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Copper-Catalyzed Arylation of Oxadiamines and Polyamines

Maxim V. Anokhin,[a] Alexei D. Averin,[a] and Irina P. Beletskaya*[a]

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Copper-catalyzed arylation of oxadiamines and polyamines aimed at the synthesis of *N*,*N*′-diaryl derivatives using bromo- and iodoarenes was studied. Conversion of the starting compounds, selectivity of the arylation of primary amino groups in the presence of the secondary amino groups, and the yields of target products were shown to be strongly dependent on the nature of the oxadiamines and polyamines, aryl halides, and halogen atom, as well as on reaction conditions such as ligand, solvent, and base applied. Reliable catalytic systems were found for each type of starting amine and aryl halide affording the highest possible yields of the products of *N*,*N*′-diarylation (65–96 %).

Introduction

Transition-metal catalysis of carbon–element bond formation has become a powerful tool of modern preparative organic chemistry. An important place among these reactions is occupied by the catalytic amination reactions.[1] Pd-catalyzed amination of aryl halides is well-studied and is now applied to the synthesis of physiologically active compounds and agrochemicals, etc.[2] Our contribution to this field covers the synthesis of polyazamacrocycles by the catalytic amination of dihaloarenes with linear polyamines.[3,4] In the last years, a renaissance of so-called catalytic Ullmann chemistry has developed, and great interest has been paid to the copper-catalyzed amination of haloarenes. Researchers from the groups of Buchwald,[5] Ma,[6] and Taillefer[7] elaborated convenient protocols for aryl halide amination, and an avalanche of publications have followed their pioneering work. Various types of N-nucleophiles, such as aliphatic amines, cyclic amines, aromatic amines, NH-heterocycles, and amides, can be converted into the corresponding *N*-aryl derivatives under relatively mild conditions, and a number of simple and readily available compounds have been employed in these reactions as ligands.[8–12] These ligands can be divided into three main groups: *N*,*N*-chelating ligands such as DMEDA,[13] phenanthroline, and its derivatives,[14] *N*,*O*-chelating ligands such as proline, *N*-methylglycine,[15–17] salicylic aldehyde oxime (salox),[18] phenylhydrazone,[19] and salicylic acid *N*,*N*-dimethylamide,[20] and *O*,*O*-chelating ligands such as tetramethylheptanedione,[21] ethylene glycol,[22] 2-acetylcyclohexanone,[23] cyclic β-keto esters,[24] and BINOL.[25] In a number of works, certain phosphorus compounds were shown to be efficient in copper-catalyzed amination,[26–28] but the use of such ligands is restricted.

Di- and polyamines occupy a special place among N-nucleophiles. On one hand, these compounds are known to form stable complexes with metal cations, including copper, which makes them valuable species for supramolecular chemistry. Thus, one may suppose that complexes of Cu^{I} formed in situ with polyamimes in the copper-catalyzed amination will influence the reaction pathway. On the other hand, *N*-aryl-substituted polyamines are of substantial interest because they have been demonstrated, for example, to regulate cancer cell growth.[29–32] From this viewpoint, the study of Cu-catalyzed arylation of polyamines is an important task. In the present research, we focused on the diarylation of primary amino groups in di- and polyamines because we considered it to be of benefit to compare Cu- and Pd-mediated aryalation of polyamines and to provide a reliable synthetic approach to *N*,*N*′-bis(bromoaryl)-substituted di- and polyamines, which are valuable precursors for polyazamacrocycles incorporating arene moieties. The Pd-catalyzed arylation of di- and polyamines was extensively studied by us previously, and excellent selectivity for primary amino group arylation in the presence of secondary amino groups was demonstrated.[33] Pd-catalyzed diarylation of 1,3-diaminopropane and *N*-(3-aminopropyl)-1,3-diaminopropane was conducted using 4-bromobiphenyl and 1-bromonaphthalene, and the reaction produced *N*,*N*′-diaryl derivatives in 75–92% yields. In contrast, copper-catalyzed arylation of diamines has not yet been investigated in detail, and there are few reports in literature on the monoarylation of linear diamines[34] or the diarylation of 1,2-diaminocyclohexane.[35] Copper-catalyzed arylation of triamine was described in only one case by Buchwald.[22]

Results and Discussion

We began our investigation with 1,3-dibromobenzene, which was important for elaborating a Cu-mediated ap-

[a] Department of Chemistry, Lomonosov Moscow State University,
Leninskie Gory, Moscow, 119991, Russian Federation
Fax: +7-495-9393618
E-mail: beletska@org.chem.msu.ru

proach to *N*,*N*′-bis(3-bromophenyl) polyamines. Initially, ligand-free arylation of tetraamine **1a** was carried out using the CuI/K_3PO_4 catalytic system in either boiling dioxane or *N*,*N*-dimethylformamide (DMF), however, the conversion of starting dibromide did not exceed 20%. The conversion was increased to 100% by replacing K_3PO_4 with K_2CO_3, but the reaction was not selective and the amination of secondary amino groups in tetraamine **1a** was substantial, thus the target N^1,N^4-diarylated product could not be isolated in a pure state. Another problem could be the formation of complexes of tetraamine and its *N*-aryl derivatives with Cu^I, which also hindered the isolation of the desired compound. These negative results prompted us to conduct a more detailed investigation into the influence of Cu^I-containing catalytic systems and the nature of aryl halides and polyamines on the amination reactions.

A study of the literature data on the copper-catalyzed amination of aryl halides prompted us to test six main, well-documented ligands: *N*,*N*′-dimethylethylenediamine (**L1**),[13] phenanthroline (**L2a**), and neocuproine (**L2b**)[14] (*N*,*N* ligands); ethylene glycol (**L3**),[22] α-acetylcyclohexanone (**L4a**), and α-isobutyrylcyclohexanone (**L4b**)[23] (*O*,*O* ligands); and salicylic aldehyde oxime (salox) (**L5**)[18] and proline (**L6**) (*N*,*O* ligands)[15–17] (Figure 1).

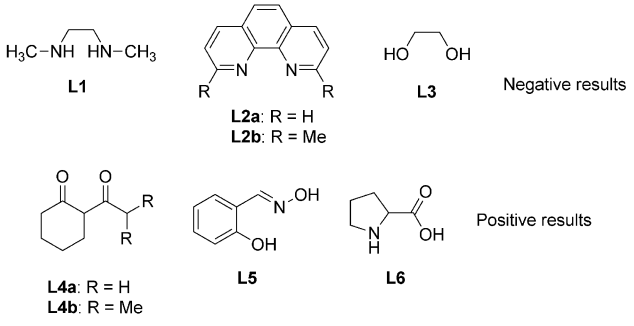


Figure 1. Ligands studied in the Cu^I-catalyzed arylation of polyamines.

Our investigation employed the following polyamines: tetraamine **1a**, triamine **1b**, trioxadiamine **1c**, and dioxadiamine **1d** (Figure 2); these compounds differ in the chain length and in the number of nitrogen and oxygen atoms and, therefore, can outline the scope and limitations of the Cu-catalyzed *N*,*N*′-diarylation.

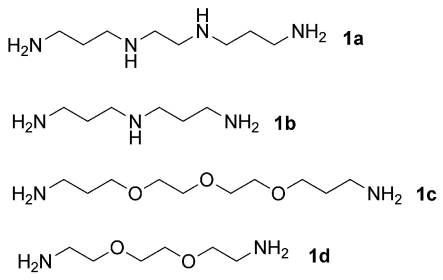


Figure 2. Polyamines studied in this research.

For the aryl halides, we first employed the simplest bromobenzene and iodobenzene, to compare the reactivity of the halogen atoms; we also examined their closest analogues 3-bromotoluene, 3-iodotoluene, and 3,5-dimethyliodobenzene to check whether the reactions are sensitive to small variations in the nature of the products. 1,3-Dibromobenzene and 1-bromo-3-iodobenzene were used to elaborate an alternative copper-mediated route to *N*,*N*′-bis(bromobenzyl)polyamines. *N*,*N*-Diethyl-3-iodobenzamide, 4-bromobiphenyl, 4-iodobiphenyl, and 4-acetoxy-4′-iodobiphenyl were applied to explore the influence of electron-withdrawing groups on the reactivity of aryl halides in the diamination processes, and 2-bromonaphthalene was used to assess the possibilities of conducting the amination of arenes with a more active bromine atom (Figure 3).

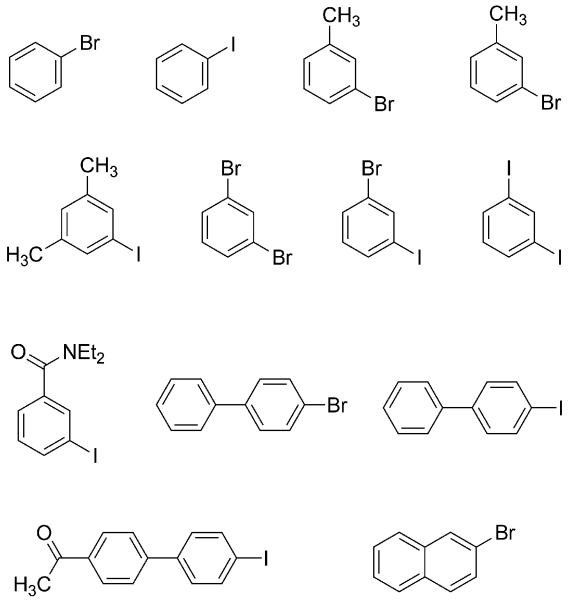
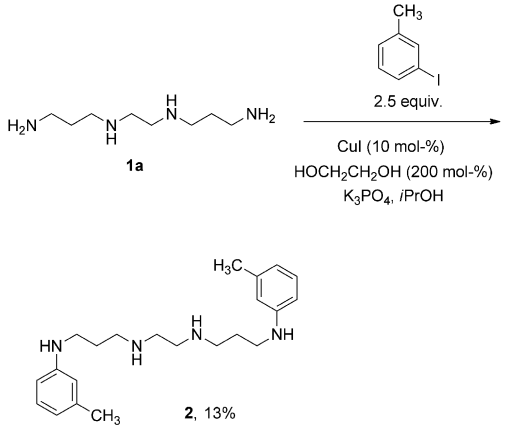


Figure 3. Aryl halides studied in this research.

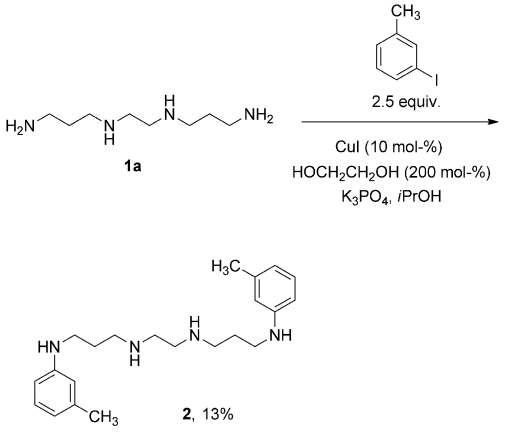
According to Buchwald, who proposed the use of the catalytic system CuI/**L3**(200 mol-%)/K_3PO_4/*i*PrOH for N^1,N^3-diarylation of triamine,[22] we applied this catalyst in the arylation of tetraamine **1a** with 2.5 equiv. of 3-iodotol-



Scheme 1. *N*,*N*′-Diarylation of tetraamine **1a** with 3-iodotoluene.

uene. The reaction was allowed to proceed for 24 h at reflux, however, we obtained the target product of N^1,N^4-diarylation **2** in only 13% yield (Scheme 1), although the conversion of starting 3-iodotoluene was complete. The selectivity of the arylation of primary amino groups was also insufficient, which led us to a search for more efficient catalytic systems for the copper-catalyzed arylation of polyamines.

