Palladium-Catalyzed Arylation of Linear and Cyclic Polyamines

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Keywords: Amines / Amination / Aromatic substitution / Homogeneous catalysis / Palladium

The palladium-catalyzed arylation of polyamines is investigated and it is shown that the C–N coupling reaction for a given substrate is strongly dependent on the nature and the concentration of the catalytic system, as well as the nature of the base employed. The arylation of the primary amino group is favored when both primary and secondary amines are present; selective arylation is then possible without using any protecting group. The reaction of dihalobenzenes with polyamines gives the monoamination products in good yields without any significant formation of diamino compounds or reduced derivatives, unlike what is observed when monoamines are used. The extent of polyarylation of polyamines as a function of the excess of aryl halide and the nature and the amount of catalyst is also studied. Finally, *N*-arylation of a macrocyclic tetraamine (cyclam) is performed by using an appropriate catalytic system.

Introduction

Polyamines are attracting a considerable and constant interest due to their widespread use in pharmacology,[1,2] coordination chemistry,[3] and supramolecular chemistry.[4] Alkyl- and benzyl-substituted linear polyamines have been investigated as polydentate ligands for complexing palladium,[5] copper,[6] and other metals,[7] and as fluorescence sensors for detecting a variety of transition metals like Ni, Zn, Cd, and Pb.[8] Linking an aromatic moiety directly to the nitrogen atom of the polyamine may favor the electronic interaction between the complexing site of the molecule and the arene moiety, which should induce a measurable response and change the sensing properties of such systems. A major area of interest is the investigation of the influence of the aryl substituent on the sensing properties of polyamines. Convenient synthetic routes to alkyl- and benzyl-substituted polyamines have already been described, but their arylated derivatives are not yet readily available.

For decades, the synthesis of arylamines was achieved by three main methods: nitration of arenes followed by the reduction of the nitro group, direct nucleophilic substitution of activated arenes, and copper-mediated (Ullmann-type) reactions of aryl halides.[9] Procedures involving nitration followed by hydrogenation are not tolerated by many functional groups and are often complicated due to the need for protection and deprotection steps. The direct nucleophilic substitution of aryl halides is a synthetic route dedicated only to substrates that contain electron-withdrawing groups, including perfluorinated compounds,[10,11] and Ullmann-type substitution reactions occur at high temperatures, giving generally diarylation products, and depend strongly on the nature of the substrate substituents.[12] These drawbacks are limiting factors for the synthesis of aryl-substituted polyamines, especially nonsymmetrical derivatives, as multistep syntheses are often required to prepare even simple species.[13] An indirect method comprising several steps has been published recently for the preparation of *N*-aryl-1,2-ethanediamines.[14] A real breakthrough in the amination of aryl halides using palladium catalysis has been achieved in recent years on the basis of innovative work conducted by the groups of Buchwald and Hartwig.[15] This soon became the most convenient method due to its obvious advantages, i.e. a wide choice of possible amines and substrates with various substituents, high yields, and, in many cases, mild conditions reactions. Over 150 publications dedicated to this field of synthesis have been published during the last five years; these bear witness to the real and urgent demand for this new synthetic method.

We have explored the possibility of applying this technique to polyamines. Polyamines are a special class of amines that are capable of forming stable chelates with a metal atom, although their use as substrates in these reactions is not obvious since the probable formation of chelates might hinder the catalytic process. Here we report

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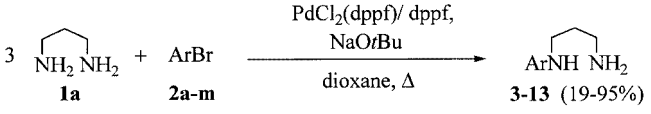
our results on selective mono-, di-, and polyarylation of polyamines. Some of the results described below have been reported previously.[16]

Results

Monoarylation of 1,3-Propanediamine

A variety of aryl bromides and aryl iodides bearing substituents with different electronic properties have been reacted with a model propane-1,3-diamine (**1a**) using Hartwig's $PdCl_2$/dppf [dppf = 1,1′-bis(diphenylphosphanyl)ferrocene] catalytic system (Scheme 1).



Scheme 1

In a typical experimental procedure, aryl halides **2a**−**m** were reacted with three equivalents of propane-1,3-diamine in the presence of 0.5−2 mol % of [$PdCl_2$(dppf)] and twice as much free dppf ligand (i.e. 1−4 mol %). Sodium *tert*-butoxide (2 equiv.) was employed as a base and the reaction mixtures were refluxed until full completion of the reactions (Table 1). The monoarylated diamines **3**−**13** were obtained in good to excellent yields in most cases. The best results were obtained with 1-bromonaphthalene (**2l**) and 9-bromoanthracene (**2m**), which afforded the corresponding arylated diamines **12** and **13** in high yields. While unsubstituted bromobenzene (**2a**) led to *N*-phenylpropane-1,3-diamine in 60% yield after refluxing for 100 h, the presence of electron-withdrawing groups in the *para* position of the benzene ring (**2c**, **2k**) gave higher yields with shorter reaction times and lower catalyst loadings. On the other hand, the presence of some other electron-withdrawing groups led to lower yields of the desired products. This is the case for the easily enolizable *p*-bromoacetophenone (**2g**) and *p*-bromo(trifluoromethyl)benzene (**2f**) — probably sensitive to sodium *tert*-butoxide — which afforded the *N*-arylated compounds in 21 and 53% yields, respectively. In the case of *p*-bromobenzonitrile (**2h**), which gave only the amidine product with $PdCl_2$/dppf, the desired product **10** was isolated in 95% yield when $Pd(dba)_2$/dppf was used as the catalyst. As expected, the use of less-reactive aryl bromides substituted by electron-donor groups (**2b**,**d**,**e**) resulted in lower yields and required higher catalyst loadings. Nevertheless, the presence of a donor methoxy group in the *ortho* position appeared to be more favorable and led to a reasonable yield (41%) of the target product **7**. Surprisingly, the use of aryl iodides (**2i**,**j**) did not result in a substantial advantage over aryl bromides in terms of yields, reaction times, and amounts of catalyst (Table 1, entries 9, 10). Selective substitution of the bromine atom was observed when the bromochloro derivative **2k** was used as the starting material (Table 1, entry 11).

Monoarylation of Linear Polyamines with *p*-Bromobiphenyl

Various linear polyamines with different chain lengths and different numbers of nitrogen atoms were successfully arylated under the conditions mentioned above by *p*-bromobiphenyl (**2c**) to give corresponding arylamines **14**−**20** in good to high yields (Scheme 2, Table 2). $PdCl_2$/dppf and three equivalents of the polyamine were employed.

The selective formation of monoarylated polyamines was observed in all these reactions as well as selective arylation of the primary amino groups. Slightly lower yields were observed when ethane-1,2-diamine (**1b**) and its derivative *N*-(2-aminoethyl)ethane-1,2-diamine (**1c**) were used. However, unsymmetrical *N*-(2-aminoethyl)propane-1,3-diamine (**1e**) afforded a 1:1 mixture of the regioisomers **17** and **18** in high yield (Table 2, entry 4).

The coupling of aryl bromides with α- and β-carbon-substituted primary diamines was also investigated (Scheme 3).

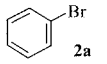
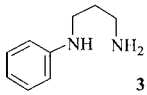
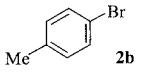
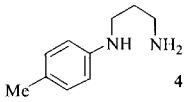
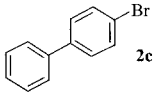
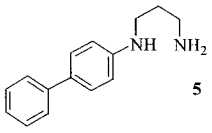
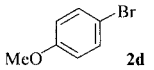
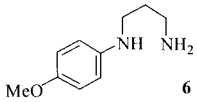
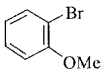
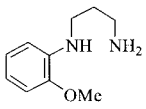
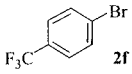
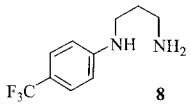
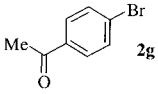
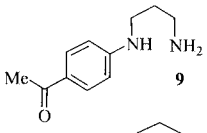
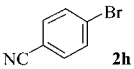
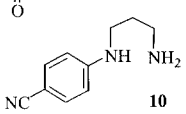
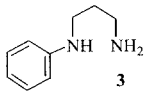
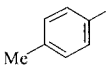
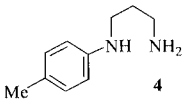
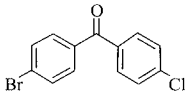
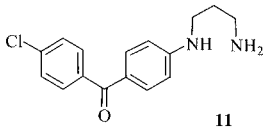
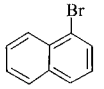
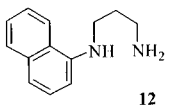
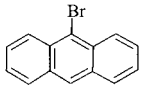
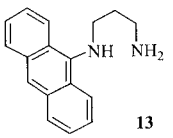
C_β-substitution did not affect the rate of the reaction since the product **21** was obtained in high yield (Table 3, entry 1). C_α-substitution, however, induced many changes, in particular a strong decrease of the reaction rate and lower yields (Table 3, entries 2,3). Moreover, even if a threefold excess of the amine was employed, diarylation became notable. The use of 1-bromonaphthalene (**2l**), which is more reactive than *p*-bromobiphenyl (**2c**), resulted in a higher yield and better regioselectivity; no diarylated product was observed (Table 3, entry 3). The presence of one methyl group at the α carbon atom makes the reaction regioselective (Table 3, entries 2 and 3), and a double substitution gives a total selectivity (Table 3, entry 4). As expected, the 1,2-disubstituted cyclohexane-1,2-diamine (**1k**) proved to be less active than the diamine **1i** since both amine groups are sterically hindered (Table 3, entry 5).

N-Arylated Cyclams

Cyclic tetraazamacrocycles, and especially 1,4,8,11-tetraazacyclotetradecane (cyclam, **1l**), are among the most widely used and studied polyamine derivatives due to their remarkable abilities to coordinate metal cations and their wide industrial and medicinal applications. Thus, the demand exists to elaborate a straightforward access to its *N*-arylated derivatives. Secondary acyclic amines are known to be versatile substrates for catalytic amination reactions.[15b] As has been demonstrated above, the secondary amino groups of linear polyamines are unreactive in the presence of primary amino groups. Although some cyclic secondary amines were found to be reactive derivatives in the aromatic C−N coupling, our investigations proved that cyclam is remarkably inert towards arylation.

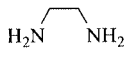
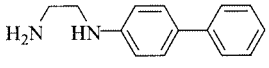
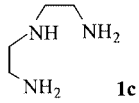
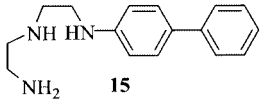
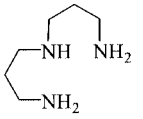
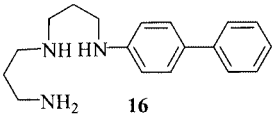
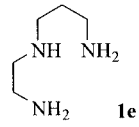
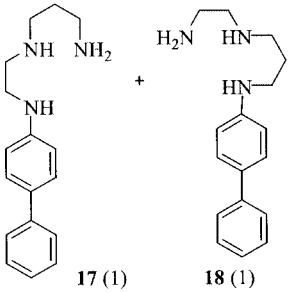
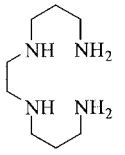
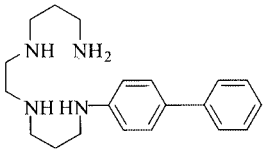
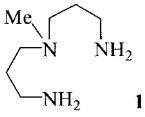
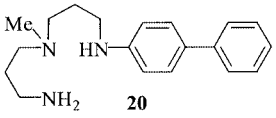
Numerous attempts to carry out the arylation of cyclam were unsuccessful. Different combinations of the catalyst precursors with supporting ligands were used in the reactions of cyclam with aryl halides (bromo- and iodo-substituted benzenes, 1-bromonaphthalene, 4-bromobiphenyl and 9-bromoanthracene): $Pd(dba)_2$, $Pd(OAc)_2$, $PdCl_2$, dppf, binap, P(*t*Bu)$_3$, PCy_3, P(*o*-tol)$_3$ but none of them led to the

Table 1. Palladium-catalyzed reactions of aryl halides with 1,3-diaminopropane[a]

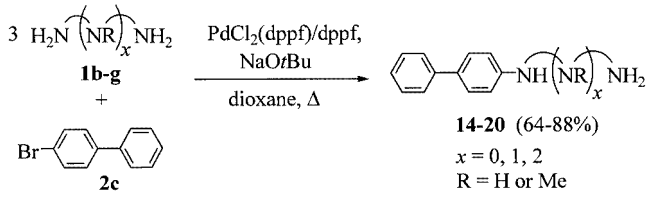
Entry	Aryl halide	mol % $PdCl_2$(dppf)/ %dppf	Time (h)	Product	Yield (%)[b]
1	 **2a**	1/2	100	 **3**	60[c]
2	 **2b**	1/2	100	 **4**	51
3	 **2c**	0.5/1	24	 **5**	75
4	 **2d**	5/10	100	 **6**	19
5	 **2e**	1.5/3	100	 **7**	41
6	 **2f**	2/4[d]	24	 **8**	53
7	 **2g**	0.5/1[d]	2	 **9**	21
8	 **2h**	4/6[e]	8	 **10**	95
9	 **2i**	1/2	100	 **3**	68[c]
10	 **2j**	0.5/1	24	 **4**	49
11	 **2k**	1/2	2	 **11**	77
12	 **2l**	0.5/1	2	 **12**	89
13	 **2m**	1/2	1	 **13**	85

[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Yields of isolated compounds based on aryl halides. [c] The product of N^1,N^3-diamination was observed by NMR spectroscopy (< 7%). [d] 1.2 Equiv. of NaO*t*Bu was used. [e] $[Pd_2(dba)_3]$/dppf catalytic system was used.

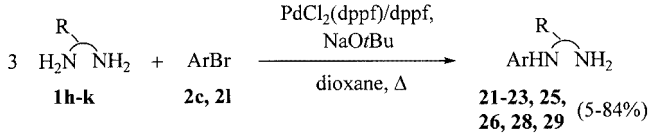
Table 2. Palladium-catalyzed reactions of 4-bromobiphenyl with polyamines[a]

Entry	Amine	mol % $PdCl_2$(dppf)/ %dppf	Time (h)	Product(ratio)	Yield (%)[b]
1	 **1b**	1/2	4	 **14**	64
2	 **1c**	1/2	4	 **15**	65
3	 **1d**	1/2	4	 **16**	77
4	 **1e**	1	24	 **17** (1) **18** (1)	85
5	 **1f**	1/2	18	 **19**	88
6	 **1g**	1/2	24	 **20**	83

[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Yields of isolated compounds based on aryl halides.



