.3; 2.83 t, 2 H, *J* = 6.7; 3.31 t, 2 H, *J* = 6.5; 3.51 t, 2 H, *J* = 5.8; 3.53–3.60 m, 10 H; 3.63 br s, 2 H; 4.80 br s, 1 H; 5.86 d, 1 H, *J* = 7.9; 5.88 d, 1 H, *J* = 7.8; 7.19 t, 1 H, *J* = 7.9. ^{13}C NMR: 28.9, 3 C; 29.2, 1 C; 31.1, 1 C; 39.1, 1 C; 39.6, 1 C; 69.3, 1 C; 69.4, 1 C; 69.9, 1 C; 70.0, 1 C; 70.3, 1 C; 70.4, 1 C; 78.5, 1 C; 98.2, 1 C; 100.1, 1 C; 139.2, 1 C; 157.2, 1 C; 163.0, 1 C. MS MALDI-TOF (*m/z*): 369.4 [M$^+$].

Typical Procedure for the Synthesis of N^{α},N^{ω}-Bis(6-halopyridin-2-yl)-polyamines **7e**, **8d**, **8e**, **8i** and **9e**

A two-neck flask equipped with a magnetic stirrer and condenser and flushed with dry argon was charged with absolute dioxane (taken in an amount to obtain 0.1 mol/l concentration of polyamine), appropriate amounts of [Pd(dba)$_2$] (4 mole %), BINAP (4.5 mole %) and 3 equiv. of 2,6-dihalopyridines **1a**, **1b**. The mixture was stirred for several minutes. Then 1 equiv. of polyamine **2** was added, followed by 2 equiv. of sodium *tert*-butoxide, and the reaction mixture was refluxed for 3–6 h. Then the reaction was cooled to ambient temperature, the solution was filtered, evaporated in vacuum and, after recording NMR spectra of the crude mixture, the residue was chromatographed on silica using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1.

N^1,$N^{1'}$-(Ethane-1,2-diyl)bis[N^3-(6-bromopyridin-2-yl)propane-1,3-diamine] (**7e**). This compound was obtained from 2,6-dibromopyridine (**1a**) (1.5 mmol, 356 mg), tetraamine **2e** (0.5 mmol, 87 mg), in the presence of Pd(dba)$_2$ (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg), in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:1, 100:20:2. Yield 69 mg (28%), yellowish oil. ^{1}H NMR: 1.77 quintet, 4 H, *J* = 6.3; 2.02 br s, 2 H; 2.73 s, 4 H; 2.74 s, 4 H, *J* = 6.3; 3.32 br s, 4 H; 5.37 br s, 2 H; 6.25 d, 2 H, *J* = 8.1; 6.66 d, 2 H, *J* = 7.4; 7.19 t, 2 H, *J* = 7.8. ^{13}C NMR: 29.2, 2 C; 40.8, 2 C; 47.7, 2 C; 49.1, 2 C; 104.5, 2 C; 115.2, 2 C; 139.2, 2 C; 140.2, 2 C; 158.8, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{18}H_{26}Br_2N_6$ calculated: 485.0664 [M$^+$ + H]; found: 485.0651.

N^1,$N^{1'}$-(Ethane-1,2-diyl)bis[N^3-(6-chloropyridin-2-yl)propane-1,3-diamine] (**8e**). This compound was obtained from 2,6-dichloropyridine (**1b**) (1.5 mmol, 222 mg), tetraamine **2e** (0.5 mmol, 87 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg), in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:1, 100:20:2. Yield 85 mg (43%), yellowish oil. ^{1}H NMR: 1.72 quintet, 4 H, *J* = 6.4; 2.67 c, 4 H; 2.68 t, 4 H, *J* = 6.2; 3.29 q, 2 H, *J* = 5.6; 5.42 br s, 2 H; 6.18 d, 2 H, *J* = 8.1; 6.46 d, 2 H, *J* = 7.5; 7.25 t, 2 H, *J* = 7.8. (2 NH protons were not unambiguously assigned) UV/VIS: 246 (23 500), 308 (9400). HRMS MALDI-TOF (*m/z*) for $C_{18}H_{26}Cl_2N_6$ calculated: 397.1674 [M$^+$ + H]; found: 397.1650.

N-{2-[(3-Aminopropyl)amino]ethyl}-N′-(6-chloropyridin-2-yl)propane-1,3-diamine (**9e**). This compound was obtained as the second compound in the synthesis of **8e**. Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 68 mg (48%), yellowish oil. ^{1}H NMR: 1.62 quintet, 2 H, *J* = 6.5; 1.74 quintet, 2 H, *J* = 6.2; 2.65 t, 2 H, *J* = 6.9; 2.69 m, 6 H; 2.75 t, 2 H, *J* = 6.5; 3.28 br s, 2 H; 3.52 br s, 4 H; 5.52 br s, 1 H; 6.21 d, 1 H, *J* = 8.1; 6.47 d, 1 H, *J* = 7.4; 7.27 t, 1 H, *J* = 7.8. ^{13}C NMR: 29.2, 1 C; 33.4, 1 C; 40.4, 1 C; 40.7, 1 C; 47.7, 2 C; 49.3, 2 C; 104.3, 1 C; 111.3, 1 C; 139.4, 1 C; 149.5, 1 C; 158.9, 1 C. UV/VIS: 248 (20 600), 310 (7800). HRMS MALDI-TOF (*m/z*) for $C_{13}H_{24}ClN_5$ calculated: 286.1798 [M$^+$ + H]; found: 286.1802.

N^1,$N^{1'}$-(Propane-1,3-diyl)bis[N^2-(6-chloropyridin-2-yl)ethane-1,2-diamine] (**8d**). This compound was obtained from 2,6-dichloropyridine (**1b**) (5.4 mmol, 801 mg), tetraamine **2d** (1.5 mmol, 240 mg), in the presence of [$Pd(dba)_2$] (46 mg, 2.5 mole %) and BINAP (55 mg, 3 mole %), sodium *tert*-butoxide (3 mmol, 300 mg), in absolute dioxane (10 ml). The yield was 43% in the reaction mixture. ^{1}H NMR: 1.63 quintet, 2 H, *J* = 6.9; 2.67 t, 2 H, 4 H, *J* = 6.7; 2.82 t, 4 H, *J* = 5.7; 3.33 q, 4 H, *J* = 5.6; 6.25 d, 2 H, *J* = 8.4; 6.52 d, 2 H, *J* = 7.9; 7.29 t, 2 H, *J* = 8.1. (NH protons were not unambiguously assigned.) ^{13}C NMR: 30.0, 1 C; 41.4, 2 C; 47.9, 2 C; 48.3, 2 C; 104.6, 2 C; 111.4, 2 C; 139.4, 2 C; 149.4, 2 C; 158.8, 2 C. HRMS MALDI-TOF (*m*/*z*) for $C_{17}H_{24}Cl_2N_6$ calculated: 383.1518 [M^+ + H]; found: 383.1520.

N,N′-{2,2′-[ethane-1,2-diylbis(oxy)]bis(ethane-2,1-diyl)}bis(6-chloropyridin-2-amine) (**8i**). This compound was obtained from 2,6-dichloropyridine (**1b**) (1.5 mmol, 222 mg), dioxadiamine **2i** (0.5 mmol, 74 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg), in absolute dioxane (5 ml). The yield was 50% in the reaction mixture. ^{1}H NMR: 3.40–3.90 m, 12 H; 6.22 d, 2 H, *J* = 8.2; 6.52 d, 2 H, *J* = 7.6; 7.28 t, 2 H, *J* = 7.9. (NH protons were not unambiguously assigned.)

