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Arylation of Adamantanamines: II.* Palladium-Catalyzed Amination of Dihalobenzenes with Adamantylalkanamines

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Abstract—Palladium-catalyzed arylation of various (1-adamantyl)alkanamines with isomeric (*ortho*, *meta*, and *para*) bromochloro- and dibromobenzenes was studied. Optimal catalytic systems were found for the synthesis of mono- and diamination products, and the dependences of their yields on the nature of the initial amine and dihalobenzene and on the amount of base were examined. Side amination products were isolated, and paths of their formation were analyzed.

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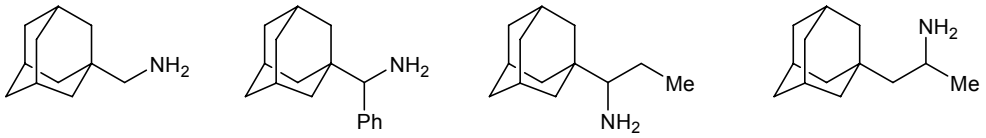
We previously reported on palladium-catalyzed arylation of 1- and 2-aminoadamantanes, which may be regarded as a convenient method for the synthesis of the corresponding *N*-aryl derivatives [1]. In the present work we tried to extend this procedure to more complex amines of the adamantane series, in which the amino group is separated from the adamantane fragment by one or two methylene or methine units. The simplest and most thoroughly studied amine of this series is (1-adamantyl)methanamine (**Ia**). Compound **Ia** was noted in more than 250 publications, whereas only a few of them were concerned with the synthesis of amine **Ia**. All other articles deal mostly with its biochemical and pharmacological applications, synthesis of ligands based thereon, and physicochemical studies. For example, amine **Ia** was used to develop potential $P2X_7$ receptor antagonists (interleukin 1β inhibitors) [2], modify 4-oxo-1,4-dihydroquinoline-3-carboxamides with a view to obtain SB_2-selective cannabioid receptor ligands [3], and modify 8-azabicyclo[3.2.1]-octane to prepare μ-opioid receptor agonists [4]. Amine **Ia** may be classed with 1-phenyl-2-aminoethanol derivatives that are β2-adrenoreceptor agonists [5], transcription factor inhibitors that weaken protein–DNA interactions [6], and metalloprotease [7] and epoxide hydrolase inhibitors [8]; it was also used in the synthesis of anticancer and antimalarial drugs (artemisinin derivatives) [9]. Finally, (1-adamantyl)methanamine (**Ia**) was used in the synthesis of Schiff bases as bidentate ligands for ruthenium complexes which catalyzed olefin metathesis [10]. Only a few aryl derivatives of aminomethyladamantane have been reported. *N*-Phenylaminomethyladamantane was synthesized in 35% yield by heating a mixture of bromomethyladamantane with aniline at the boiling point over a period of 3 h [11]. *N*-(1-Adamantylmethyl)benzene-1,2-diamine was obtained as intermediate product in the synthesis of complex biologically active ligands [12]. Another aryl derivative, *N*-(1-adamantylmethyl)-4-bromoaniline was prepared by reaction of adamantane-1-carbonyl chloride with 4-bromoaniline, followed by reduction of the amide thus formed with lithium tetrahydridoaluminate [13].

(1-Adamantyl)phenylmethanamine (**Ib**) was poorly studied. We have found only one publication on the synthesis of its *N*-phenyl derivative (yield 20%) via electrochemical reduction of the product obtained by reaction of the corresponding Schiff base with 1-bromoadamantane [14]. Biochemical and pharmaceutical applications of 1-(1-adamantyl)propan-1-amine (**Ic**) were studied much better: it was noted in 40 publications. On the other hand, 1-(1-adamantyl)-

* For communication I, see [1].



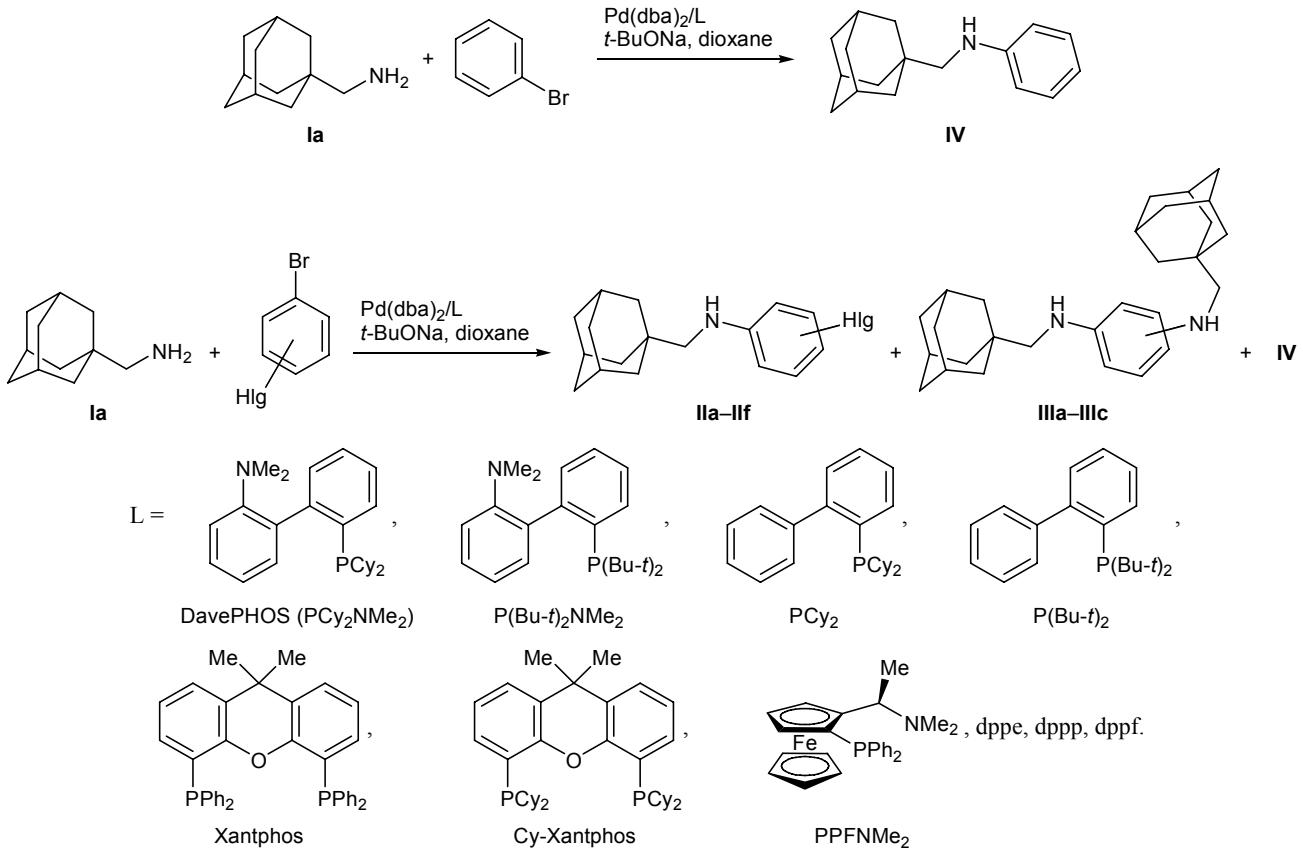
Ia **Ib** **Ic** **Id**

propan-2-amine (**Id**) which is isomeric to **Ic**, was studied to a considerably lesser extent; moreover, no its *N*-aryl derivatives were reported prior to our studies.

Taking the above stated into account, it seemed reasonable to examine palladium-catalyzed arylation of adamantyl-containing amines **Ia**–**Id** with isomeric dihalo benzenes with a view to obtain the corresponding *N*-(halophenyl) derivatives which were expected to possess a significant pharmacological potential. It was also interesting to elucidate how the nature of initial amines and dihalo benzenes (i.e., nature of the halogen atoms and their mutual position) affect the mono- and diamination processes, as well as reduction.

Arylation of (1-adamantyl)methanamine. We examined palladium-catalyzed arylation of (1-adamantyl)methanamine (**Ia**) with isomeric bromochloro- and dibromobenzenes (Scheme 1). The reactions were carried out using equimolar amounts of the initial compounds in dioxane at concentrations of 0.1 M. Initially, standard $Pd(dba)_2$/BINAP system was selected as catalyst [15]. The results are collected in Table 1. First of all we made sure that no reaction occurred in the absence of catalyst. For this purpose, amine **Ia** was heated with bromobenzene in the presence of 1.5 equiv of sodium *tert*-butoxide in boiling dioxane over a period of 7 h. The reaction mixture contained only the initial reactants, and even traces of the expected product were not detected. When the reaction was carried out in the presence of $Pd(dba)_2$/BINAP (4/4.5 mol %) as catalytic system, *N*-phenyl derivative **IV** was formed in 82% yield (Table 1, run no. 1). The reactions of **Ia** with isomeric bromochlorobenzenes smoothly occurred under standard conditions [$Pd(dba)_2$/BINAP

Scheme 1.