Scheme 2



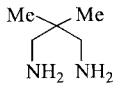
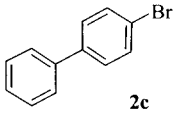
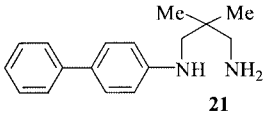
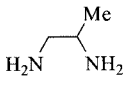
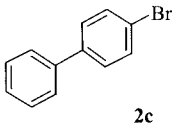
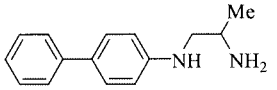
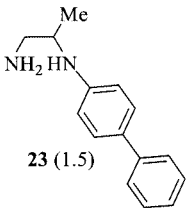
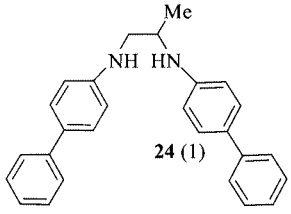
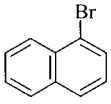
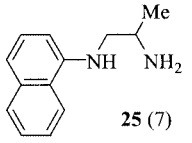
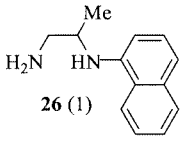
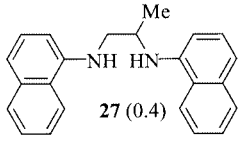
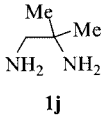
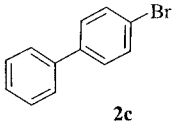
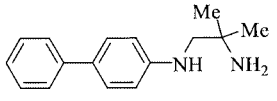
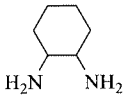
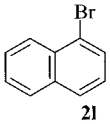
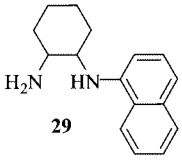
Scheme 3

hoped-for derivatives — we observed only full or partial reduction of the aryl halides into the corresponding arenes. However, the reaction of cyclam with *p*-bromobiphenyl (**2c**) and *p*-bromobenzonitrile (**2h**) using $Pd(dba)_2$/PPF-OMe[17] as catalyst afforded the corresponding *N*-arylated derivatives **30** and **31** in rather modest 20% yield (Scheme 4). This success opens the way to the catalytic preparation of *N*-arylated cyclams, which are, to date, very rare.[11,18]

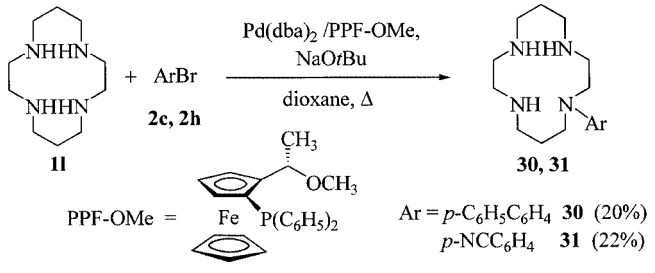
Monoamination of Dihalobenzenes by Polyamines

We have applied the standard procedure used for the arylation of linear polyamines with dihalobenzenes as the arylating agents; haloaryl-substituted polyamines, which may serve as valuable precursors in organic synthesis, are the target derivatives (Scheme 5).

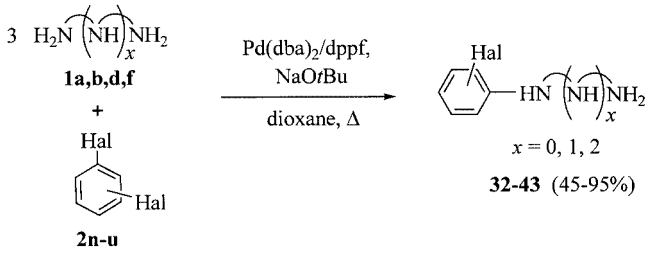
Table 3. Palladium-catalyzed reactions of aryl halides with polyamines[a]

Entry	Amine	Aryl halide	mol % $PdCl_2$(dppf)/ % dppf	Time (h)	Product(ratio)	Yield (%)[b]
1	 **1h**	 **2c**	1	3	 **21**	75
2	 **1i**	 **2c**	2/3	20	 **22** (9) +  **23** (1.5) +  **24** (1)	42
3	 **2l**		2/3	12	 **25** (7) +  **26** (1) +  **27** (0.4)	64
4	 **1j**	 **2c**	2/3[c]	8	 **28**	84
5	 **1k**	 **2l**	1/2	8	 **29**	42

[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Yields of isolated compounds based on aryl halides. [c] $[Pd(dba)_2]$/dppf catalytic system was used.



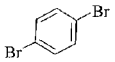
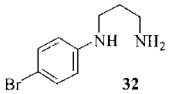
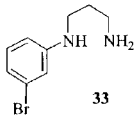
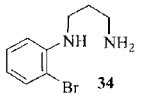
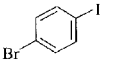
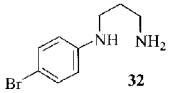
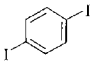
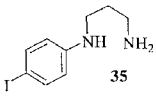
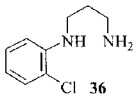
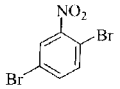
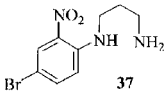
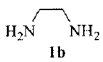
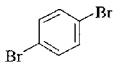
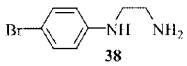
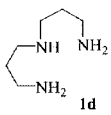
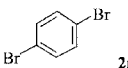
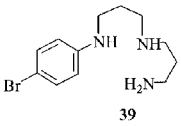
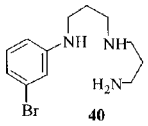
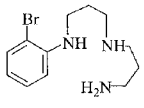
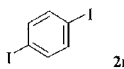
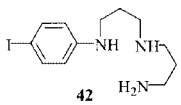
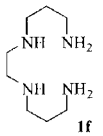
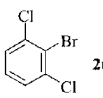
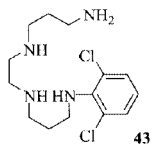
Scheme 4



Scheme 5

The standard procedure employed 2−4 mol % $Pd(dba)_2$ with 2−6 mol % dppf as a catalyst, NaO*t*Bu (2 equiv.) as a base, and a 3:1 polyamine to dihalobenzene ratio. Various substituted polyamines were obtained in good to excellent yields (Table 4). The results obtained in this series of reactions closely resemble those described in the case of the amination of aryl halides (Table 1). Again, ethane-1,2-di-

Table 4. Palladium-catalyzed reactions of aryl dihalides with polyamines[a]

Entry	Amine	Aryl dihalide	mol %Pd(dba)$_2$/ % dppf	Time (h)	Product	Yield (%)[b]
1	 **1a**	 **2n**	2/2	30	 **32**	93
2		 **2o**	2/4	30	 **33**	93
3		 **2p**	2/3	30	 **34**	71[c]
4		 **2q**	4/6	30	 **32**	72
5		 **2r**	4/6	48	 **35**	57[d]
6		 **2s**	4/6	2	 **36**	75[e]
7[f]		 **2t**	2/3	30	 **37**	79[g]
8	 **1b**	 **2n**	2/4	30	 **38**	45
9	 **1d**	 **2n**	2/4	30	 **39**	95
10		 **2o**	2/4	30	 **40**	93
11		 **2p**	2/4	30	 **41**	74
12		 **2r**	4/6	30	 **42**	48[h]
13	 **1f**	 **2u**	4/6	30	 **43**	85

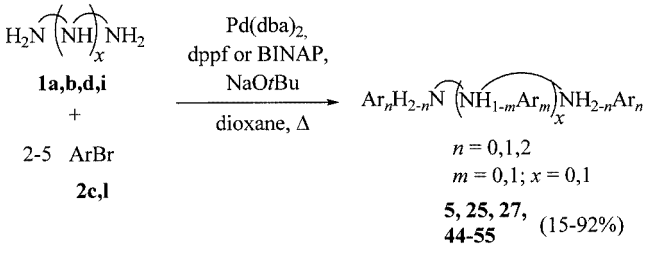
[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Yields of isolated compounds based on aryl halides. [c] A minor amount (8%) of tetrahydrobenzodiazepine **57** (diamination product) was observed. [d] 65% conversion of *p*-diiodobenzene. [e] A minor amount (15%) of tetrahydrobenzodiazepine **57** was also obtained. [f] Cs_2CO_3 was employed as the base. [g] In the absence of palladium catalyst the reaction proceeds slowly to give the desired product in 50% yield together with 15% of 1-bromo-3-nitrobenzene and 16% of 1,4-dibromo-2-nitrobenzene. [h] 60% conversion of *p*-diiodobenzene.

amine (**1b**) proved to be less reactive — the reaction led to **38** in only modest yield (Table 4, entry 8) — because polymeric by-products were formed. *p*-Diiodobenzene appeared to be less efficient in the coupling — its conversion did not exceed 60−65% even with greater loadings of catalyst (Table 4, entries 5,12). A further increase of the amount of catalyst favored the conversion but did not improve the yields of the target compounds. However, fully selective substitution of an iodine atom in the presence of a bromine atom (Table 4, entry 4), as well as of a bromine atom in the presence of a chlorine atom (Table 4, entry 6), was possible. In the case of 1,4-dibromo-2-nitrobenzene (**2t**) selective substitution of the more-activated bromine atom took place (Table 4, entry 7). As in the case of the previous experiments, only the primary amino groups of the triamine **1d** and the tetraamine **1f** were selectively arylated (Table 4, entries 9−13).

The reduction of the second halogen atom in the course of the amination of dihaloarenes is an usual side reaction. Nevertheless, in the case of polyamines the reduced derivatives were formed in much lower quantities than in the reactions of dihalobenzenes with primary monoamines.[16b] We did not observe diamination of dihalobenzenes under these conditions, which is not the case with secondary cyclic amines.[19] When applied to substrates which contain more than two bromine atoms, this reaction gave inseparable mixtures of products.

Polyarylation of Polyamines

The next step of our investigations was to find the appropriate conditions for di- and polyarylation of polyamines (Scheme 6). The coupling of equimolar amounts of aryl halides and polyamines led to different results depending on the nature of the amine. Thus, the reaction of 1-bromonaphthalene with propane-1,3-diamine afforded a mixture of mono- and diarylated products in a 14:1 ratio, which is close to the ratio obtained with a threefold excess of the diamine (18:1). However, in the case of *N*-(3-aminopropyl)-propane-1,3-diamine the reaction with an equimolar amount of the same bromide led to a 2:1 ratio of mono- and diarylated compounds.



Scheme 6

Selective diarylation of polyamines was carried out successfully with the active 1-bromonaphthalene (**2l**) by using two equivalents of aryl halide (Table 5, entries 1,2), the corresponding products **44** and **45** being obtained in excellent yields (88−92%). Less-active *p*-bromobiphenyl (**2c**) required a higher catalyst loading and provided a mixture of the mono-, di-, and triarylated diamines **5**, **46**, **47**, and **48** in high overall yields (87%; Table 5, entry 3). It is interesting to note that replacement of the dppf ligand by binap led to a highly selective reaction affording symmetrical diarylated molecules **46**, **49**, and **50** in high yields (Table 5, entries 4−6). The substituted diamine **1i** appeared to be reluctant to undergo diarylation (Table 5, entry 7), and neither the Pd/dppf nor the Pd/binap catalytic systems allowed us to avoid the formation of the monoarylated derivative **25**.

Only monoarylation of primary amino groups has been discussed, although we also found that, with generous catalytic loadings and binap as a supporting ligand, arylation of the secondary amino groups was also possible. Thus, tetraarylated propane-1,3-diamine (**51**) and ethane-1,2-diamine (**52**) were obtained in remarkable 95% yields (Table 5, entries 8,9), as well as the pentasubstituted triamine **53** and the tetrasubstituted product **54**. It is interesting to note that the reaction of the triamine **1d** with four equivalents of *p*-bromobiphenyl resulted in the formation of a complex mixture of pentasubstituted **53**, tetrasubstituted **54** and **55**, and trisubstituted **56** triamines. The difference in the reactivity of both types (aliphatic and aniline-type) of secondary amino groups present in the symmetrically diarylated triamine **50** is significantly smaller than the difference in the reactivity of the primary and secondary amino groups in unsubstituted linear polyamines (Table 2).

Diamination of Dibromoarenes

Previously published results on the diamination of dihaloarenes deal mainly with secondary amines;[19,20] the main side-products were reported to be arylamines and haloarylamines. We have described above (Table 4) the successful monoamination of dihaloarenes by diamines without reduction of the remaining halogen atom. Attempts to conduct the double amination gave modest results: the reaction of *o*-dibromobenzene (**2p**) with propane-1,3-diamine (**1a**) required higher catalyst loadings and led to 75% yield of a mixture of benzodiazepine (**57**), *N*-(2-bromophenyl)propane-1,3-diamine (**34**), and *N*-phenylpropane-1,3-diamine (**3**) in a 1:1:1 ratio (Scheme 7).

The coupling of the same diamine **1a** with *m*-dibromobenzene (**2o**) gave the desired diaminated product **58** in 23% yield along with the reduced product **3** as the major compound (Scheme 8). In both cases the substitution of the second bromine atom required prolonged heating, which may also accelerate the reduction reaction. Indeed, independent experiments revealed that heating the haloaryl diamines of type **32**−**43** in the presence of the Pd catalyst resulted in a slow formation of the reduction products.

Amination of Aryl Chlorides by Polyamines

Amination of aryl chlorides has been the topic of several recent surveys.[15a,15d,21] In a previous study we have found, from many examples, that 1-bromonaphthalene is more reactive in the amination coupling than *p*-bromobiphenyl. Taking into account this observation, we decided to use 1-chloronaphthalene (**2v**) in the amination reaction with pro-

Table 5. Palladium-catalyzed polyarylation of polyamines[a]

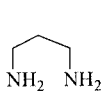
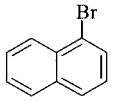
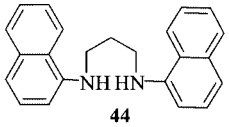
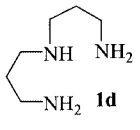
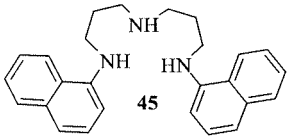
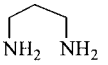
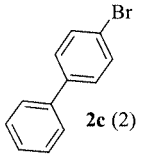
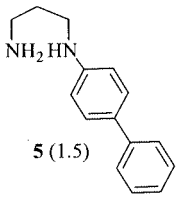
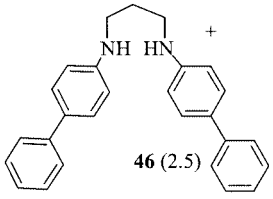
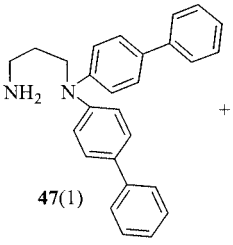
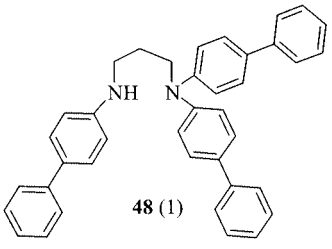
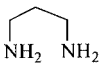
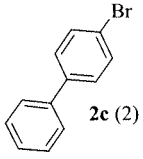
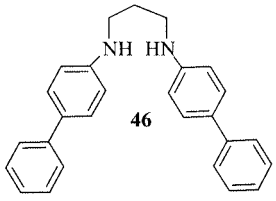
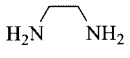
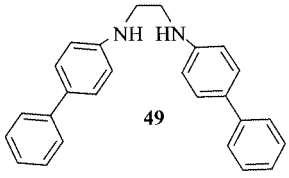
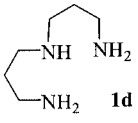
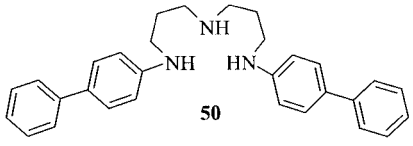
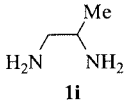
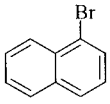
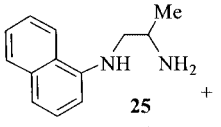
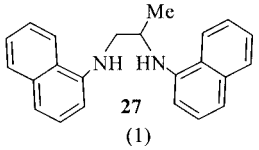
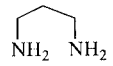
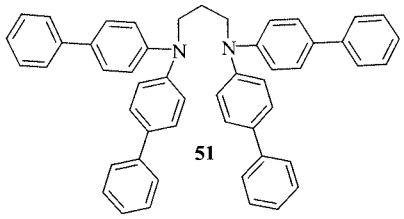
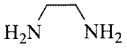
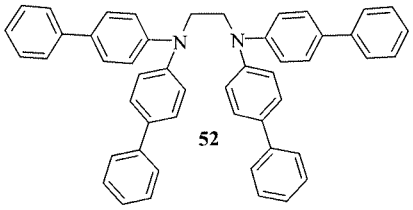
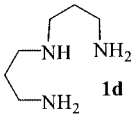
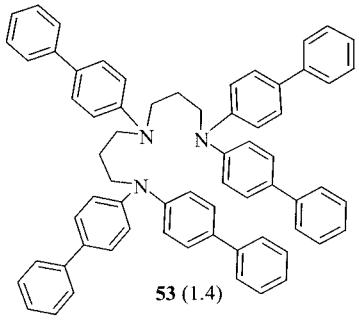
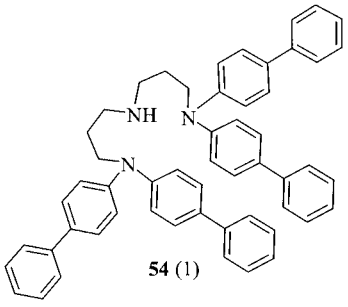
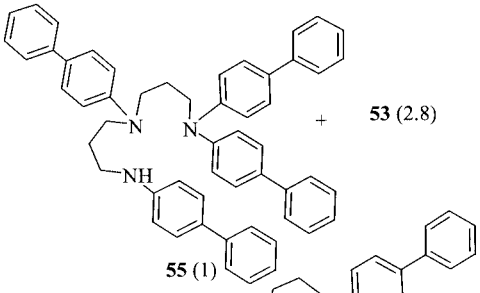
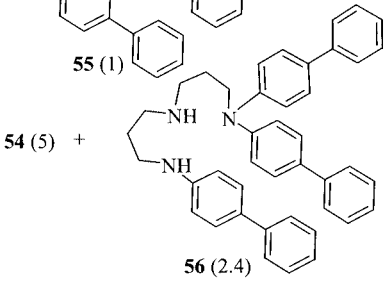
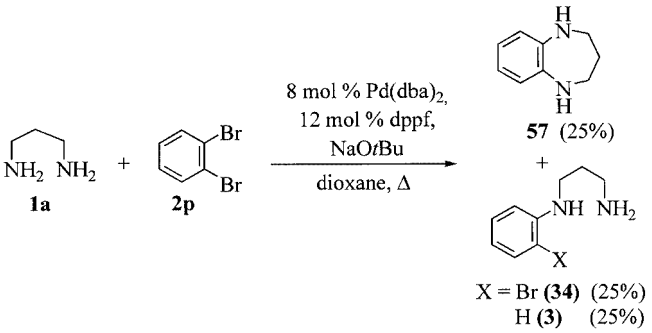
Entry	Amine	Aryl halide (equiv.)	mol % Pd/ % ligand	Time (h)	Products (ratio)	Yield (%)[b]
1	 **1a**	 **2l** (2)	1/2[c]	18	 **44**	88
2	 **1d**	**2l** (2)	1/2[c]	24	 **45**	92
3	 **1a**	 **2c** (2)	2/4[c]	48	 **5** (1.5) +  **46** (2.5) +  **47**(1) +  **48** (1)	87
4	 **1a**	 **2c** (2)	2/4[d]	72	 **46**	85
5	 **1b**	**2c** (2)	2/4[d]	72	 **49**	75
6	 **1d**	**2c** (2)	2/4[d]	72	 **50**	89
7	 **1i**	 **2l** (2.2)	2/3[c]	24	 **25** (2) +  **27** (1)	65
			2/3[d]	48	(2) (1)	70
			6/9[c]	48	(1) (2)	60