Typical Procedure for the Synthesis of 2,6-Bis(polyamine)-Substituted Polyamines **10a**–**10e**, **10g**–**10j**

A two-neck flask equipped with a magnetic stirrer and condenser, flushed with dry argon, was charged with absolute dioxane (taken in an amount to obtain the 0.2–0.04 mol/l concentration of 2,6-dibromopyridine), appropriate amounts of [$Pd(dba)_2$] (4–8 mole %), BINAP (4.5–9 mole %) and 1 equiv. of 2,6-dibromopyridine (**1a**), the mixture was stirred for several minutes, then 4–6 equiv. of polyamine **2** was added, followed by 2 equiv. of sodium *tert*-butoxide, and the reaction mixture was refluxed for 2–5 h. Then the reaction was cooled to ambient temperature, the solution was filtered, evaporated in vacuum and, after recording NMR spectra of the crude mixture, the residue can be treated with CH_2Cl_2/H_2O as described above and/or chromatographed on silica using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1. The residue can be also dissolved in dichloromethane (20 ml), then treated with 20 ml of conc. HCl, the acid layer treated with aqueous KOH or NaOH solution to adjust pH 10 and then the aqueous phase was extracted with dichloromethane (3 × 20 ml). Combined organic phases were dried over anhydrous sodium sulfate, the solvent was evaporated in vacuum and the residue analyzed by NMR. In ^{1}H NMR spectra of compounds **10**, pyridine ring signals often give a complicated picture: instead of one doublet and one triplet, a set of close doublets and triplets are observed, with the same coupling constants, but of different intensities. The patterns depend on the concentration and on the amount of free polyamines. For the sake of clarity we give the data for the biggest signals in said sets of signals.

N^1,$N^{1'}$-(Pyridine-2,6-diyl)bis[N^2-(2-aminoethyl)ethane-1,2-diamine] (**10a**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), triamine **2a** (2 mmol, 206 mg), in the presence of [$Pd(dba)_2$] (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (12 ml). The yield in the reaction mixture was 72%. ^{1}H NMR: 2.65 t, 4 H, *J* = 5.7; 2.78 t, 4 H, *J* = 5.9; 2.82 t, 4 H, *J* = 5.4; 3.31 t, 4 H, *J* = 5.4; 5.71 d, 2 H, *J* = 8.0; 7.20 t, 1 H, *J* = 8.0. (NH protons were not unambiguously assigned.) ^{13}C NMR: 41.2, 2 C; 41.3, 2 C; 48.3, 2 C; 51.6, 2 C; 94.1, 2 C; 138.2,1 C; 157.8, 2 C. HRMS MALDI-TOF (*m*/*z*) for $C_{13}H_{27}N_7$ calculated: 282.2406 [M^+ + H]; found: 282.2400.

When using 2,6-dibromopyridine (1 mmol, 237 mg), triamine **2a** (4 mmol, 412 mg), in the presence of $[Pd(dba)_2]$ (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in absolute dioxane (10 ml), the yield of **10a** in the reaction mixture was 60%. The actual yield of *N*-(2-aminoethyl)-*N′*-(6-bromopyridin-2-yl)ethane-1,2-diamine was 11%. ^{1}H NMR: 2.62 t, 2 H, *J* = 5.3; 2.74 t, 2 H, *J* = 5.6; 2.79 t, 2 H, *J* = 5.0; 3.29 t, 2 H, *J* = 5.3; 6.26 d, 1 H, *J* = 8.3; 6.64 d, 1 H, *J* = 7.5; 7.15 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 41.7, 1 C; 48.2, 1 C; 48.6, 1 C; 51.9, 1 C; 105.0, 1 C; 115.3, 1 C; 139.2, 1 C; 140.1, 1 C; 158.9, 1 C.

N^1,$N^{1'}$-(Pyridine-2,6-diyl)bis[N^3-(3-aminopropyl)propane-1,3-diamine] (**10b**). This compound was obtained from 2,6-dibromopyridine (1 mmol, 237 mg), triamine **2b** (4 mmol, 524 mg), in the presence of $[Pd(dba)_2]$ (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in absolute dioxane (10 ml). The yield in the reaction mixture was 82%. After treatment with CH_2Cl_2/aqHCl the yield was 25%. ^{1}H NMR: 1.59 quintet, 4 H, *J* = 7.0; 1.72 quintet, 4 H, *J* = 6.5; 2.62 t, 4 H, *J* = 7.0; 2.67 t, 4 H, *J* = 6.9; 2.70 t, 4 H, *J* = 6.7; 3.22 t, 4 H, *J* = 6.2; 5.64 d, 2 H, *J* = 7.9; 7.16 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 29.2, 2 C; 33.2, 2 C; 39.8, 2 C; 40.0, 2 C; 47.2, 2 C; 47.4, 2 C; 93.7, 2 C; 138.2, 1 C; 157.8, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{17}H_{35}N_7$ calculated: 338.3032 [M^+ + H]; found: 338.2999.

N^1,$N^{1'}$-{2,2′-[Pyridine-2,6-diylbis(azanediyl)]bis(ethane-2,1-diyl)}bis[N^2-(2-aminoethyl)ethane-1,2-diamine] (**10c**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), tetraamine **2c** (2 mmol, 292 mg), in the presence of $[Pd(dba)_2]$ (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (12 ml). The yield in the reaction mixture was 42%. ^{1}H NMR: 2.59 t, 4 H, *J* = 5.9; 2.66 s, 8 H; 2.71 t, 4 H, *J* = 5.7; 2.76 t, 4 H, *J* = 5.9; 3.25 t, 4 H, *J* = 5.9; 5.65 d, 2 H, *J* = 8.0; 7.13 t, 1 H, *J* = 8.0. (NH protons were not unambiguously assigned.)

N^1,$N^{1'}$-{2,2′-[Pyridine-2,6-diylbis(azanediyl)]bis(ethane-2,1-diyl)}bis[N^3-(2-aminoethyl)propane-1,3-diamine] (**10d**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), tetraamine **2d** (2 mmol, 320 mg), in the presence of $[Pd(dba)_2]$ (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (12 ml). The yield in the reaction mixture was 54%. After treatment with CH_2Cl_2/H_2O 3:1, the yield was 6%. ^{1}H NMR: 1.56 quintet, 4 H, *J* = 7.0; 2.52–2.60 m, 8 H; 2.61 t, 4 H, *J* = 6.1; 2.67 t, 4 H, *J* = 5.7; 2.71 t, 4 H, *J* = 5.9; 3.21 t, 4 H, *J* = 5.7; 5.62 d, 2 H, *J* = 7.9; 7.09 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 29.6, 2 C; 41.0, 2 C; 41.1, 2 C; 47.5, 2 C; 47.6, 2 C; 48.4, 2 C; 51.9, 2 C; 94.0, 2 C; 138.1, 1 C; 157.8, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{19}H_{41}N_9$ calculated: 396.3563 [M^+ + H]; found: 396.3558.

N^1,$N^{1'}$-(Pyridine-2,6-diyl)bis(N^3-{2-[(3-aminopropyl)amino]ethyl}propane-1,3-diamine) (**10e**). This compound was obtained from 2,6-dibromopyridine (1 mmol, 237 mg), tetraamine **2e** (6 mmol, 1.044 g), in the presence of $[Pd(dba)_2]$ (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 91%. Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 133 mg of the 1:1 mixture of **10e** with **2e** (22%), yellowish oil. ^{1}H NMR: 1.57 quintet, 4 H, *J* = 7.0; 1.70 quintet, 4 H, *J* = 6.7; 2.61 t, 4 H, *J* = 7.0; 2.65 s, 8 H; 2.68 t, 4 H, *J* = 7.0; 2.69 t, 4 H, *J* = 6.9; 3.20 t, 4 H, *J* = 6.7; 5.62 d, 2 H, *J* = 7.9; 7.14 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 29.2, 2 C; 32.9, 2 C; 39.9, 2 C; 40.0, 2 C; 47.2, 4 C; 48.9, 4 C; 93.7, 2 C; 138.2, 1 C; 157.5, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{21}H_{45}N_9$ calculated: 424.3876 [M^+ + H]; found: 424.3867.