II, Hlg = *p*-Cl (**a**), *m*-Cl (**b**), *o*-Cl (**c**), *p*-Br (**d**), *m*-Br (**e**), *o*-Br (**f**); **III**, *para* isomer (**a**), *meta* isomer (**b**), *ortho* isomer (**c**).

Table 1. Synthesis of *N*-aryl 1-aminomethyladamantane derivatives **IIa**–**IIf** (dihaloarene–amine ratio 1 : 1)

Run no.	Halobenzene	Pd/L (mol %)	Product (yield, %)
1	Bromobenzene	$Pd(dba)_2$/BINAP (4/4.5)	**IV** (82)
2	*p*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**IIa** (79)
3	*p*-Br,Cl	$Pd(dba)_2$/BINAP (2/2.5)	**IIa** (71)
4	*m*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**IIb** (81)
5	*o*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**IIc** (93)
6	*p*-Br,Br	$Pd(dba)_2$/BINAP (4/4.5)	**IId** (23), **IV** (11)
7	*p*-Br,Br	$Pd(dba)_2$/DavePHOS (4/5)	**IId** (11), **IIIa** (30), **IV** (13)
8	*p*-Br,Br	$Pd(dba)_2/PCy_2$ (4/8)	**IId** (13), **IIIa** (24), **IV** (15)
9[a]	*p*-Br,Br	$Pd(dba)_2/P(Bu\text{-}t)_2$ (4/8)	**IId** (42), **IIIa** (33)
10[b]	*p*-Br,Br	$Pd(OAc)_2$/dppe (5/10)	**IId** (0)
11[b]	*p*-Br,Br	$Pd(OAc)_2$/dppf (5/10)	**IId** (traces)
12[c]	*p*-Br,Br	$Pd(OAc)_2$/dppp (5/10)	**IId** (9)
13[d]	*p*-Br,Br	$Pd(dba)_2$/dppp (5/7.5)	**IId** (7)
14[a]	*p*-Br,Br	$Pd(dba)_2$/Xantphos (10/10)	**IId** (34)
15[e]	*p*-Br,Br	$Pd(dba)_2$/Cy-Xantphos (10/10)	**IId** (17), **IV** (7)
16[f]	*m*-Br,Br	$Pd(dba)_2$/BINAP (4/4.5)	**IIe** (47, 39[g]), **IIIb** (10), 4[g]), **IV** (17, 7[g])
17	*o*-Br,Br	$Pd(dba)_2$/BINAP (4/4.5)	**IIe** (38, 30[g]), **IIIc** (38, 34[g]), **IV** (19, 5[g])

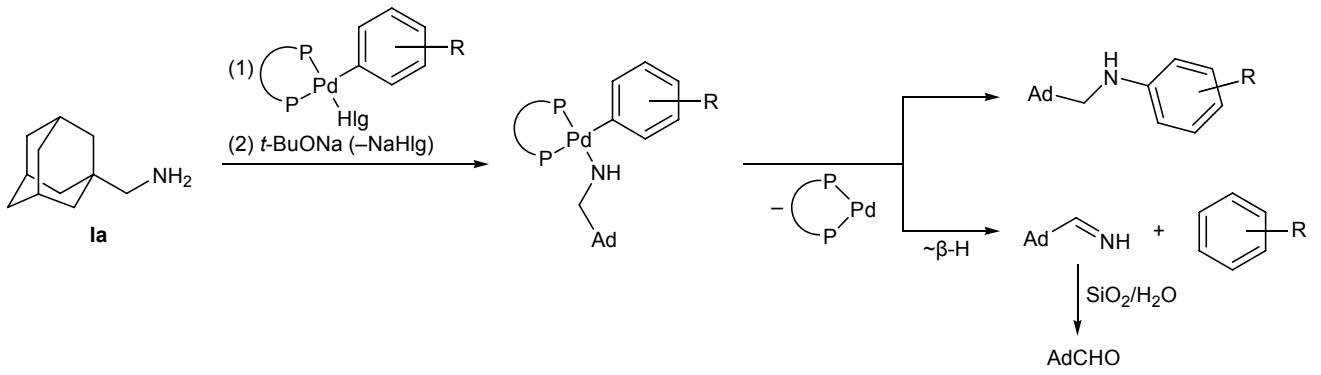
[a] Joint chromatographic separation of the products obtained in run nos. 9 and 14; yield of **IId** 33%.
[b] Conversion of *p*-dibromobenzene 100%.
[c] Conversion of *p*-dibromobenzene 55%.
[d] Conversion of *p*-dibromobenzene 65%.
[e] Conversion of *p*-dibromobenzene 78%.
[f] Adamantane-1-carbaldehyde (12%).
[g] After chromatographic separation.

4/4.5 mol %, 1.5 equiv of *t*-BuONa, c = 0.1 M] and were complete in 5–7 h; target compounds **IIa**–**IIc** were obtained in high yields, and only in the reaction with *m*-bromochlorobenzene an insignificant amount of side diamination product was detected. Considerably lower reactivity of chlorine atom compared to bromine in catalytic amination ensured selective formation of just chloro-substituted anilines **IIa**–**IIc**.

Reduction of the amount of catalyst to 2 mol % resulted in slight decrease of the yield (Table 1, run no. 3). The reaction mixtures were analyzed by ^{1}H and ^{13}C NMR spectroscopy and treated with water, and the products were extracted into methylene chloride. If several products were formed, they were isolated as individual substances by chromatography on silica gel. The reactions with isomeric dibromobenzenes followed a considerably more complex pattern. Surprisingly, the strongest difficulties were encountered in the reaction with *p*-dibromobenzene, and the yield of compound **IId** in the presence of standard catalytic system did not exceed 23% (Table 1, run no. 6). The use of a more active amination catalyst containing P-donor ligand DavePHOS [16] led to formation of an appreciable amount of *p*-diamino-substituted benzene **IIIa**, whereas the yield of compound **IId** was even smaller (Table 1, run no. 7). The results were not improved when another donor ligand, 2-(dicyclohexylphosphino)-biphenyl (PCy_2), was used (Table 1, run no. 8), while in the presence of structurally related ligand, 2-(di-*tert*-butylphosphino)biphenyl [$P(t\text{-}Bu_2)$] the yield of **IId** increased to 45%, though the amount of diamination product **IIIa** remained significant (Table 1, run no. 9). The catalytic system including Xantphos as ligand was also quite successful for the formation of target compound **IId** (Table 1, run no. 14), while the yield of **IId** decreased in the presence of a Xantphos analog containing dicyclohexylphosphino groups (Cy-Xantphos); in addition, the conversion of initial dibromobenzene was not complete (Table 1, run no. 15).

Other bidentate phosphine ligands, such as dppe, dppp, and dppf, turned out to be completely ineffective (Table 1; run nos. 10–13). In some cases, poor yield of

Scheme 2.



IId was observed together with incomplete conversion of initial *p*-dibromobenzene (Table 1; run nos. 12, 13), whereas in other cases the conversion of *p*-dibromobenzene was complete, but even traces of the amination product were not detected (Table 1, run nos. 10, 11). The main side processes in the reactions with dibromobenzenes are reduction and double amination. The reaction of **Ia** with *o*-dibromobenzene gave comparable amounts of the target monoamination product **IIf** and *o*-phenylenediamine derivative **IIIc**. The reaction was also accompanied by formation of reduction product **IV** (Table 1, run no. 17). The yield of compound **IIe** obtained from *m*-dibromobenzene was higher, while the yield of by-product **IIIb** decreased; reduction product **IV** was also formed (Table 1, run no. 16). Presumably, compound **IV** is formed according to a catalytic mechanism which involves β-hydride shift in intermediate palladium complex (Scheme 2). Schiff base formed during the reduction process is hydrolytically unstable, and it decomposes into adamantane-1-carbaldehyde and amine **IV** upon chromatography on silica gel. Furthermore, reduction of one bromine atom in the initial dihalobenzene could give chloro- or bromobenzene. However, the yields of these compounds were not determined, for they were readily removed from the reaction mixture under reduced pressure together with dioxane (the boiling points of chlorobenzene and bromobenzene are 132 and 156°C, respectively).

On the whole, the reactions with bromochlorobenzenes provide better results than those obtained in analogous reactions with dibromobenzenes (the same applies to reactions with other amines; see below), which is consistent with the higher reactivity of bromine atom in other catalytic reactions. The conversion of dibromobenzenes is generally higher than the conversion of the amine; this means that the reactions are accompanied by other side processes which do not involve amines. By special experiment we showed that *m*-dibromobenzene under standard amination conditions but in the absence of amine in 7 h largely undergoes transformation into a complex mixture of unidentifiable compounds.