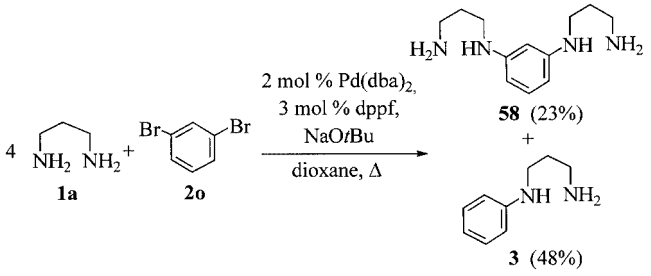
Table 5. *(continued)*

Entry	Amine	Aryl halide (equiv.)	mol % Pd/ % ligand	Time (h)	Products (ratio)	Yield (%)[b]
8	 **1a**	**2c** (4)	4/8[d]	72	 **51**	95
9	 **1b**	**2c** (4)	4/8[d]	72	 **52**	95
10	 **1d**	**2c** (5.6)	8/16[d]	72	 **53** (1.4)	89
11	**1d**	**2c** (4.1)	4/8[d]	72	 **54** (1)  **55** (1) + **53** (2.8)  **54** (5) + **56** (2.4)	88

[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Yields of isolated compounds based on aryl halides. [c] $[Pd(dba)_2]$/dppf was used as the catalytic system. [d] $[Pd(dba)_2]$/binap was used as the catalytic system.

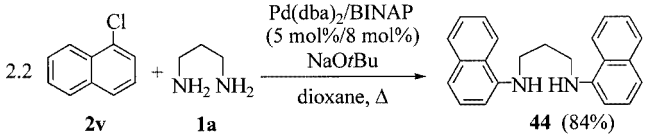


Scheme 7



Scheme 8

pane-1,3-diamine. The most efficient ligand for this purpose proved to be binap, and a standard procedure with a threefold excess of amine afforded a 5:1 mixture of mono- and diarylated products **12** and **44** in 83% total yield (Table 6, entry 1). A lower selectivity of monoarylation is observed when compared to the results obtained with 1-bromonaphthalene (Table 1, entry 12). This may be ascribed to the lower reactivity of **2v**, which requires a longer reaction time and a greater amount of catalyst. The pure diarylated product was obtained when 2.2 equivalents of aryl chloride were used, and the target compound **44** was obtained in 84% yield (Scheme 9, Table 6, entry 2).



Scheme 9

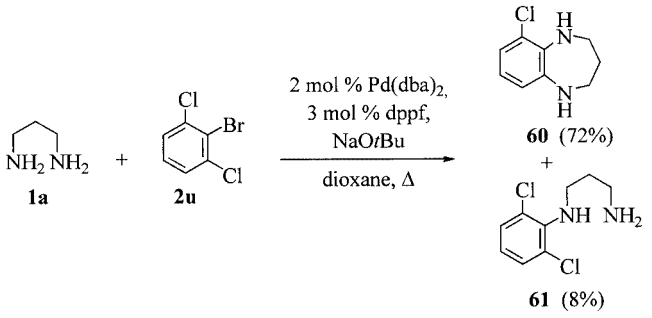
It is clear that dppf is less efficient than binap in this coupling reaction. The reaction of less-reactive *p*-chlorotoluene (**2w**) was also successful and produced the corresponding product **4** in 31% yield. These results encouraged us to use a monoamine in the coupling reaction with aryl chloride. The reaction of 1-chloronaphthalene (**2v**) with an excess of *n*-hexylamine (**1m**) gave the corresponding 1-(*N*-hexyl)naphthylamine (**59**) in 76% yield (Table 6, entry 5). An important feature of aryl chlorides is that they undergo re-

Table 6. Palladium-catalyzed reactions of aryl chlorides with polyamines[a]

Entry	Amine	Aryl halide(equiv)	mol % Pd/ % BINAP	Time (h)	Product(ratio)	Yield (%)[b]
1	**1a**	**2v** (0.33)	2/3	72	**12** (5) + **44** (1)	83
2		(2)	5/8	72	**44**	84
3		**2 w**	5/8	72	**4**	31
4		**2x**	2/3	36	**36**	53[c]
5	*n*HexNH$_2$ **1m**	**2v** (0.33)	2/3	72	**59**	76

[a] NaO*t*Bu was used as the base and dioxane as solvent. [b] Reported yields correspond to isolated compounds based on aryl halides. [c] 60% conversion of *o*-dichlorobenzene.

duction to arenes at a lower rate than the corresponding aryl bromides. Thus, the reaction of *o*-dichlorobenzene (**2x**) with propane-1,3-diamine gave the product **36** in 53% yield. The substitution of chlorine was also observed in the reaction of 1-bromo-2,6-dichlorobenzene (**2u**) with the same diamine. Indeed, the first step was the nucleophilic substitution of the bromine atom, followed by chlorine substitution and cyclization to give 6-chloro-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine (**60**) and *N*-(2,6-dichlorophenyl)propane-1,3-diamine (**61**) as an 8:1 mixture in 80% yield (Scheme 10).



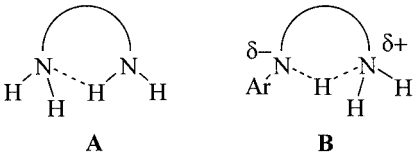
Scheme 10

The synthesis of diaminoanthracenes and diaminoanthraquinones starting from dichloro derivatives and using a Pd catalyst will be published elsewhere.[22]

Discussion

The compilation of a large amount of material dealing with the arylation of polyamines by aryl halides leads us to some general and distinctive features when different combinations of starting molecules are used. The main characteristic of all the studied reactions is the high selectivity for the arylation of primary amino groups in the presence of secondary amino groups, which is consistent with previous results reported by Senanayake.[23] Moreover, the selective monoarylation of di- and polyamines proceeds smoothly and no di- and polyarylation or reduction reactions are observed. However, an appropriate catalytic system has to be chosen for a given combination of aryl halide and polyamine in order to obtain the target product in the highest yield. The amount of catalyst employed in the coupling is strongly dependent on the nature of the starting compounds — an excess of supporting ligand increases the yield only in a few cases. Another important factor is the nature of the base employed. Sodium *tert*-butoxide proved to be efficient in all cases except when aryl halides containing substituents sensitive to this strong base were used; cesium carbonate was employed successfully in these latter cases. Surprisingly, sodium hydroxide could also be used as a base in this coupling reaction, alhtough lower yields were observed; for example, the reaction of the triamine **1d** with *p*-bromobiphenyl (**2c**) in the presence of sodium hydroxide afforded the product **16** in a relatively moderate 53% yield (77% with NaO*t*Bu). Sodium carbonate was not efficient, possibly due to its lower solubility in dioxane compared to that of cesium carbonate.

The key factors acting on the C−N coupling mentioned above were observed for both mono- and polyamines, although some particularities of the coupling of aryl halides with polyamines have to be considered. For example, polyamines could have acted as strong chelating molecules towards zero-valent palladium, thus diminishing its catalytic activity. Fortunately this was not the case, and the existence of intramolecular hydrogen bonds in polyamines (structure **A**) probably explains why no stable chelates with Pd^0 are formed; the chelating ligands in the catalytic process during the oxidative-addition step are bidentate phosphorus compounds such as dppf, or binap. The reaction of the unsymmetrical triamine **1e** with **2c**, which led to an equimolar mixture of the two regioisomers **17** and **18** (Table 2), also supports the idea that no polyamine chelates are formed during the catalytic cycle corresponding to oxidative addition. Indeed, intermediate five- and six-membered chelates would certainly produce two regioisomers in different quantities due to their different stability.

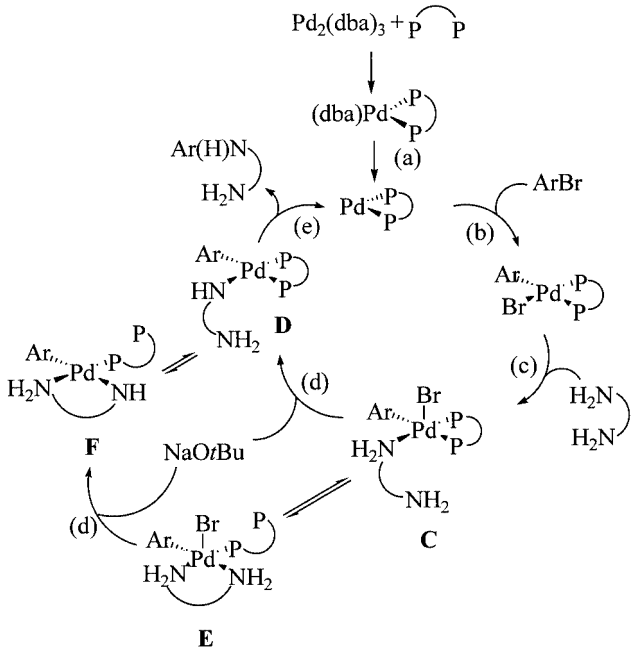


The experiments concerning the selective monoarylation of propane-1,3-diamine (**1a**) with an equivalent amount of **2c**, as well as with perfluorinated aryl halides,[11] show that the second primary amino group is less reactive in the arylation process. This may be explained by the fact that the existing intramolecular hydrogen bond in the diamine becomes stronger in the monoarylated derivative due to the difference of the basicity of the two nitrogen atoms (structure **B**). The nitrogen atom of the remaining primary amino group coordinates the hydrogen atom more strongly and its participation in arylation reaction is therefore not favored. Diarylation becomes possible either with the most active aryl halides or in the presence of higher catalyst loadings. Even exhaustive arylation, which leads to the formation of tetra- and pentasubstituted diamines and triamines, is possible under these conditions (Table 5).

There are still some common features of the reactions of polyamines with aryl halides which have to be reasonably explained: a) the better efficiency of binap over dppf for the selective di- and polyarylation of polyamines; b) the poorer selectivity of less-reactive aryl halides (like *p*-bromobiphenyl or 1-chloronaphthalene vs. 1-bromonaphthalene); and c) the decrease of the selectivity of monoarylation with higher catalyst loadings.

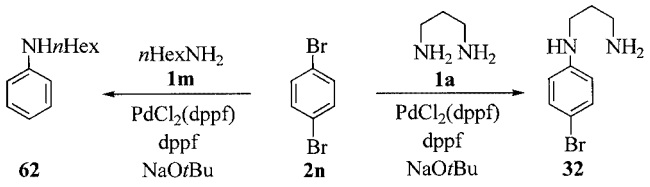
The mechanism of the amination reaction is one of the most complicated among Pd-catalyzed carbon−carbon and carbon−element bond-formation processes. The currently

accepted mechanism for the arylation of amines is presented in Scheme 11.[15a−15c]



Scheme 11

It includes the following steps: (a) formation of the active catalytic species, (b) oxidative addition of the aryl halide, (c) coordination of the amine, (d) deprotonation, and (e) reductive elimination of the product. Although detailed mechanistic studies have been undertaken,[24,25] several experimental results are not yet entirely clear. For example, so far there is no exhaustive explanation of the influence of the ligand nature and concentration, or the applicability of a weak base like cesium carbonate. The true mechanism of the competing reduction of the aryl halide to an arene is also not clear, nor is the enhanced reduction of the second halogen atom in the course of diamination of dihaloarenes. Full information is also lacking concerning the complexation with amine, the dissociation of the bidentate ligand in the catalytic cycle, and the coordination state of palladium. Also the possible exchange of halogen by an alkoxide group remains unclear. Many of these questions have been discussed frequently in the literature but some answers are still missing. The use of polyamines instead of monoamines in the amination of aryl halides certainly cannot be regarded as a convenient tool to solve some existing mechanistical problems, but, nevertheless, we believe that some particular features which make polyamines advantageous over monoamines can be clarified. One of these peculiarities is a dramatic decrease in the formation of the arene by-product, which is the main side-reaction in the amination reaction. As has already been demonstrated (Table 4), polyamines form the corresponding haloaryl-substituted derivatives in good to excellent yields, while the reduction side-reaction of the remaining halogen atom is insignificant. On the contrary, the reaction of *n*-hexylamine with *p*-dibromobenzene leads exclusively to the corresponding reduced product *N*-hexylaniline **62** (Scheme 12).



Scheme 12

A possible explanation may be as follows. We fully agree with Hartwig's opinion that the formation of the arene side-product is due not only to the competing reductive elimination and β-hydride elimination,[24d] but also to other reduction pathways. We suppose that dihaloarenes are especially prone to undergo reduction because the electron-donating amino group hinders the second amination, and that the prolonged heating required leads to reduction by the excess of amine. The formation of the reduced product could occur not only from the amidopalladium complex **D**, but also from the amino, bisamino, and amino-amidopalladium complexes **C**, **E**, and **F** respectively (Scheme 11). We suppose that the formation of such complexes in the case of polyamines includes substitution of one phosphorus atom of the chelate phosphane by the second amino group coordinated to palladium. While a Pd−P bond is stronger than a Pd−N bond, this process is nevertheless possible, as shown by Buchwald in the reaction of [ArPdX{P(*o*-tol)$_3$}] with an excess of amine;[25] formation of a complex containing two amines was observed. In our case this process is favored by the formation of five- or six-membered chelates. According to the hypothesis formulated by Whitesides,[26] β-hydride elimination from such chelate complexes is thermodynamically unfavorable.