N^1,$N^{1'}$-(2,2′-{2,2′-[Pyridine-2,6-diylbis(azanediyl)]bis(ethane-2,1-diyl)}bis(azanediyl)bis(ethane-2,1-diyl))bis[N^2-(2-aminoethyl)ethane-1,2-diamine] (**10g**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), pentaamine **2g** (2 mmol, 378 mg), in the presence of [Pd(dba)$_2$] (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (12 ml). The yield in the reaction mixture was 46%. ^{1}H NMR: 2.61 t, 4 H, *J* = 6.0; 2.68 s, 16 H; 2.73 t, 4 H, *J* = 5.9; 2.81 br s, 4 H; 3.28 br s, 4 H; 5.67 d, 2 H, *J* = 7.9; 7.15 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.)

N^1,$N^{1'}$-[2,2′-(2,2′-{2,2′-[Pyridine-2,6-diylbis(azanediyl)]bis(ethane-2,1-diyl)}bis(azanediyl)bis(ethane-2,1-diyl))bis(azanediyl)bis(ethane-2,1-diyl)]bis[N^2-(2-aminoethyl)ethane-1,2-diamine] (**10h**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), hexaamine **2h** (2 mmol, 464 mg), in the presence of [Pd(dba)$_2$] (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (12 ml). The yield in the reaction mixture was 50%. ^{1}H NMR: 2.61 t, 4 H, *J* = 6.0; 2.68 s, 24 H; 2.74 t, 4 H, *J* = 6.0; 2.82 t, 4 H, *J* = 5.8; 3.27 t, 4 H, *J* = 5.7; 5.69 d, 2 H, *J* = 8.0; 7.15 t, 1 H, *J* = 8.0. (NH protons were not unambiguously assigned.)

N,N′-Bis{2-[2-(2-aminoethoxy)ethoxy]ethyl}pyridine-2,6-diamine (**10i**). This compound was obtained from 2,6-dibromopyridine (1 mmol, 237 mg), dioxadiamine **2i** (3 mmol, 222 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 80%. ^{1}H NMR: 2.82 t, 4 H, *J* = 5.3; 3.38 t, 4 H, *J* = 5.6; 3.47 t, 4 H, *J* = 5.2; 3.58 s, 8 H; 3.62 t, 4 H, *J* = 5.6; 5.62–5.68 m, 2 H; 7.10–7.16 m, 1 H. (NH protons were not unambiguously assigned.) ^{13}C NMR: 40.8, 4 C; 69.3, 4 C; 72.5, 4 C; 94.2, 2 C; 138.8, 1 C; 157.3, 2 C.

N^2,N^6-Bis(3-{2-[2-(3-aminopropoxy)ethoxy]ethoxy}propyl)pyridine-2,6-diamine (**10j**). This compound was obtained from 2,6-dibromopyridine (0.5 mmol, 119 mg), trioxadiamine **2j** (2 mmol, 440 mg), in the presence of [Pd(dba)$_2$] (12 mg, 4 mole %) and BINAP (20 mg, 6 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 64%. ^{1}H NMR: 1.67 quintet, 4 H, *J* = 6.5; 1.80 quintet, 4 H, *J* = 6.2; 2.72 t, 4 H, *J* = 6.7; 3.24 t, 4 H, *J* = 5.7; 3.46–3.62 m, 24 H; 5.63 d, 2 H, *J* = 7.9; 7.13 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 28.7, 2 C; 32.5, 2 C; 38.6, 4 C; 68.6, 4 C; 69.3, 4 C; 69.7, 4 C; 93.4, 2 C; 137.7, 1 C; 157.5, 2 C. HRMS MALDI-TOF (*m*/*z*) for $C_{25}H_{49}N_5O_6$ calculated: 516.3716 [M^+ + H]; found: 516.3714.

Typical Procedure for the Synthesis of Cyclodimers **11d**, **11e**, **11i**–**11l**

Method (*A*). A two-neck flask equipped with a magnetic stirrer and a condenser, flushed with dry argon, was charged with [Pd(dba)$_2$] (7–18 mole %) and BINAP (7.5–18 mole %) in absolute dioxane (taken in an amount to obtain the 0.01–0.05 mol/l concentration of starting compounds) equimolar amounts of N^{α},N^{ω}-bis(6-halopyridin-2-yl)-substituted polyamines **7e**, **8d**, **8e**, **8i**, appropriate polyamine **2**, 2 equiv. of sodium *tert*-butoxide, and the reaction mixture was refluxed for 5–10 h. After cooling to ambient temperature and evaporation of the solvent, the residue was chromatographed on silica using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1.

2,5,9,12,18,21,25,28,33,34-Decaazatricyclo[27.3.1.1^{13,17}]tetratriaconta-1(33),13(34),14,16,29,31-hexaene (**11d**)

Method (*A*). **11d** was obtained from the in situ obtained **8d** (0.6 mmol, 230 mg), tetraamine **2d** (0.6 mmol, 96 mg), in the presence of [Pd(dba)$_2$] (23 mg, 7 mole %) and BINAP (28 mg, 7.5 mole %), sodium *tert*-butoxide (1.2 mmol, 120 mg) in absolute dioxane (12 ml).

Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 39 mg (14%), yellow oil. ^{1}H NMR: 1.62 quintet, 4 H, *J* = 6.9; 2.64 t, 8 H, *J* = 6.8; 2.74 br s, 8 H; 3.26 br s, 8 H; 5.65 d, 4 H, *J* = 7.8; 7.18 t, 2 H, *J* = 7.8. (NH protons were not unambiguously assigned.) ^{13}C NMR: 30.0, 2 C; 41.6, 4 C; 48.0, 4 C; 48.9, 4 C; 94.5, 4 C; 138.3, 2 C; 158.2, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{24}H_{42}N_{10}$ calculated: 471.3672 [M^+ + H]; found: 471.3624.

2,6,9,13,19,23,26,30,35,36-Decaazatricyclo[29.3.1.1^{14,18}]hexatriaconta-1(35),14(36),15,17,31,33-hexaene (**11e**)

Method (*A*). **11e** was obtained from **7e** (0.103 mmol, 50 mg), tetraamine **2e** (0.1 mmol, 17 mg), in the presence of [Pd(dba)$_2$] (6 mg, 10 mole %) and BINAP (9 mg, 14.5 mole %), sodium *tert*-butoxide (0.25 mmol, 24 mg) in absolute dioxane (10 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 8 mg (16%), yellow oil.

From **8e** (0.174 mmol, 69 mg), tetraamine **2e** (0.17 mmol, 30 mg), in the presence of [Pd(dba)$_2$] (18 mg, 18 mole %) and BINAP (20 mg, 18 mole %), sodium *tert*-butoxide (0.36 mmol, 34 mg) in absolute dioxane (10 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 33 mg (38%), yellow oil.

Method (*B*). From the in situ obtained **10e** (0.45 mmol, 190 mg), 2,6-dibromopyridine (**1a**) (1.5 mmol, 357 mg), in the presence of [Pd(dba)$_2$] (33 mg, 13 mole %) and BINAP (39 mg, 14 mole %), sodium *tert*-butoxide (3.5 mmol, 350 mg) in absolute dioxane (17 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 123 mg (49%), yellow oil. ^{1}H NMR: 1.73 quintet, 8 H, *J* = 6.3; 2.70 t, 8 H, *J* = 6.2; 2.71 s, 8 H; 3.25 t, 8 H, *J* = 6.4; 4.29 br s, 4 H; 5.64 d, 4 H, *J* = 7.9; 7.16 t, 2 H, *J* = 7.9. (4 NH protons were not unambiguously assigned.) ^{13}C NMR: 29.3, 4 C; 40.7, 4 C; 47.6, 4 C; 48.8, 4 C; 94.1, 4 C; 138.9, 2 C; 158.4, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{26}H_{46}N_{10}$ calculated: 499.3985 [M^+ + H]; found: 499.3995.