We have become interested in relatively ready formation of diaminobenzene derivatives **IIIa**–**IIIc**, specifically of *ortho*-diamination product **IIIc**. In order to synthesize compounds containing two adamantane fragments as potential physiologically active substances [12], we performed reactions of isomeric

Table 2. Synthesis of diaminobenzene derivatives **IIIa**–**IIIc** (dibromobenzene–amine ratio 1 : 3)

Run no.	Dibromobenzene	Pd/L (mol %)	Product (yield, %)
1	*para*	$Pd(dba)_2$/BINAP (4/4.5)	**IV** (96)
2[a]	*para*	$Pd(dba)_2$/DavePHOS (8/16)	**IIIa** (43), **IV** (30)
3[a]	*para*	$Pd(dba)_2$/P(*t*-Bu)$_2$ (8/16)	**IIIa** (90), **IV** (9)
4	*meta*	$Pd(dba)_2$/BINAP (8/9)	**IIIb** (99)
5	*ortho*	$Pd(dba)_2$/BINAP (8/9)	**IIIc** (66), **IV** (15), **IIf** (15), **IIIb** (2)
6	*ortho*	$Pd(dba)_2$/ DavePHOS (8/10)	**IIIc** (36), **IV** (33), **IIf** (12), **IIIb** (2)
7	*ortho*	$Pd(dba)_2$/P(*t*-Bu)$_2$ (8/16)	**IIIc** (24), **IV** (21)

[a] Joint chromatographic separation of the products obtained in run nos. 2 and 3; yield of **IIIa** 50%.

dibromobenzenes with 3 equiv of amine **Ia**. The use of $Pd(dba)_2$/BINAP as catalytic system in the reaction with *p*-dibromobenzene led to exclusive formation of reduction product **IV** (Table 2, run no. 1). Donor phosphine ligands DavePHOS and especially $P(t\text{-}Bu)_2$ favored considerable increase in the yield of diamination product **IIIa** (up to 90%; Table 2, run nos. 2, 3), and the yield of reduction product **IV** decreased. Compound **IIIa** displayed in the ^1H NMR spectrum of the reaction mixture narrow signals at δ 2.71 (d, 2H, CH_2N) and 6.54 ppm (s, 4H, H_{arom}). The corresponding carbon signals appeared in the ^{13}C NMR spectrum at δ_C 58.0 (2C), 114.5 (4C), and 141.4 ppm (2C). However, the ^1H NMR spectrum of the product isolated by chromatography contained very broad lines (about 500 Hz), whereas signals from the corresponding carbon atoms were not observed at all. As will be shown below, such pattern is typical of all *p*-diamino-substituted benzenes synthesized in this work.

Diamination of *m*-dibromobenzene was characterized by almost quantitative yield (Table 2, run no. 4) when $Pd(dba)_2$/BINAP was used as catalytic system. This system turned out to ensure the best results in the reaction with *o*-dibromobenzene: the yield of target diaminobenzene **IIIc** was 66% (Table 2, run no. 5). Catalytic systems based on donor phosphine ligands were less effective (Table 2; run nos. 6, 7). In these cases, monoamino derivative **IId** and reduced compound **IV** were formed as by-products. In addition, a small amount of isomeric *m*-diamino derivative **IIIb** was detected in two experiments (Table 2; run nos. 5, 6). Compound **IIIb** was formed following the elimination–addition pattern (benzyne mechanism) rather than the catalytic path.

We previously studied diamination of isomeric dibromobenzenes with linear polyamines and found that *meta*-diamination products can be obtained in high yield [17] and that *ortho*- or *para*-diamination almost does not occur; in almost no cases reduction products were formed. As follows from the above data, a different pattern is observed in the reactions with (1-adamantyl)methanamine (**Ia**). According to PM3 calculations,** lone electron pair on the nitrogen atom in molecule **IIf** (N-substituted *o*-bromoaniline) is partly forced out from conjugation with π-electron system of the benzene ring; therefore, positive mesomeric effect of the amino group is weakened, and oxidative addition at the C–Br bond to Pd(0), followed by replacement of bromine by the second amino group, becomes more facile. This may be responsible for relatively easy formation of *o*-diamino derivative **IIIc** even in the presence of an equimolar amount of amine **Ia**.

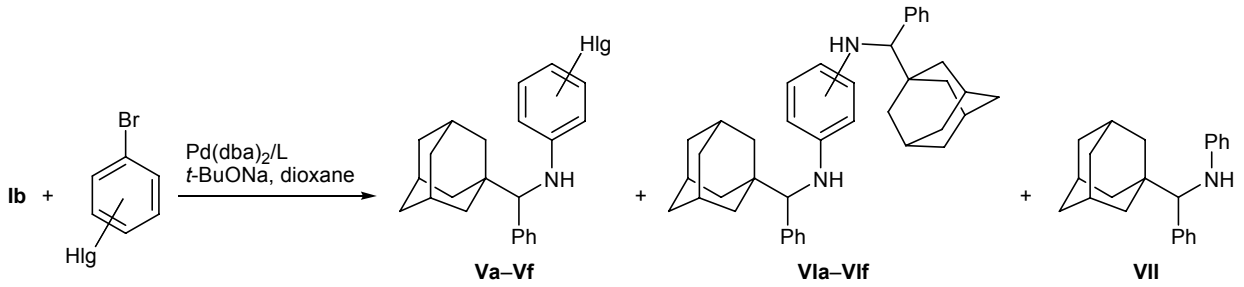
Arylation of (1-adamantyl)phenylmethanamine (Ib). The arylation of sterically hindered amine **Ib** (Scheme 3) with *p*-bromochlorobenzene was successful in the presence of 4 mol % of standard catalytic system, and the yield of arylation product **Va** was 65% (Table 3, run no. 1). Likewise, compound **Ib** reacted with *m*-bromochlorobenzene, yielding 75% of monoamination product **Vc**. The yield of compound **Vc** in the reaction with more sterically hindered *o*-bromochlorobenzene was 48%, and it increased to 56% in the presence of a larger amount of the catalyst (8 mol %) (Table 3; run nos. 2–4). The lower yields of compounds **Va**–**Vc** as compared to the yields of **IIa**–**IIc** in the reactions with amine **Ia** should be attributed to stronger steric hindrances at the nitrogen atom in amine **Ib**.

Fairly high yield of amination product **Vd** (60%) was obtained in the reaction with *p*-dibromobenzene (Table 3, run no. 5). Analogous reaction with *m*-dibromobenzene gave N-substituted bromoaniline **Ve** in a lower yield (44%; Table 3, run no. 6). The yield further decreased when Xantphos was used as ligand instead of BINAP (Table 3, run no. 7), and in the presence of donor phosphine ligand DavePHOS the major product was diaminobenzene **VIb** (Table 3, run no. 8). The reaction of **Ib** with *o*-dibromobenzene afforded 40% of amination product **Vf** and 22% of reduction product **VII**. Raising the amount of the catalyst did not increase the yield of **Vf** (Table 3; run nos. 9, 10). In this case, DavePHOS also favored formation of diamination product **VIc**, while the yield of **Vf** was several times lower (Table 3, run no. 11). It should be noted that the conversion of *o*-dibromobenzene did not exceed 90%. In some cases, oxidation product of amine **Ib**, 1-adamantyl phenyl ketone, was isolated by chromatography (Table 3; run nos. 3, 6, 9).

With a view to synthesize the corresponding diamino derivatives, isomeric dibromobenzenes were reacted with 3 equiv of amine **Ib** in the presence of different catalytic systems. No diaminobenzene **VIa** was formed in the reaction of *p*-dibromobenzene catalyzed by palladium complex with BINAP. Instead, monoamination product **Vd** and reduction product **VII** were obtained in approximately similar yields (Table 4, run no. 1). A more effective ligand was DavePHOS; in this case, the yield of **VIa** was 33%. As in the reaction

** In collaboration with Prof. T.V. Magdesieva and post-graduate student A.V. Dolganov (Lomonosov Moscow State University).

Scheme 3.



V, Hlg = *p*-Cl (**a**), *m*-Cl (**b**), *o*-Cl (**c**), *p*-Br (**d**), *m*-Br (**e**), *o*-Br (**f**); **VI**, *para* isomer (**a**), *meta* isomer (**b**), *ortho* isomer (**c**).

of *o*-dibromobenzene with amine **Ia**, an appreciable amount of *m*-diamino derivative **VIb** was formed (6%; Table 4, run no. 2). The amination of *m*-dibromobenzene was performed in the presence of six phosphine ligands (Table 4; run nos. 3–8). Among them, the most efficient for the synthesis of **VIb** was DavePHOS; it ensured 68% yield of the target compound (Table 4, run no. 6). Reduction product **VII** was formed in all the above reactions. The yield of *o*-diamino derivative **VIc** weakly depended on the nature of phosphine ligand, and it ranged from 30 to 37% (Table 4; run nos. 9, 10); the amount of reduction product **VII** was comparable.