Conclusion

In conclusion, the palladium-catalyzed arylation of polyamines has been shown to be a convenient one-pot procedure for the selective introduction of one or several aryl moieties in polyamines without using any protecting groups. This method is applicable for a wide range of polyamines.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, on a Bruker AM200 spectrometer and referenced to the residual protons of the deuterated solvent. Infrared spectroscopy was carried out on a Perkin−Elmer 1600 Series FT-IR spectrometer. Elemental analyses were performed with a Fisons EA 1108 CHNS. Gas chromatographic analyses were carried out on a Hewlett−Packard HP-5890 Series II gas chromatograph fitted with an HP-1 capillary column (25 m, 0.20 mm, 0.11 mm). Thin-layer chromatography was carried out on E. Merck Silica Gel 60F-254 TLC plates.

Reactions under argon atmosphere were carried out using standard Schlenk techniques. All reagents were used directly as obtained commercially, unless otherwise noted. Dioxane was distilled under argon from sodium benzophenone ketyl. 1,8-Dichloroanthraquinone was purchased from Acros Chemical Co. Sodium *tert*-butoxide was purchased from Aldrich Chemical Co. and stored under nitrogen. Small amounts were taken as needed, stored in a Schlenk tube for up to two weeks, and quickly weighed in the air. Propane-1,3-diamine (**1a**), ethane-1,2-diamine (**1b**), *N*-(2-aminoethyl)ethane-1,2-diamine (**1c**), *N*-(3-aminopropyl)propane-1,3-diamine (**1d**), *N*-(2-aminoethyl)propane-1,3-diamine (**1e**), N^1-2-[(3-aminopropyl)amino]ethylpropane-1,3-diamine (**1f**), N^1-(3-aminopropyl)-N^1-methylpropane-1,3-diamine (**1g**), 2,2-dimethylpropane-1,3-diamine (**1h**), 1,2-propanediamine (**1i**), 2-methyl-1,2-propanediamine (**1j**), *trans*-1,2-diaminocyclohexane (**1k**), bromobenzene (**2a**), 4-bromotoluene (**2b**), 4-bromobiphenyl (**2c**), *p*-bromoanisole (**2d**), *o*-bromoanisole (**2e**), 1-bromo-4-(trifluoromethyl)benzene (**2f**), 4-bromoacetophenone (**2g**), 4-bromobenzonitrile (**2h**), iodobenzene (**2i**), 4-iodotoluene (**2j**), 4-bromo-4′-chlorobenzophenone (**2k**), 1-bromonaphthalene (**2l**), 9-bromoanthracene (**2m**), *o*-dibromobenzene (**2n**), *m*-dibromobenzene (**2o**), *p*-dibromobenzene (**2p**), 4-bromo-1-iodobenzene (**2q**), *p*-diiodobenzene (**2r**), *o*-bromochlorobenzene (**2s**), 1,4-dibromo-3-nitrobenzene (**2t**), 1-bromo-2,6-dichlorobenzene (**2u**), 1-chloronaphthalene (**2v**), 4-chlorotoluene (**2w**), *o*-dichlorobenzene (**2x**), [$PdCl_2$(dppf)], dppf, and PPF-OMe were purchased from Aldrich Chemical Co.; binap was purchased from Strem Chemical Company and used as supplied. $Pd(dba)_2$ and $[Pd_2(dba)_3]\cdot CHCl_3$ were synthesized by a literature procedure.[27] Cyclam (**1l**) was also synthesized by a literature procedure.[28]

General Procedure for the Palladium-Catalyzed Monoarylation of Polyamines using the [$PdCl_2$(dppf)]/dppf Catalytic System: Dioxane (10 mL), the indicated amount of [$PdCl_2$(dppf)] with dppf ligand, and the amine (3 mmol) were added to an argon-flushed, two-necked flask and stirred for 2 min. The aryl halide (1 mmol) and sodium *tert*-butoxide (2 mmol) were then added to the reaction mixture. The vial was flushed with argon and the mixture was refluxed whilst stirring. After the indicated period of time the mixture was cooled down to room temperature, 1 mL of water was added, and the reaction mixture was concentrated under reduced pressure. The residue was taken up with CH_2Cl_2 and the product was extracted from the organic layer with aqueous HCl (ca. 10%). After addition of NaOH aqueous solution until pH 12, the product was extracted with CH_2Cl_2. The organic layers were dried over anhydrous Na_2SO_4 and the solvents evaporated in vacuo. The crude material was purified by column chromatography on silica gel. The following compounds were prepared by the described procedure, and the results are summarized in Tables 1−3.

***N*¹-Phenylpropane-1,3-diamine[29] (3):** See Table 1, entries 1 and 9. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (10:3:1) to yield a yellow oil. Yield: 90 mg (60%). ^{1}H NMR ($CDCl_3$): δ = 1.98 (br. m, 2 H), 2.82 (br. t, J = 8.4 Hz, 2 H), 3.39 (br. t, J = 8.4 Hz, 2 H), 6.62 (d, J = 8.4 Hz, 2 H), 7.37 (m, 1 H), 7.88 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 33.9 (1 C), 41.1 (1 C), 42.9 (1 C), 113.6 (2 C), 117.9 (1 C), 129.9 (2 C), 149.5 (1 C) ppm. MS (EI): m/z = 151 (4), 150 (35) [M^+], 133 (27), 132 (37), 120 (10), 118 (8), 107 (11), 106 (100), 104 (15), 93 (25), 77 (35).

***N*¹-(4-Methylphenyl)propane-1,3-diamine[30] (4):** See Table 1, entries 2 and 10. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a yellow oil. Yield: 84 mg (51%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (q, J = 6.8 Hz, 2 H), 2.21 (s, 3 H), 2.81 (t, J = 6.6 Hz, 2 H), 2.85 (s, 2 H), 2.92 (s, 1 H), 3.17 (t, J = 6.6 Hz, 2 H), 6.52 (AA′, J = 8.3 Hz, 2 H), 6.96 (BB′, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.9 (1 C), 33.6 (1 C), 40.9 (1 C), 42.9 (1 C), 113.5 (2 C), 126.9 (1 C), 130.3 (2 C), 146.8 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3317 cm^{-1}, 1617, 1523, 1303, 1123, 804. MS (EI): m/z = 165 (5), 164 (40) [M^+], 140 (17), 132 (22), 120 (100), 107 (27), 91 (24), 77 (13).

***N*¹-[(1,1′-Biphenyl)-4-yl]propane-1,3-diamine (5):** See Table 1, entry 3. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (10:3:1) to yield a white solid. M.p. 72−76 °C. Yield: 170 mg (75%). ^{1}H NMR [CD_3OD + NH_3 (1 drop)]: δ = 2.08 (q, J = 6.8 Hz, 2 H), 3.07 (t, J = 7.2 Hz, 2 H), 3.47 (t, J = 6.8 Hz, 2 H), 7.02 (d, J = 8.8 Hz, 2 H), 7.47 (t, J = 8.8 Hz, 1 H), 7.71 (m, 6 H) ppm; NH signals are not given. ^{13}C NMR [CD_3OD + NH_3 (1 drop)]: δ = 32.6 (1 C), 39.9 (1 C), 42.0 (1 C), 113.8 (2 C), 126.6 (3 C), 128.2 (2 C), 129.3 (2 C), 130.3 (1 C), 142.0 (1 C), 149.1 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3419 cm^{-1}, 3267, 1611, 824, 764. MS (EI): m/z = 227 (17), 226 (100) [M^+], 209 (11), 208 (18), 196 (12), 183 (16), 182 (91), 169 (46), 154 (13), 153 (17), 152 (40), 141 (13), 115 (15). $C_{15}H_{18}N_2$ (226.32): calcd. C 79.61, H 8.02, N 12.38; found C 79.41, H 8.03, N 12.14.

***N*¹-(4-Methoxyphenyl)propane-1,3-diamine (6):**[30] See Table 1, entry 4. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (4:2:1) to yield a brown oil. Yield: 34 mg (19%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (q, J = 6.8 Hz, 2 H), 2.81 (t, J = 6.8 Hz, 2 H), 3.03 (t, J = 6.6 Hz, 2 H), 3.66 (s, 3 H), 4.05 (br. s, 3 H), 6.52 (AA′, J = 9.0 Hz, 2 H), 6.70 (BB′, J = 9.0 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.9 (1 C), 40.2 (1 C), 43.3 (1 C), 56.4 (1 C), 114.9 (2 C), 115.5 (2 C), 143.3 (1 C), 152.7 (1 C) ppm. MS (EI): m/z = 181 (5), 180 (43) [M^+], 162 (9), 148 (13), 137 (10), 136 (100), 134 (10), 123 (28), 122 (10), 121 (14), 120 (10), 107 (22). $C_{10}H_{16}N_2O\cdot 0.33CH_2Cl_2$ ($180.25\cdot 0.33CH_2Cl_2$): calcd. C 59.58, H 8.07, N 13.46; found C 60.09, H 8.04, N 13.10.

***N*¹-(2-Methoxyphenyl)propane-1,3-diamine (7):** See Table 1, entry 5. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a brown oil. Yield: 74 mg (41%). ^{1}H NMR ($CDCl_3$): δ = 1.77 (br. q, J = 6.6 Hz, 2 H), 2.81 (br. t, J = 6.6 Hz, 2 H), 3.17 (br. t, J = 6.6 Hz, 2 H), 3.81 (s, 3 H), 6.71 (m, 4 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 33.6 (1 C), 40.7 (1 C), 42.1 (1 C), 56.0 (1 C), 110.0 (1 C), 110.4 (1 C), 116.9 (1 C), 121.9 (1 C), 139.0 (1 C), 147.4 (1 C) ppm. MS (EI): m/z = 181 (7), 180 (59) [M^+], 162 (12), 133 (17), 132 (15), 136 (100), 131 (15), 123 (54), 121 (58), 120 (72). $C_{10}H_{16}N_2O\cdot 0.33CH_3OH$ ($180.25\cdot 0.33CH_3OH$): calcd. C 65.00, H 9.15, N 14.67; found C 65.27, H 8.66, N 15.13.

***N*¹-[4-(Trifluoromethyl)phenyl]propane-1,3-diamine (8):** See Table 1, entry 6. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a yellow solid. Yield: 116 mg (53%). ^{1}H NMR ($CDCl_3$): δ = 1.67 (q, J = 6.6 Hz, 2 H), 1.94 (br. s, 2 H), 2.76 (t, J = 6.6 Hz, 2 H), 3.11 (t, J = 6.6 Hz, 2 H), 4.73 (br. s, 1 H), 6.53 (AA′, J = 8.4 Hz, 2 H), 7.34 (BB′, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.8 (1 C), 40.9 (1 C), 42.5 (1 C), 112.3 (2 C), 118.4 (q, J = 33 Hz, 1 C), 125.9 (q, J = 273 Hz, 1 C), 127.2 (br. s, 2 C), 151.7 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3406 cm^{-1}, 3326, 1620, 1331, 1066, 823. MS (EI): m/z = 219 (5), 218 (37) [M^+], 201 (53), 200 (49), 199 (12), 188 (9), 175 (13), 174 (100), 172 (25), 161 (14), 145 (30), 132 (12), 127 (13). $C_{10}H_{13}F_3N_2\cdot H_2O$ ($218.22\cdot H_2O$): calcd. C 50.82, H 6.40, N 11.86; found C 51.01, H 5.57, N 11.50.

1-[4-(3-Aminopropyl)aminophenyl]ethanone (9): See Table 1, entry 7. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield an orange solid. M.p.

80 to 82 °C. Yield: 40 mg (21%). ^{1}H NMR ($CDCl_3$): δ = 1.47 (br. s, 2 H), 1.73 (q, J = 6.6 Hz, 2 H), 2.45 (s, 3 H), 2.82 (t, J = 6.6 Hz, 2 H), 3.21 (br. m, 2 H), 4.92 (br. s, 1 H), 6.51 (d, J = 8.8 Hz, 2 H), 7.79 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 26.6 (1 C), 32.8 (1 C), 40.8 (1 C), 42.2 (1 C), 111.8 (2 C), 131.5 (2 C), 131.8 (1 C), 153.3 (1 C), 197.0 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3356 cm^{-1}, 3027, 1665, 1598, 1477, 1426, 1307, 1281, 1179, 824. MS (EI): m/z = 193 (7), 192 (50) [M$^+$], 175 (32), 174 (16), 160 (61), 148 (100), 146 (13), 136 (33), 132 (48), 120 (36), 119 (14), 106 (22), 105 (28), 104 (12), 91 (19).

4-[(3-Aminopropyl)amino]benzonitrile (10): See Table 1, entry 8. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (10:3:1) to yield a yellow oil. Yield: 166 mg (95%). ^{1}H NMR ($CDCl_3$): δ = 1.43 (br. s, 2 H), 1.56 (br. m, 2 H), 2.78 (br. s, 2 H), 3.14 (br. s, 2 H), 5.22 (br. s, 1 H), 6.47 (d, J = 8.6 Hz, 2 H), 7.30 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.7 (1 C), 40.1 (1 C), 41.5 (1 C), 97.3 (1 C), 111.9 (2 C), 120.8 (1 C), 133.5 (2 C), 151.7 (1 C) ppm.

4-[(3-Aminopropyl)amino]phenyl(4-chlorophenyl)methanone (11): See Table 1, entry 11. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a yellow oil. Yield: 221 mg (77%). ^{1}H NMR ($CDCl_3$): δ = 1.79 (q, J = 6.6 Hz, 2 H), 2.24 (br. s, 2 H), 2.89 (t, J = 6.4 Hz, 2 H), 3.26 (t, J = 6.6 Hz, 2 H), 5.10 (br. s, 1 H), 6.54 (d, J = 8.6 Hz, 2 H), 7.38 (d, J = 8.6 Hz, 2 H), 7.64 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.6 (1 C), 40.8 (1 C), 42.2 (1 C), 111.8 (2 C), 125.5 (1 C), 129.0 (2 C), 131.6 (2 C), 133.6 (2 C), 137.9 (1 C), 138.2 (1 C), 153.4 (1 C), 194.4 (1 C) ppm. MS (EI): m/z = 290 (20), 289 (12), 288 (56) [M$^+$], 271 (40), 244 (90), 232 (37), 180 (7), 160 (31), 141 (33), 139 (100), 132 (58). $C_{16}H_{17}ClN_2O\cdot CHCl_3$ (288.10·$CHCl_3$): calcd. C 59.71, H 8.53, N 5.39; found C 59.10, H 9.01, N 5.32.

***N*^{1}-Naphthalen-1-ylpropane-1,3-diamine (12):** See Table 1, entry 12. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a white solid. M.p. 95−98 °C. Yield: 178 mg (89%). ^{1}H NMR ($CDCl_3$): δ = 1.87 (q, J = 6.4 Hz, 2 H), 2.92 (t, J = 6.4 Hz, 2 H), 3.34 (t, J = 6.5 Hz, 2 H), 6.59 (br. d, J = 7.5 Hz, 1 H), 7.40 (m, 4 H), 7.81 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 32.7 (1 C), 41.7 (1 C), 43.8 (1 C), 104.5 (1 C), 117.5 (1 C), 121.0 (1 C), 124.1 (1 C), 125.2 (1 C), 126.4 (1 C), 127.4 (1 C), 129.3 (1 C), 134.4 (1 C), 144.1 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3405 cm^{-1}, 1580, 1519, 1469, 1407, 1388, 764. MS (EI): m/z = 201 (14), 200 (92) [M$^+$], 183 (11), 182 (30), 168 (19), 167 (17), 166 (13), 165 (13), 157 (33), 156 (100), 143 (80), 129 (53), 128 (51), 127 (42), 126 (16), 115 (50). $C_{13}H_{16}N_2\cdot CH_3OH$ (200.13·CH_3OH): calcd. C 72.38, H 8.68, N 12.06; found C 71.66, H 8.16, N 12.34.