Except for this modest result, numerous other attempts to apply ligands **L1**, **L2a**, **L2b**, and **L3** in the arylation of di- and polyamines were unsuccessful due either to low conversion of starting compounds or to non-selective transformations leading to inseparable mixtures of unidentified compounds. On the other hand, ligands **L4a**, **L4b**, **L5**, and **L6** were found to be applicable to the arylation of polyamines. Initially, we studied the reactions of the simplest bromobenzene and iodobenzene with tetraamine **1a** (Scheme 2). The reactions were performed using 2.5 equiv. of halobenzene and 1 equiv. of tetraamine in the presence of 10 mol-% CuI and 20 mol-% ligand at reflux temperature (or at 110 °C with DMF) for 24 h. The appropriate solvent and base were generally chosen according to the literature data in which certain ligands are often associated with a



Scheme 1. *N*,*N*′-Diarylation of tetraamine **1a** with 3-iodotoluene.

Table 1. Copper-catalyzed arylation of tetraamine **1a** [CuI /L (10/20 mol-%), 24 h].

Entry	ArHal	Ligand	Base	Solvent	Conc. [M]	Yield of **3** [%][a]
1	PhBr	**L4a**	Cs_2CO_3	DMF	0.5	35
2	PhBr	**L4a**	Cs_2CO_3	CH_3CN	0.5	33
3	PhBr	**L5**	Cs_2CO_3	PhMe	0.5	0[b]
4	PhBr	**L5**	Cs_2CO_3	PhMe	0.25	43
5	PhBr	**L5**	K_2CO_3	PhMe	0.25	39
6	**PhBr**	**L6**	**Cs_2CO_3**	**CH_3CN**	**0.5**	**65**
7	PhI	**L5**	Cs_2CO_3	PhMe	0.5	0[b]
8	PhI	**L5**	Cs_2CO_3	PhMe	0.25	30
9	PhI	**L5**	K_2CO_3	PhMe	0.13	10[c]
10	PhI	**L4a**	Cs_2CO_3	DMF	0.5	43
11	**PhI**	**L6**	**Cs_2CO_3**	**CH_3CN**	**0.5**	**59**

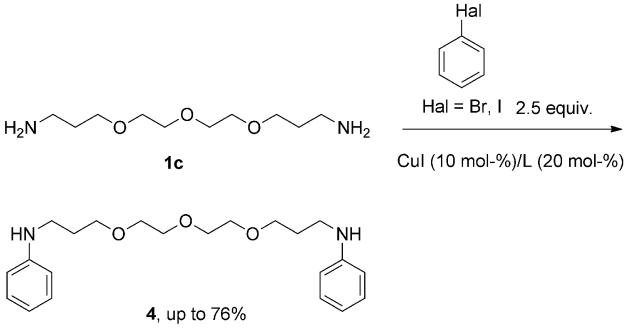
[a] Yields after column chromatography. [b] 100% conversion of halobenzenes, complex mixture of products. [c] 100% conversion of iodobenzene, mainly non-selective monoarylation of tetraamine **1a**.

corresponding base and solvent. The results are presented in Table 1.

Use of bromobenzene gave similar moderate yields of N^1,N^4-diphenyl tetraamine **3** with 2-acetylcyclohexanone (**L4a**) in DMF and acetonitrile (Table 1, entries 1 and 2), the result with salox (**L5**) in toluene at the same concentration (0.5 M) was negative because the reaction proceeded non-selectively (Table 1, entry 3) due to competitive arylation of secondary amino groups. The desired product **3** thus could not be isolated in pure state from a mixture of tri-, di-, and monoaryl derivatives. However, use of a lower concentration (0.25 M) substantially improved the result (Table 1, entry 4). It was possible to use less expensive potassium carbonate instead of cesium carbonate with almost the same yield of product (Table 1, entry 5). The best result (65% of **3**) was achieved by the application of proline (**L6**) in acetonitrile.

Initially it was assumed that the more active iodobenzene would provide better results, however, in many cases, the selectivity of arylation was lower than with bromobenzene. Again, salox (**L5**) provided a moderate yield of **3** only at 0.25 M concentration (Table 1, entry 8), at higher concentration (0.5 M) the selectivity of the process was very low because arylation of the secondary amino groups occurred (Table 1, entry 7), and at lower concentration (0.13 M) mainly monoarylation of tetraamine **1c** took place that was also non-selective, thus preventing the isolation of individual monoaryl derivatives (Table 1, entry 9). Acetylcyclohexanone (**L4a**) afforded 43% yield of **3** (Table 1, entry 10), which is comparable to the reaction with bromobenzene (Table 1, entry 1), and the best result (59%) was again achieved with proline (**L6**; Table 1, entry 11). Slightly lower yield of compound **3** in the reaction with iodobenzene might be explained by a lower selectivity of the arylation process due to the higher reactivity of iodine compared with bromine.

The catalytic system CuI/**L6**/Cs_2CO_3/CH_3CN was also thought to be suitable for *N*,*N*′-diarylation of trioxadimaine **1c** (Scheme 3). However, the results were quite different with this compound. Proline (**L6**) provided insufficient conversion of starting halobenzenes, thus *N*,*N*′-diphenyl deriv-



Scheme 3. *N*,*N*′-Diarylation of trioxadiamine **1c** with bromo- and iodobenzenes.

ative **4** was not obtained in either case (Table 2, entries 1 and 5). On the other hand, the reaction catalyzed by salox (**L5**) at 0.5 M concentration was more efficient than in the case of tetraamine **1a**, providing moderate yields of **4** (Table 2, entries 2 and 6). Acetylcyclohexanone (**L4a**) as well as its more bulky analogue 2-isopropylcarboxycyclohexanone (**L4b**) were inefficient in the amination of bromobenzene due to the absence of any diarylation process, and only monoaryl derivatives of **1c** were noted in the reaction mixtures (Table 2, entries 3 and 4) together with 100% conversion of bromobenzene. The latter result suggests that the catalytic reduction of the halogen took place to a large extent, but the monoaryl derivative could not be isolated in a pure state possibly due to the formation of its complexes with Cu^{I} and the presence of unreacted **1c** (which has a very similar R_f value) in the mixture. It is to be mentioned that, in all further reactions with trioxadiamine in which mainly monoarylation took place, we failed to isolate pure *N*-aryl derivatives of this diamine using column chromatography, unlike the case with *N*-aryl derivatives of triamine **1b** (see below). Fortunately, the reaction of iodobenzene was efficiently catalyzed by **L4b**, giving target compound **4** in 76% yield (Table 2, entry 7). From the data obtained, one can conclude that polyamines and oxadiamines require different catalytic systems to provide preparative diarylation of primary amino groups, and that iodoarenes are preferable for the arylation of oxadiamines, whereas bromoarenes can equally be used for the arylation of polyamines. To support this assumption, we made a series of reactions with 3-bromo- and 3-iodotoluenes, which are the closest analogues of bromo- and iodobenzenes (Scheme 4).

First we checked whether salox (**L5**) ligand could be employed for the arylation of tetraamine **1a** and trioxadiamine **1c**. It was found that neither 3-bromotoluene nor 3-iodotoluene could provide the target N^1,N^4-diarylated product **2** using this ligand due to low selectivity of the arylation of primary and secondary amino groups, as described above, although the consumption of aryl halide was complete (Table 3, entries 1 and 2). This ligand afforded the *N*,*N*′-diarylation product **7** in the reaction with trioxadiamine, but only in low yields (Table 3, entries 8 and 11). A better result was achieved in the amination of 3-bromotoluene with tetraamine using acetylcyclohexanone (**L4a**) in toluene (Table 3, entry 3). Because similar yields were obtained for the diarylation of tetraamine **1a** with bromobenzene using the same ligand in acetonitrile and DMF, it can be supposed that this ligand is not too sensitive to the nature of the solvent. The best yield (67%) of the product **2** in the reaction with 3-iodotoluene was obtained using proline (**L6**) in acetonitrile (Table 3, entry 5), and the arylation using 3-bromotoluene catalyzed with the same ligand (Table 3, entry 4) gave the product **2** in 55% yield. These

Table 2. Copper-catalyzed arylation of trioxadiamine **1c** [CuI/L (10/20 mol-%), Cs_2CO_3, 24 h, c = 0.5 M].

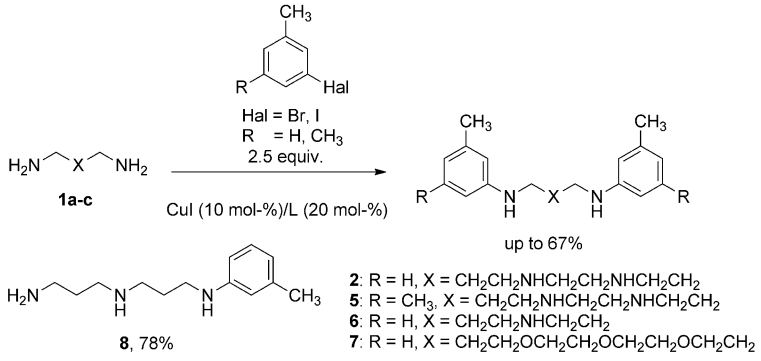
Entry	ArHal	Ligand	Solvent	Yield of **4** [%][a]
1	PhBr	**L6**	CH_3CN	0[b]
2	PhBr	**L5**	PhMe	37
3	PhBr	**L4a**	DMF	0[c]
4	PhBr	**L4b**	DMF	0[c]
5	PhI	**L6**	CH_3CN	0[d]
6	PhI	**L5**	PhMe	26
7	**PhI**	**L4b**	**DMF**	**76**

[a] Yields after column chromatography. [b] 5% conversion of bromobenzene. [c] 100% conversion of bromobenzene. [d] 50% conversion of iodobenzene.

Table 3. Cu-catalyzed amination of bromo- and iodotoluenes [CuI/L (10/20 mol-%), Cs_2CO_3, 24 h, c = 0.5 M].

Entry	ArHal	Amine	Ligand	Solvent	Prod.	Yield [%][a]
1	*m*-$BrC_6H_4CH_3$	**1a**	**L5**	PhMe	**2**	0[b]
2	*m*-$IC_6H_4CH_3$	**1a**	**L5**	PhMe	**2**	0[b]
3	*m*-$IC_6H_4CH_3$	**1a**	**L4a**	PhMe	**2**	38
4	*m*-$BrC_6H_4CH_3$	**1a**	**L6**	**CH_3CN**	**2**	**55**
5	*m*-$BrC_6H_4CH_3$	**1a**	**L6**	**CH_3CN**	**2**	**67**
6	3,5-dimethyl iodobenzene	**1a**	**L4a**	DMF	**5**	54
7	*m*-$IC_6H_4CH_3$	**1b**	**L6**	CH_3CN	**8**	78
8	*m*-$BrC_6H_4CH_3$	**1c**	**L5**	PhMe	**7**	7[c]
9	*m*-$BrC_6H_4CH_3$	**1c**	**L4a**	DMF	**7**	0[c]
10	*m*-$BrC_6H_4CH_3$	**1c**	**L4b**	DMF	**7**	15[c]
11	*m*-$IC_6H_4CH_3$	**1c**	**L5**	PhMe	**7**	20[c]
12	***m*-$IC_6H_4CH_3$**	**1c**	**L4a**	**DMF**	**7**	**63**
13	***m*-$IC_6H_4CH_3$**	**1c**	**L4b**	**DMF**	**7**	**65**

[a] Yield after column chromatography. [b] 100% conversion of aryl halides, complex mixture of products. [c] 100% conversion of 3-bromotoluene.