A number of signals in the ^{1}H and ^{13}C NMR spectra of *o*- and *m*-diaminobenzene derivatives **VIb** and **VIc** were doubled, indicating that these compounds are mixtures of two couples of diastereoisomers. The ^{1}H NMR spectrum of the reaction mixture containing *p*-diamino derivative **VIa** displayed fairly narrow signals from protons in the adamantane fragments, CH groups [δ 3.50 ppm, s (2H)], and 1,4-disubstituted benzene ring [δ 6.27 ppm, s, (4H)]. Analogous pattern was observed in the ^{13}C NMR spectrum: the CH signal was located at δ_C 65.9 ppm (2C), and carbon atoms in the 1,4-disubstituted benzene ring resonated at δ_C 114.5 ppm (4C). After chromatographic purification, the same signals in the ^{1}H NMR spectrum of **VIa** were very broad, while no signals were observed in the ^{13}C NMR spectrum, as noted above for *p*-diamino derivative **IIIa**.

Arylation of 1-(1-adamantyl)propan-1-amine (Ic). The reactions of 1-(1-adamantyl)propan-1-amine (**Ic**) with *p*- and *m*-bromochlorobenzenes (Scheme 4) were not so successful as analogous reactions with less

Table 3. Reaction of dihalobenzenes with (1-adamantyl)phenylmethanamine (**Ib**) (dihalobenzene–amine ratio 1 : 1)

Run no.	Dihalobenzene	Pd/L (mol %)	Product (yield, %)
1	*p*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**Va** (65)
2	*m*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**Vb** (75)
3[a]	*o*-Br,Cl	$Pd(dba)_2$/BINAP (4/4.5)	**Vc** (48, 40[b])
4	*o*-Br,Cl	$Pd(dba)_2$/BINAP (8/9)	**Vc** (56)
5	*p*-Br,Br	$Pd(dba)_2$/BINAP (4/5)	**Vd** (60)
6[c]	*m*-Br,Br	$Pd(dba)_2$/BINAP (4/4.5)	**Ve** (44, 37[b])
7	*m*-Br,Br	$Pd(dba)_2$/Xantphos (10/10)	**Ve** (24)
8	*m*-Br,Br	$Pd(dba)_2$/DavePHOS (4/8)	**Ve** (11), **VII** (4), **VIb** (43)
9[d]	*o*-Br,Br	$Pd(dba)_2$/BINAP (4/4.5)	**Vf** (40, 40[b])
10	*o*-Br,Br	$Pd(dba)_2$/BINAP (8/9)	**Vf** (44), **VII** (22)
11[e]	*o*-Br,Br	$Pd(dba)_2$/DavePHOS (4/8)	**Vf** (9), **VII** (19), **VIc** (36)

[a] Yield of 1-adamantyl phenyl ketone 18%.
[b] After chromatographic separation.
[c] Yield of 1-adamantyl phenyl ketone 12%.
[d] Conversion of *o*-dibromobenzene 86%; yield of 1-adamantyl phenyl ketone 12%.
[e] Conversion of *o*-dibromobenzene 87%.

Table 4. Synthesis of diaminobenzene derivatives **VIa**–**VIc** (dibromobenzene–amine ratio 1 : 3)

Run no.	Dibromobenzene	Pd/L (mol %)	Product (yield, %)
1	*para*	$Pd(dba)_2$/BINAP (4/4.5)	**VIa** (0), **VII** (48), **Vd** (51)
2[a]	*para*	$Pd(dba)_2$/DavePHOS (8/16)	**VIa** (33, 17[b]), **VII** (30, 19[b]), **VIb** (6, 6[b])
3	*meta*	$Pd(dba)_2$/BINAP (4/4.5)	**VIb** (34), **VII** (45)
4	*meta*	$Pd(dba)_2/PCy_2$ (8/16)	**VIb** (31), **VII** (18)
5	*meta*	$Pd(dba)_2/P(t\text{-Bu})_2$ (8/16)	**VIb** (48), **VII** (15)
6	*meta*	$Pd(dba)_2$/DavePHOS (8/16)	**VIb** (68, 63[b]), **VII** (9, 6[b])
7	*meta*	$Pd(dba)_2/P(t\text{-Bu})_2NMe_2$ (8/16)	**VIb** (24), **VII** (15), **Ve** (12)
8	*meta*	$Pd(dba)_2/PPFNMe_2$ (8/16)	**VIb** (49), **VII** (27)
9	*ortho*	$Pd(dba)_2$/BINAP (4/4.5)	**VIc** (37), **VII** (36)
10[c]	*ortho*	$Pd(dba)_2$/DavePHOS (8/16)	**VIc** (30), 26[b]), **VII** (33, 25[b])

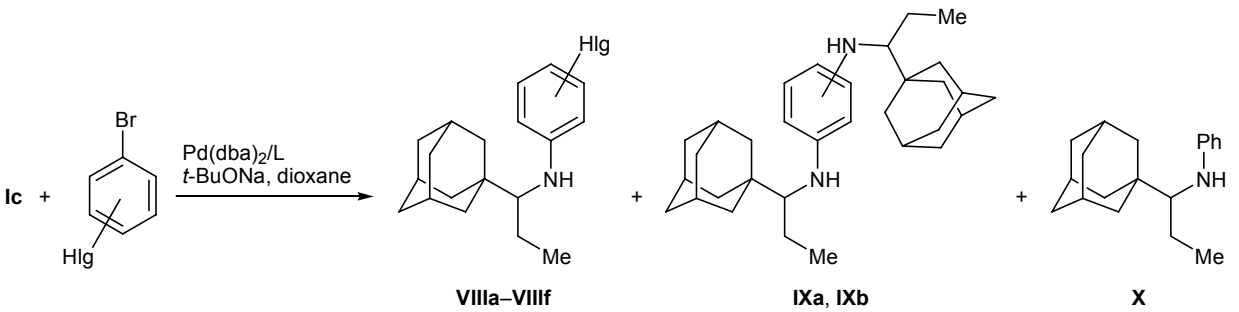
[a] Yield of 1-adamantyl phenyl ketone 13%.
[b] After chromatographic separation.
[c] Yield of 1-adamantyl phenyl ketone 18%.

sterically hindered amines **Ia** and **Ib**, and target compounds **VIIIa** and **VIIIb** were formed in 50 and 53% yield, respectively, under standard conditions (7 h under reflux; Table 5; run nos. 1, 2). In the reaction of *o*-bromochlorobenzene with amine **Ic** we initially obtained only 35% of compound **VIIIc**, the conversion of the dihalobenzene being no more than 75% (Table 5, run no. 3). Prolonged heating (14 h) allowed us to raise the yield of **VIIIc** to 50% (Table 5, run no. 4). Moderate yield of the target product may be rationalized by considerable steric hindrances in amine **Ic**. The reaction of **Ic** with *o*-dibromobenzene was even more difficult: the yield of compound **VIIIf** did not exceed 20%, and the reaction was accompanied by formation of reduction product **X** (Table 5, run no. 7). In this case, the conversion of *o*-dibromobenzene was also incomplete. *p*- and *m*-Dibromobenzenes reacted appreciably better, though the yields of **VIIId** and **VIIIe** did not exceed 50% (Table 5, run nos. 5, 6). In the reactions with *p*-bromochloro- and *p*-dibromobenzene appreciable amounts of *p*-chloro- and *p*-bromoanilines were formed (Table 5; run nos. 1, 5). The latter could result from arylation of intermediate Schiff base (β-hydride elimination product; Scheme 5).

The arylation of amine **Ic** was characterized by formation of a considerable amount of 1-adamantyl ethyl ketone as a result of redox process.

p-Diamino derivative **IXa** was detected only in the reaction mixture obtained from 3 equiv of amine **Ic**; its yield was estimated at 36%. However, attempts to isolate compound **IXa** by chromatography were unsuccessful; we isolated only reduction product **X** and 1-adamantyl ethyl ketone (Table 5, run no. 8). In the ^{1}H NMR spectrum of the reaction mixture *p*-diaminobenzene **IXa** gave rise to a singlet from aromatic protons at δ 6.42 ppm (4H), and the ^{13}C NMR spectrum contained signals at δ_C 114 (4C) and 142 ppm (2C). The formation of **IXa** was also proved by the MALDI-TOF mass spectrum of the reaction mixture (*m*/*z* 460.41 $[M]^+$). The synthesis of *m*-diaminobenzene

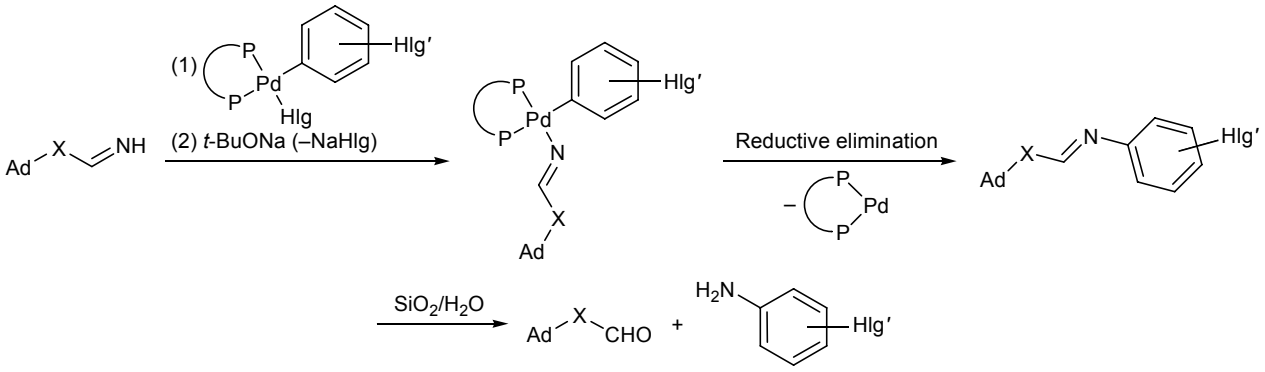
Scheme 4.