***N*^{1}-Anthracen-9-ylpropane-1,3-diamine (13):** See Table 1, entry 13. The crude product was crystallized from CH_2Cl_2/hexane (1:1). Yield: 212 mg (85%). ^{1}H NMR ($CDCl_3$): δ = 1.88 (q, J = 6.6 Hz, 2 H), 2.50 (br. s, 3 H), 2.91 (t, J = 6.6 Hz, 2 H), 3.42 (t, J = 6.8 Hz, 2 H), 7.48 (m, 4 H), 8.00 (m, 2 H), 8.15 (s, 1 H), 8.28 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 35.3 (1 C), 41.4 (1 C), 51.2 (1 C), 122.0 (2 C), 122.1 (1 C), 123.9 (2 C), 125.5 (2 C), 125.9 (2 C), 129.7 (2 C), 133.0 (2 C), 142.7 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3331 cm^{-1}, 1610, 1530, 1489, 820, 759. MS (EI): m/z = 251 (18), 250 (94) [M$^+$], 220 (10), 217 (10), 215 (22), 207 (14), 206 (52), 205 (26), 204 (52), 193 (75), 192 (35), 191 (18), 179 (39), 178 (100), 176 (29), 165 (63), 164 (25), 163(14).

***N*^{1}-[(1,1′-Biphenyl)-4-yl]ethane-1,2-diamine (14):**[29] See Table 2, entry 1. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) to yield a yellow oil. Yield: 136 mg (64%). ^{1}H NMR ($CDCl_3$): δ = 1.41 (br. s, 2 H), 2.95 (br. t, J = 5.8 Hz, 2 H), 3.21 (br. t, J = 5.8 Hz, 2 H), 4.20 (br. s, 1 H), 6.71 (d, J = 10 Hz, 2 H), 7.26 (m, 1 H), 7.44 (m, 4 H), 7.56 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 41.9 (1 C), 47.2 (1 C), 113.9 (2 C), 126.9 (1 C), 127.0 (2 C), 128.6 (2 C), 129.4 (2 C), 130.9 (1 C), 141.9 (1 C), 148.6 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3380 cm^{-1}, 3226, 1610, 1531, 1494, 1475, 771. MS (EI): m/z = 170 (14), 169 (100), 168 (24), 167 (14), 152 (3), 141 (8), 139 (5), 115 (9).

***N*^{1}-(2-Aminoethyl)-*N*^{2}-[(1,1′-biphenyl)-4-yl]ethane-1,2-diamine (15):** See Table 2, entry 2. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (2:2:1) to yield a white solid. M.p. 145 to 150 °C. Yield: 166 mg (65%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (br. s, 3 H), 2.66 (m, 2 H), 2.75 (m, 2 H), 2.85 (m, 2 H), 3.21 (m, 2 H), 4.40 (br. s, 1 H), 6.70 (d, J = 8.6 Hz, 2 H), 7.28 (m, 1 H), 7.43 (m, 4 H), 7.57 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 42.4 (1 C), 44.2 (1 C), 49.2 (1 C), 52.8 (1 C), 113.9 (2 C), 126.7 (1 C), 126.9 (2 C), 128.6 (2 C), 129.4 (2 C), 130.7 (1 C), 141.9 (1 C), 148.7 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3380 cm^{-1}, 2930, 1608, 1531, 1303, 1183, 826. MS (EI): m/z = 256 (5), 255 (19) [M$^+$], 196 (27), 195 (41), 183 (100), 182 (96), 181 (16), 154 (15), 153 (21), 152 (59), 151 (14), 141 (14), 115 (16), 73 (86). $C_{16}H_{21}N_3\cdot 0.5CHCl_3$ (255.18·0.5$CHCl_3$): calcd. C 64.88, H 7.51, N, 12.28; found C 65.09, H 7.80, N 12.24.

***N*^{1}-(3-Aminopropyl)-*N*^{3}-[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (16):** See Table 2, entry 3. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (2:1:1) to yield a creamy white solid. Yield: 218 mg (77%). ^{1}H NMR ($CDCl_3$): δ = 1.61 (br. q, J = 6.8 Hz, 2 H), 1.78 (br. q, J = 6.4 Hz, 2 H), 2.68 (m, 6 H), 3.19 (br. t, J = 6.4 Hz, 2 H), 6.66 (d, J = 8.4 Hz, 2 H), 7.28 (m, 1 H), 7.39 (m, 4 H), 7.56 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 30.0 (1 C), 34.3 (1 C), 41.2 (1 C), 43.6 (1 C), 48.6 (1 C), 49.2 (1 C), 113.6 (2 C), 126.7 (1 C), 126.9 (2 C), 128.6 (2 C), 129.4 (2 C), 130.4 (1 C), 142.0 (1 C), 148.8 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3359 cm^{-1}, 1612, 1560, 1528, 1489, 1323, 826. MS (EI): m/z = 284 (30), 283 (100) [M$^+$], 209 (38), 196 (29), 183 (21), 182 (68), 169 (52), 152 (34), 84 (45), 71 (35).

***N*^{1}-{2-[(1,1′-Biphenyl)-4-yl]aminoethyl}propane-1,3-diamine (17) and *N*^{1}-(2-Aminoethyl)-*N*^{3}-[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (18):** See Table 2, entry 4. These compounds were separated by column chromatography on SiO_2 with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:2:1) as eluent. Yield: 229 mg (85%).

17: Obtained as a white solid. ^{1}H NMR [$CDCl_3$ + CD_3OD + NH_3 (1 drop)]: δ = 1.89 (q, J = 6.8 Hz, 2 H), 2.87 (t, J = 7.2 Hz, 2 H), 2.96 (t, J = 7.0 Hz, 2 H), 3.01 (t, J = 6.8 Hz, 2 H), 3.45 (br. t, J = 6.4 Hz, 2 H), 6.90 (d, J = 8.6 Hz, 2 H), 7.36 (m, 1 H), 7.54 (m, 6 H) ppm; NH signals are not given. ^{13}C NMR [$CDCl_3$ + CD_3OD + NH_3 (1 drop)]: δ = 30.9 (1 C), 40.1 (1 C), 43.7 (1 C), 47.8 (1 C), 49.1 (1 C), 114.1 (2 C), 126.8 (3 C), 128.5 (2 C), 129.5 (2 C), 130.8 (1 C), 142.2 (1 C), 149.2 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3421 cm^{-1}, 3275, 1611, 1528, 1489, 828, 762. MS (EI): m/z = 269 (15) [M$^+$], 196 (54), 195 (18), 184 (13),183 (100), 182 (81), 181 (16), 169 (17), 154 (11), 153 (15), 152 (33), 99 (22), 98 (120), 87 (50), 70 (12). $C_{17}H_{23}N_3\cdot CH_3OH$ (269.19·CH_3OH): calcd. C 71.72, H 9.03, N 13.96; found C 71.37, H 8.68, N 14.24.

18: ^{1}H NMR [$CDCl_3$ + CD_3OD + NH_3 (1 drop)]: δ = 1.80 (q, J = 6.8 Hz, 2 H), 2.65 (m, 4 H), 2.75 (t, J = 6.8 Hz, 2 H), 3.16 (t, J = 6.8 Hz, 2 H), 6.69 (d, J = 8.8 Hz, 2 H), 7.23 (m, 1 H), 7.45 (m, 4 H), 7.72 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR [$CDCl_3$ + CD_3OD + NH_3 (1 drop)]: δ = 29.3 (1 C), 40.9 (1 C), 42.3 (1 C), 47.7 (1 C), 51.7 (1 C), 113.5 (2 C), 126.4 (3 C), 128.1 (2 C), 129.0 (2 C), 130.0 (1 C), 141.6 (1 C), 148.5 (1 C) ppm.

$C_{17}H_{23}N_3 \cdot CH_3OH$ (269.19·CH_3OH): calcd. C 71.72, H 9.03, N 13.96; found C 71.41, H 8.03, N 12.14.

***N*¹-2-[(3-Aminopropyl)amino]ethyl-*N*³-[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (19):** See Table 2, entry 5. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (2:1:1) to yield a white solid. Yield: 287 mg (88%). ^{1}H NMR [$CDCl_3$ + CD_3OD + NH_3 (1 drop)]: δ = 1.65 (m, 2 H), 1.81 (m, 2 H), 2.65 (m, 10 H), 3.53 (t, J = 7.9 Hz, 2 H), 6.71 (d, J = 10.7 Hz, 2 H), 7.58 (m, 1 H), 7.75 (m, 4 H), 7.90 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$ + CD_3OD): δ = 30.0 (1 C), 32.5 (1 C), 40.5 (1 C), 43.0 (1 C), 48.2 (1 C), 48.5 (1 C), 50.0 (2 C), 114.3 (2 C), 127.0 (3 C), 128.8 (2 C), 129.9 (2 C), 130.5 (1 C), 142.4 (1 C), 149.6 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3386 cm^{-1}, 1611, 1528, 780. MS (EI): *m*/*z* = 327 (11), 326 (26) [M$^+$], 252 (11), 240 (28), 239 (27), 238 (27), 226 (27), 196 (100), 182 (42), 169 (17), 152 (18), 87 (44), 71 (11).

***N*¹-(3-Aminopropyl)-*N*³-[(1,1′-biphenyl)-4-yl]-*N*¹-methylpropane-1,3-diamine (20):** See Table 2, entry 6. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (2:1:1) to yield a white solid. Yield: 247 mg (83%). ^{1}H NMR ($CDCl_3$): δ = 1.26 (br. s, 2 H), 1.62 (m, 2 H), 1.78 (m, 2 H), 2.25 (s, 3 H), 2.40 (t, J = 8.0 Hz, 2 H), 2.45 (t, J = 8.0 Hz, 2 H), 2.75 (br. t, J = 7.7 Hz, 2 H), 3.20 (br. t, J = 7.7 Hz, 2 H), 4.75 (br. s, 1 H), 6.66 (d, J = 10.0 Hz, 2 H), 7.25 (m, 1 H), 7.43 (m, 4 H), 7.58 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.1 (1 C), 31.9 (1 C), 41.3 (1 C), 42.9 (1 C), 44.0 (1 C), 56.4 (1 C), 57.4 (1 C), 113.6 (2 C), 126.6 (1 C), 126.9 (2 C), 128.6 (2 C), 129.4 (2 C), 130.3 (1 C), 142.0 (1 C), 148.9 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3410 cm^{-1}, 3299, 1611, 1526, 1477, 765, 700. MS (EI): *m*/*z* = 298 (22), 297 (100) [M$^+$], 209 (31), 208 (22), 182 (61), 169 (15), 153 (16), 152 (38),141 (11), 115 (13), 98 (21), 85 (28), 84 (15), 72 (34), 71 (21). $C_{19}H_{27}N_3 \cdot CH_3OH$ (297.22·CH_3OH): calcd. C 72.89, H 9.49, N 12.76; found C 72.46, H 9.23, N 13.15.

***N*¹-[(1,1′-Biphenyl)-4-yl]-2,2-dimethylpropane-1,3-diamine (21):** See Table 3, entry 1. The crude product was crystallized from CH_2Cl_2/Et_2O/hexane (2:1:1) to yield a white solid. M.p. 78 to 80 °C. Yield: 191 mg (75%). ^{1}H NMR ($CDCl_3$): δ = 1.02 (s, 6 H), 2.66 (s, 2 H), 3.06 (s, 2 H), 6.74 (d, J = 8.6 Hz, 2 H), 7.28 (m, 1 H), 7.47 (m, 4 H), 7.60 (m, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 24.6 (2 C), 36.1 (1 C), 52.1 (1 C), 53.9 (1 C), 113.6 (2 C), 126.7 (1 C), 126.9 (2 C), 128.6 (2 C), 129.4 (2 C), 130.3 (1 C), 142.1 (1 C), 149.4 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3353 cm^{-1}, 3310, 1613, 1530, 1488, 1277, 1252, 829, 761. MS (EI): *m*/*z* = 255 (14), 254 (100) [M$^+$], 224 (7), 183 (18), 182 (100), 181 (7), 169 (22), 152 (20), 141 (9), 73 (14). $C_{17}H_{22}N_2 \cdot 0.5CH_3OH$ (254.18·0.5CH_3OH): calcd. C 71.73, H 8.95, N 10.36; found C 71.36, H 8.45, N 10.29.

***N*¹-[(1,1′-Biphenyl)-4-yl]propane-1,2-diamine (22):** See Table 3, entry 2. This compound was separated from *N*²-[(1,1′-biphenyl)-4-yl]-1,2-propanediamine (**23**) and *N*¹,*N*²-bis[(1,1′-biphenyl)-4-yl]-1,2-propanediamine (**24**) by column chromatography on SiO_2 using, successively CH_2Cl_2, CH_2Cl_2/CH_3OH (9:1), and $CH_2Cl_2/CH_3OH/NH_3$ (30:4:1) as eluents. Yield: 74 mg (33%). ^{1}H NMR ($CDCl_3$): δ = 1.16 (d, J = 6.2 Hz, 3 H), 1.34 (br. s, 2 H), 2.90 (m, 1 H), 3.18 (m, 2 H), 4.53 (br. s, 1 H), 6.69 (d, J = 8.4 Hz, 2 H), 7.27 (m, 1 H), 7.45 (m, 4 H), 7.49 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.0 (1 C), 46.3 (1 C), 52.0 (1 C), 113.2 (2C), 126.1 (1 C), 126.3 (2 C), 128.0 (2 C), 128.7 (2 C), 130.2 (1 C), 141.3 (1 C), 147.9 (1 C) ppm. MS (EI): *m*/*z* = 227 (8), 226 (24) [M$^+$], 184 (200), 183 (100), 182 (83), 181 (11), 153 (11), 152 (30), 44 (75).

***N*²-[(1,1′-Biphenyl)-4-yl]propane-1,2-diamine (23):** Yield: 12 mg (5%). ^{1}H NMR ($CDCl_3$): δ = 1.19 (d, J = 6.2 Hz, 3 H), 1.49 (br. s, 2 H), 2.84 (m, 2 H), 3.47 (m, 1 H), 4.20 (br. s, 1 H), 6.69 (d, J = 8.4 Hz, 2 H), 7.27 (m, 1 H), 7.41 (m, 4 H), 7.51 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 18.7 (1 C), 47.5 (1 C), 50.9 (1 C), 113.7 (2 C), 126.2 (2 C), 126.4 (1 C), 128.1 (2 C), 128.8 (2 C), 130.3 (1 C), 141.4 (1 C), 147.3 (1 C) ppm.

***N*¹,*N*²-Bis[(1,1′-biphenyl)-4-yl]propane-1,2-diamine (24):** Yield: 14 mg (4%). ^{1}H NMR ($CDCl_3$): δ = 1.31 (d, J = 6.2 Hz, 3 H), 1.60 (br. s, 1 H), 3.20 (m, 1 H), 3.38 (m, 1 H), 3.85 (m, 2 H), 6.71 (d, J = 8.8 Hz, 2 H), 6.73 (d, J = 8.8 Hz, 2 H), 7.24 (m, 2 H), 7.43 (m, 8 H), 7.59 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.45 (1 C), 48.8 (1 C), 49.8 (1 C), 113.4 (2 C), 114.0 (2 C), 126.4 (2 C), 126.4 (4 C), 128.1 (2 C), 128.2 (2 C), 128.8 (4 C), 130.7 (1 C), 130.9 (1 C), 141.2 (1 C), 141.2 (1 C), 146.9 (1 C), 147.7 (1 C) ppm. MS (EI): *m*/*z* = 379 (12), 378 (28) [M$^+$], 197 (40), 196 (40), 196 (100), 195 (14), 184 (20), 183 (87), 182 (25), 181 (11), 180 (12), 154 (13), 153 (14), 152 (29).