5,8,20,23-Tetraoxa-2,11,17,26,31,32-hexaazatricyclo[25.3.1.1^{12,16}]dotriaconta-1(31),12(32),13,15,27,29-hexaene (**11i**)

Method (*A*). **11i** was prepared from in situ obtained **8i** (0.5 mmol, 185 mg), dioxadiamine **2i** (1.5 mmol, 222 mg), in the presence of [Pd(dba)$_2$] (24 mg, 8 mole %) and BINAP (28 mg, 9 mole %), sodium *tert*-butoxide (2 mmol, 200 mg) in absolute dioxane (20 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 87 mg (39%), yellow oil. Also obtained as a by-product in the synthesis of **3i**. Yield 20 mg (9%). ^{1}H NMR: 3.50 m, 8 H; 3.55–3.80 m, 16 H; 3.88 t, 2 H, *J* = 6.4; 4.37 t, 2 H, *J* = 6.6; 5.92 d, 1 H, *J* = 7.4; 5.93 d, 1 H, *J* = 7.5; 6.39 d, 1 H, *J* = 7.9; 6.47 d, 1 H, *J* = 7.9; 7.17 t, 1 H, *J* = 7.9; 7.21 t, *J* = 7.9. ^{13}C NMR: 41.6, 2 C; 42.1, 1 C; 47.8, 1 C; 69.9, 1 C; 70.1, 1 C; 70.3, 3 C; 70.9, 3 C; 99.2, 1 C; 100.7, 1 C; 102.5, 1 C; 102.9, 1 C; 137.8, 1 C; 138.4, 1 C; 156.0, 2 C; 158.0, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{22}H_{34}N_6O_4$ calculated: 446.2642 [M^+]; found: 446.2689.

6,8,11,25,28,31-Hexaoxa-2,15,21,35,40,41-hexaazatricyclo[34.3.1.1^{16,20}]hentetraconta-1(40),16(41),17,19,36,38-hexaene (**11j**). This compound was obtained as a by-product in the synthesis of **3j**. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:3. Yield 25 mg (8%), yellow oil. ^{1}H NMR: 1.70 quintet, 4 H, *J* = 6.5; 1.86 quintet, 2 H, *J* = 6.1; 1.87 quintet, 2 H, *J* = 6.4; 2.77 t, 2 H, *J* = 6.8; 3.35 m, 8 H; 3.50–3.70 m, 24 H; 4.26 t, 2 H, *J* = 7.5; 5.91 d, 1 H, *J* = 7.8; 5.92 d, 1 H, *J* = 7.5; 6.37 d, 1 H, *J* = 8.1; 6.41 d, 1 H, *J* = 7.5; 7.16 t, 1 H, *J* = 8.0; 7.23 t, 1 H, *J* = 7.5. ^{13}C NMR: 28.5, 1 C; 29.4, 1 C; 29.6, 1 C; 32.8, 1 C; 39.5, 1 C; 39.7, 1 C; 40.6, 1 C; 44.6, 1 C; 69.3, 1 C; 69.5, 2 C; 69.9, 1 C; 70.1, 2 C; 70.2, 2 C; 70.4, 1 C; 70.6, 2 C; 71.1, 1 C; 96.5, 1 C; 98.9, 1 C; 102.2, 1 C; 104.1, 1 C; 137.7, 1 C; 138.1, 1 C; 156.4, 1 C; 156.7, 1 C; 158.3, 2 C. HRMS MALDI-TOF (*m/z*) for $C_{30}H_{50}N_6O_6$ calculated: 591.3870 [M^+ + H]; found: 591.3886.

2,5,9,12,18,22,25,29,34,35-Decaazatricyclo[28.3.1.1^{13,17}]pentatriaconta-1(34),13(35),14,16,30,32-hexaene (**11k**)

Method (*A*). **11k** was prepared from the in situ obtained **8d** (0.6 mmol, 230 mg), tetraamine **2e** (0.6 mmol, 104 mg), in the presence of [Pd(dba)$_2$] (23 mg, 7 mole %) and BINAP (28 mg, 7.5 mole %), sodium *tert*-butoxide (1.2 mmol, 120 mg) in absolute dioxane (12 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 55 mg (19%), yellow oil. ^{1}H NMR: 1.59 br s, 2 H; 1.70 br s, 4 H; 2.50–2.90 m, 16 H; 3.26 br s, 8 H; 5.63 br s, 4 H; 7.14 br s, 2 H. (NH protons were not unambiguously assigned.) ^{13}C NMR: 29.5, 1 C; 29.6, 2 C; 40.4, 2 C; 41.5, 2 C; 47.6, 2 C; 47.9, 2 C; 48.8, 2 C; 49.3, 2 C; 94.3, 4 C; 138.2, 1 C; 138.7, 1 C; 158.2, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{25}H_{44}N_{10}$ calculated: 485.3829 [M^+ + H]; found: 485.3833.

2,6,10,16,19,23,26,31,32-Nonaazatricyclo[25.3.1.1^{11,15}]dotriaconta-1(31),11,13,15(32),27,29-hexaene (**11l**)

Method (*A*). **11l** was prepared from the in situ obtained **8d** (0.6 mmol, 230 mg), triamine **2b** (0.6 mmol, 79 mg), in the presence of [Pd(dba)$_2$] (23 mg, 7 mole %) and BINAP (28 mg, 7.5 mole %), sodium *tert*-butoxide (1.2 mmol, 120 mg) in absolute dioxane (12 ml). Eluent CH_2Cl_2/MeOH/aqNH_3 10:3:1. Yield 29 mg (11%), yellow oil. ^{1}H NMR: 1.60 quintet, 2 H, *J* = 5.5; 1.73 quintet, 4 H, *J* = 7.0; 2.60–2.80 m, 12 H; 3.20–3.35 m, 8 H; 5.64 d, 2 H, *J* = 7.9; 5.66 d, 2 H, *J* = 7.9; 7.17 t, 1 H, *J* = 7.9; 7.19 t, 1 H, *J* = 7.9. (NH protons were not unambiguously assigned.) ^{13}C NMR: 28.9, 2 C; 29.7, 1 C; 40.8, 2 C; 41.8, 2 C; 47.8, 2 C; 48.1, 2 C; 48.9, 2 C; 94.4, 4 C; 138.0, 1 C; 138.3, 1 C; 158.3, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{23}H_{39}N_9$ calculated: 442.3407 [M^+ + H]; found: 442.3413.

Typical Procedure for the Synthesis of N^{α},N^{ω}-Bis(6-*tert*-butoxypyridin-2-yl)-Substituted Polyamines **12a**–**12e**, **12g**–**12j**

A two-neck flask equipped with a magnetic stirrer and condenser, flushed with dry argon, was charged with 2 equiv. of 2-bromo-6-*tert*-butoxypyridine (**5**), [Pd(dba)$_2$] (4 mole %), BINAP (4.5 mole %) and absolute dioxane (taken in an amount to obtain 0.1–0.2 mol/l concentration of polyamine), the mixture was stirred for several minutes, then 1 equiv. of appropriate polyamine **2** was added, followed by the addition of sodium *tert*-butoxide (2 equiv.). The mixture was refluxed for 5–10 h, cooled and evaporated in vacuum. The residue was dissolved in dichloromethane (10 ml), washed with water (10 ml), and then the water layer was extracted with dichloromethane (2 × 10 ml). Combined organic layers were dried over anhydrous sodium sulfate, evaporated in vacuum, and the residue, after recording NMR spectra of the crude compound, was chromatographed on silica using the sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 100:1–3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1–10:3:1.