VIIIa–VIIIf **IXa**, **IXb** **X**

VIII, Hlg = *p*-Cl (**a**), *m*-Cl (**b**), *o*-Cl (**c**), *p*-Br (**d**), *m*-Br (**e**), *o*-Br (**f**); **IX**, *para* isomer (**a**), *meta* isomer (**b**).

Scheme 5.



derivative **IXb** was more successful; it was obtained in 43% yield using BINAP as ligand (Table 5, run no. 9). Though compound **IXb** was a mixture of two couples of diastereoisomers, its ^{1}H and ^{13}C NMR spectra were considerably simpler: only the C^2 atom in the benzene ring appeared as a doubled signal (δ_C 96.6, 96.7 ppm). No desired *o*-diamino derivative was obtained in the reaction of amine **Ic** with *o*-dibromobenzene. In all cases, monoamination with subsequent reduction to compound **X** was observed, and the reaction was also accompanied by oxidation of amine **Ic** to 1-adamantyl ethyl ketone (Table 5; run nos. 10, 11). Presumably, the reason is stronger steric hindrances at the nitrogen atom, as compared to amine **Ib**.

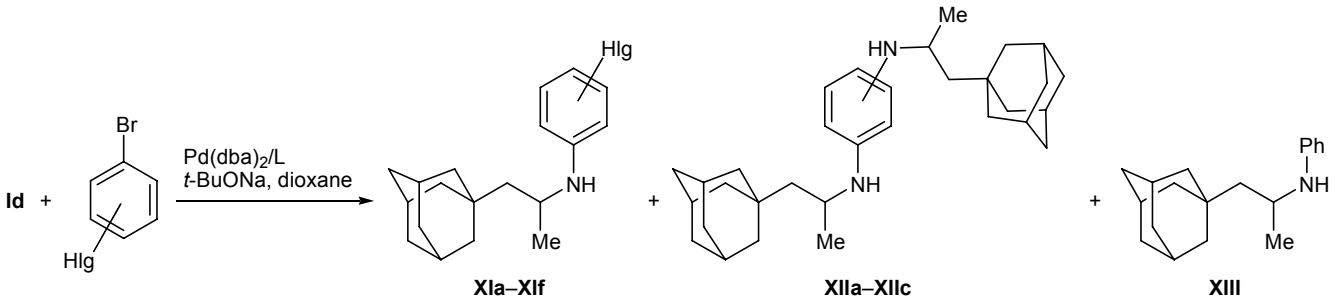
Arylation of 1-(1-adamantyl)propan-2-amine (Id). 1-(1-Adamantyl)propan-2-amine (**Id**) turned out to be appreciably more reactive than isomeric amine **Ic**, which may be due to lesser steric hindrances at the nitrogen atom. Its reactions with bromochlorobenzenes gave the corresponding *N*-substituted chloroanilines **XIa**–**XIc** in 81–89% yield (Scheme 6; Table 6, run nos. 1–3). The reaction of **Id** with *p*-dibromobenzene was also successful, though the conversion of the latter was 83% (Table 6, run no. 4). In the reaction with *m*-dibromobenzene the yield of diamination product **XIIb** was considerably lower than the yield of analogous compound **XIIc** in the amination of *o*-dibromobenzene, and *m*-bromoaniline **XIe** was obtained in

Table 5. Synthesis of *N*-aryl derivatives of 1-(1-adamantyl)propan-1-amine (**Ic**)

Run no.	Dihalobenzene	Amin–dihalobenzene ratio	Pd/L (mol %)	Product (yield, %)
1[a]	*p*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIa** (50)
2	*m*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIb** (53)
3[b]	*o*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIc** (35)
4[c]	*o*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIc** (50)
5[d]	*p*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIId** (48), **X** (10)
6	*m*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIe** (48), **X** (8), **IXb** (3)
7[e]	*o*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**VIIIf** (20, 13[f]), **X** (8, 4.5[f])
8[g]	*p*-Br,Br	3 : 1	$Pd(dba)_2$/DavePHOS (8/16)	**IXa** (36), **X** (42, 25[f])
9	*m*-Br,Br	3 : 1	$Pd(dba)_2$/BINAP (8/9)	**IXb** (43, 33[f]), **X** (33, 24[f])
10[h]	*o*-Br,Br	3 : 1	$Pd(dba)_2$/BINAP (8/9)	**X** (36)
11[i]	*o*-Br,Br	3 : 1	$Pd(dba)_2$/DavePHOS (8/16)	**X** (57)

[a] Yield of *p*-chloroaniline 7%.
[b] Conversion of *o*-bromochlorobenzene 75%; yield of 1-(1-adamantyl)propan-1-one 24%.
[c] The reaction time was twice as long; yield of 1-(1-adamantyl)propan-1-one 20%.
[d] Yield of *p*-bromoaniline 12%.
[e] Conversion of *o*-dibromobenzene 82%; yield of 1-(1-adamantyl)propan-1-one 38% (21% after chromatographic separation).
[f] After chromatographic separation.
[g] Compound **IXa** was not isolated; yield of 1-(1-adamantyl)propan-1-one 40% (after chromatographic separation).
[h] Yield of 1-(1-adamantyl)propan-1-one 28%.
[i] Yield of 1-(1-adamantyl)propan-1-one 30%.

Scheme 6.



XI, Hlg = *p*-Cl (**a**), *m*-Cl (**b**), *o*-Cl (**c**), *p*-Br (**d**), *m*-Br (**e**), *o*-Br (**f**); **XII**, *para* isomer (**a**), *meta* isomer (**b**), *ortho* isomer (**c**).

67% yield (Table 6, run no. 5). The reaction of amine **Id** with *o*-dibromobenzene followed a more complex pattern due to formation of both *o*-diaminobenzene derivative **XIIc** and reduction product **XIII**; therefore, the yield of target compound **XIf** was lower (Table 6; run nos. 6, 7).

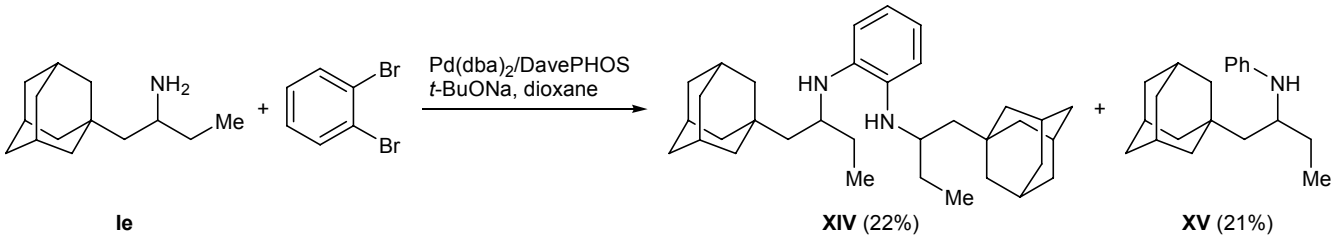
All these reactions were performed in the presence of standard catalytic system $Pd(dba)_2$/BINAP (4/4.5 mol %). The amination of *m*- and *o*-dibromobenzenes with 3 equiv of amine **Id** in the presence of BINAP and DavePHOS as ligands gave 51 and 46% of compounds **XIIb** and **XIIc**, respectively (Table 6; run nos. 9, 10). In both cases, a considerable amount of reduction product **XIII** was formed. In the reaction of *p*-dibromobenzene with excess amine **Id** *p*-diaminobenzene derivative **XIIa** partly crystallized from the reaction mixture on cooling (28%; Table 6, run no. 8). However, we failed to isolate an additional amount of compound **XIIa** from the reaction mixture by chromatography. As with *p*-diamino derivative **IXa**, chromatographic separation gave mainly reduction product **XIII**, whereas only a small amount of compound **XIIa** was isolated as a mixture with other unidentified compounds. The yield of reduction product **XIII** considerably increased in the presence of excess amine **Id**. A number of signals in the ^1H and ^{13}C NMR spectra of compounds **XIIb** and **XIIc** were either doubled or broadened, indicating that they exist as mixtures of equal amounts of two couples of diastereoisomers. By contrast, neither doubling nor broadening of signals was observed in the spectra of *p*-diamino derivative **XIIa**. All amines of the adamantane series characteristically displayed in the MALDI mass spectra a strong peak belonging to the $[M - H_2]^+$ ion which is likely to contain dehydroadamantane fragment. The highest intensity of the $[M - H_2]^+$ peaks was observed in the mass spectra of **XIa**–**XIf** and **XIIa**–**XIIc**, and the MALDI mass spectra of **XId** and **XIe** contained only