***N*¹-(Naphthalen-1-yl)propane-1,2-diamine (25):** See Table 3, entry 3. This compound was separated from *N*²-[1-naphthyl]-1,2-propanediamine (**26**) and *N*¹,*N*²-bis(1-naphthyl)-1,2-propanediamine (**27**) by column chromatography on SiO_2 using, successively, CH_2Cl_2, CH_2Cl_2/CH_3OH (9:1), and $CH_2Cl_2/CH_3OH/NH_3$ (30:4:1) as eluents. Yield: 107 mg (53%). ^{1}H NMR ($CDCl_3$): δ = 1.21 (d, J = 6.0 Hz, 3 H), 1.82 (br. s, 2 H), 2.99 (m, 1 H), 3.29 (m, 2 H), 4.94 (br. s, 1 H), 6.59 (d, J = 7.4 Hz, 1 H), 7.31 (m, 4 H), 7.84 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.5 (1 C), 46.1 (1 C), 51.9 (1 C), 104.4 (1 C), 117.3 (1 C), 120.2 (1 C), 123.6 (1 C), 124.7 (1 C), 125.8 (1 C), 126.7 (1 C), 128.6 (1 C), 134.4 (1 C), 143.7 (1 C) ppm. MS (EI): *m*/*z* = 202 (27), 201 (42), 200 (100) [M$^+$], 158 (22), 157 (88), 156 (83), 155 (20), 154 (28), 143 (10), 129 (30), 128 (25), 127 (24), 115 (12), 44 (64).

***N*²-(Naphthalen-1-yl)propane-1,2-diamine (26):** Yield: 15 mg (8%). ^{1}H NMR ($CDCl_3$): δ = 1.28 (d, J = 6.2 Hz, 3 H), 1.56 (br. s, 2 H), 2.85 (m, 1 H), 3.68 (m, 2 H), 4.95 (br. s, 1 H), 6.65 (d, J = 7.6 Hz, 1 H), 7.34 (m, 4 H), 7.81 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 18.4 (1 C), 47.1 (1 C), 50.5 (1 C), 105.0 (1 C), 117.2 (1 C), 120.1 (1 C), 123.7 (1 C), 124.7 (1 C), 125.8 (1 C), 126.7 (1 C), 128.7 (1 C), 134.5 (1 C), 142.8 (1 C) ppm. MS (EI): *m*/*z* = 186 (17), 185 (35), 175 (15), 173 (100), 141 (100), 128 (13), 116 (18), 105 (13), 104 (45), 100 (12), 99 (38), 98 (9), 97 (9), 87 (33), 86 (12), 85 (71), 71 (19), 70 (12), 58 (31), 56 (36), 44 (62).

***N*¹,*N*²-Di(naphthalen-1-yl)propane-1,2-diamine (27):** Yield: 10 mg (3%). ^{1}H NMR ($CDCl_3$): δ = 1.53 (d, J = 6.2 Hz, 3 H), 3.51 (m, 2 H), 4.20 (m, 1 H), 4.44 (br. s, 1 H), 4.89 (br. s, 1 H), 6.84 (d, J = 7.2 Hz, 1 H), 6.93 (d, J = 7.2 Hz, 1 H), 7.41 (m, 8 H), 7.89 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.3 (1 C), 48.7 (1 C), 50.0 (1 C), 104.7 (1 C), 105.8 (1 C), 117.8 (1 C), 118.0 (1 C), 120.1 (2 C), 123.7 (2 C), 124.0 (2 C), 124.9 (2 C), 125.9 (1 C), 126.7 (1 C), 128.6 (1 C), 128.8 (1 C), 134.4 (1 C), 134.6 (1 C), 142.6 (1 C), 143.6 (1 C) ppm. MS (EI): *m*/*z* = 327 (5), 326 (19) [M$^+$], 170 (100), 171 (16), 157 (75), 154 (12), 128 (18), 127 (14).

***N*¹-[(1,1′-Biphenyl)-4-yl]-2-methylpropane-1,2-diamine (28):** See Table 3, entry 4. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (30:6:1) to yield a white solid. M.p. 116 to 118 °C. Yield: 202 mg (84%). ^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 6 H), 1.77 (br. s, 2 H), 3.05 (s, 2 H), 4.28 (br. s, 1 H), 6.74 (d, J = 8.6 Hz, 2 H), 7.28 (m, 1 H), 7.44 (m, 4 H), 7.57 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.9 (2 C), 50.5 (1 C), 55.4 (1 C), 113.1 (2 C), 126.0 (1 C), 126.2 (2 C), 127.9 (2 C), 128.7 (2 C), 130.0 (1 C), 141.3 (1 C), 148.4 (1 C) ppm. MS (EI): *m*/*z* = 241 (4), 240 (17) [M$^+$], 184 (14), 183 (68), 182 (28), 152 (22), 58

(100). $C_{16}H_{20}N_2 \cdot 0.5H_2O$ (240.35·0.5H_2O): calcd. C 77.07, H 8.49, N 11.23; found C 76.56, H 8.16, N 11.02.

***N*¹-(Naphthalen-1-yl)cyclohexane-1,2-diamine (29):** See Table 3, entry 5. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (30:6:1) to yield a yellow oil. Yield: 101 mg (42%). ^{1}H NMR ($CDCl_3$): δ = 0.85 (m, 1 H), 1.20 (m, 3 H), 1.61 (m, 2 H), 1.93 (m, 1 H), 2.18 (m, 1 H), 2.47 (m, 1 H), 3.27 (br. s, 1 H), 4.04 (br. s, 2 H), 4.27 (br. s, 1 H), 6.70 (d, J = 6.8 Hz, 1 H), 7.44 (m, 4 H), 7.74 (m, 1 H), 7.96 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.3 (1 C), 25.5 (1 C), 32.1 (1 C), 34.6 (1 C), 55.9 (1 C), 58.9 (1 C), 106.2 (1 C), 118.1 (1 C), 121.4 (1 C), 124.6 (1 C), 125.4 (1 C), 126.5 (1 C), 127.3 (1 C), 129.4 (1 C), 135.2 (1 C), 143.5 (1 C) ppm. MS (EI): m/z = 241 (11), 240 (55) [M^+], 197 (5), 194 (6), 183 (9), 182 (43), 168 (56), 167 (42), 144 (47), 143 (100), 127 (41), 97 (27), 43 (22). $C_{16}H_{20}N_2 \cdot 0.5CH_2Cl_2$ (240.35·0.5CH_2Cl_2): calcd. C 70.07, H 9.91, N 7.48; found C 69.40, H 10.16, N 7.54.

Attempts at the Pd-Catalyzed Arylation of Cyclam (1l). Typical Procedure: dioxane (15 mL) and the catalyst precursor were placed in an argon-flushed, two-necked flask. The reaction mixture was stirred for 5 min. The aryl halide (1 mmol), 1.0 equiv. of cyclam (**1l**), and 2.0 equiv. of NaO*t*Bu were then added and the mixture was refluxed for 24−72 h. After cooling down to room temperature and concentrating in vacuo, the residue was taken up with CH_2Cl_2 (30 mL), washed with water, dried over Na_2SO_4, and the solvents evaporated in vacuo. The residue was analysed by ^{1}H and ^{13}C NMR spectroscopy. Arylation of cyclam was carried out with the following aryl halides:

1) 1-Bromonaphthalene in the presence of: a) 4 mol % $Pd(dba)_2$ and 6 mol % P(*t*Bu)$_3$; b) 5 mol % $Pd(OAc)_2$ and 20 mol % P(*t*Bu)$_3$; c) 2 mol % [$PdCl_2$(dppf)] and 4 mol % dppf; d) 2 mol % $Pd(dba)_2$ and 3 mol % P(PPF-OMe)$_3$.

2) 4-Bromobiphenyl in the presence of: a) 4 mol % $Pd(OAc)_2$ and 6 mol % P(*t*Bu)$_3$; b) 4 mol % $Pd(dba)_2$ and 5 mol % binap; c) 2 mol % [$PdCl_2$(dppf)] and 4 mol % dppf; d) 1 mol % [$Pd_2(dba)_3$[·$CHCl_3$ and 4 mol % P(*o*-tol)$_3$.

3) *p*-Tolyl bromide in the presence of 5 mol % $Pd(OAc)_2$ and 30 mol % P(*t*Bu)$_3$.

4) *p*-Tolyl chloride in the presence of 4 mol % $Pd(dba)_2$ and 16 mol % P(cy)$_3$.

5) 1,3-Dibromobenzene in the presence of 4 mol % $Pd(dba)_2$ and 16 mol % P(*o*-tol)$_3$.

No aryl-substituted cyclams were formed in any of these reactions: either the reaction did not occur at all or only partial or complete reduction of the aryl halide to the corresponding arene was observed.

General Procedure for the Palladium-Catalyzed Arylation of Cyclam (1l) using the $Pd(dba)_2$/PPF-OMe Catalytic System: Dioxane (15 mL), $Pd(dba)_2$ (6 mg, 0.01 mmol), and PPF-OMe (6 mg, 0.014 mmol) were added to an argon-flushed, two-necked flask. The reaction mixture was stirred for 5 min. Cyclam (100 mg, 0.5 mmol), the aryl halide (0.5 mmol), and NaO*t*Bu (96 mg, 1 mmol) were then added and the mixture was refluxed for 100 h. After cooling down to room temperature and concentrating in vacuo, the residue was taken up with CH_2Cl_2 (30 mL), washed with water, dried over Na_2SO_4, and the solvents evaporated in vacuo. The residue was chromatographed on silica using, successively, CH_2Cl_2 and CH_2Cl_2/MeOH/NH_3 (16:4:1) as eluents.

1-[(1,1′-Biphenyl)-4-yl]-1,4,8,11-tetraazacyclotetradecane (30): This compound was prepared from cyclam and 4-bromobiphenyl (117 mg). Yield: 35 mg (20%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (m, 4 H), 3.10 (m, 19 H), 7.06 (d, J = 8.5 Hz, 2 H), 7.45 (m, 7 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 26.1 (1 C), 26.5 (1 C), 46.8 (1 C), 47.0 (1 C), 47.5 (1 C), 48.3 (1 C), 48.9 (1 C), 50.1 (1 C), 50.9 (1 C), 50.6 (1 C), 118.7 (2 C), 126.1 (1 C), 126.6 (2 C), 128.1 (2 C), 128.8 (2 C), 133.5 (1 C), 140.7 (1 C), 148.9 (1 C) ppm.

4-(1,4,8,11-Tetraazacyclotetradec-1-yl)benzonitrile (31): This compound was prepared from cyclam and 4-bromobenzonitrile (91 mg). Yield: 33 mg (22%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (m, 4 H), 2.40 (br. s, 3 H), 2.85 (m, 12 H), 3.50 (m, 4 H), 6.62 (d, J = 8.6 Hz, 2 H), 7.39 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.9 (1 C), 29.1 (1 C), 45.6 (1 C), 47.6 (1 C), 48.2 (2 C), 48.5 (2 C), 48.9 (1 C), 51.7 (1 C), 97.5 (1 C), 112.2 (2 C), 120.8 (1 C), 133.7 (2 C), 151.7 (1 C) ppm.

General Procedure for the Palladium-Catalyzed Reactions of Aryl Dihalides with Polyamines using the $[Pd_2(dba)_3]$/dppf Catalytic System: Dioxane (10 mL), the indicated amount of $[Pd_2(dba)_3]\cdot CHCl_3$ {or $[Pd(dba)_2]$}, dppf, and the amine (3 mmol) were added to an argon-flushed, two-necked flask and the mixture was stirred for 10 min. The aryl halide (1 mmol) and sodium *tert*-butoxide (2 mmol) were then added, the vial was flushed with argon, and the mixture was refluxed with stirring. After the indicated period of time it was cooled down to room temperature, 1 mL of water was added, and the reaction mixture was concentrated in vacuo. The residue was taken up with CH_2Cl_2 (30 mL). The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the solvents evaporated in vacuo. The crude material was purified by column chromatography on silica gel. The following compounds were prepared by the described procedure; the results are summarized in Table 4.

***N*¹-(4-Bromophenyl)propane-1,3-diamine (32):** See Table 4, entries 1,4. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:2:1) to yield a white solid. Yield: 213 mg (93%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (q, J = 6.6 Hz, 2 H), 2.82 (t, J = 6.6 Hz, 2 H), 3.14 (t, J = 6.9 Hz, 2 H), 6.46 (AA′, J = 8.6 Hz, 2 H), 7.15 (BB′, J = 8.6 Hz, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 32.0 (1 C), 39.9 (1 C), 41.9 (1 C), 108.3 (1 C), 114.2 (2 C), 131.0 (2 C), 147.5 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3342 cm^{-1}, 3050, 820, 777. $C_9H_{13}BrN_2$ (229.12): calcd. C 47.18, H 5.72, Br 34.87, N 12.23; found C 47.43, H 6.08, Br 34.41, N 12.38.

***N*¹-(3-Bromophenyl)propane-1,3-diamine (33):** See Table 4, entry 2. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:2:1) to yield a white solid. Yield: 212 mg (93%). ^{1}H NMR ($CDCl_3$): δ = 1.67 (q, J = 6.6 Hz, 2 H), 2.75 (br. s, 2 H), 3.09 (t, J = 6.6 Hz, 2 H), 6.43 (d, J = 8.5 Hz, 1 H), 6.74 (d, J = 6.3 Hz, 2 H), 6.94 (t, J = 7.4 Hz, 1 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 31.6 (1 C), 39.5 (1 C), 41.2 (1 C), 110.8 (1 C), 114.3 (1 C), 118.8 (1 C), 122.6 (1 C), 129.9 (1 C), 149.3 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3300 cm^{-1}, 3055, 910, 842, 760, 733. $C_9H_{13}BrN_2$ (229.12): calcd. C 47.18, H 5.72, Br 34.87, N 12.23; found C 47.34, H 5.92, Br 34.49, N 12.42.

***N*¹-(2-Bromophenyl)propane-1,3-diamine (34):** See Table 4, entry 3. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:2:1) to yield a yellow oil. Yield: 163 mg (71%). ^{1}H NMR ($CDCl_3$): δ = 1.74 (q, J = 6.8 Hz, 2 H), 2.18 (br. s, 2 H), 2.79 (t, J = 6.7 Hz, 2 H), 3.16 (t, J = 6.8 Hz, 2 H), 4.57 (br. s, 1 H), 6.51 (dt, J = 7.5, 1.0 Hz, 1 H), 6.59 (dd, J = 8.5, 1.0 Hz, 1 H), 7.13 (dt, J = 7.6, 1.0 Hz, 1 H), 7.38 (dd, J = 8.5, 1.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.3 (1 C), 38.6 (1 C), 40.9 (1 C), 109.6 (1 C), 111.2 (1 C), 117.6 (1 C), 128.4 (1 C), 132.3 (1 C), 145.1 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3392 cm^{-1}, 3080, 791, 745.

$C_9H_{13}BrN_2$ (229.12): calcd. C 47.18, H 5.72, Br 34.87, N 12.23; found C 47.51, H 5.48, Br 34.61, N 11.88.

***N*¹-(4-Iodophenyl)propane-1,3-diamine (35):** See Table 4, entry 5. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:3:1) to yield a brown oil. Yield: 157 mg (57%). ^{1}H NMR ($CDCl_3$): δ = 1.73 (q, J = 6.6 Hz, 2 H), 2.82 (t, J = 6.6 Hz, 2 H), 3.15 (t, J = 6.5 Hz, 2 H), 6.65 (AA′, J = 8.6 Hz, 2 H), 7.38 (BB′, J = 8.6 Hz, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 32.3 (1 C), 40.1 (1 C), 41.9 (1 C), 88.1 (1 C), 114.5 (2 C), 137.6 (2 C), 147.9 (1 C) ppm.