N-(6-tert-Butoxypyridin-2-yl)-N′-{2-[(6-tert-butoxypyridin-2-yl)amino]ethyl}ethane-1,2-diamine (**12a**). **12a** was obtained from **5** (1 mmol, 230 mg), triamine **2a** (0.5 mmol, 52 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 90%. ^{1}H NMR: 1.54 s, 18 H; 2.86 t, 4 H, *J* = 5.7; 3.37 q, 4 H, *J* = 5.7; 4.63 t, 2 H, *J* = 5.0; 5.91 d, 2 H, *J* = 7.8; 5.93 d, 2 H, *J* = 7.8; 7.25 t, 2 H, *J* = 7.8. (1 NH proton was not unambiguously assigned.) ^{13}C NMR: 28.9, 6 C; 41.9, 2 C; 48.7, 2 C; 78.7, 2 C; 98.4, 2 C; 100.7, 2 C; 139.4, 2 C; 157.3, 2 C; 163.1, 2 C. MS MALDI-TOF (*m/z*): 402.2 [M^+ + H], 347.1 [$M^+ - C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{22}H_{35}N_5O_2$ calculated: 402.2869 [M^+ + H]; found: 402.2879.

N-(6-tert-Butoxypyridin-2-yl)-N′-{3-[(6-tert-butoxypyridin-2-yl)amino]propyl}propane-1,3-diamine (**12b**). **12b** was obtained from **5** (1 mmol, 230 mg), triamine **2b** (0.5 mmol, 66 mg), in the

presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH 10:1, 3:1. Yield 183 mg (85%), pale-yellow oil. ^{1}H NMR: 1.46 s, 18 H; 2.09 quintet, 4 H, *J* = 6.3; 2.97 t, 4 H, *J* = 6.7; 3.42 t, 4 H, *J* = 6.0; 5.19 br s, 2 H; 5.93 d, 2 H, *J* = 7.8; 6.01 d, 2 H, *J* = 7.9; 7.21 t, 2 H, *J* = 7.8. (1 NH proton was not unambiguously assigned.) ^{13}C NMR: 26.5, 2 C; 28.8, 6 C; 38.5, 2 C; 45.5, 2 C; 79.0, 2 C; 100.3, 2 C; 100.8, 2 C; 139.8, 2 C; 157.5, 2 C; 162.6, 2 C. MS MALDI-TOF (*m/z*): 430.2 [M^+ + H], 374.1 [$M^+ - C_4H_8$ + H], 318.1 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{24}H_{39}N_5O_2$ calculated: 430.3182 [M^+ + H]; found: 430.3169.

N^1,*N*$^{1'}$*-(Ethane-1,2-diyl)bis[N*^{2}*-(6-tert-butoxypyridin-2-yl)ethane-1,2-diamine]* (**12c**). This compound was obtained from **5** (1 mmol, 230 mg), tetraamine **2c** (0.5 mmol, 73 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 86%. ^{1}H NMR: 1.54 s, 18 H; 2.74 s, 4 H; 2.84 t, 4 H, *J* = 6.0; 3.35 t, 4 H, *J* = 4.5; 4.63 br s, 2 H; 5.91 d, 2 H, *J* = 7.8; 5.94 d, 2 H, *J* = 7.8; 7.24 t, 1 H, *J* = 7.8. (2 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.9, 6 C; 41.8, 2 C; 48.7, 2 C; 48.9, 2 C; 78.5, 2 C; 98.3, 2 C; 100.4, 2 C; 139.3, 2 C; 157.3, 2 C; 163.0, 2 C. MS MALDI-TOF (*m/z*): 445.4 [M^+ + H], 389.3 [$M^+ - C_4H_8$ + H], 333.3 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{24}H_{40}N_6O_2$ calculated: 445.3291 [M^+ + H]; found: 445.3230.

N^1,*N*$^{1'}$*-(Propane-1,3-diyl)bis[N*^{2}*-(6-tert-butoxypyridin-2-yl)ethane-1,2-diamine]* (**12d**). This compound was obtained from **5** (1 mmol, 230 mg), tetraamine **2d** (0.5 mmol, 80 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 85%. ^{1}H NMR: 1.56 s, 18 H; 1.75 quintet, 2 H, *J* = 6.6; 2.68 t, 4 H, *J* = 5.7; 2.78 t, 4 H, *J* = 6.6; 3.42 q, 4 H, *J* = 5.7; 4.92 br s, 2 H; 5.96 d, 2 H, *J* = 7.9; 5.97 d, 2 H, *J* = 7.9; 7.26 t, 2 H, *J* = 7.9. (2 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.8, 1 C; 29.0, 6 C; 41.4, 2 C; 48.4, 2 C; 48.7, 2 C; 78.6, 2 C; 98.7, 2 C; 100.6, 2 C; 139.4, 2 C; 157.3, 2 C; 163.1, 2 C. MS MALDI-TOF (*m/z*): 459.1 [M^+ + H], 403.1 [$M^+ - C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{25}H_{42}N_6O_2$ calculated: 459.3447 [M^+ + H]; found: 459.3436.

N^1,*N*$^{1'}$*-(Ethane-1,2-diyl)bis[N*^{3}*-(6-tert-butoxypyridin-2-yl)propane-1,3-diamine]* (**12e**). This compound was obtained from **5** (6.6 mmol, 1.52 g), tetraamine **2e** (3 mmol, 522 mg), in the presence of [Pd(dba)$_2$] (110 mg, 3 mole %) and BINAP (130 mg, 3.5 mole %), sodium *tert*-butoxide (6.6 mmol, 660 mg) in absolute dioxane (33 ml). Eluent CH_2Cl_2/MeOH 3:1, CH_2Cl_2/MeOH/aqNH_3 100:20:1. Yield 358 mg (25%), pale-yellow oil. ^{1}H NMR: 1.54 s, 18 H; 1.76 quintet, 4 H, *J* = 6.7; 2.72 s, 4 H; 2.73 t, 4 H, *J* = 6.6; 3.31 t, 4 H, *J* = 6.6; 4.69 br s, 2 H; 5.88 d, 2 H, *J* = 7.9; 5.93 d, 2 H, *J* = 7.9; 7.24 t, 2 H, *J* = 7.9. (2 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.8, 6 C; 29.5, 2 C; 40.6, 2 C; 47.8, 2 C; 49.3, 2 C; 78.4, 2 C; 97.8, 2 C; 100.2, 2 C; 139.2, 2 C; 157.3, 2 C; 163.0, 2 C. IR: 3412, 3297, 2967, 2923, 2836, 1602, 1586, 1501, 1445, 1387, 1362, 1176, 1036, 884, 782, 728. UV/VIS: 246 (23 800), 302 (15 200). HRMS MALDI-TOF (*m/z*) for $C_{26}H_{44}N_6O_2$ calculated: 473.3604 [M^+ + H]; found: 473.3607.

N^1*-(6-tert-Butoxypyridin-2-yl)-N*^{2}*-(2-{[2-({2-[(6-tert-butoxypyridin-2-yl)amino]ethyl}amino)ethyl]-amino}ethyl)ethane-1,2-diamine* (**12g**). This compound was obtained from **5** (1 mmol, 230 mg), pentaamine **2g** (0.5 mmol, 95 mg), in the presence of [Pd(dba)$_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 80%. ^{1}H NMR: 1.52 s, 18 H; 2.68 s, 8 H; 2.80 br s, 4 H; 3.33 br s, 4 H; 4.86 br s, 2 H; 5.89 d, 2 H, *J* = 8.1; 5.90 d, 2 H, *J* = 7.8; 7.19 t, 2 H, *J* = 8.0. (3 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.8, 6 C; 41.5, 2 C; 48.5,

2 C; 48.7, 2 C; 48.8, 2 C; 78.3, 2 C; 98.3, 2 C; 100.2, 2 C; 139.1, 2 C; 157.2, 2 C; 162.9, 2 C. MS MALDI-TOF (*m/z*): 488.3 [M^+ + H], 432.3 [$M^+ - C_4H_8$ + H], 376.3 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{26}H_{45}N_7O_2$ calculated: 488.3713 [M^+ + H]; found: 488.3758.