Scheme 4. *N*,*N*′-Diarylation of polyamines **1a**–**c** with bromo- and iodotoluenes.

results are similar to those obtained with bromo- and iodotoluenes (Table 1, entries 6 and 11), which demonstrates the reliability of the present catalytic system (CuI/proline/CH_3CN) for the diarylation of tetraamine. Use of the more bulky 3,5-dimethyliodobenzene also provided good yield of N^1,N^4-diarylated product **5** (54%; Table 3, entry 6) in the reaction mediated by a less selective CuI/**L4a** catalyst, probably due to greater steric hindrance of the arylation of secondary amino groups, which made the reaction more selective towards arylation of the primary amino groups. For comparison, the same aryl halide reacted smoothly with *n*-hexylamine at room temperature with the same catalyst,[23] which clearly demonstrates that diarylation of polyamines needs much harsher reaction conditions. Only monoarylation occurred in the case of triamine **1b** when the CuI/**L6** system was used (Table 3, entry 7), probably due to the reduction of 3-iodotoluene; in this case the corresponding *N*-(*m*-tolyl)-substituted triamine **8** was isolated in 78% yield.

Trioxadiamine **1c** was not normally diarylated with 3-bromotoluene (Table 3, entries 8–10), and the use of 3-iodotoluene with CuI/**L5** catalyst was also not efficient (Table 3, entry 11). In all these reactions, although the bromo- and iodotoluenes were fully converted, the catalytic reduction of the halogen atom was significant, which mainly led to formation of the monoaryl derivatives. The situation changed with the application of acetylcyclohexanone (**L4a**) or its more bulky analogue **L4b**, which provided 63–65% yield of *N*,*N*′-diarylation product **7** (Table 3, entries 12 and 13). These results are again in a good agreement with the data described above for the arylation of trioxadiamine **1c** with halobenzenes (Table 2). We investigated the possibility of reducing the catalyst loading to 5 mol-%, but found that the conversion of the aryl halides decreased dramatically, thus, in all further investigations 10 mol-% catalyst was always used.

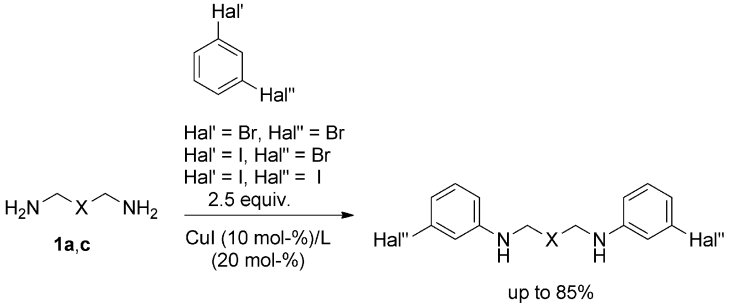
Synthesis of *N*,*N*′-bis(halophenyl)-substituted polyamines is of special importance because these compounds can be further transformed into polyazamacrocycles by reaction with a second molecule of polyamine under Pd catalysis. This process was described by us previously,[36] where the synthesis of diarylated linear polyamines from dibromobenzenes and polyamines was also conducted by applying a Pd-mediated amination protocol. The main drawback of this approach was found to be the formation of oligomeric by-products due to the diamination of dibromobenzenes, which resulted in 29–64% yields of *N*,*N*′-bis(3-bromophenyl)-substituted polyamines. Thus, it was interesting to elaborate a copper-catalyzed version of this reaction. For this purpose, tetraamine **1a** and trioxadiamine **1c** were reacted with 2.5 equiv. of 1,3-dibromo-, 1-bromo-3-iodo-, and 1,3-diiodobenzenes (Scheme 5).

The reaction between 1,3-dibromobenzene and tetraamine **1a** catalyzed by the CuI/**L5** complex was successful to some extent only in the presence of K_2CO_3 as base (Table 4, entry 1); with Cs_2CO_3, the conversion of starting aryl dihalide was only partial and the arylation was totally non-selective (Table 4, entry 2). A better result (26%) was obtained with proline (**L6**; Table 4, entry 3), but only in the presence of K_2CO_3 and at lower concentration. The main obstacle was, again, low selectivity of the process, which resulted in arylation of the secondary amino groups and consequently a drastic reduction in the isolated yield of the

Table 4. Copper-catalyzed arylation of tetraamine **1a** and trioxadiamine **1c** with dihalobenzenes [CuI/L (10/20 mol-%), Cs_2CO_3, 24 h, c = 0.5 M, 24 h].

Entry	ArHal	Amine	Ligand	Solvent	Prod.	Yield [%][a]
1[b]	1,3-$Br_2C_6H_4$	**1a**	**L5**	PhMe[c]	**9**	13
2	1,3-$Br_2C_6H_4$	**1a**	**L5**	PhMe[c]	**9**	0[d]
3[b]	1,3-$Br_2C_6H_4$	**1a**	**L6**	CH_3CN[e]	**9**	26
4	1,3-$Br_2C_6H_4$	**1a**	**L4a**	DMF	**9**	28
5	1,3-$Br_2C_6H_4$	**1a**	**L4a**	PhMe	**9**	27
6	1-Br-3-IC_6H_4	**1a**	**L6**	CH_3CN	**9**	0[f]
7	1-Br-3-IC_6H_4	**1a**	**L6**	EtCN	**9**	27
8	1-Br-3-IC_6H_4	**1a**	**L6**	EtCN	**10**	24
9	**1-Br-3-IC_6H_4**	**1c**	**L4b**	**DMF**	**11**	**85**
10	1,3-$I_2C_6H_4$	**1c**	**L5**	PhMe	**12**	0[g]
11	1,3-$I_2C_6H_4$	**1c**	**L4b**	DMF	**12**	53

[a] Yield after column chromatography. [b] K_2CO_3 was used as base. [c] c = 0.25 M. [d] 70% conversion of 1,3-dibromobenzene, complex mixture of products. [e] c = 0.13 M. [f] 70% conversion of 1-bromo-3-iodobenzene, complex mixture of products. [g] 45% conversion of 1,3-diiodobenzene.



9: Hal'' = Br, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
10: Hal'' = I, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
11: Hal'' = Br, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
12: Hal'' = I, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$

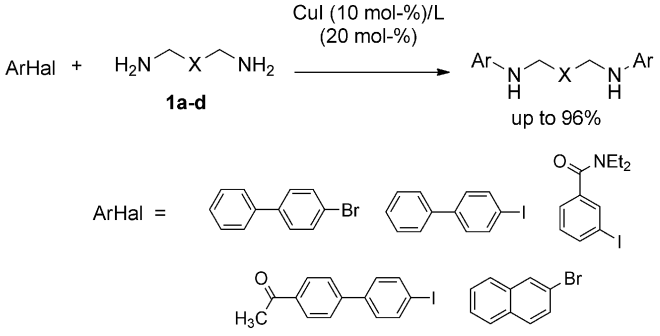
Scheme 5. *N*,*N*′-Diarylation of polyamines **1a** and **1c** with dihaloarenes.

target product **9**. Almost the same results were obtained when acetylcyclohexanone (**L4a**) was applied either in DMF or toluene (Table 4, entries 4 and 5). The use of 1-bromo-3-iodobenzene in the reaction with tetraamine **1a** under conditions that were optimal for iodobenzene and 3-iodotoluene (CuI/**L6**, CH_3CN) led to a non-selective reaction, and the conversion of 1-bromo-3-iodobenzene was not complete (Table 4, entry 6); however, changing acetonitrile for propionitrile (with a higher boiling point) provided the target diarylated product in 27% yield (Table 4, entry 7). It is interesting that the arylation with 1,3-diiodobenzene under the same conditions was of the same efficiency due to the low selectivity of the process, and compound **10** was isolated in 24% yield (Table 4, entry 8).

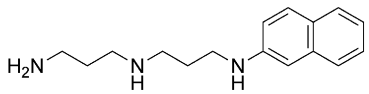
The reactions of 1,3-dibromobenzene with trioxadiamine **1c** were all inefficient, although the CuI/**L5** catalytic system, which promoted the synthesis of diarylation products with bromobenzene and 3-bromotolune, was tried. Even with 1,3-diiodobenzene, this catalyst provided only 45% conversion of dihaloarene (Table 4, entry 10). However, switching to 1-bromo-3-iodobenzene afforded an excellent 85% yield of the target diarylated compound **11** (Table 4, entry 9) in the reaction catalyzed by CuI/**L4b**, which was also the most efficient for 3-iodotoluene amination with the same trioxadiamine (Table 3, entry 13). The formation of *N*,*N*′-bis(3-iodophenyl)-substituted trioxadiamine **12** under the same conditions was somewhat less efficient (Table 4, entry 11), possibly due to the higher reactivity of the C–I bond in the reduction process.

A comparison of Pd and Cu-catalyzed amination reactions for the synthesis of *N*,*N*′-bis(3-bromophenyl)-substituted oxadiamines and polyamines favors the Pd chemistry in the case of the tetraamine derivative because the yields of the corresponding derivatives with polyamines reached 64%.[36] For *N*,*N*′-bis(3-bromophenyl)-substituted trioxadiamine, the Cu-mediated diarylation using 1-bromo-3-iodobenzene was found to be much more efficient than the Pd-catalyzed process, which provided only 29% yield of the same product.

To gain information on the behavior of aryl halides with more active halogen atoms in the *N*,*N*′-diarylation process, we introduced 4-bromo- and 4-iodobiphenyl, *N*,*N*-diethyl-3-iodobenzamide, 4-acetoxy-4′-iodobiphenyl, and 2-bromonaphthalene into the Cu-catalyzed reactions with di-, tri-, and tetraamines (Scheme 6). The reaction of 4-bromobiphenyl with tetraamine **1a** gave a modest result (Table 5, entry 1), and with trioxadiamine **1c** the arylation did not occur at all (Table 5, entry 2). Better results were achieved with 4-iodobiphenyl (Table 5, entries 3 and 4), in which two catalytic systems were found to be suitable for tetraamine and trioxadiamine and both gave similar results. The introduction of an electron-withdrawing acetoxy group improved the results of *N*,*N*′-diarylation; with tetraamine **1a**, the target product **15** was isolated in 68% yield (Table 5, entry 5), triamine **1b** gave a moderate yield of **16** (Table 5, entry 6), whereas *N*,*N*′-diarylation of oxadiamines **1c** and **1d** resulted in good yields of corresponding products **17** and **18** (Table 5, entries 7 and 8). The reactions with another iodoarene containing an electron-withdrawing amide group were all successful for di- and polyamines **1a**–**d**, and the highest observed yield in this investigation was obtained with triamine **1b** (96%; Table 5, entry 10). In all cases the



13: Ar = 4-biphenyl, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
14: Ar = 4-biphenyl, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
15: Ar = 4-acetoxybiphenyl, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
16: Ar = 4-acetoxybiphenyl, X = $CH_2CH_2NHCH_2CH_2$
17: Ar = 4-acetoxybiphenyl, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
18: Ar = 4-acetoxybiphenyl, X = $CH_2OCH_2CH_2OCH_2$
19: Ar = 3-(diethylaminocarboxy)phenyl, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
20: Ar = 3-(diethylaminocarboxy)phenyl, X = $CH_2CH_2NHCH_2CH_2$
21: Ar = 3-(diethylaminocarboxy)phenyl, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
22: Ar = 3-(diethylaminocarboxy)phenyl, X = $CH_2OCH_2CH_2OCH_2$
23: Ar = 2-naphthyl, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$



24, 99%

Scheme 6. *N*,*N*′-Diarylation of polyamines **1a**–**d** with activated haloarenes.