***N*¹-(2-Chlorophenyl)propane-1,3-diamine (36):** See Table 4, entry 6. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (30:6:1) to yield a yellow oil. Yield: 139 mg (75%). ^{1}H NMR ($CDCl_3$): δ = 1.40 (br. s, 2 H), 1.76 (br. t, J = 6.8 Hz, 2 H), 2.82 (br. s, 2 H), 3.20 (br. t, J = 6.8 Hz, 2 H), 4.60 (br. s, 1 H), 6.58 (t, J = 8.6 Hz, 1 H), 6.62 (d, J = 7.3 Hz, 1 H), 7.10 (t, J = 7.3 Hz, 1 H), 7.20 (t, J = 8.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.6 (1 C), 40.1 (1 C), 41.7 (1 C), 111.0 (1 C), 116.9 (1 C), 119.0 (1 C), 127.8 (1 C), 129.0 (1 C), 144.2 (1 C) ppm.

***N*¹-(4-Bromo-2-nitrophenyl)propane-1,3-diamine (37):** See Table 4, entry 7. The reaction mixture was chromatographed with CH_2Cl_2/CH_3OH (4:1) to yield an orange solid. Yield: 216 mg (79%). ^{1}H NMR ($CDCl_3$): δ = 1.26 (br. s, 2 H), 1.85 (q, J = 6.8 Hz, 2 H), 2.85 (t, J = 6.8 Hz, 2 H), 3.40 (t, J = 6.8 Hz, 2 H), 6.76 (d, J = 8.5 Hz, 1 H), 7.44 (dd, J = 8.5, 2.5 Hz, 1 H), 8.20 (br. s, 1 H), 8.26 (d, J = 2.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.1 (1 C), 39.7 (1 C), 41.2 (1 C), 106.3 (1 C), 115.6 (1 C), 128.9 (1 C), 132.1 (1 C), 138.9 (1 C), 144.5 (1 C) ppm.

***N*¹-(4-Bromophenyl)ethane-1,2-diamine (38):** See Table 4, entry 8. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:3:1) to yield a yellow oil. Yield: 97 mg (45%). ^{1}H NMR ($CDCl_3$): δ = 2.81 (br. s, 3 H), 3.03 (br. s, 4 H), 6.41 (d, J = 7.9 Hz, 2 H), 7.15 (d, J = 7.9 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 40.5 (1 C), 45.7 (1 C), 108.6 (1 C), 114.4 (2 C), 131.8 (2 C), 147.3 (1 C) ppm. $C_8H_{11}BrN_2$ (215.09): calcd. C 44.67, H 5.15; found C 45.26, H 4.77.

***N*¹-(3-Aminopropyl)-*N*³-(4-bromophenyl)propane-1,3-diamine (39):** See Table 4, entry 9. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:3:1) to yield a yellow oil. Yield: 272 mg (95%). ^{1}H NMR ($CDCl_3$): δ = 1.54 (q, J = 6.9 Hz, 2 H), 1.68 (q, J = 6.6 Hz, 2 H), 2.57 (t, J = 6.9 Hz, 2 H), 2.64 (t, J = 6.6 Hz, 2 H), 2.68 (t, J = 6.9 Hz, 2 H), 3.04 (t, J = 6.6 Hz, 2 H), 6.37 (AA′, J = 8.5 Hz, 2 H), 7.14 (BB′, J = 8.5 Hz, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 28.8 (1 C), 33.4 (1 C), 40.1 (1 C), 42.6 (1 C), 47.5 (1 C), 48.2 (1 C), 107.9 (1 C), 113.8 (2 C), 131.5 (2 C), 147.3 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3305 cm^{-1}, 3037, 815, 764, 699. $C_{12}H_{20}BrN_3$ (285.08): calcd. C 50.36, H 7.04, Br 27.92, N 14.68; found C 50.09, H 6.91, Br 28.07, N 14.52.

***N*¹-(3-Aminopropyl)-*N*³-(3-bromophenyl)propane-1,3-diamine (40):** See Table 4, entry 10. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:2:1) to yield a yellow oil. Yield: 266 mg (93%). ^{1}H NMR ($CDCl_3$): δ = 1.54 (q, J = 6.9 Hz, 2 H), 1.68 (q, J = 6.5 Hz, 2 H), 2.57 (t, J = 6.9 Hz, 2 H), 2.63 (t, J = 6.6 Hz, 2 H), 2.68 (t, J = 6.9 Hz, 2 H), 3.05 (t, J = 6.6 Hz, 2 H), 6.40 (d, J = 7.9 Hz, 1 H), 6.62 (t, J = 1.7 Hz, 1 H), 6.68 (d, J = 7.6 Hz, 1 H), 6.90 (t, J = 8.2 Hz, 1 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 28.7 (1 C), 33.3 (1 C), 40.2 (1 C), 42.5 (1 C), 47.6 (1 C), 48.2 (1 C), 111.1 (1 C), 114.6 (1 C), 119.1 (1 C), 122.9 (1 C), 130.1 (1 C), 149.7 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3333 cm^{-1}, 3050, 912, 852, 764, 735. $C_{12}H_{20}BrN_3$ (285.08): calcd. C 50.36, H 7.04, Br 27.92, N 14.68; found C 50.19, H 6.91, Br 27.73, N 14.61.

***N*¹-(3-Aminopropyl)-*N*³-(2-bromophenyl)propane-1,3-diamine (41):** See Table 4, entry 11. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:3:1) to yield a yellow oil. Yield: 212 mg (74%). ^{1}H NMR ($CDCl_3$): δ = 1.55 (q, J = 6.6 Hz, 2 H), 1.74 (q, J = 6.4 Hz, 2 H), 2.01 (br. s, 3 H), 2.66 (m, 6 H), 3.13 (br. t, J = 6.2 Hz, 2 H), 4.80 (br. s, 1 H), 6.46 (d, J = 7.6 Hz, 1 H), 6.53 (t, J = 8.2 Hz, 1 H), 7.08 (d, J = 8.2 Hz, 1 H), 7.32 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.5 (1 C), 33.1 (1 C), 39.9 (1 C), 42.1 (1 C), 47.3 (1 C), 47.6 (1 C), 108.9 (1 C), 110.4 (1 C), 116.6 (1 C), 127.8 (1 C), 131.6 (1 C), 144.7 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3392 cm^{-1}, 3084, 795, 747. $C_{12}H_{20}BrN_3$ (285.08): calcd. C 50.36, H 7.04, Br 27.92, N 14.68; found C 50.10, H 7.10, Br 27.67, N 14.65.

***N*¹-(3-Aminopropyl)-*N*³-(4-iodophenyl)propane-1,3-diamine (42):** See Table 4, entry 12. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (12:3:1) to yield a yellow oil. Yield: 160 mg (48%). ^{1}H NMR ($CDCl_3$): δ = 1.58 (br. s, 2 H), 1.68 (br. s, 2 H), 2.71 (br. s, 6 H), 3.08 (br. s, 2 H), 6.34 (AA′, J = 8.5 Hz, 2 H), 7.33 (BB′, J = 8.5 Hz, 2 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 28.8 (1 C), 33.4 (1 C), 40.1 (1 C), 42.6 (1 C), 47.5 (1 C), 48.2 (1 C), 89.1 (1 C), 114.8 (2C), 138.4 (2 C), 148.0 (1 C) ppm. IR (nujol): $\tilde{\nu}$ = 3382 cm^{-1}, 3080, 798, 755.

***N*¹-2-[(3-Aminopropyl)amino]ethyl-*N*³-(2,6-dichlorophenyl)propane-1,3-diamine (43):** See Table 4, entry 13. The reaction mixture was chromatographed with CH_2Cl_2 and then with $CH_2Cl_2/CH_3OH/NH_3$ (8:3:1) to yield a yellow oil. Yield: 271 mg (85%). ^{1}H NMR ($CDCl_3$): δ = 1.25 (m, 8 H), 2.45 (m, 10 H), 3.15 (m, 2 H), 4.20 (br. s, 1 H), 6.48 (t, J = 8.5 Hz, 1 H), 6.92 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 30.4 (1 C), 33.1 (1 C), 39.9 (1 C), 45.5 (1 C), 47.3 (2 C), 49.0 (2 C), 120.7 (1 C), 125.3 (2 C), 128.3 (2 C), 142.4 (1 C) ppm. MS (EI): m/z = 174 (10), 173 (100), 171 (95), 149 (13), 145 (5), 143 (5), 92 (60), 84 (20), 65 (70).

2,3,4,5-Tetrahydro-1*H*-1,5-benzodiazepine (57): The reaction of *o*-dibromobenzene (**2p**; 472 mg, 2 mmol) with 1,3-diaminopropane (**1a**; 148 mg, 2 mmol) was carried out using the general procedure for the amination of aryl dibromides, in the presence of 8 mol % $Pd(dba)_2$ and 12 mol % dppf. The reaction mixture was refluxed for 4 days. The product **57** (25% yield) was separated from the compounds **3** and **34** by chromatography on SiO_2 using CH_2Cl_2/CH_3OH (10:1) and then $CH_2Cl_2/CH_3OH/NH_3$ (12:4:1) as eluents. ^{1}H NMR ($CDCl_3$): δ = 1.76 (m, 2 H), 3.01 (m, 4 H), 3.80 (br. s, 2 H), 6.70 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 32.6 (1 C), 47.3 (2 C), 120.0 (2 C), 121.0 (2 C), 140.6 (2 C) ppm. MS (EI): m/z = 149 (6), 148 (53) [M$^+$], 147 (8), 134 (2), 133 (4), 132 (8), 130 (4), 120 (15), 119 (12), 107 (2), 106 (2), 92 (14), 77 (6), 65 (15).

***N*¹,*N*³-Bis(3-aminopropyl)benzene-1,3-diamine (58):** The reaction of *m*-dibromobenzene (**2o**; 236 mg, 1 mmol) with 1,3-diaminopropane (**1a**; 296 mg, 4 mmol) was carried out using the general procedure for the amination of aryl dibromides, in the presence of 2 mol % [$PdCl_2$(dppf)] and 2 mol % dppf. The reaction mixture was refluxed for 1 day. The product **58** (23% yield) was separated from compound **3** by column chromatography on SiO_2 using CH_2Cl_2/CH_3OH/NH_3 (12:3:1) as eluent. ^{1}H NMR ($CDCl_3$): δ = 1.73 (q, J = 6.6 Hz, 4 H), 2.75 (br. s, 4 H), 3.09 (t, J = 6.6 Hz, 4 H), 5.83 (br. s, 1 H), 5.97 (d, J = 7.7 Hz, 2 H), 6.95 (t, J = 7.7 Hz, 1 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 32.7 (2

C), 39.9 (2 C), 41.6 (2 C), 96.7 (1 C), 102.3 (2 C), 129.6 (1 C), 149.4 (2 C) ppm.

General Procedure for the Palladium-Catalyzed Double Arylation and Polyarylation of Polyamines using the Pd/dppf and Pd/binap Catalytic Systems: Dioxane (10 mL), the indicated amount of $Pd(dba)_2$, dppf or binap, and the amine (1 mmol) were added to an argon-flushed, two-necked flask and the mixture was stirred for 10 min. The aryl halide (2−5 mmol) and sodium *tert*-butoxide (2 mmol) were then added to the reaction mixture, the vial was flushed with argon, and the mixture was refluxed whilst stirring. After cooling down to room temperature, 1 mL of water was added and the reaction mixture was concentrated in vacuo. The residue was taken up with CH_2Cl_2 (30 mL). The organic layer was washed with water, dried over anhydrous Na_2SO_4, and the solvents evaporated in vacuo. The crude material was purified by column chromatography on silica gel. The following compounds were prepared by the above procedure, and the results are summarized in Table 5.

***N*¹,*N*³-Di(naphthalen-1-yl)propane-1,3-diamine (44):** See Table 5, entry 1. The reaction mixture was chromatographed with CH_2Cl_2 to yield a brown solid. M.p. 115−117 °C. Yield: 287 mg (88%). ^{1}H NMR ($CDCl_3$): δ = 2.19 (q, J = 6.8 Hz, 2 H), 3.48 (t, J = 6.8 Hz, 4 H), 4.65 (br. s, 2 H), 6.72 (dd, J = 7.5, 1.2 Hz, 2 H), 7.49 (m, 8 H), 7.88 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.7 (1 C), 43.9 (2 C), 105.8 (2 C), 118.7 (2 C), 120.8 (2 C), 124.7 (2 C), 125.6 (2 C), 126.5 (2 C), 127.4 (2 C), 129.5 (2 C), 135.4 (2 C), 144.1 (2 C) ppm. IR (KBr): $\tilde{\nu}$ = 3358 cm^{-1}, 1628, 1581, 1522, 1471, 1262, 788. MS (EI): *m*/*z* = 327 (26), 326 (100) [M$^+$], 182 (37), 156 (71), 143 (49), 129 (48), 128 (57), 127 (45), 115 (56).

***N*¹-(Naphthalen-1-yl)-*N*³-[3-(naphthalen-1-ylamino)propyl]propane-1,3-diamine (45):** See Table 5, entry 2. The crude product was crystallized from CH_2Cl_2/Et_2O/hexane (2:1:1) to yield a brown solid. Yield: 353 mg (92%). ^{1}H NMR ($CDCl_3$): δ = 1.97 (q, J = 6.1 Hz, 4 H), 2.83 (t, J = 6.1 Hz, 4 H), 3.37 (t, J = 6.1 Hz, 4 H), 5.10 (br. s, 3 H), 6.61 (d, J = 7.3 Hz, 2 H), 7.41 (m, 8 H), 7.85 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.8 (2 C), 44.3 (2 C), 49.7 (2 C), 104.6 (2 C), 117.6 (2 C), 121.1 (2 C), 124.3 (2 C), 125.3 (2 C), 126.5 (2 C), 127.5 (2 C), 129.4 (2 C), 135.1 (2 C), 144.7 (2 C) ppm. IR (KBr): $\tilde{\nu}$ = 3375 cm^{-1}, 1581, 1528, 1479, 1409, 1129, 786, 768. MS (EI): *m*/*z* = 384 (31), 383 (100) [M$^+$], 200 (15), 170 (33), 157 (31), 156 (44), 143 (22), 128 (18), 127 (12), 84 (16). $C_{26}H_{29}N_3$·CH_3OH (383.24·CH_3OH): calcd. C 78.02, H 8.01, N 10.12; found C 77.84, H 7.42, N 10.43.

***N*¹,*N*³-Bis[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (46):** See Table 5, entry 3,4. Compound **46** was separated from *N*¹,*N*¹-bis[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (**47**) and *N*¹,*N*¹,*N*²-tris[(1,1′-biphenyl)-4-yl]ethane-1,2-diamine (**48**) by chromatography on SiO_2 using CH_2Cl_2/CH_3OH (20:1) as eluent as a white solid. M.p. 120 to 122 °C. Yield: 137 mg (35%). ^{1}H NMR ($CDCl_3$): δ = 1.98 (q, J = 6.6 Hz, 2 H), 3.32 (t, J = 6.6 Hz, 4 H), 3.68 (br. s, 2 H), 6.71 (d, J = 8.4 Hz, 4 H), 7.30 (m, 2 H), 7.47 (m, 12 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 29.3 (1 C), 42.1 (2 C), 113.2 (4 C), 126.4 (6 C), 128.1 (4 C), 128.8 (4 C), 130.5 (2 C), 141.3 (2 C), 147.7 (2 C) ppm. MS (EI): *m*/*z* = 380 (14), 379 (99), 378 (100) [M$^+$], 209 (41), 208 (36), 196 (10), 195 (10), 192 (10), 189 (10), 169 (38), 168 (10), 167 (10), 154 (11), 153 (11), 152 (21), 132 (11).

***N*¹,*N*¹-Bis[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (47):** Yield: 55 mg (15%). ^{1}H NMR (CD_3OD): δ = 2.04 (br. q, 2 H), 3.30 (br. t, 2 H), 3.30 (br. t, 2 H), 7.08 (d, J = 8.8 Hz, 4 H), 7.25 (m, 2 H), 7.34 (m, 12 H) ppm; NH signals are not given. ^{13}C NMR (CD_3OD): δ = 28.2 (1 C), 31.4 (1 C), 39.7 (1 C), 123.3 (4 C), 128.2 (4 C), 128.6 (2 C), 129.7 (4 C), 130.6 (4 C), 136.6 (2 C), 142.6 (2 C), 149.1 (2 C) ppm.