N^1,$N^{1'}$-[Ethane-1,2-diyldiaminobis(ethane-2,1-diyl)]bis[N^2-(6-tert-butoxypyridin-2-yl)ethane-1,2-diamine] (**12h**). This compound was obtained from **5** (1 mmol, 230 mg), hexaamine **2h** (0.5 mmol, 116 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). The yield in the reaction mixture was 55%. ^{1}H NMR: 1.54 s, 18 H; 2.70 s, 4 H; 2.72 s, 8 H; 2.83 t, 4 H, *J* = 5.8; 3.35 t, 4 H, *J* = 4.6; 4.75 br s, 2 H; 5.91 d, 2 H, *J* = 8.1; 5.93 d, 2 H, *J* = 8.1; 7.23 t, 2 H, *J* = 8.1. (4 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.8, 6 C; 41.6, 2 C; 48.6, 2 C; 48.7, 2 C; 48.9, 4 C; 78.3, 2 C; 98.3, 2 C; 100.2, 2 C; 139.1, 2 C; 157.2, 2 C; 162.9, 2 C. MS MALDI-TOF (*m/z*): 531.2 [M^+ + H], 475.2 [$M^+ - C_4H_8$ + H], 419.5 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{28}H_{50}N_8O_2$ calculated: 531.4135 [M^+ + H]; found: 531.4116.

N,N′-{[(Ethane-1,2-diyl)bis(oxy)]bis(ethane-2,1-diyl)}bis(6-tert-butoxypyridin-2-amine) (**12i**). This compound was obtained from **5** (1.5 mmol, 345 mg), dioxadiamine **2i** (0.75 mmol, 111 mg), in the presence of $Pd(dba)_2$ (36 mg, 4 mole %) and BINAP (42 mg, 4.5 mole %), sodium *tert*-butoxide (1.5 mmol, 150 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH 100:1. Yield 265 mg (79%), pale-yellow oil. ^{1}H NMR: 1.55 s, 18 H; 3.48 t, 4 H, *J* = 5.3; 3.63 s, 4 H; 3.66 t, 4 H, *J* = 5.2; 5.90 d, 2 H, *J* = 7.9; 5.95 d, 2 H, *J* = 7.8; 7.22 t, 2 H, *J* = 7.8. (2 NH protons were not unambiguously assigned.) ^{13}C NMR: 28.8, 6 C; 41.6, 2 C; 69.9, 2 C; 70.1, 2 C; 78.4, 2 C; 98.6, 2 C; 100.4, 2 C; 139.3, 2 C; 157.0, 2 C; 163.0, 2 C. MS MALDI-TOF (*m/z*): 447.0 [M^+ + H], 391.0 [$M^+ - C_4H_8$ + H], 373.0 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{24}H_{38}N_4O_4$ calculated: 447.2971 [M^+ + H]; found: 447.2903.

N,N′-(3,3′-{Oxybis[(ethane-2,1-diyl)oxy(propane-3,1-diyl)]}bis(6-tert-butoxypyridin-2-amine) (**12j**). This compound was obtained from **5** (1 mmol, 230 mg), trioxadiamine **2j** (0.44 mmol, 97 mg), in the presence of [$Pd(dba)_2$] (24 mg, 4.4 mole %) and BINAP (28 mg, 5 mole %), sodium *tert*-butoxide (1 mmol, 100 mg) in absolute dioxane (5 ml). Eluent CH_2Cl_2/MeOH 100:1. Yield 50 mg (22%), pale-yellow oil. ^{1}H NMR: 1.54 s, 18 H; 1.86 quintet, 4 H, *J* = 6.2; 3.35 q, 4 H, *J* = 6.2; 3.58 t, 4 H, *J* = 5.5; 3.59–3.61 m, 4 H; 3.64–3.67 m, 4 H; 4.62 br s, 2 H; 5.88 d, 2 H, *J* = 7.6; 5.91 d, 2 H, *J* = 7.9; 7.23 t, 2 H, *J* = 7.8. ^{13}C NMR: 29.0, 6 C; 29.4, 2 C; 40.0, 2 C; 69.7, 2 C; 70.2, 2 C; 70.6, 2 C; 78.6, 2 C; 98.0, 2 C; 100.3, 2 C; 139.3, 2 C; 157.5, 2 C; 163.2, 2 C. MS MALDI-TOF (*m/z*): 519.0 [M^+ + H], 463.0 [$M^+ - C_4H_8$ + H], 407.0 [$M^+ - 2\ C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{28}H_{46}N_4O_5$ calculated: 519.3546 [M^+ + H]; found: 519.3532.

N^1,N^1-Bis(6-*tert*-butoxypyridin-2-yl)-N^3-{3-[bis(6-*tert*-butoxypyridin-2-yl)amino]propyl}-propane-1,3-diamine (**14b**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser was charged with [$Pd(dba)_2$] (71 mg, 12 mole %) and BINAP (84 mg, 13.5 mole %), 2-bromo-6-*tert*-butoxypyridine (**5**) (3 mmol, 690 mg) in absolute dioxane (10 ml), and the reaction mixture was stirred for several minutes. Then triamine **2b** (0.5 mmol, 66 mg) was added, followed by sodium *tert*-butoxide (3 mmol, 300 mg) and the reaction mixture was refluxed for 12 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. Eluent CH_2Cl_2/MeOH 25:1. Yield 38 mg (10%), pale-yellow oil. ^{1}H NMR: 1.46 s, 36 H; 2.16 quintet, 4 H, *J* = 6.1; 2.93 t, 4 H, *J* = 6.8; 4.25 t,

4 H, *J* = 6.0; 6.30 d, 4 H, *J* = 7.8; 6.65 d, 4 H, *J* = 7.9; 7.35 t, 4 H, *J* = 7.9. ^{13}C NMR: 23.6, 2 C; 28.7, 12 C; 44.4, 2 C; 44.9, 2 C; 80.0, 4 C; 106.6, 4 C; 107.5, 4 C; 140.0, 4 C; 154.8, 4 C; 162.3, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{42}H_{61}N_7O_4$ calculated: 728.4863 [M^+ + H]; found: 728.4873.

N^1,*N*^{1}-Bis(6-*tert*-butoxypyridin-2-yl)-*N*^{3}-{3-[(6-*tert*-butoxypyridin-2-yl)amino]propyl}-propane-1,3-diamine (**13b**)

13b was obtained as the by-product in the synthesis of **14b**. Eluent CH_2Cl_2/MeOH 25:1. Yield 72 mg (25%), pale-yellow oil. ^{1}H NMR: 1.44 s, 9 H; 1.46 s, 18 H; 2.16 quintet, 4 H, *J* = 6.1; 2.90 t, 2 H, *J* = 5.8; 3.09 t, 2 H, *J* = 7.0; 3.44 t, 2 H, *J* = 6.0; 4.19 t, 2 H, *J* = 6.0; 5.28 br s, 1 H; 5.86 d, 1 H, *J* = 7.8; 5.97 d, 1 H, *J* = 8.0; 6.23 d, 2 H, *J* = 7.8; 6.58 d, 2 H, *J* = 7.8; 7.16 t, 1 H, *J* = 7.9; 7.34 t, 2 H, *J* = 7.8. (1 NH proton was not unambiguously assigned.) ^{13}C NMR: 23.7, 1 C; 25.2, 1 C; 28.7, 6 C; 28.9, 3 C; 38.4, 1 C; 43.8, 1 C; 43.9, 1 C; 44.1, 1 C; 78.4, 1 C; 79.5, 2 C; 99.6, 1 C; 100.3, 1 C; 106.3, 2 C; 107.0, 2 C; 139.2, 1 C; 139.6, 2 C; 154.8, 2 C; 157.1, 1 C; 162.6, 2 C; 162.8, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{33}H_{50}N_6O_3$ calculated: 579.4022 [M^+ + H]; found: 579.4000.