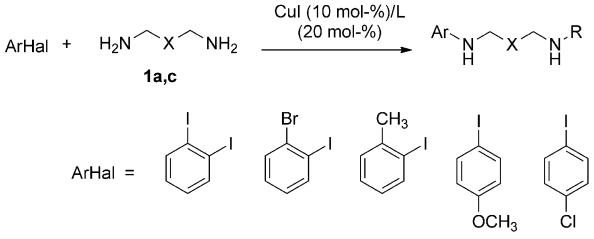
Table 5. Copper-catalyzed arylation of di- and polyamines **1a**–**d** with activated haloarenes [CuI/L (10/20 mol-%), Cs_2CO_3, c = 0.5 M, 24 h].

Entry	ArHal	Amine	Ligand	Solvent	Prod.	Yield [%][a]
1	4-bromobiphenyl	**1a**	**L5**	PhMe[b]	**13**	27
2	4-bromobiphenyl	**1c**	**L5**	PhMe	**14**	0[c]
3	4-iodobiphenyl	**1a**	**L6**	CH_3CN	**13**	43
4	**4-iodobiphenyl**	**1c**	**L4b**	**DMF**	**14**	**46**
5	4-acetoxy-4′-iodobiphenyl	**1a**	**L6**	EtCN	**15**	68
6	4-acetoxy-4′-iodobiphenyl	**1b**	**L6**	EtCN	**16**	32
7	**4-acetoxy-4′-iodobiphenyl**	**1c**	**L4b**	**DMF**	**17**	**72**
8	4-acetoxy-4′-iodobiphenyl	**1d**	**L4b**	DMF	**18**	60
9	*N*,*N*-diethyl-3-iodobenzamide	**1a**	**L6**	EtCN	**19**	58
10	***N*,*N*-diethyl-3-iodobenzamide**	**1b**	**L6**	**EtCN**	**20**	**96**
11	*N*,*N*-diethyl-3-iodobenzamide	**1c**	**L4b**	DMF	**21**	52
12	*N*,*N*-diethyl-3-iodobenzamide	**1d**	**L4b**	DMF	**22**	52
13	2-bromonaphtalene	**1a**	**L6**	CH_3CN	**23**	0[d]
14	2-bromonaphtalene	**1a**	**L4b**	DMF	**23**	28[e]
15	2-bromonaphtalene	**1b**	**L6**	CH_3CN	**24**	99[f]
16	2-bromonaphtalene	**1c**	**L4b**	DMF	—[g]	
17	2-bromonaphtalene	**1d**	**L4b**	DMF	—[h]	

[a] Yield after column chromatography. [b] c = 0.25 M. [c] 2% conversion of 4-bromobiphenyl. [d] 50% conversion of 2-bromonaphthalene. [e] 40% conversion of 2-bromonaphthalene. [f] 60% conversion of 2-bromonaphthalene. [g] 20% conversion of 2-bromonaphthalene. [h] 3% conversion of 2-bromonaphthalene.

CuI/**L6** catalyst was applied in propionitrile for the diarylation of tri- and tetraamines, and CuI/**L4b** catalyst in DMF in the case of oxadiamines. Surprisingly, 2-bromonaphthalene, which proved to be an active substrate in Pd-catalyzed amination according to our previous investigations,[37] was more problematic in copper catalysis. The CuI/**L6** system was not efficient in the reaction with tetraamine **1a** (Table 5, entry 13), however, although the CuI/**L4b** catalyst was of similar activity, compound **23** could be isolated in a moderate 28% yield (Table 5, entry 14). With triamine **1b**, due to only partial conversion of 2-bromonaphthalene, only the product of monoarylation **24** could be obtained, but in almost quantitative yield (Table 5, entry 15). The contrasting behavior of tetraamine **1a** and triamine **1b** is notable: the former afforded the diarylated derivative with a lower degree of conversion of 2-bromonaphthalene (40%), whereas the latter gave only the product of monoarylation with a higher degree of conversion (60%) of 2-bromonaphthalene. Attempts to introduce oxadiamines in the reaction with 2-bromonaphthalene failed (Table 5, entries 16 and 17), also due to very low conversion of the aryl bromide.

We then investigated the dependence of the reactivity of substituted aryl iodides on the nature of the substituent on the phenyl ring (electron-donating or electron-withdrawing group), and also assessed several *ortho*-substituted aryl halides to delineate the influence of steric factors (Scheme 7). Optimized catalytic systems were chosen in accordance with previously obtained data: CuI/**L6**/boiling EtCN for the arylation of tetraamine **1a** and CuI/**L4b**/DMF (110 °C) for the arylation of trioxadiamine **1c**.



25: Ar = R = *o*-MeC_6H_4, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
26: Ar = *o*-MeC_6H_4, R = H, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
27: Ar = R = *o*-MeC_6H_4, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
28: Ar = *o*-MeC_6H_4, R = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
29: Ar = R = *p*-$MeOC_6H_4$, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
30: Ar = R = *p*-$MeOC_6H_4$, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
31: Ar = *p*-$MeOC_6H_4$, R = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
32: Ar = R = *p*-ClC_6H_4, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
33: Ar = R = *p*-ClC_6H_4, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
34: Ar = *p*-ClC_6H_4, R = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$

35: $R^1 = R^2 = R^3$ = *p*-$NO_2C_6H_4$, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
36: $R^1 = R^2$ = *p*-$NO_2C_6H_4$, R^3 = H, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
37: R^2 = *p*-$NO_2C_6H_4$, $R^1 = R^3$ = H, X = $CH_2CH_2NHCH_2CH_2NHCH_2CH_2$
38: $R^1 = R^2 = R^3$ = *p*-$NO_2C_6H_4$, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
39: $R^1 = R^2$ = *p*-$NO_2C_6H_4$, R^3 = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
40: R^2 = *p*-$NO_2C_6H_4$, $R^1 = R^3$ = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
41: R^1 = *p*-$NO_2C_6H_4$, $R^2 = R^3$ = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$
42: $R^1 = R^2 = R^3$ = H, X = $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2$

Scheme 7. Copper-catalyzed arylation of polyamines **1a** and **1c** with iodoarenes.

The reactions with *o*-diiodobenzene and *o*-bromoiodobenzene with tetraamine **1a** did not proceed at all due to the steric hindrance in these molecules (Table 6, entries 1 and 2), and only starting compounds were detected in the reaction mixtures after prolonged heating. The reaction with *o*-iodotoluene was somewhat more successful (Table 6, entry 3), however, in this case the yield of diarylated product **25** was too small, and N^1-aryl-substituted compound **26** was also isolated in a moderate 27% yield due to competitive arylation of the dialkylamino group. Arylation of tri-

oxadiamine **1c** with the same aryl iodide provided a slightly better result, giving 7% yield of the diaryl-substituted product **27** and 39% yield of the mono-arylated compound **28** (Table 6, entry 4). These data show that copper-catalyzed arylation of polyamines is more sensitive to steric factors than palladium-catalyzed reactions because previously we showed that facile amination of *o*-dibromobenzene and 2,6-dichlorobromobenzene occurred.[39]

Table 6. Copper-catalyzed arylation of tetraamine **1a** and trioxadiamine **1c** with aryl iodides [CuI/L (10/20 mol-%), Cs_2CO_3, *c* = 0.5 M, 24 h].

Entry	ArHal	Amine	Ligand	Solvent	Prod.	Yield [%][a]
1	1,2-$I_2C_6H_4$	**1a**	**L6**	EtCN	–	
2	1-Br-2-I-C_6H_4	**1a**	**L6**	EtCN	–	
3	2-iodotoluene	**1a**	**L6**	EtCN	**25**	2
					26	27
4	2-iodotoluene	**1c**	**L4b**	DMF	**27**	7
					28	39
5	4-$MeOC_6H_4I$	**1a**	**L6**	EtCN	**29**	52
6	4-$MeOC_6H_4I$	**1c**	**L4b**	DMF	**30**	17
					31	51
7	1-Cl-4-IC_6H_4	**1a**	**L6**	EtCN	**32**	42
8	1-Cl-4-IC_6H_4	**1c**	**L4b**	DMF	**33**	28
					34	42
9	4-$NO_2C_6H_4I$	**1a**	**L6**	EtCN	**35 + 36**	35[b]
					36	33
					37	12
10	4-$NO_2C_6H_4I$	**1c**	**L4b**	DMF	**38 + 39**	25[b]
					39	5
					40	26
					40 + 41	16[b]
					42	28

[a] Yield after column chromatography. [b] Yields of inseparable mixtures.

The N^1,N^4-diarylation of tetraamine **1a** with electron-rich *p*-methoxyiodobenzene proceeded normally, and the target product **29** was isolated in 52% yield (Table 6, entry 5). In this reaction other isomeric diaryl and monoaryl compounds were also obtained as inseparable fractions. The reaction with trioxadiamine **1c** was not so successful, and the main product was the monarylated derivative **31**, whereas the diarylated product **30** was obtained in a small amount (Table 6, entry 6). Similar results were obtained when the substrate contained a moderate electron-withdrawing group, for example, *p*-chloroiodobenzene; in this case, the reaction with tetraamine **1a** resulted in 42% preparative yield of the product of N^1,N^4-diarylation **32** (Table 6, entry 7), and the formation of N^1,N^2,N^4-triaryl derivative was notable. However, the latter compound was observed only as a mixture with the target product **32**, and it was identified by a characteristic signal in its ^{1}H NMR spectrum (triplet at δ = 3.65 ppm, which corresponds to $ArNHCH_2CH_2CH_2NArCH_2$ protons). The reaction of the same iodide with trioxadiamine afforded *N*,*N*′-diaryl product **33** in 28% yield, whereas monoaryl derivative **34** was isolated in 42% yield (Table 6, entry 8).

Finally, the arylation of polyamines using more electron-withdrawing *p*-nitroiodobenzene was investigated. The results of the reactions were found to be notably different to those described above. In the coupling with tetraamine **1a**, the reaction produced only 12% of the desired N^1,N^4-diaryl derivative **37** (Table 6, entry 9); the main products were N^1,N^1,N^4,N^4-tetraaryl-substituted tetraamine **35** and N^1,N^1,N^4-triaryl-substituted tetraamine **36**, which were isolated as a mixture in approximately 35% yield. Compound **36** was additionally obtained as an individual product in 33% yield. The formation of the products of *N*,*N*-diarylation was shown by a strong downfield shift of the protons of the CH_2NAr_2 group (δ_H = 4.0 ppm) and the benzene ring (δ_H = 7.3 and 8.15 ppm). For comparison, the protons of the CH_2NHAr group have ^{1}H NMR shifts at δ = 3.2 ppm, and benzene protons at δ = 6.6 and 7.9 ppm. The formation of tetraaryl derivative **35** was also proven by the presence of the corresponding pseudomolecular peak in the MALDI mass-spectrum (*m*/*z* = 659 $[M + H]^+$). Trioxadiamine **1c** was less reactive, nevertheless, its reaction with *p*-nitroiodobenzene (Table 6, entry 10) also afforded a mixture of tri- and tetraaryl-substituted compounds **38** and **39** (combined yield approximately 25%), and the triarylated derivative **39** was also isolated separately in 5% yield. Target N^1,N^2-diaryl compound **40** was obtained in 26% yield, and a part of it was isolated as a mixture with N^1,N^1-diaryl derivative **41** (combined yield 16%), whereas monoarylated product **42** was obtained in 28% yield. These reactions demonstrated for the first time the possibility of *N*,*N*-diarylation of primary alkylamines; such processes until now have been well-known for only Pd-catalyzed reactions.[1] We tried to reduce the ratio of polyaryl derivatives by using a less active catalytic system and by lowering the reaction temperature [CuI/**L6**/MeCN and CuI/**L5**/MeCN for the reactions with **1a**, CuI/**L4a**/DMF (80 °C) with **1c**], however, this approach did not notably decrease the formation of the products of *N*,*N*-diarylation but, rather, led to insufficient conversion of the starting aryl iodide (60% in the case of **1a** and 40% in the case of **1c**). These results suggest that the reactions with aryl halides containing strong electron-withdrawing substituents need individually tailored catalytic systems, and changing the more reactive iodine for less active bromine atom; these questions will be addressed in further investigations into heteroaromatic halides possessing halogen atoms. Conditions for exhaustive *N*,*N*-diarylation of primary alkylamines will also be established.