Table 6. Synthesis of *N*-aryl derivatives of 1-(1-adamantyl)propan-2-amine (**Id**)

Run no.	Dihalobenzene	Amine–dihalobenzene ratio	Pd/L (mol %)	Product (yield, %)
1	*p*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XIa** (89)
2	*m*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XIb** (81)
3	*o*-Br,Cl	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XIc** (82)
4[a]	*p*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XId** (75)
5	*m*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XIe** (67), **XIII** (6), **XIIb** (7)
6	*o*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XId** (65), **XIII** (7), **XIIc** (20)
7	*o*-Br,Br	1 : 1	$Pd(dba)_2$/BINAP (4/4.5)	**XId** (50), **XIII** (7), **XIIc** (27)
8[b]	*p*-Br,Br	3 : 1	$Pd(dba)_2$/DavePHOS (8/16)	**XIIa** (37[c], 0[d]), **XIII** (24[c], 13[d])
9	*m*-Br,Br	3 : 1	$Pd(dba)_2$/BINAP (8/9)	**XIIb** (51, 50[d]), **XIII** (27, 23[d])
10	*o*-Br,Br	3 : 1	$Pd(dba)_2$/DavePHOS (8/16)	**XIIc** (46, 35[d]), **XIII** (33, 32[d])

[a] Conversion of *p*-dibromobenzene 83%.
[b] Compound **XIIc** crystallized from the reaction solution (yield 28%).
[c] Isolated from the reaction mixture.
[d] After chromatographic separation.

Scheme 7.



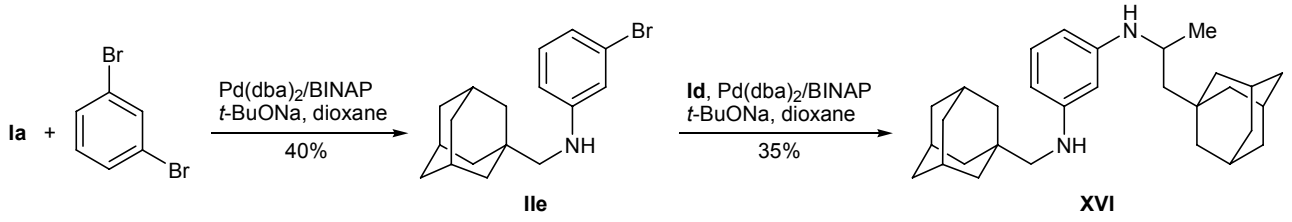
$[M - H_2]^+$ peaks, $[M]^+$ peaks being almost lacking. Diamino derivatives **XIIa**–**XIIc** also displayed strong $[M - 2H_2]^+$ ion peaks.

We tried to elucidate the reason why amine **Ic** (in contrast to isomeric amine **Id**) does not give *ortho*-diamination product in the reaction with *o*-dibromobenzene. For this purpose, the reaction of excess amine **Ie** with *o*-dibromobenzene was examined. Like amine **Ic**, molecule **Ie** possesses an ethyl substituent, but the adamantane fragment therein is separated from the amino group by two carbon atoms (as in amine **Id**). This reaction afforded *orto*-diamino derivative **XIV** in 22% yield (Scheme 7), and compound **XV** was obtained as by-product (21%). These findings indicated that the presence of an ethyl group at the α-carbon atom in adamantylalkylamine does not hamper formation of *o*-diamination products provided that the adamantyl substituent is sufficiently distant from the nitrogen atom. Most signals in the ^{13}C NMR spectrum of compound **XIV** were doubled, for it was formed as a mixture of two couples of diastereoisomers in equal amounts.

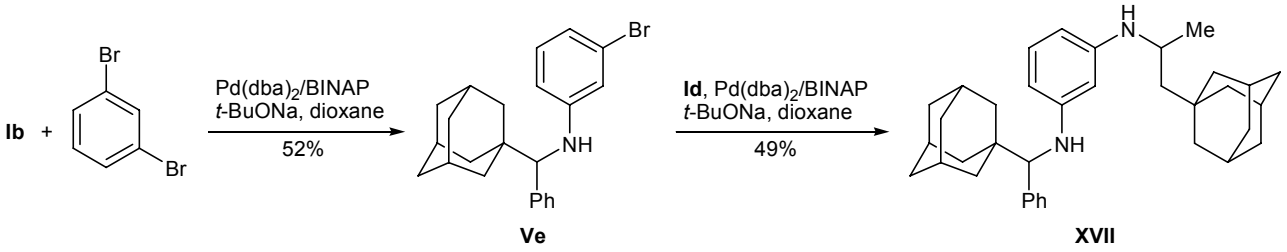
Synthesis of unsymmetrically substituted diaminobenzenes and *N*,*N*′-bis(haloaryl)-substituted diamines. Successful synthesis of a number of substituted diaminobenzenes containing two adamantylalkyl fragments prompted us to extend the scope of this procedure with a view to obtain derivatives containing two different adamantylalkyl fragments. In the first step, by reaction of equimolar amounts of aminomethyladamantane **Ia** and *m*-dibromobenzene we synthesized compound **IIe** in 40% yield (in the reaction mixture) and brought it (without isolation) into reaction with another amine (**Id**) taken in excess. As a result, we isolated 35% of unsymmetrically substituted *m*-phenylenediamine **XVI** (Scheme 8). Likewise, the reaction of compound **Ve** (generated *in situ* from amine **Ib** and *m*-dibromobenzene in 52% yield) with excess amine **Id** gave 49% of *N*,*N*′-disubstituted *m*-phenylenediamine **XVII** (Scheme 9). Compound **XVII** was a mixture of two couples of diastereoisomers in equimolar amounts, so that most signals in its NMR spectra were doubled. In addition, compounds **XVI** and **XVII** characteristically displayed in the MALDI mass spectra very strong peaks belonging to $[M - 2H_2]^+$ ions.

Effect of the $AdXNH_2$–ArHlg–*t*-BuONa ratio on the yield of mono- and diamination products of dihalobenzenes. While performing experiments we found that the product yield considerably depends on the amount of sodium *tert*-butoxide taken as a base. Therefore, we specially examined how the ratio amine–dihalobenzene–base affects the reaction direction, i.e., predominant formation of one or another product. The use of equimolar amounts of the above reactants in the reaction with amine **Ia** did not lead to reduced yield of monoamination product **IIe**, as compared to the reaction carried out under standard conditions (1.5 equiv of *t*-BuONa; Table 7, run no. 1). When the amount of the base was reduced to 0.6 equiv, the yield decreased to 30%, the conversion of amine **Ia** was 35%, and the conversion of *m*-dibromobenzene was 64% (Table 7, run no. 2). A more complicated pattern was observed in the reaction with excess amine **Ia** (3 equiv). Neither mono- nor diamination product was detected in the reaction mixture obtained from

Scheme 8.



Scheme 9.



m-dibromobenzene in the presence of 1.5 equiv of sodium *tert*-butoxide and 4 mol % of the catalyst [$Pd(dba)_2$/BINAP] despite 100% conversion of the initial reactants (Table 7, run no. 3).

Raising the amount of the same catalyst to 8 mol % resulted in the formation of monoamination product **IIe** approximately in the same amount as under standard conditions (54%), and 7.5% of diamination product **IIIb** was detected (Table 7, run no. 4). The use of DavePHOS as more efficient diamination ligand allowed us to synthesize diamination product in the presence of a smaller than equivalent amount of sodium *tert*-butoxide (Table 7; run nos. 5, 6). Somewhat different results were obtained in the amination of *o*-dibromobenzene in the presence of insufficient *t*-BuONa. The yield of monoamination product **IIf** was 57–63% with the use of 8 mol % of $Pd(dba)_2$/BINAP, and the yield of diamination product **IIIc** in the same reaction was 18–26% (Table 7; run nos. 7, 8). Donor phosphine ligand DavePHOS impaired the results (Table 7, run no. 9). The yield of diamination product **IIIc** sharply increased (66%) in the reaction with excess amine **Ia** (6 equiv) in the presence of 4 equiv of *t*-BuONa (Table 7, run no. 10), indicating that excess amine over the base is critical only within a definite range. If the amounts of these components considerably exceed the amount of aryl halide, this factor is no longer significant. In the reaction with *p*-dibromobenzene, as with *m*-dibromobenzene, the use of a sufficient amount of DavePHOS ensures successful formation of compound **IIIa** in the presence of a small amount of *t*-BuONa (Table 7; run nos. 11, 12). By contrast, another donor ligand, $P(t\text{-Bu})_3$, provides a good yield of **IId** (Table 7, run no. 13).