***N*¹,*N*¹,*N*²-Tris[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (48):** Yield: 77 mg (15%). ^{1}H NMR ($CDCl_3$): δ = 2.09 (q, J = 6.6 Hz, 2 H), 3.31 (t, J = 6.6 Hz, 2 H), 3.74 (br. s, 1 H), 3.97 (t, J = 6.6 Hz, 2 H), 6.68 (d, J = 8.8 Hz, 2 H), 7.18 (d, J = 8.8 Hz, 4 H), 7.28 (m, 3 H), 7.48 (m, 18 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.7 (1 C), 41.9 (1 C), 50.1 (1 C), 113.3 (2 C), 121.4 (4 C), 126.3 (1 C), 126.4 (2 C), 126.8 (4 C), 126.9 (2 C), 128.2 (6 C), 128.9 (6 C), 130.5 (1 C), 134.4 (2 C), 140.7 (2 C), 141.2 (1 C), 147.2 (2 C), 147.7 (1 C) ppm. MS (EI): *m*/*z* = 532 (11), 531 (45), 530 (100) [M$^+$], 360 (11), 335 (22), 334 (50), 322 (20), 321 (75), 265 (14), 209 (13), 208 (13), 207 (18), 193 (16), 182 (32), 181 (14), 180 (17), 169 (18), 167 (20), 154 (12), 153 (29), 152 (31), 115 (9). $C_{39}H_{34}N_2$·H_2O (530.70·H_2O): calcd. C 84.88, H 7.19, N 4.69; found C 85.37, H 6.61, N 5.11.

***N*¹,*N*²-Bis[(1,1′-biphenyl)-4-yl]ethane-1,2-diamine (49):** See Table 5, entry 5. The reaction mixture was chromatographed with CH_2Cl_2/toluene (1:1) to yield a white solid. M.p. 190−192 °C. Yield: 273 mg (75%). ^{1}H NMR ($CDCl_3$): δ = 3.47 (s, 4 H), 3.96 (br. s, 2 H), 6.73 (d, J = 8.8 Hz, 4 H), 7.24 (m, 8 H), 7.48 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 43.5 (2 C), 113.4 (4 C), 125.4 (2 C), 126.4 (4 C), 128.2 (4 C), 129.2 (4 C), 130.9 (2 C), 141.2 (2 C), 146.9 (2 C) ppm. MS (EI): *m*/*z* = 366 (14), 365 (23), 364 (75) [M$^+$], 194 (28), 184 (95), 183 (100), 182 (18), 181 (19), 154 (17), 153 (19), 152 (41), 151 (12).

***N*¹-[(1,1′-biphenyl)-4-yl]-*N*³-[3-([(1,1′-biphenyl)-4-yl]amino)propyl]-propane-1,3-diamine (50):** See Table 5, entry 6. The reaction mixture was chromatographed with CH_2Cl_2/MeOH (9:1) and then with CH_2Cl_2/CH_3OH/NH_3 (16:3:1) to yield a white solid. M.p. 95−97 °C. Yield: 524 mg (89%). ^{1}H NMR ($CDCl_3$): δ = 1.85 (q, J = 6.5 Hz, 4 H), 2.79 (t, J = 6.5 Hz, 4 H), 3.28 (t, J = 6.6 Hz, 4 H), 6.70 (d, J = 8.2 Hz, 4 H), 7.29 (m, 2 H), 7.43 (m, 8 H), 7.58 (m, 4 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 29.6 (2 C), 43.0 (2 C), 48.5 (2 C), 113.1 (4 C), 126.2 (2 C), 126.3 (4 C), 128.0 (4 C), 128.8 (4 C), 130.0 (2 C), 141.4 (2 C), 148.1 (2 C) ppm. MS (EI): *m*/*z* = 436 (38), 435 (100) [M$^+$], 237 (20), 226 (23), 209 (28), 208 (22), 196 (43), 195 (18), 183 (29), 182 (74), 181 (21), 180 (16), 169 (38), 167 (100), 154 (11), 153 (17), 152 (28).

***N*¹,*N*¹,*N*³,*N*³-Tetrakis[(1,1′-biphenyl)-4-yl]propane-1,3-diamine (51):** See Table 5, entry 8. The reaction mixture was chromatographed with CH_2Cl_2/toluene (1:1) to yield a white solid. M.p. 198 to 200 °C. Yield: 648 mg (95%). ^{1}H NMR ($CDCl_3$): δ = 2.21 (q, J = 6.5 Hz, 2 H), 3.97 (t, J = 6.5 Hz, 4 H), 7.11 (d, J = 8.2 Hz, 8 H), 7.48 (m, 28 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.5 (1 C), 49.9 (2 C), 121.4 (8 C), 126.6 (8 C), 126.8 (4 C), 128.0 (8 C), 128.8 (8 C), 134.2 (4 C), 140.7 (4 C), 147.0 (4 C) ppm. MS (EI): *m*/*z* = 669 (10), 668 (13), 530 (2), 335 (40), 334 (100), 322 (5), 243 (2), 181 (3), 180 (7), 154 (4), 153 (18), 152 (12), 151 (5).

***N*¹,*N*¹,*N*²,*N*²-Tetrakis[(1,1′-biphenyl)-4-yl]ethane-1,2-diamine (52):** See Table 5, entry 9. The reaction mixture was chromatographed with CH_2Cl_2/toluene (1:1) to yield a white solid. M.p. > 250 °C (dec.). Yield: 635 mg (95%). ^{1}H NMR ($CDCl_3$): δ = 4.15 (s, 4 H), 7.08 (d, J = 8.8 Hz, 8 H), 7.44 (m, 28 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 50.1 (2 C), 121.2 (8 C), 126.8 (8 C), 126.8 (4 C), 128.2 (8 C), 128.9 (8 C), 134.5 (4 C), 140.8 (4 C), 146.9 (4 C) ppm. MS (EI): *m*/*z* = 669 (11), 668 (18) [M$^+$], 336 (11), 335 (67), 334 (100), 321 (10), 180 (17), 167 (17), 153 (41), 152 (27).

***N*¹,*N*¹,*N*³-Tris[(1,1′-biphenyl)-4-yl]-*N*³-[3-(bis[(1,1′-biphenyl)-4-yl]-amino)propyl]propane-1,3-diamine (53):** See Table 5, entry 10. Compound **53** (white crystals. M.p. 158 to 160 °C) was separated from *N*¹,*N*¹-bis[(1,1′-biphenyl)-4-yl]-*N*³-[3-(bis[(1,1′-biphenyl)-4-

yl]amino)propyl]propane-1,3-diamine (**54**) by column chromatography on SiO_2 using CH_2Cl_2/hexane (1:1) as eluent. Yield: 463 mg (52%). ^1H NMR ($CDCl_3$): δ = 2.05 (q, J = 6.6 Hz, 4 H), 3.45 (t, J = 6.6 Hz, 4 H), 3.92 (t, J = 6.6 Hz, 4 H), 6.68 (d, J = 8.9 Hz, 2 H), 7.12 (d, J = 8.8 Hz, 8 H), 7.48 (m, 35 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.5 (2 C), 49.1 (2 C), 49.8 (2 C), 113.2 (2 C), 121.5 (8 C), 126.1 (1 C), 126.2 (2 C), 126.5 (br. s, 12 C), 128.1 (br. s, 10 C), 128.9 (br. s, 10 C), 139.5 (1 C), 140.4 (4 C), 140.7 (4 C), 141.5 (1 C), 147.2 (4 C), 148.1 (1 C) ppm. MS (EI): m/z = 531 (2), 530 (4), 361 (6), 335 (12), 321 (23), 196 (26), 193 (12), 182 (11), 180 (16), 166 (17), 153 (36), 152 (22), 115 (14), 97 (10), 91 (12), 77 (21). $C_{66}H_{57}N_3 \cdot H_2O$ (891.46·H_2O): calcd. C 87.09, H 6.53, N 4.62; found C 87.17, H 6.70, N 4.82.

N^1,N^1-Bis[(1,1′-biphenyl)-4-yl]-N^3-[3-(bis[(1,1′-biphenyl)-4-yl]amino)propyl]propane-1,3-diamine (54): Yield: 274 mg (37%). ^1H NMR ($CDCl_3$): δ = 1.96 (br. q, 4 H), 2.75 (br. t, 4 H), 3.90 (br. t, 4 H), 7.15 (d, J = 8.2 Hz, 8 H), 7.48 (m, 28 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 27.9 (2 C), 47.4 (2 C), 50.2 (2 C), 121.3 (8 C), 126.6 (8 C), 126.8 (4 C), 128.0 (8 C), 128.8 (8 C), 134.2 (4 C), 140.7 (4 C), 147.1 (4 C) ppm.

Reaction of *N*-(3-Aminopropyl)propane-1,3-diamine (1d) with Four Equivalents of 4-Bromobiphenyl (2c): See Table 5, entry 11. The reaction was carried out using the general procedure for the polyarylation of polyamines. Compounds **53**−**56** were separated by column chromatography on SiO_2 using, successively, CH_2Cl_2/hexane (1:1), CH_2Cl_2, and CH_2Cl_2/CH_3OH (10:1) as eluents.

N^1,N^1,N^3-Tris[(1,1′-biphenyl)-4-yl]-N^3-[3-([(1,1′-biphenyl)-4-yl]amino)propyl]propane-1,3-diamine (55): This compound was obtained as white crystals. M.p. 116−118 °C. Yield: 58 mg (8%). ^1H NMR ($CDCl_3$): δ = 1.94 (br. q, J = 6.6 Hz, 2 H), 2.10 (br. q, J = 6.6 Hz, 2 H), 3.22 (t, J = 6.6 Hz, 2 H), 3.48 (br. q, J = 6.6 Hz, 4 H), 3.92 (br. t, J = 6.6 Hz, 2 H), 6.68 (d, J = 8.6 Hz, 2 H), 6.76 (d, J = 8.8 Hz, 2 H), 7.14 (d, J = 8.8 Hz, 4 H), 7.38 (m, 28 H) ppm; NH signals are not given. ^{13}C NMR ($CDCl_3$): δ = 25.4 (1 C), 27.4 (1 C), 41.9 (1 C), 49.3 (2 C), 49.8 (1 C), 113.3 (4 C), 121.5 (4 C), 126.3 (br. s, 6 C), 126.7 (br. s, 6 C), 128.1 (br. s, 8 C), 128.8 (4 C), 128.9 (4 C), 129.7 (1 C), 130.5 (1 C), 134.4 (2 C), 140.7 (2 C), 141.0 (1 C), 141.3 (1 C), 147.1 (3 C), 147.7 (1 C) ppm. MS (EI): m/z = 362 (7), 361 (17), 348 (10), 347 (33), 346 (9), 335 (33), 322 (23), 321 (100), 243 (10), 180 (16), 167 (12), 153 (17), 152 (43), 115 (12), 77 (22).

N^1,N^1-Bis[(1,1′-biphenyl)-4-yl]-N^3-[3-([(1,1′-biphenyl)-4-yl]amino)-propyl]propane-1,3-diamine (56): Yield: 111 mg (19%). ^1H NMR ($CDCl_3$): δ = 1.85 (q, J = 6.6 Hz, 2 H), 2.00 (q, J = 6.6 Hz, 2 H), 2.77 (br. q, J = 6.6 Hz, 4 H), 3.21 (t, J = 6.6 Hz, 2 H), 3.47 (br. s, 2 H), 3.86 (t, J = 6.6 Hz, 2 H), 6.62 (d, J = 8.6 Hz, 2 H), 7.26 (d, J = 8.8 Hz, 4 H), 7.38 (m, 21 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.6 (1 C), 28.6 (1 C), 42.7 (1 C), 47.3 (1 C), 48.2 (1 C), 50.2 (1 C), 113.1 (2 C), 121.3 (4 C), 126.1 (1 C), 126.3 (2 C), 126.7 (6 C), 128.1 (6 C), 128.9 (6 C), 130.1 (1 C), 134.3 (2 C), 140.8 (2 C), 141.1 (1 C), 147.2 (2 C), 147.9 (1 C) ppm.

General Procedure for the Palladium-Catalyzed Reactions of Amines with Aryl Chlorides using the [Pd(dba)$_2$]/dppf and [Pd(dba)$_2$]/binap Catalytic Systems: Dioxane (10 mL), the indicated amount of $Pd(dba)_2$, and the ligand were added successively to an argon-flushed, two-necked flask. The reaction mixture was stirred for 5 min. The amine (3 mmol), aryl chloride (1−6 mmol), and sodium *tert*-butoxide (1−6 mmol) were then added and the mixture was refluxed with stirring. After cooling down to room temperature, 1 mL of water was added and the mixture was concentrated in vacuo. The residue was taken up with a mixture of CH_2Cl_2 and water. The organic layer was separated, washed with water, dried over anhydrous Na_2SO_4, and the solvents evaporated in vacuo. The crude material was purified by column chromatography on silica gel. The results are summarized in Table 6.

***N*-Hexylnaphthalen-1-ylamine (59):** See Table 6, entry 5. The reaction mixture was chromatographed with CH_2Cl_2/pentane (1:1) to yield a yellow oil. Yield: 173 mg (76%). ^1H NMR ($CDCl_3$): δ = 1.06 (t, J = 7.0 Hz, 3 H), 1.48 (m, 6 H), 1.82 (q, J = 7.0 Hz, 2 H), 3.32 (t, J = 6.9 Hz, 2 H), 4.28 (br. s, 1 H), 6.70 (d, J = 7.6 Hz, 1 H), 7.34 (d, J = 8.2 Hz, 1 H), 7.50 (m, 3 H), 7.85 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2 (1 C), 22.8 (1 C), 27.1 (1 C), 29.5 (1 C), 31.8 (1 C), 44.3 (1 C), 104.2 (1 C), 117.1 (1 C), 119.9 (1 C), 123.4 (1 C), 124.6 (1 C), 125.7 (1 C), 126.8 (1 C), 128.7 (1 C), 134.4 (1 C), 143.7 (1 C) ppm.

6-Chloro-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine (60): The reaction of 1-bromo-2,6-dichlorobenzene (**2u**; 225 mg, 1 mmol) with 1,3-propanediamine (**1a**; 220 mg, 3 mmol) was carried out using the general procedure for the amination of aryl chlorides in the presence of 2 mol % $Pd(dba)_2$ and 3 mol % dppf. The reaction mixture was refluxed for 4 days. The products **60** (132 mg, 72%) and **61** (7 mg, 8%) were separated by column chromatography on SiO_2 using CH_2Cl_2/hexane (1:1) as eluent. ^1H NMR ($CDCl_3$): δ = 1.82 (m, 2 H), 3.11 (m, 4 H), 4.50 (br. s, 2 H), 6.60 (m, 2 H), 6.88 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.9 (1 C), 46.5 (1 C), 46.9 (1 C), 118.4 (1 C), 120.4 (1 C), 121.4 (1 C), 123.8 (1 C), 137.2 (1 C), 141.7 (1 C) ppm.

N^1-(2,6-Dichlorophenyl)propane-1,3-diamine (61): ^1H NMR ($CDCl_3$): δ = 1.41 (br. s, 2 H), 1.67 (q, J = 6.9 Hz, 2 H), 2.77 (t, J = 6.9 Hz, 2 H), 3.35 (br. t, J = 6.9 Hz, 2 H), 4.10 (br. s, 1 H), 7.16 (d, J = 8.2 Hz, 2 H), 6.70 (d, J = 8.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 34.5 (1 C), 40.0 (1 C), 45.5 (1 C), 121.7 (1 C), 126.2 (2 C), 128.9 (2 C), 142.9 (1 C) ppm.

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Received July 1, 2004