Conclusions

The experimental data obtained in this research demonstrate that primary amino groups of di- and polyamines can be preparatively diarylated with aryl bromides and aryl iodides under Cu^I catalysis. Generally, the arylation of tetraamine was more exhaustive than the arylation of oxadiamines, possibly due to additional coordination of copper by ethylenediamine and trimethylenediamine fragments. However, the main problem was a lower selectivity of the arylation of primary amino groups in the presence of secondary amino groups compared to Pd-mediated amination. The general idea is that more bulky ligands should prevent

arylation of more sterically hindered secondary amino groups, however, this may simultaneously hinder the *N*,*N*′-diarylation process, giving rise to monoarylated derivatives. In the present investigation, proline was found to be optimal for the synthesis of N^1,N^4-diaryl derivatives of a model tetraamine. Another consistent feature is that tetraamines can be successfully diarylated not only with aryl iodides but also with aryl bromides, at least in some cases, whereas oxadiamines, due to their lower reactivity, can be successfully transformed into their *N*,*N*′-diaryl derivatives only using aryl iodides. The main advantage of the copper-catalyzed amination of dihalobenzenes over the palladium-mediated protocol is the total absence of a diamination process, which could lead to linear oligomers. Unlike the Pd-catalyzed arylation of polyamines, the reactions catalyzed by Cu^I demanded a tailored approach to each particular aryl halide/polyamine pair. The following catalytic systems were found to be most suitable: CuI/**L6**/Cs_2CO_3/MeCN or EtCN for the *N*,*N*′-diarylation of tetraamines, and CuI/**L4a**,**b**/Cs_2CO_3/DMF for the *N*,*N*′-diarylation of oxadiamines. Thus, the best catalytic systems for the synthesis of almost all the desired *N*,*N*′-diaryl-substituted polyamines were established and the products were obtained in high yields. Cu-catalyzed arylation of polyamines was found to be sensitive to steric hindrance in the aryl halides, and the application of *ortho*-substituted substrates retarded the process. By investigating the reactions with an active *p*-nitroiodobenzene, we revealed an easy *N*,*N*-diarylation process that was previously unknown for Cu-catalyzed arylation of primary alkylamines. The study will be continued to extend the approach to a greater variety of benzene functional derivatives, condensed aromatics, and heteroaromatic compounds.

Experimental Section

General: Aryl halides, di- and polyamines **1a**–**d**, ligands **L1**–**L6**, and CuI were purchased from commercial suppliers and used without further purification. Silica gel 40–60 mesh was purchased from Fluka Chemical Co. Acetonitrile and DMF were purified by distillation over CaH_2, toluene was distilled from sodium, propionitrile was used as purchased, dichloromethane and methanol were freshly distilled before use. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance-400 spectrometer; chemical shifts are given in ppm and are referenced to TMS. Mass spectra were recorded with a Bruker Ultraflex spectrometer using 1,8,9-trihydroxyanthracene as matrix and PEGs as internal standards.

General Procedure for the Synthesis of *N*,*N*′-Diaryl-Substituted Oxadiamines and Polyamines: A two-necked flask equipped with magnetic stirrer and condenser, flushed with dry argon, was charged with aryl halide (0.625–2.5 mmol), CuI (4.8–19.2 mg, 10 mol-%), appropriate ligand (20 mol-%), and solvent (1–2 mL). The reaction mixture was stirred for several minutes, then amine (0.25–1 mmol) and base (0.625–2.5 mmol) were added and the reaction mixture was stirred for 24 h either at reflux temperature (acetonitrile, propionitrile, toluene) or at 110 °C (DMF). Upon completion of reaction, the reaction mixture was diluted with CH_2Cl_2 (5 mL), the solution was filtered, evaporated in vacuo, and the residue was subjected to column chromatography using the following sequence of eluents: petroleum ether/CH_2Cl_2 10:1–1:1, CH_2Cl_2, CH_2Cl_2/MeOH 500:1–3:1, CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–10:4:1. As the majority of diaryl-substituted oxadiamines and polyamines were obtained by using several catalytic systems, only the best methods are described below for each compound.

***N*^{1},*N*$^{1'}$-(Ethane-1,2-diyl)bis(*N*^{3}-*m*-tolylpropane-1,3-diamine) (2):** Synthesized from 3-iodotoluene (1.25 mmol, 273 mg), and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg), in acetonitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 118 mg (67%); pale-yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.78 (quint., J = 6.6 Hz, 4 H), 2.26 (s, 6 H), 2.73 (t, J = 6.6 Hz, 4 H), 2.74 (s, 4 H), 3.16 (t, J = 6.6 Hz, 4 H), 6.41 (d, J = 7.6 Hz, 2 H), 6.42 (s, 2 H), 6.50 (d, J = 7.5 Hz, 2 H), 7.05 (t, J = 7.5 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.5 (2 C), 29.4 (2 C), 42.5 (2 C), 48.0 (2 C), 49.3 (2 C), 109.7 (2 C), 113.3 (2 C), 117.9 (2 C), 128.9 (2 C), 138.7 (2 C), 148.4 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{34}N_4 + H]^+$ 355.2862; found 355.2898.

***N*^{1},*N*$^{1'}$-(Ethane-1,2-diyl)bis(*N*^{3}-phenylpropane-1,3-diamine) (3):** Synthesized from bromobenzene (1.25 mmol, 196 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in acetonitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 107 mg (65%); pale-yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.82 (quint., J = 6.0 Hz, 4 H), 2.80 (t, J = 5.7 Hz, 4 H), 2.85 (s, 4 H), 3.16 (t, J = 5.9 Hz, 4 H), 4.16 (br. s, 2 H), 6.61 (d, J = 7.7 Hz, 4 H), 6.67 (t, J = 7.3 Hz, 2 H), 7.14 (t, J = 7.4 Hz, 4 H) ppm ; 2 NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.1 (2 C), 42.4 (2 C), 47.8 (2 C), 48.8 (2 C), 112.6 (4 C), 117.0 (2 C), 129.1 (4 C), 148.4 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{20}H_{30}N_4 + H]^+$ 327.2549; found 327.2557.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}dianiline (4):** Synthesized from iodobenzene (1.25 mmol, 255 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4a** (14 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2; yield 144 mg (76%); pale-yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.91 (quint., J = 6.2 Hz, 4 H), 3.25 (t, J = 6.5 Hz, 4 H), 3.62 (t, J = 5.9 Hz, 4 H), 3.63–3.67 (m, 4 H), 3.68–3.72 (m, 4 H), 3.98 (br. s, 2 H), 6.63 (d, J = 8.5 Hz, 4 H), 6.71 (t, J = 7.3 Hz, 2 H), 7.20 (t, J = 7.8 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.8 (2 C), 41.5 (2 C), 69.5 (2 C), 70.1 (2 C), 70.4 (2 C), 112.5 (2 C), 116.7 (2 C), 129.0 (2 C), 148.4 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{32}N_2O_3 + H]^+$ 373.2491; found 373.2448.

***N*^{1},*N*$^{1'}$-(Ethane-1,2-diyl)bis[*N*^{3}-(3,5-dimethylphenyl)propane-1,3-diamine] (5):** Synthesized from 3,5-dimethyliodobenzene (1.25 mmol, 290 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L4a** (14 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 103 mg (54%); pale-yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.89 (br. s, 4 H), 2.20 (s, 12 H), 2.90 (br. s, 4 H), 3.01 (br. s, 4 H), 3.16 (br. s, 4 H), 5.25 (br. s, 2 H), 6.26 (br. s, 4 H), 6.34 (br. s, 1 H) ppm; 2 NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.4 (4 C), 27.3 (2 C), 41.8 (2 C), 45.9 (2 C), 46.8 (2 C), 111.0 (4 C), 119.6 (2 C), 138.7 (4 C), 148.1 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{24}H_{38}N_4 + H]^+$ 383.3175; found 383.3128.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(3-methylaniline) (7):** Synthesized from 3-iodotoluene (1.25 mmol, 273 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3

(408 mg) in DMF (1 mL). Eluent: CH_2Cl_2, CH_2Cl_2/MeOH 500:1; yield 130 mg (65%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.92 (quint., J = 6.2 Hz, 4 H), 2.32 (s, 6 H), 3.25 (t, J = 6.5 Hz, 4 H), 3.63 (t, J = 5.9 Hz, 4 H), 3.64–3.68 (m, 4 H), 3.70–3.74 (m, 4 H), 3.83 (br. s, 2 H), 6.46 (d, J = 6.2 Hz, 2 H), 6.47 (s, 2 H), 6.55 (d, J = 7.3 Hz, 2 H), 7.10 (t, J = 8.1 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.5 (2 C), 29.0 (2 C), 41.5 (2 C), 69.5 (2 C), 70.1 (2 C), 70.5 (2 C), 109.7 (2 C), 113.3 (2 C), 117.8 (2 C), 128.9 (2 C), 138.7 (2 C), 148.4 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{24}H_{36}N_2O_3 + H]^+$ 401.2804; found 401.2820.

***N*^{1}-(3-Aminopropyl)-*N*^{3}-*m*-tolylpropane-1,3-diamine (8):** Synthesized from 3-iodotoluene (1.25 mmol, 273 mg) and triamine **1b** (0.5 mmol, 65 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in acetonitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:3–100:25:5; yield 86 mg (78%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (quint., J = 6.8 Hz, 2 H), 1.78 (quint., J = 6.6 Hz, 2 H), 2.25 (s, 3 H), 2.66 (t, J = 7.0 Hz, 2 H), 2.72 (t, J = 6.7 Hz, 2 H), 2.76 (t, J = 6.9 Hz, 2 H), 6.40 (d, J = 7.0 Hz, 1 H), 6.41 (s, 1 H), 6.49 (d, J = 7.5 Hz, 1 H), 7.03 (t, J = 7.4 Hz, 1 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.6, 29.4, 33.2, 40.3, 42.7, 47.8, 48.3, 109.9, 113.4, 118.0, 129.0, 138.8, 148.5 ppm. HRMS (MALDI-TOF): calcd. for $[C_{13}H_{23}N_3 + H]^+$ 222.1970; found 222.1968.