The relations found for the reactions with amine **Ia** were checked out in reactions with other amines, **Ib**

Table 7. Reaction of amine **Ia** with isomeric dibromobenzenes

Run no.	Dibromobenzene	Amine–dibromobenzene–*t*-BuONa ratio	Pd/L (mol %)	Product (yield, %)
1	*meta*	1:1:1	$Pd(dba)_2$/BINAP (4/4.5)	**IIe** (49)
2[a]	*meta*	1:1:0.6	$Pd(dba)_2$/BINAP (4/4.5)	**IIe** (30)
3	*meta*	3:1:1.5	$Pd(dba)_2$/BINAP (4/4.5)	**IIIb** (0)
4	*meta*	3:1:1.5	$Pd(dba)_2$/BINAP (8/9)	**IIe** (54), **IIIb** (7.5)
5[b]	*meta*	3:1:1.5	$Pd(dba)_2$/DavePHOS (4/5)	**IIe** (7.5), **IIIb** (39), **IV** (12)
6[b]	*meta*	3:1:1.5	$Pd(dba)_2$/DavePHOS (10/10)	**IIIb** (76), **IV** (24)
7	*ortho*	3:1:1.5	$Pd(dba)_2$/BINAP (8/9)	**IIf** (63), **IIIc** (26), **IV** (6)
8	*ortho*	3:1:1.5	$Pd(dba)_2$/BINAP (8/9)	**IIf** (57), **IIIc** (18), **IV** (7.5)
9	*ortho*	3:1:1.5	$Pd(dba)_2$/DavePHOS (10/10)	**IIf** (9), **IIIc** (13.5), **IV** (9)
10	*ortho*	6:1:4	$Pd(dba)_2$/BINAP (8/9)	**IIIc** (66), **IV** (12)
11[c]	*para*	3:1:1.5	$Pd(dba)_2$/DavePHOS (4/5)	**IId** (10), **IIIa** (7.5), **IV** (15)
12	*para*	3:1:1.5	$Pd(dba)_2$/DavePHOS (10/10)	**IId** (21), **IIIa** (53), **IV** (26)
13[c]	*para*	3:1:1.5	$Pd(dba)_2$/$P(t\text{-Bu})_2$ (10/10)	**IId** (54), **IIIa** (27)

[a] Conversion of *m*-dibromobenzene 64%.
[b] Joint chromatographic separation of the products obtained in run nos. 5 and 6 gave compound **IIIb** in 25% yield.
[c] Joint chromatographic separation of the products obtained in run nos. 11 and 13 gave 9% of **IV**, 6% of **IId**, and 6% of adamantane-1-carbaldehyde.

Table 8. Reaction of amine **Ib** with isomeric dibromobenzenes

Run no.	Dibromobenzene	Amine–dibromobenzene–*t*-BuONa ratio	Pd/L (mol %)	Product (yield, %)
1	*meta*	3:1:1.5	$Pd(dba)_2$/BINAP (8/9)	**VII** (traces)
2	*ortho*	3:1:1.5	$Pd(dba)_2$/BINAP 8/9)	**Vf** (84)
3	*ortho*	3:1:9	$Pd(dba)_2$/DavePHOS (8/16)	**VIc** (36), **VII** (27)
4	*para*	3:1:9	$Pd(dba)_2$/DavePHOS (8/16)	**VIa** (55), **VII** (18)

Table 9. Reaction of amine **Id** with *m*-dibromobenzene

Run no.	Amine–dibromobenzene–*t*-BuONa ratio	Pd/L (mol %)	Yield, %		
			XIe	**XIII**	**XIIb**
1	3:1:1.5	$Pd(dba)_2$/BINAP (8/9)	57	15	3.6
2	3:1:2	$Pd(dba)_2$/BINAP (8/9)	72	22	4.5
3	3:1:3	$Pd(dba)_2$/BINAP (8/9)	0	42	27
4	2:1:1.5	$Pd(dba)_2$/BINAP (8/9)	51	39	9
5	2:1:2	$Pd(dba)_2$/BINAP (8/9)	0	45	17

and **Id**. The reaction of **Ib** with *m*-dibromobenzene at a **Ib**–dibromobenzene–*t*-BuONa ratio of 3:1:1.5 (catalyzed by palladium complex with BINAP) gave neither mono- nor diamination product (Table 8, run no. 1). Quite different pattern was observed in the reaction of **Ib** with *o*-dibromobenzene; under analogous conditions, monoamination product **Vf** was obtained in 84% yield which is appreciably higher than under standard conditions (Table 8, run no. 2). Diamination experiments were carried out with amine **Ib** in the presence of a large excess of sodium *tert*-butoxide, and the yields of both *o*- and *p*-diaminobenzene derivatives were slightly improved (Table 8; run nos. 3, 4).

Using amine **Id** as the most reactive among the examined amines, we studied the dependence of the yields of mono- and diamination products in the reactions with *m*-dibromobenzene upon the ratio amine–*m*-dibromobenzene–sodium *tert*-butoxide. When the latter was equal to 3:1:1.5, monoamination product **XIe** was obtained in a good yield (Table 9, run no. 1). Increase in the amount of the base (3:1:2) resulted in improved yield of **XIe**, while the contribution of the diamination process was insignificant (Table 9, run no. 2). When the above reactant ratio changed to 3:1:3, no monoamination product was formed, and the yield of diamination product **XIIb** increased to 27% (Table 9, run no. 3). Simultaneously, the yield of reduction product **XIII** appreciably increased in parallel with the amount of sodium *tert*-butoxide. Analogous pattern was observed in the reaction with 2 equiv of amine **Id**. Smaller amount of the base favored formation of monoamination product **XIe** (Table 9, run no. 4), while at an equimolar ratio of amine **Id** and the base the yield of diamination product **XIIb** increased (Table 9, run no. 5). However, in this case the yield of **XIIb** was lower and the yield of reduction product **XIII** was higher than the yields of the same compounds obtained using 3 equiv of **Id** and *t*-BuONa.

Thus the optimal amine–dihaloarene–sodium *tert*-butoxide ratio for the monoamination of dihaloarenes is 1:1:1.5, and for the diamination, 3:1:3 (and more). The conversion of the initial amine in the examined reaction remains incompletely studied. In some cases, the amine conversion is comparable with the overall amount of the amination products, whereas in other cases it is appreciably higher presumably due to redox processes with participation of that amine.

General relations holding in the arylation of adamantyl-substituted amines. The data obtained in the present and preceding studies [1] should be generalized (if possible) in order to use them in practice and predict the results of amination reactions with participation of other amines of the adamantane series. The examined amines differ fairly strongly in their reactivity which is related to steric hindrances at the nitrogen atom. Amines in which the hydrocarbon radical is not branched at the α-carbon atom or those in which such branching does not give rise to considerable steric hindrances (e.g., amines **Ia** and **Id**) ensure

better yields of mono- and diamination products. Correspondingly, amines having bulky substituents at the α-carbon atom react with dihalobenzenes more difficultly, and in some cases *ortho*-diamination does not occur at all. Simultaneously, the fraction of reduction products increases (these products are formed with participation of the same palladium complex).

Among dihalobenzenes, higher yields of monoamination products were obtained with bromochlorobenzenes. This is consistent with the lower reactivity of the chlorine atom which is involved in concurrent side processes (such as diamination or reduction) at a much lower rate; bromochlorobenzenes are also less prone to undergo transformations other than amination, as compared to dibromobenzenes. Finally, the chlorine atom is smaller than bromine, so that N-substituted 2-chloroanilines are formed more readily than analogous N-substituted 2-bromoanilines. This factor is responsible for the lower yields of monoamination products in the reactions of *o*-dibrombenzene with sterically hindered amines **Ib** and **Ic**. On the other hand, *ortho*-diamination in the reactions with less sterically hindered amines such as **Ia** and adamantan-2-amine [1] smoothly occurs and even competes with the monoamination when equimolar amounts of the reactants are used. On the whole, diamination of *m*-dibromobenzene with different amines involves no difficulties, in contrast to *para*-diamination (only in a few cases it was possible to isolate the corresponding *p*-diaminobenzene derivatives by chromatography). The reason is that the amino group in the *para* position exerts a positive mesomeric effect thus hampering replacement of the second bromine atom. In the case of *o*-bromoanilines, mesomeric effect of the amino group is weakened for steric reasons (see above).

While studying the reactions of admantane-containing amines with dihalobenzenes, a number of various phosphine ligands were tested. The most appropriate ligand was BINAP; in most cases it ensured the best yields of monoamination and *meta*-diamination products; in some cases it was also more effective for *ortho*-diamination. DavePHOS turned out to be the best ligand for the preparation of *para*- and *ortho*-diamination products. The yield of diamination products depends on the amount of the catalyst: increase of the latter from 4 to 8–10% appreciably improves the yield.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded from solutions in chloroform-*d* on a Bruker Avance-400 spectrometer at 400 and 100.6 MHz, respectively, using the solvent signals as reference ($CHCl_3$, δ 7.25 ppm; $CDCl_3$, δ_C 77.00 ppm). The mass spectra (MALDI-TOF, positive ion detection) were obtained on a Bruker Daltonics Ultrafex mass spectrometer with 1,8,9-trihydroxyanthracene as matrix and polyethylene glycols as internal standards. Preparative column chromatography was performed on silica gel (40–60 μm, Merck). Commercially available isomeric bromochloro- and dibromobenzenes, sodium *tert*-butoxide, and phosphine ligands were used without additional purification. Amine **Ia** was synthesized according to the procedure reported in [18], amines **Ib**–**Ie** were prepared as described in [19], and $Pd(dba)_2$ was prepared as described in [20] and used without additional recrystallization. Dioxane was distilled first over alkali and then over metallic sodium; methylene chloride and methanol were distilled.