N,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}-bis[6-*tert*-butoxy-*N*-(6-*tert*-butoxypyridin-2-yl)pyridin-2-amine] (**14j**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with [Pd(dba)$_2$] (47 mg, 4 mole %) and BINAP (56 mg, 4.5 mole %), 2-bromo-6-*tert*-butoxypyridine (**5**) (2 mmol, 460 mg) in absolute dioxane (5 ml), and the reaction mixture was stirred for several minutes. Then trioxadiamine **2j** (0.5 mmol, 110 mg) was added followed by sodium *tert*-butoxide (2 mmol, 200 mg), and the reaction mixture was refluxed for 12 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. Eluent CH_2Cl_2/MeOH 100:1. Yield 65 mg (16%), pale-yellow oil. ^{1}H NMR: 1.56 s, 36 H; 1.98 br s, 4 H; 3.47–3.54 m, 4 H; 3.55–3.65 m, 8 H; 4.19 t, 4 H, *J* = 7.3; 6.19 d, 4 H, *J* = 7.6; 6.62 d, 4 H, *J* = 7.9; 7.32 t, 4 H, *J* = 7.8. ^{13}C NMR: 28.9, 12 C; 29.4, 2 C; 45.3, 2 C; 69.4, 2 C; 70.2, 2 C; 70.6, 2 C; 78.9, 4 C; 105.1, 4 C; 106, 4 C; 139.1, 4 C; 155.4, 4 C; 163.0, 4 C. HRMS MALDI-TOF (*m/z*) for $C_{46}H_{68}N_6O_7$ calculated: 816.5149 [M^+]; found: 816.5150.

6-*tert*-Butoxy-*N*-(6-*tert*-butoxypyridin-2-yl)-*N*-{3-[2-(2-{3-[(6-*tert*-butoxypyridin-2-yl)-amino]propoxy}ethoxy)ethoxy]propyl}pyridin-2-amine (**13j**)

13j was obtained as the by-product in the synthesis of **14j**. Eluent CH_2Cl_2/MeOH 100:1, 50:1. Yield 98 mg (29%), pale-yellow oil. ^{1}H NMR: 1.55 s, 9 H; 1.56 s, 18 H; 1.86 quintet, 2 H, *J* = 6.0; 1.98 br s, 2 H; 3.35 t, 2 H, *J* = 5.8; 3.47–3.54 m, 4 H; 3.53–3.65 m, 8 H; 4.19 t, 2 H, *J* = 7.3; 4.64 br s, 1 H; 5.88 d, 1 H, *J* = 7.9; 5.92 d, 1 H, *J* = 7.8; 6.19 d, 2 H, *J* = 7.6; 6.62 d, 2 H, *J* = 7.9; 7.22 t, 1 H, *J* = 7.9; 7.32 t, 2 H, *J* = 7.8. ^{13}C NMR: 28.8, 1 C; 28.9, 6 C; 29.0, 3 C; 29.4, 1 C; 40.0, 1 C; 45.3, 1 C; 69.4, 1 C; 69.7, 1 C; 70.2, 2 C; 70.6, 2 C; 79.0, 1 C; 79.5, 2 C; 98.0, 1 C; 100.3, 1 C; 105.1, 2 C; 106.4, 2 C; 139.1, 2 C; 139.4, 1 C; 155.4, 2 C; 157.5, 1 C; 163.0, 2 C; 163.2, 1 C. HRMS MALDI-TOF (*m/z*) for $C_{37}H_{57}N_5O_6$ calculated: 667.4309 [M^+]; found: 667.4301.

N^1,*N*$^{1'}$-*(Ethane-1,2-diyl)bis(N*^{3}-pyridin-2-ylpropane-1,3-diamine) (**16**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with [Pd(dba)$_2$] (23 mg, 4 mole %) and BINAP (28 mg, 4.5 mole %), 2-bromopyridine (**15**) (2.2 mmol, 332 mg) in absolute dioxane (5 ml), and the reaction mixture was stirred for several minutes. Then tetraamine **2e** (1 mmol, 174 mg) was added followed by sodium *tert*-butoxide (3 mmol, 300 mg), and the reaction mixture was refluxed for 1 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. The NMR yield in the reaction mixture was 71%. Eluent CH_2Cl_2/MeOH/aqNH_3 100:20:1, 100:20:2. Yield 78 mg (24%), pale-yellow oil. ^{1}H NMR: 1.76 quintet, 4 H, *J* = 6.6; 2.70 s, 4 H; 2.71 t, 4 H, *J* = 6.5; 3.31 t, 4 H, *J* = 6.7; 5.14 br s, 2 H; 6.33 d, 2 H, *J* = 8.4; 6.49 ddd, 2 H, *J* = 6.9, 4.9, 1.0; 7.34 ddd, 2 H, *J* = 8.5, 7.0, 2.0; 8.01 dd, 2 H, *J* = 5.0, 1.4. (The observed coupling constants are given. 2 NH protons were not unambiguously assigned.) ^{13}C NMR: 29.1, 2 C; 40.2, 2 C; 47.4, 2 C; 48.9, 2 C; 106.6, 2 C; 111.9, 2 C; 136.8, 2 C; 147.6, 2 C; 158.7, 2 C. HRMS MALDI-TOF (*m*/*z*) for $C_{18}H_{28}N_6$ calculated: 328.2375 [M^+]; found: 328.2394.

N^1-(6-*tert*-Butoxypyridin-2-yl)-*N*^{3}-[3-(pyridin-2-ylamino)propyl]propane-1,3-diamine (**17**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with [Pd(dba)$_2$] (20 mg, 4 mole %) and BINAP (24 mg, 4.5 mole %), 2-bromopyridine (**15**) (0.85 mmol, 136 mg) in absolute dioxane (5 ml), and the reaction mixture was stirred for several minutes. Then compound **4b** (0.85 mmol, 238 mg) was added followed by sodium *tert*-butoxide (0.9 mmol, 86 mg), and the reaction mixture was refluxed for 9 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. Eluent CH_2Cl_2/MeOH 3:1. Yield 82 mg (27%), pale-yellow oil. ^{1}H NMR: 1.44 s, 9 H; 2.12 quintet, 4 H, *J* = 6.1; 2.90–3.00 m, 4 H; 3.45 br s, 4 H; 5.46 br s, 1 H; 5.79 br s, 1 H; 5.88 d, 1 H, *J* = 7.5; 6.03 d, 1 H, *J* = 7.5; 6.41 t, 1 H, *J* = 6.2; 6.57 d, 1 H, *J* = 8.6; 7.15 t, 1 H, *J* = 7.5; 7.27 t, 1 H, *J* = 7.0; 7.74 d, 1 H, *J* = 5.3. (1 NH proton was not unambiguously assigned.) ^{13}C NMR: 26.3, 1 C; 26.6, 1 C; 28.9, 3 C; 37.8, 1 C; 38.3, 1 C; 44.8, 1 C; 45.3, 1 C; 78.7, 1 C; 100.2, 1 C; 100.5, 1 C; 109.9, 1 C; 112.7, 1 C; 137.7, 1 C; 139.4, 1 C; 145.7, 1 C; 156.5, 1 C; 158.8, 1 C; 162.7, 1 C. MS MALDI-TOF (*m*/*z*): 358.3 [M^+ + H], 302.3 [M^+ – C_4H_8 + H].

N^3-{3-[(6-*tert*-Butoxypyridin-2-yl)amino]propyl}-*N*^{1},*N*^{1}-di(pyridin-2-yl)propane-1,3-diamine (**18**)

18 was obtained as the by-product in the synthesis of **17**. Eluent CH_2Cl_2/MeOH 10:1, 3:1. Yield 195 mg (53%), yellow crystals, m.p. 71–73 °C. ^{1}H NMR: 1.48 s, 9 H; 2.16 quintet, 2 H, *J* = 6.6; 2.18 quintet, 2 H, *J* = 6.6; 2.96 t, 2 H, *J* = 6.4; 3.07 t, 2 H, *J* = 7.0; 3.51 q, 2 H, *J* = 5.6; 4.29 t, 2 H, *J* = 6.0; 5.55 t, 1 H, *J* = 5.6; 5.88 d, 1 H, *J* = 7.9; 6.04 d, 1 H, *J* = 8.1; 6.85 dd, 2 H, *J* = 7.3, 5.1; 7.05 d, 2 H, *J* = 8.6; 7.16 t, 1 H, *J* = 7.9; 7.52 ddd, 2 H, *J* = 8.6, 7.4, 1.9; 8.15 dd, 2 H, *J* = 5.0, 1.3. (Observed coupling constants are given. 1 NH proton was not unambiguously assigned.) ^{13}C NMR: 22.9, 1 C; 26.5, 1 C; 28.9, 3 C; 38.6, 1 C; 44.4, 1 C; 45.2, 1 C; 45.5, 1 C; 78.5, 1 C; 100.0, 1 C; 100.4, 1 C; 115.0, 2 C; 118.0, 2 C; 138.2, 2 C; 139.3, 1 C; 147.8, 2 C; 157.0, 1 C; 157.4, 2 C; 162.9, 1 C. MS MALDI-TOF (*m*/*z*): 435.4 [M^+ + H], 379.4 [M^+ – C_4H_8 + H].