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis[*N*^{3}-(3-bromophenyl)propane-1,3-diamine] (9):** Synthesized from 1,3-dibromobenzene (1.25 mmol, 295 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L4a** (14 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 65 mg (28%); pale-yellow oil. Spectral data have previously been reported.[36]

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis[*N*^{3}-(3-iodophenyl)propane-1,3-diamine] (10):** Synthesized from 1,3-diiodobenzene (1.25 mmol, 412 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 69 mg (24%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.79 (quint., J = 5.9 Hz, 4 H), 2.78 (br. s, 8 H), 3.14 (t, J = 5.9 Hz, 4 H), 6.53 (d, J = 7.8 Hz, 2 H), 6.84 (t, J = 7.8 Hz, 2 H), 6.93 (s, 2 H), 6.97 (d, J = 7.5 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 28.7 (2 C), 42.4 (2 C), 47.9 (2 C), 48.6 (2 C), 95.3 (2 C), 112.1 (2 C), 121.1 (2 C), 126.0 (2 C), 130.6 (2 C), 149.7 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{20}H_{28}I_2N_4 + H]^+$ 579.0482; found 579.0471.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(3-bromoaniline) (11):** Synthesized from 1-bromo-3-iodobenzene (1.25 mmol, 353 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2, CH_2Cl_2/MeOH 500:1; yield 226 mg (85%); pale-yellow oil. Spectral data have previously been reported.[36]

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(3-iodoaniline) (12):** Synthesized from 1,3-diiodobenzene (1.25 mmol, 412 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 500:1–200:1; yield 165 mg (53%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 (quint., J = 6.1 Hz, 4 H), 3.16 (t, J = 6.4 Hz, 4 H), 3.58 (t, J = 5.9 Hz, 4 H), 3.59–3.63 (m, 4 H), 3.65–3.69 (m, 4 H), 4.21 (br. s, 2 H), 6.51 (dd, J = 8.2, 2.3 Hz), 6.83 (t, J = 7.9 Hz, 2 H), 6.91 (t, J = 1.9 Hz, 2 H), 6.99 (dd, J = 7.7, 1.5 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 28.7 (2 C), 41.6 (2 C), 69.7 (2 C), 70.2 (2 C), 70.5 (2 C), 70.5 (2 C), 95.3 (2 C), 111.9 (2 C), 121.0 (2 C), 125.6 (2 C), 130.5 (2 C), 149.7 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{30}I_2N_2O_3 + H]^+$ 625.0424; found 625.0480.

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis[*N*^{3}-(biphenyl-4-yl)propane-1,3-diamine] (13):** Synthesized from 4-iodobiphenyl (1.25 mmol, 351 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in acetonitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 90 mg (43%); beige crystals; m.p. 72–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81 (quint., 4 H, J = 6.5 Hz), 2.75 (s, 4 H), 2.76 (t, J = 6.7 Hz, 4 H), 3.22 (t, J = 6.5 Hz, 4 H), 6.66 (d, J = 8.6 Hz, 4 H), 7.25 (t, J = 7.3 Hz, 2 H), 7.38 (t, J = 7.5 Hz, 4 H), 7.43 (d, J = 8.5 Hz, 4 H), 7.53 (d, J = 7.2 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.4 (2 C), 42.6 (2 C), 48.0 (2 C), 49.3 (2 C), 112.9 (4 C), 125.9 (2 C), 126.1 (4 C), 127.8 (4 C), 128.6 (4 C), 129.9 (2 C), 141.2 (2 C), 147.9 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{32}H_{38}N_4 + H]^+$ 479.3175; found 479.3205.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}dibiphenyl-4-amine (14):** Synthesized from 4-iodobiphenyl (1.25 mmol, 351 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 500:1–100:1; yield 121 mg (46%); pale-yellow oil. Spectral data have previously been reported.[38]

1,1′-(4′,4′′-{3,3′-[Ethane-1,2-diylbis(azanediyl)]bis(propane-3,1-diyl)}bis(azanediyl)bis(biphenyl-4′,4-diyl))diethanone (15): Synthesized from 4-acetoxy-4′-iodobiphenyl (2.5 mmol, 808 mg) and tetraamine **1a** (1 mmol, 174 mg), in the presence of CuI (19.2 mg), ligand **L6** (23 mg), and Cs_2CO_3 (816 mg) in propionitrile (2 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:3; yield 381 mg (68%); beige crystals; m.p. 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82 (quint., J = 6.4 Hz, 4 H), 2.59 (s, 6 H), 2.76 (s, 6 H), 2.78 (t, J = 6.6 Hz, 4 H), 3.24 (t, J = 6.1 Hz, 4 H), 6.65 (d, J = 8.3 Hz, 4 H), 7.46 (d, J = 8.6 Hz, 4 H), 7.59 (d, J = 8.6 Hz, 4 H), 7.95 (d, J = 8.3 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 26.5 (2 C), 29.0 (2 C), 41.0 (2 C), 47.1 (2 C), 49.0 (2 C), 112.2 (4 C), 124.9 (4 C), 127.6 (4 C), 128.9 (4 C), 133.8 (2 C), 141.6 (2 C), 145.0 (2 C), 149.5 (2 C), 197.1 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{36}H_{42}N_4O_2 + H]^+$ 563.3386; found 563.3407.

1,1′-{4′,4′′-[3,3′-Azanediylbis(propane-3,1-diyl)bis(azanediyl)]bis(biphenyl-4′,4-diyl)}diethanone (16): Synthesized from 4-acetoxy-4′-iodobiphenyl (2.5 mmol, 808 mg) and triamine **1b** (1 mmol, 131 mg), in the presence of CuI (19.2 mg), ligand **L6** (23 mg), and Cs_2CO_3 (816 mg), in propionitrile (2 mL). Eluent: CH_2Cl_2/MeOH 3:1, CH_2Cl_2/MeOH/NH_3(aq) 100:20:1; yield 167 mg (32%); beige crystals; m.p. 190–192 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.81 (quint., J = 7.2 Hz, 4 H), 2.55 (s, 6 H), 2.88 (t, J = 7.0 Hz, 4 H), 3.14 (br. s, 4 H), 6.05 (br. s, 2 H), 6.67 (d, J = 8.6 Hz, 4 H), 7.53 (d, J = 8.7 Hz, 4 H), 7.69 (d, J = 8.5 Hz, 4 H), 7.93 (d, J = 8.5 Hz, 4 H) ppm; 1 NH proton was not assigned. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 26.0 (2 C), 26.6 (2 C), 39.9 (2 C), 45.5 (2 C), 112.4 (4 C), 125.0 (4 C), 125.7 (2 C), 127.7 (4 C), 128.9 (4 C), 134.0 (2 C), 144.9 (2 C), 149.1 (2 C), 197.2 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{34}H_{37}N_3O_2 + H]^+$ 520.2964; found 520.2897.

1,1′-(4′,4′′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(azanediyl)bis(biphenyl-4′,4-diyl))diethanone (17): Synthesized from 4-acetoxy-4′-iodobiphenyl (2.5 mmol, 808 mg) and trioxadiamine **1c** (1 mmol, 220 mg), in the presence of CuI (19.2 mg), ligand **L4b** (34 mg), and Cs_2CO_3 (816 mg), in DMF (2 mL). Eluent: CH_2Cl_2/MeOH 100:1–50:1 Yield: 463 mg (72%);

beige crystals; m.p. 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.90 (quint., J = 6.1 Hz, 4 H), 2.58 (s, 6 H), 3.27 (t, J = 6.4 Hz, 4 H), 3.61 (t, J = 5.8 Hz, 4 H), 3.63–3.65 (m, 4 H), 3.68–3.71 (m, 4 H), 4.33 (br. s, 2 H), 6.65 (d, J = 8.6 Hz, 4 H), 7.46 (d, J = 8.6 Hz, 4 H), 7.59 (d, J = 8.3 Hz, 4 H), 7.94 (d, J = 8.3 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 26.5 (2 C), 29.0 (2 C), 41.6 (2 C), 69.7 (2 C), 70.2 (2 C), 70.6 (2 C), 112.8 (4 C), 125.7 (4 C), 127.8 (2 C), 128.0 (4 C), 128.9 (4 C), 134.5 (2 C), 145.8 (2 C), 148.8 (2 C), 197.6 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{38}H_{44}N_2O_5 + H]^+$ 609.3328; found 609.3361.

1,1′-(4′,4′′-{2,2′-[Ethane-1,2-diylbis(oxy)]bis(ethane-2,1-diyl)}bis(azanediyl)bis(biphenyl-4′,4-diyl))diethanone (18): Synthesized from 4-acetoxy-4′-iodobiphenyl (2.5 mmol, 808 mg) and dioxadiamine **1d** (1 mmol, 148 mg), in the presence of CuI (19.2 mg), ligand **L4b** (34 mg), and Cs_2CO_3 (816 mg), in DMF (2 mL). Eluent: CH_2Cl_2/MeOH 50:1–20:1 Yield: 322 mg (60%); beige crystals; m.p. 180–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (s, 6 H), 3.36 (t, J = 5.2 Hz, 4 H), 3.69 (s, 4 H), 3.75 (t, J = 5.2 Hz, 4 H), 4.30 (br. s, 2 H), 6.68 (d, J = 8.6 Hz, 4 H), 7.46 (d, J = 8.6 Hz, 4 H), 7.59 (d, J = 8.3 Hz, 4 H), 7.95 (d, J = 8.3 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 26.5 (2 C), 42.5 (2 C), 69.0 (2 C), 69.8 (2 C), 112.4 (4 C), 124.9 (4 C), 125.5 (2 C), 127.6 (4 C), 128.9 (4 C), 133.9 (2 C), 144.9 (2 C), 149.2 (2 C), 197.1 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{34}H_{36}N_2O_4 + H]^+$ 537.2753; found 537.2702.

3,3′-{3,3′-[Ethane-1,2-diylbis(azanediyl)]bis(propane-3,1-diyl)}bis(azanediyl)bis(*N*,*N*-diethylbenzamide) (19): Synthesized from *N*,*N*-diethyl-3-iodobenzamide (1.25 mmol, 379 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 151 mg (58%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (br. s, 6 H), 1.18 (br. s, 6 H), 1.73 (quint., J = 6.5 Hz, 4 H), 2.68 (t, J = 6.4 Hz, 4 H), 2.69 (s, 4 H), 3.11 (t, J = 6.5 Hz, 4 H), 3.21 (br. s, 4 H), 3.47 (br. s, 4 H), 4.48 (br. s, 2 H), 6.52 (s, 2 H), 6.56 (d, J = 7.6 Hz, 4 H), 7.08 (t, J = 7.6 Hz, 2 H) ppm; 2 NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 12.8 (2 C), 14.2 (2 C), 28.8 (2 C), 39.0 (2 C), 42.2 (2 C), 43.1 (2 C), 47.7 (2 C), 48.7 (2 C), 110.0 (2 C), 113.2 (2 C), 114.2 (2 C), 129.0 (2 C), 137.9 (2 C), 148.6 (2 C), 171.8 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{30}H_{48}N_6O_2 + H]^+$ 525.3917; found 525.3881.

3,3′-[3,3′-Azanediylbis(propane-3,1-diyl)bis(azanediyl)]bis(*N*,*N*-diethylbenzamide) (20): Synthesized from *N*,*N*-diethyl-3-iodobenzamide (1.25 mmol, 379 mg) and triamine **1b** (0.5 mmol, 65 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH 3:1, CH_2Cl_2/MeOH/NH_3(aq) 100:20:1; yield 230 mg (96%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01 (br. s, 6 H), 1.14 (br. s, 6 H), 1.69 (quint., J = 6.1 Hz, 4 H), 2.63 (br. s, 4 H), 3.05 (br. s, 4 H), 3.18 (br. s, 4 H), 3.42 (br. s, 4 H), 4.46 (br. s, 2 H), 6.47 (s, 2 H), 6.51 (d, J = 7.7 Hz, 4 H), 7.04 (t, J = 7.7 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 12.6 (2 C), 14.0 (2 C), 28.2 (2 C), 38.9 (2 C),41.8 (2 C), 43.0 (2 C), 47.4 (2 C), 109.7 (2 C), 113.1 (2 C), 114.0 (2 C), 128.9 (2 C), 137.8 (2 C), 148.4 (2 C), 171.7 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{28}H_{43}N_5O_2 + H]^+$ 482.3495; found 482.3560.

3,3′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(azanediyl)bis(*N*,*N*-diethylbenzamide) (21): Synthesized from *N*,*N*-diethyl-3-iodobenzamide (1.25 mmol, 379 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 50:1; yield 148 mg (52%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (br. s, 6 H), 1.20 (br. s, 6 H), 1.84 (quint., J = 6.0 Hz, 4 H), 3.19 (t, J = 6.4 Hz, 4 H), 3.23 (br. s, 4 H), 3.49 (br. s, 4 H), 3.56 (t, J = 5.8 Hz, 4 H), 3.57–3.60 (m, 4 H), 3.62–3.65 (m, 4 H), 6.53 (s, 2 H), 6.57 (d, J = 7.6 Hz, 2 H), 6.59 (d, J = 7.6 Hz, 2 H), 7.11 (t, J = 7.6 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 12.8 (2 C), 14.2 (2 C), 28.8 (2 C), 38.9 (2 C), 41.7 (2 C), 43.1 (2 C), 69.7 (2 C), 70.2 (2 C), 70.5 (2 C), 110.1 (2 C), 113.4 (2 C), 114.4 (2 C), 129.0 (2 C), 138.1 (2 C), 148.5 (2 C), 171.8 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{32}H_{50}N_4O_5 + H]^+$ 571.3859; found 571.3829.

3,3′-{2,2′-[Ethane-1,2-diylbis(oxy)]bis(ethane-2,1-diyl)}bis(azanediyl)bis(*N*,*N*-diethylbenzamide) (22): Synthesized from *N*,*N*-diethyl-3-iodobenzamide (1.25 mmol, 379 mg) and dioxadiamine **1c** (0.5 mmol, 74 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg), in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 50:1–20:1; yield 130 mg (52%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (br. s, 6 H), 1.18 (br. s, 6 H), 3.23 (br. s, 4 H), 3.25 (t, J = 5.0 Hz, 4 H), 3.47 (br. s, 4 H), 3.60 (s, 4 H), 3.65 (t, J = 5.0 Hz, 4 H), 4.22 (br. s, 2 H), 6.55 (s, 2 H), 6.57 (d, J = 8.3 Hz, 2 H), 6.61 (d, J = 7.5 Hz, 2 H), 7.10 (t, J = 7.6 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 12.8 (2 C), 14.1 (2 C), 38.9 (2 C), 43.1 (2 C), 43.2 (2 C), 69.4 (2 C), 70.1 (2 C), 110.3 (2 C), 113.7 (2 C), 114.9 (2 C), 129.1 (2 C), 138.1 (2 C), 148.2 (2 C), 171.6 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{28}H_{42}N_4O_4 + H]^+$ 499.3284; found 499.3300.

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis[*N*^{3}-(naphthalen-2-yl)propane-1,3-diamine] (23):** Synthesized from 2-bromonaphthalene (1.25 mmol, 258 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg), in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 61 mg (28%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83 (quint., J = 6.6 Hz, 4 H), 2.75 (s, 4 H), 2.77 (t, J = 6.7 Hz, 4 H), 3.27 (t, J = 6.6 Hz, 4 H), 6.78 (d, J = 2.0 Hz, 2 H), 6.84 (dd, J = 8.6, 2.0 Hz, 2 H), 7.18 (t, J = 7.5 Hz, 2 H), 7.35 (t, ^3J = 7.5 Hz, 2 H), 7.59 (d, J = 8.8 Hz, 2 H), 7.60 (d, J = 8.1 Hz, 2 H), 7.65 (d, J = 8.1 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.3 (2 C), 42.7 (2 C), 48.2 (2 C), 49.3 (2 C), 104.0 (2 C), 118.0 (2 C), 121.7 (2 C), 125.8 (2 C), 126.2 (2 C), 127.3 (2 C), 127.6 (2 C), 128.8 (2 C), 135.2 (2 C), 146.1 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{28}H_{34}N_4 + H]^+$ 427.2862; found 427.2810.

***N*^{1}-(3-Aminopropyl)-*N*^{3}-(naphthalen-2-yl)propane-1,3-diamine (24):** Synthesized from 2-bromonaphthalene (1.25 mmol, 258 mg) and triamine **1b** (0.5 mmol, 65 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg), in acetonitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:3–100:25:5; yield 120 mg (99%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65 (quint., J = 6.7 Hz, 2 H), 1.86 (quint., J = 6.4 Hz, 2 H), 2.69 (t, J = 6.9 Hz, 2 H), 2.78 (t, J = 6.4 Hz, 4 H), 6.77 (s, 2 H), 3.28 (t, J = 6.5 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 7.16 (t, J = 7.3 Hz, 2 H), 7.33 (t, J = 7.4 Hz, 2 H), 7.59 (d, J = 8.5 Hz, 4 H), 7.64 (d, J = 8.1 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.0, 33.1, 40.5, 42.9, 47.9, 48.4, 104.0, 118.1, 121.7, 125.8, 126.2, 127.3, 127.6, 128.8, 135.3, 146.2 ppm. HRMS (MALDI-TOF): calcd. for $[C_{16}H_{23}N_3 + H]^+$ 258.1970; found 258.1988.

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis(*N*^{3}-*o*-tolylpropane-1,3-diamine) (25):** Synthesized from 2-iodotoluene (1.25 mmol, 273 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 4 mg (2%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83 (quint., J =

6.4 Hz, 4 H), 2.12 (s, 6 H), 2.75 (s, 4 H), 2.77 (t, J = 6.4 Hz, 4 H), 3.21 (t, J = 6.6 Hz, 4 H), 6.58 (d, J = 8.0 Hz, 2 H), 6.62 (t, J = 7.1 Hz, 2 H), 7.03 (d, J = 7.1 Hz, 2 H), 7.10 (t, J = 7.6 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.6 (2 C), 29.3 (2 C), 42.9 (2 C), 48.4 (2 C), 49.4 (2 C), 109.4 (2 C), 116.6 (2 C), 121.9 (2 C), 127.1 (2 C), 130.0 (2 C), 146.5 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{34}N_4 + H]^+$ 355.2862; found 355.2810.

N^1-[2-(3-Aminopropylamino)ethyl]-N^3-*o*-tolylpropane-1,3-diamine (26): Obtained as the second product in the synthesis of compound **25**. Eluent: CH_2Cl_2/MeOH/NH_3(aq) 10:4:1; yield 36 mg (27%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.60 (quint., J = 6.9 Hz, 2 H), 1.83 (quint., J = 6.4 Hz, 2 H), 2.10 (s, 3 H), 2.64 (t, J = 6.9 Hz, 2 H), 2.71 (s, 4 H), 2.73 (t, J = 7.1 Hz, 2 H), 2.75 (t, J = 6.4 Hz, 2 H), 3.20 (t, J = 6.3 Hz, 2 H), 6.57 (d, J = 8.1 Hz, 1 H), 6.61 (t, J = 7.6 Hz, 1 H), 7.01 (d, J = 6.8 Hz, 1 H), 7.09 (t, J = 7.1 Hz, 1 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.5, 29.3, 33.4, 40.3, 42.8, 47.7, 48.4, 49.3, 49.4, 109.4, 116.5, 121.8, 127.0, 129.9, 146.5 ppm. HRMS (MALDI-TOF): calcd. for $[C_{15}H_{28}N_4 + H]^+$ 265.2392; found 265.2336.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(2-methylaniline) (27):** Synthesized from 2-iodotoluene (1.25 mmol, 273 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 100:1–50:1; yield 14 mg (7%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94 (quint., J = 6.1 Hz, 4 H), 2.12 (s, 4 H), 3.26 (t, J = 6.4 Hz, 4 H), 3.59–3.67 (m, 12 H), 3.93 (br. s, 2 H), 6.59 (d, J = 8.2 Hz, 2 H), 6.63 (t, J = 7.3 Hz, 2 H), 7.03 (d, J = 7.1 Hz, 2 H), 7.11 (t, J = 7.6 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.5 (2 C), 29.2 (2 C), 42.0 (2 C), 70.2 (2 C), 70.4 (2 C), 70.6 (2 C), 109.4 (2 C), 116.5 (2 C), 121.8 (2 C), 127.0 (2 C), 129.9 (2 C), 146.5 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{24}H_{36}N_2O_3 + H]^+$ 401.2804; found 401.2790.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-2-methylaniline (28):** Obtained as the second product in the synthesis of compound **27**. Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:1–100:20:2; yield 61 mg (39%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (quint., J = 6.4 Hz, 2 H), 1.92 (quint., J = 6.0 Hz, 2 H), 2.10 (s, 3 H), 2.77 (t, J = 6.4 Hz, 2 H), 3.24 (t, J = 6.3 Hz, 2 H), 3.51 (t, J = 6.2 Hz, 2 H), 3.52–3.65 (m, 10 H), 6.57 (d, J = 8.0 Hz, 1 H), 6.60 (t, J = 7.5 Hz, 1 H), 7.01 (d, J = 7.0 Hz, 1 H), 7.08 (t, J = 7.6 Hz, 1 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.4, 29.1, 32.6, 39.4, 41.9, 69.4, 70.0, 70.1, 70.3, 70.5 (2 C), 109.3, 116.5, 121.8, 126.9, 129.9, 146.4 ppm. HRMS (MALDI-TOF): calcd. for $[C_{17}H_{30}N_2O_3 + H]^+$ 311.2335; found 311.2286.

N^1,$N^{1\prime}$-(Ethane-1,2-diyl)bis[N^3-(4-methoxyphenyl)propane-1,3-diamine] (29): Synthesized from 4-iodoanisole (1.25 mmol, 293 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 101 mg (52%); beige crystals; m.p. 85–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74 (quint., J = 6.6 Hz, 4 H), 2.68–2.72 (m, 8 H), 3.09 (t, J = 6.4 Hz, 4 H), 3.70 (s, 6 H), 6.54 (d, J = 8.7 Hz, 4 H), 6.74 (d, J = 8.7 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.3 (2 C), 43.3 (2 C), 47.8 (2 C), 48.9 (2 C), 55.6 (2 C), 113.9 (4 C), 114.7 (4 C), 142.6 (2 C), 151.8 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{34}N_4O_2 + H]^+$ 387.2760; found 387.2760.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(4-methoxyaniline) (30):** Synthesized from 4-iodoanisole (1.25 mmol, 293 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 100:1; yield 36 mg (17%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (quint., J = 6.0 Hz, 4 H), 3.16 (t, J = 6.0 Hz, 4 H), 3.55–3.61 (m, 8 H), 3.63–3.67 (m, 4 H), 3.72 (s, 6 H), 6.56 (d, J = 8.6 Hz, 4 H), 6.76 (d, J = 8.6 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.2 (2 C), 42.6 (2 C), 55.7 (2 C), 69.8 (2 C), 70.2 (2 C), 70.6 (2 C), 114.0 (4 C), 114.8 (4 C), 142.8 (2 C), 151.8 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{24}H_{36}N_2O_5 + H]^+$ 433.2702; found 433.2712.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-4-methoxyaniline (31):** Obtained as the second product in the synthesis of compound **30**. Eluent: CH_2Cl_2/MeOH 3:1, CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 83 mg (51%); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (quint., J = 6.4 Hz, 2 H), 1.85 (quint., J = 6.2 Hz, 2 H), 2.76 (br. s, 2 H), 3.15 (t, J = 6.5 Hz, 2 H), 3.52 (t, J = 6.2 Hz, 2 H), 3.53–3.63 (m, 10 vH), 3.71 (s, 3 H), 6.53–6.57 (m, 2 H), 6.72–6.76 (m, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.2, 33.0, 39.5, 42.6, 55.8, 69.4, 69.7, 70.1, 70.2, 70.5 (2 C), 114.0 (2 C), 114.8 (2 C), 142.8, 151.8 ppm. HRMS (MALDI-TOF): calcd. for $[C_{17}H_{30}N_2O_4 + H]^+$ 327.2284; found 327.2236.