6-*tert*-Butoxy-*N*-(2-{2-[2-(dipyridin-2-ylamino)ethoxy]ethoxy}ethyl)-*N*-(pyridin-2-yl)-pyridin-2-amine (**19**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with $[Pd(dba)_2]$ (26 mg, 4 mole %) and BINAP (30 mg, 4.5 mole %), 2-bromopyridine (**15**) (1.44 mmol, 226 mg) in absolute dioxane (5 ml), and the reaction mixture was stirred for several minutes. Then compound **4i** (0.36 mmol, 105 mg) was added followed by sodium *tert*-butoxide (1.125 mmol, 108 mg), and the reaction mixture was refluxed for 11 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. Eluent CH_2Cl_2/MeOH 100:1. Yield 14 mg (7%), pale-yellow oil. ^{1}H NMR: 1.52 s, 9 H; 3.46 br s, 4 H; 3.70 t, 2 H, *J* = 6.6; 3.73 t, 2 H, *J* = 6.2; 4.29 t, 2 H, *J* = 6.6; 4.34 t, 2 H, *J* = 6.2; 6.20 d, 1 H, *J* = 7.5; 6.59 d, 1 H, *J* = 7.6; 6.79–6.84 m, 3 H; 7.13 d, 1 H, *J* = 8.3; 7.14 d, 2 H, *J* = 8.3; 7.32 t, 1 H, *J* = 7.6; 7.44–7.50 m, 3 H; 8.27–8.31 m, 3 H. ^{13}C NMR: 28.7, 3 C; 47.7, 1 C; 47.9, 1 C; 69.1, 1 C; 69.2, 1 C; 70.3, 2 C; 105.3, 1 C; 114.8, 2 C; 114.9, 1 C; 115.7, 1 C; 116.9, 1 C; 117.0, 2 C; 136.9, 1 C; 137.1, 2 C; 139.3, 1 C; 148.0, 1 C; 148.1, 2 C; 155.0, 1 C; 157.4, 2 C; 157.6, 1 C; 162.9, 1 C. (The quaternary carbon in *tert*-butoxy group was not unambiguously assigned.) MS MALDI-TOF (*m/z*): 529.0 [M^+ + H], 473.0 [$M^+ - C_4H_8$ + H]. HRMS MALDI-TOF (*m/z*) for $C_{30}H_{36}N_6O_3$ calculated: 529.2927 [M^+ + H]; found: 529.2917.

6-*tert*-Butoxy-*N*-(2-{2-[2-(dipyridin-2-ylamino)ethoxy]ethoxy}ethyl)-pyridin-2-amine (**20**)

This compound was obtained as the by-product in the synthesis of **19**. Eluent CH_2Cl_2/MeOH 100:1, 50:1. Yield 80 mg (49%), pale-yellow oil. ^{1}H NMR: 1.54 s, 9 H; 3.42 q, 2 H, *J* = 4.8; 3.50–3.54 m, 2 H; 3.56–5.61 m, 4 H; 3.81 t, 2 H, *J* = 6.2; 4.40 t, 2 H, *J* = 6.2; 4.65 br s, 1 H; 5.89 d, 1 H, *J* = 7.8; 5.93 d, 1 H, *J* = 7.9; 6.83 ddd, 2 H, *J* = 7.3, 5.0, 1.0; 7.14 dt, 2 H, *J* = 8.4, 1.0; 7.23 t, 1 H, *J* = 7.8; 7.49 ddd, 2 H, *J* = 8.6, 7.3, 2.0; 8.31 ddd, 2 H, *J* = 4.8, 2.0, 1.0. (The observed coupling constants are given.) ^{13}C NMR: 29.0, 3 C; 41.8, 1 C; 47.9, 1 C; 69.4, 1 C; 70.0, 1 C; 70.3, 2 C; 98.7, 1 C; 100.5, 1 C; 114.9, 2 C; 117.1, 2 C; 137.2, 2 C; 139.4, 1 C; 148.2, 2 C; 157.2, 1 C; 157.4, 2 C; 163.1, 1 C. (The quaternary carbon in *tert*-butoxy group was not unambiguously assigned.) HRMS MALDI-TOF (*m/z*) for $C_{25}H_{33}N_5O_3$ calculated: 452.2661 [M^+ + H]; found: 452.2674.

6-*tert*-Butoxy-*N*-[2-(2-{2-[(6-*tert*-butoxypyridin-2-yl)amino]ethoxy}ethoxy)ethyl]-*N*-(pyridin-2-yl)pyridin-2-amine (**21**)

A two-neck flask flushed with dry argon, equipped with a magnetic stirrer and condenser, was charged with $[Pd(dba)_2]$ (16 mg, 4 mole %) and BINAP (19 mg, 4.5 mole %), 2-bromopyridine (**15**) (0.68 mmol, 107 mg) in absolute dioxane (5 ml), and the reaction mixture was stirred for several minutes. Then compound **12i** (0.68 mmol, 303 mg) was added followed by sodium *tert*-butoxide (71 mmol, 68 mg), and the reaction mixture is refluxed for 11 h. After cooling to ambient temperature, the solvent was evaporated in vacuum, and the residue was chromatographed on silica. Eluent CH_2Cl_2/MeOH 50:1. Yield 89 mg (25%), pale- yellow oil. ^{1}H NMR: 1.54 s, 18 H; 3.43 q, 2 H, *J* = 5.3; 3.51–3.54 m, 2 H; 3.55–3.59 m, 2 H; 3.59 t, 2 H, *J* = 5.3; 3.79 t, 2 H, *J* = 6.5; 4.36 t, 2 H, *J* = 6.5; 4.64 t, 1 H, *J* = 4.0; 5.88 d, 1 H, *J* = 7.8; 5.93 d, 1 H, *J* = 7.8; 6.22 d, 1 H, *J* = 7.8; 6.61 d, 1 H, *J* = 8.1; 6.81 dd, 1 H, *J* = 7.3, 5.1; 7.15 d, 1 H, *J* = 8.3; 7.22 t, 1 H, *J* = 7.8; 7.34 t, 1 H, *J* = 7.8; 7.46 ddd, 1 H, *J* = 8.6, 7.4, 2.0;

8.31 d, 1 H, J = 4.8. (The observed coupling constants are given.) ^{13}C NMR: 28.8, 3 C; 28.9, 3 C; 41.7, 1 C; 47.6, 1 C; 69.3, 1 C; 69.9, 1 C; 70.2, 1 C; 70.3, 1 C; 78.5, 1 C; 78.9, 1 C; 98.6, 1 C; 100.4, 1 C; 105.3, 1 C; 105.4, 1 C; 115.5, 1 C; 116.9, 1 C; 136.9, 1 C; 139.3, 2 C; 148.1, 1 C; 155.0, 1 C; 157.1, 1 C; 157.6, 1 C; 162.9, 1 C; 163.1, 1 C. HRMS MALDI-TOF (m/z) for $C_{29}H_{41}N_5O_4$ calculated: 524.3237 [M^+ + H]; found: 524.3226.

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