N^1,$N^{1\prime}$-(Ethane-1,2-diyl)bis[N^3-(4-chlorophenyl)propane-1,3-diamine] (32): Synthesized from 1-chloro-4-iodobenzene (1.25 mmol, 298 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 83 mg (42%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74 (quint., J = 6.6 Hz, 4 H), 2.70 (s, 4 H), 2.71 (t, J = 6.6 Hz, 4 H), 3.11 (t, J = 6.6 Hz, 4 H), 6.48 (d, J = 8.8 Hz, 4 H), 7.07 (d, J = 8.8 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 29.2 (2 C), 42.7 (2 C), 48.0 (2 C), 49.3 (2 C), 113.6 (4 C), 121.3 (2 C), 128.8 (4 C), 147.0 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{20}H_{28}Cl_2N_4 + H]^+$ 395.1769; found 395.1810.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(4-chloroaniline) (33):** Synthesized from 1-chloro-4-iodobenzene (1.25 mmol, 293 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 500:1–100:1; yield 62 mg (28%); pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (quint., J = 6.1 Hz, 4 H), 3.18 (t, J = 6.4 Hz, 4 H), 3.58 (t, J = 5.9 Hz, 4 H), 3.59–3.61 (m, 4 H), 3.64–3.67 (m, 4 H), 4.12 (br. s, 2 H), 6.47–6.51 (m, 4 H), 7.06–7.10 (m, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 28.9 (2 C), 42.0 (2 C), 69.7 (2 C), 70.2 (2 C), 70.6 (2 C), 113.7 (4 C), 121.4 (2 C), 128.9 (4 C), 147.1 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{30}Cl_2N_2O_3 + H]^+$ 441.1712; found 441.1642.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-4-chloroaniline (34):** Obtained as the second product in the synthesis of compound **33**. Eluent: CH_2Cl_2/MeOH 5:1; yield 69 mg (42%); yellow oil. ^{1}H NMR (400 MHz, CDCl3): δ = 1.89 (quint., J = 6.1 Hz, 4 H), 3.11 (t, J = 5.9 Hz, 2 H), 3.12 (t, J = 6.4 Hz, 2 H), 3.55–3.65 (m, 12 H), 6.60 (d, J = 8.7 Hz, 2 H), 7.03 (d, J = 8.7 Hz, 2 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 25.7, 28.6, 40.1, 41.5, 69.4 (2 C), 69.5, 69.7, 70.0, 70.1, 114.2 (2 C), 121.6, 128.7 (2 C), 146.9 ppm. HRMS (MALDI-TOF): calcd. for $[C_{16}H_{28}ClN_2O_3 + H]^+$ 331.1788; found 331.1748.

N^1,$N^{1\prime}$-(Ethane-1,2-diyl)bis[N^3-(4-nitrophenyl)propane-1,3-diamine] (37): Synthesized from 4-nitroiodobenzene (1.25 mmol,

311 mg) and tetraamine **1a** (0.5 mmol, 87 mg), in the presence of CuI (9.6 mg), ligand **L6** (11.5 mg), and Cs_2CO_3 (408 mg) in propionitrile (1 mL). Eluent: CH_2Cl_2/MeOH/NH_3(aq) 100:20:2; yield 24 mg (12%); dark-yellow oil. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.63 (quint., 4 H, J = 6.4 Hz), 2.54 (br. s, 8 H), 3.11 (q, J = 5.2 Hz, 4 H), 6.55 (d, J = 8.9 Hz, 4 H), 7.32 (br. s, 2 H), 7.89 (d, J = 8.9 Hz, 4 H) ppm; 2 NH protons were not assigned. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 28.4 (2 C), 40.5 (2 C), 46.6 (2 C), 48.5 (2 C), 110.7 (4 C), 126.2 (4 C), 135.4 (2 C), 154.6 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{20}H_{28}N_6O_4 + H]^+$ 417.2250; found 417.2311.

***N*^{1},*N*^{1}-Bis(4-nitrophenyl)-*N*^{3}-{2-[3-(4-nitrophenylamino)propylamino]ethyl}propane-1,3-diamine (36):** Obtained as the second product in the synthesis of compound **37**. Eluent: CH_2Cl_2/MeOH 3:1; yield 75 mg (33%); dark-yellow oil. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.79 (br. s, 4 H), 2.68 (br. s, 2 H), 2.77 (br. s, 2 H), 2.80 (br. s, 4 H), 3.20 (br. s, 2 H), 4.00 (br. s, 2 H), 6.62 (d, J = 8.6 Hz, 2 H), 7.31 (d, J = 8.5 Hz, 4 H), 7.93 (d, J = 8.6 Hz, 2 H), 8.14 (d, J = 8.5 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 26.1, 26.6, 45.4, 45.6, 45.9, 46.3, 49.9, 110.9 (2 C), 121.1 (4 C), 125.7 (4 C), 126.3 (2 C), 135.8 (1 C), 141.5 (2 C), 151.6 (2 C), 154.6 (1 C) ppm; one carbon atom of polyamine chain was not assigned. HRMS (MALDI-TOF): calcd. for $[C_{26}H_{31}N_7O_6 + H]^+$ 538.2414; found 538.2497.

***N*^{1},*N*$^{1\prime}$-(Ethane-1,2-diyl)bis[*N*^{3},*N*^{3}-bis(4-nitrophenyl)propane-1,3-diamine] (35):** Obtained as the third product in the synthesis of compound **37**. Eluent: CH_2Cl_2/MeOH 10:1, isolated in a mixture with compound **36**. Yield of the mixture 77 mg (*ca* 35%); dark-yellow oil. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.77 (br. s, 4 H), 2.63 (s, 4 H), 2.65 (br. s, 4 H), 3.98 (br. s, 4 H), 7.29 (d, J = 8.3 Hz, 8 H), 8.13 (d, J = 8.3 Hz, 8 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 26.5 (2 C), 45.7 (2 C), 49.7 (2 C), 49.9 (2 C), 121.0 (8 C), 125.6 (8 C), 141.5 (4 C), 151.6 (4 C) ppm. MS (MALDI-TOF): calcd. for $[C_{32}H_{34}N_8O_8 + H]^+$ 659.26; found 659.38.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis(4-nitroaniline) (40):** Synthesized from 4-nitroiodobenzene (1.25 mmol, 311 mg) and trioxadiamine **1c** (0.5 mmol, 110 mg), in the presence of CuI (9.6 mg), ligand **L4b** (17 mg), and Cs_2CO_3 (408 mg) in DMF (1 mL). Eluent: CH_2Cl_2/MeOH 100:1; yield 61 mg (26%); dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (quint., J = 5.9 Hz, 4 H), 3.27 (q, J = 5.9 Hz, 4 H), 3.55–3.60 (m, 8 H), 3.63–3.67 (m, 4 H), 5.45 (br. s, 2 H), 6.46 (d, J = 9.2 Hz, 4 H), 7.97 (d, J = 9.2 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 28.3 (2 C), 41.5 (2 C), 69.5 (2 C), 70.0 (2 C), 70.3 (2 C), 110.7 (4 C), 126.2 (4 C), 137.1 (2 C), 153.7 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{30}N_4O_7 + H]^+$ 463.2193; found 463.2179.

4-Nitro-*N*-(4-nitrophenyl)-*N*-[3-(2-{2-[3-(4-nitrophenylamino)-propoxy]ethoxy}ethoxy)propyl]aniline (39): Obtained as the second product in the synthesis of compound **40**. Eluent: CH_2Cl_2/MeOH 200:1; yield 13 mg (5%); dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88–1.95 (m, 4 H), 3.31 (q, J = 5.9 Hz, 2 H), 3.47 (t, J = 5.6 Hz, 2 H), 3.56–3.70 (m, 12 H), 5.39 (br. s, 1 H), 6.48 (d, J = 9.2 Hz, 2 H), 7.17 (d, J = 9.2 Hz, 4 H), 8.00 (d, J = 9.2 Hz, 2 H), 8.14 (d, J = 9.2 Hz, 4 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 27.5, 28.4, 41.8, 49.2, 67.3, 69.9, 70.2, 70.4, 70.7 (2 C), 110.8 (2 C), 120.6 (4 C), 125.7 (4 C), 126.4 (2 C), 137.0 (1 C), 142.2 (2 C), 151.7 (2 C), 153.7 (1 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{28}H_{33}N_5O_9 + H]^+$ 584.2357; found 584.2389.

***N*,*N*′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}bis[4-nitro-N-(4-nitrophenyl)aniline] (38):** Obtained as the third product in the synthesis of compound **40**. Eluent: CH_2Cl_2/MeOH 500:1, isolated in a mixture with compound **39**. Yield of the mixture 64 mg (*ca* 25%); dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.92 (quint., J = 5.8 Hz, 4 H), 3.50 (t, J = 5.8 Hz, 4 H), 3.58–3.72 (m, 8 H), 4.03 (t, J = 7.1 Hz, 4 H), 7.18 (d, J = 9.0 Hz, 8 H), 8.12 (d, J = 9.0 Hz, 8 H) ppm. MS (MALDI-TOF): calcd. for $[C_{34}H_{36}N_6O_{10} - O + H]^+$ 689.26; found 689.38.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-4-nitro-*N*-(4-nitrophenyl)aniline (41):** Obtained as the fourth product in the synthesis of compound **40**. Eluent: CH_2Cl_2/MeOH 50:1, isolated in a mixture with compound **40**. Yield of the mixture 37 mg (16%); dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86–1.94 (m, 4 H), 3.29 (t, J = 5.3 Hz, 2 H), 3.46 (t, J = 5.4 Hz, 2 H), 3.58–3.68 (m, 10 H), 4.02 (t, J = 6.1 Hz, 2 H), 7.17 (d, J = 9.1 Hz, 4 H), 8.14 (d, J = 9.1 Hz, 4 H) ppm; NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 27.4, 28.4, 41.5, 49.3, 69.6, 70.1, 70.2, 70.3, 70.4, 72.4, 120.6 (4 C), 126.4 (4 C), 142.1 (2 C), 151.7 (2 C) ppm. HRMS (MALDI-TOF): calcd. for $[C_{22}H_{30}N_4O_7 + H]^+$ 463.2193; found 463.2178.

***N*-(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-4-nitroaniline (42):** Obtained as the fifth product in the synthesis of compound **40**. Eluent: CH_2Cl_2/MeOH 20:1; yield 48 mg (28%); dark-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.73 (quint., J = 5.5 Hz, 2 H), 1.86 (quint., J = 5.4 Hz, 2 H), 3.27 (br. s, 2 H), 3.35 (q, J = 5.4 Hz, 2 H), 3.51–3.62 (m, 12 H), 5.61 (br. s, 1 H), 6.48 (d, J = 8.3 Hz, 2 H), 7.97 (d, J = 8.3 Hz, 2 H) ppm; 2 NH protons were not assigned. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 28.4 (2 C), 36.6, 41.2, 69.3, 69.6, 69.9, 70.0, 70.2, 70.3, 110.7 (2 C), 126.3 (2 C), 137.0, 153.8 ppm. HRMS (MALDI-TOF): calcd. for $[C_{16}H_{27}N_3O_5 + H]^+$ 342.2029; found 342.2004.

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