N*-Aryl-substituted (1-adamantyl)alkanamines IIa–IIf, Va–Vf, VIIIa–VIIIf, and XIa–XIf (general procedure*).** A two-necked flask was charged under argon with the corresponding dihalobenzene (0.25 mmol), $Pd(dba)_2$ (4–10 mol %), and phosphine ligand (4.5–16 mol %), anhydrous dioxane (2 ml), amine **Ia**–**Id** (0.25 mmol), and sodium *tert*-butoxide (0.38 mmol) were added, and the mixture was heated for 7 h under reflux. The mixture was cooled, the precipitate was filtered off, the filtrate was evaporated under reduced pressure, the solid residue was dissolved in methylene chloride, the solution was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure, and the residue was subjected (if necessary) to chromatography on silica gel using the following solvents as eluents (in succession): petroleum ether–methylene chloride (10 : 1 to 1 : 4), methylene chloride.

N,N′*-Bis[(1-adamantyl)alkyl]benzenediamines IIIa–IIIc, VIa–VIc, IXa, IXb, XIIa–XIIc, and XIV (general procedure*).** A two-necked flask was charged under argon with the corresponding dihalobenzene (0.1–0.15 mmol), $Pd(dba)_2$ (4–16 mol %), and BINAP or DavePHOS (4.5–18 mol %), anhydrous dioxane (1–1.5 ml), amine **Ia**–**Ie** (0.2–0.6 mmol), and sodium *tert*-butoxide (0.38–0.7 mmol) were added, and the mixture was heated for 6–8 h under reflux. The mixture was cooled, the precipitate was filtered off, the filtrate was evaporated under reduced pressure, the solid residue was dissolved in methylene chloride, the solution was washed with water, dried over anhydrous sodium sulfate, and evaporated under reduced pressure, and the residue was subjected (if necessary) to chromatography on silica gel using the following

solvents as eluents (in succession): petroleum ether–methylene chloride (4:1 to 1:4), methylene chloride, methylene chloride–methanol (100:1).

***N*-(1-Adamantylmethyl)-4-chloroaniline (IIa)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (48 mg) of *p*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 54 mg (79%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.57 br.s (6H) 1.63–1.78 m (6H), 2.01 br.s (3H), 2.76 d (2H, ^3J = 5.8 Hz), 3.67 br.s (1H), 6.53 d (2H, ^3J = 8.7 Hz), 7.09 d (2H, ^3J = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 33.9 (1C), 37.0 (3C), 40.7 (3C), 56.3 (1C), 113.5 (2C), 125.0 (1C), 128.9 (2C), 147.8 (1C). MALDI-TOF mass spectrum: *m*/*z* 275.1 $[M]^+$.

***N*-(1-Adamantylmethyl)-3-chloroaniline (IIb)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (48 mg) of *m*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 56 mg (81%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.55–1.59 m (6H), 1.64–1.78 m (6H), 2.01 br.s (3H), 2.78 d (2H, ^3J = 5.3 Hz), 3.76 br.s (1H), 6.47 d.d.d (1H, ^3J = 8.3, ^4J = 2.2, 0.7 Hz), 6.59 t (1H, ^4J = 2.1 Hz), 6.61 d.d.d (1H, ^3J = 7.9, ^4J = 1.9, 0.7 Hz), 7.04 t (1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 33.9 (1C), 37.0 (3C), 40.6 (3C), 55.9 (1C), 110.9 (1C), 112.0 (1C), 116.4 (1C), 130.0 (1C), 134.9 (1C), 150.3 (1C).

***N*-(1-Adamantylmethyl)-2-chloroaniline (IIc)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (48 mg) of *o*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 64 mg (93%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.61–1.64 m (6H), 1.66–1.81 m (6H), 2.04 br.s (3H), 2.86 d (2H, ^3J = 5.8 Hz), 4.39 br.s (1H), 6.59 t.d (1H, ^3J = 7.6 Hz, ^4J = 1.3 Hz), 6.69 d (1H, ^3J = 8.2 Hz), 7.12 t.d (1H, ^3J = 7.8 Hz, ^4J = 1.4 Hz), 7.25 d.d (1H, ^3J = 7.8 Hz, ^4J = 1.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 34.0 (1C), 37.0 (3C), 40.7 (3C), 55.8 (1C), 111.0 (1C), 116.4 (1C), 118.9 (1C), 127.6 (1C), 128.9 (1C), 144.8 (1C). MALDI-TOF mass spectrum: *m*/*z* 275.1398 $[M]^+$. $C_{17}H_{22}ClN$. Calculated: *M* 275.1441.

***N*-(1-Adamantylmethyl)-4-bromoaniline (IId)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 15 mg (10 mol %) of $Pd(dba)_2$, 15 mg (10 mol %) of Xantphos, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. In another experiment, the reaction was carried out in the presence of 6 mg (4 mol %) of $Pd(dba)_2$ and 6 mg (8 mol %) of 2-(di-*tert*-butylphosphino)biphenyl, other conditions being equal. The products isolated in the two experiments were combined and subjected to chromatography using petroleum ether–methylene chloride (4:1) as eluent. Yield 53 mg (33%), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.56 br.s (6H) 1.61–1.77 m (6H), 2.00 br.s (3H), 3.68 br.s (1H), 6.48 d (2H, ^3J = 8.8 Hz), 7.21 d (2H, ^3J = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 33.9 (1C), 37.0 (3C), 40.6 (3C), 56.2 (1C), 108.0 (1C), 114.0 (2C), 131.8 (2C), 148.2 (1C). MALDI-TOF mass spectrum: *m*/*z* 319.0975 $[M]^+$. $C_{17}H_{22}BrN$. Calculated: *M* 319.0936.

***N*-(1-Adamantylmethyl)-3-bromoaniline (IIe)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. The product was isolated by chromatography using petroleum ether–methylene chloride (4:1) as eluent. Yield 31 mg (39%), colorless crystalline powder, mp 90–92°C. ^{1}H NMR spectrum, δ, ppm: 1.54–1.57 m (6H), 1.61–1.77 m (6H), 2.00 br.s (3H), 2.75 d (2H, ^3J = 4.3 Hz), 3.73 br.s (1H), 6.51 d.d.d (1H, ^3J = 8.3, ^4J = 2.3, 0.8 Hz), 6.73–6.77 m (2H), 6.98 t (1H, ^3J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 33.9 (1C), 37.0 (3C), 40.6 (3C), 55.9 (1C), 111.3 (1C), 114.9 (1C), 119.3 (1C), 123.3 (1C), 130.3 (1C), 150.4 (1C). MALDI-TOF mass spectrum: *m*/*z* 319.0938 $[M]^+$. $C_{17}H_{22}BrN$. Calculated: *M* 319.0936. Elution with petroleum ether–methylene chloride (2:1) gave 4 mg (7%) of reduction product **IV** and 5 mg (12%) of adamantane-1-carbaldehyde. ^{1}H NMR spectrum, δ, ppm: 1.69–1.81 m (12H), 2.06 br.s (3H), 9.31 s (1H). Elution with petroleum ether–methylene chloride (1:2) gave 2 mg (4%) of diamination product **IIIb**.

***N*-(1-Adamantylmethyl)-2-bromoaniline (IIf)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. After chromatographic separation using petroleum ether–methylene chloride (4:1), yield 24 mg (30%),

colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.60 br.s (6H), 1.65–1.78 m (6H), 2.02 br.s (3H), 2.83 s (2H), 4.38 br.s (1H), 6.51 t.d (1H, ^3J = 7.5, ^4J = 1.2 Hz), 6.64 d (1H, ^3J = 8.1 Hz), 7.14 t.d (1H, ^3J = 7.7, ^4J = 1.2 Hz), 7.39 d.d (1H, ^3J = 8.0, ^4J = 1.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 34.0 (1C), 37.0 (3C), 40.7 (3C), 56.0 (1C), 109.7 (1C), 111.2 (1C), 117.0 (1C), 128.4 (1C), 132.2 (1C), 145.7 (1C). MALDI-TOF mass spectrum: *m*/*z* 319.2 $[M]^+$. Subsequent elution with the same solvent system gave 17 mg (34%) of diamino derivative **IIIc** and 3 mg (5%) of reduction product **IV**.

***N*,*N*′-Bis(1-adamantylmethyl)benzene-1,2-diamine (IIIc)** [12]. ^{1}H NMR spectrum, δ, ppm: 1.65 br.s (12H), 1.66–1.80 m (12H), 2.03 br.s (6H), 2.74 s (4H), 3.34 br.s (2H), 6.65–6.70 m (2H), 6.73–6.78 m (2H). ^{13}C NMR spectrum, δ_C, ppm: 28.5 (6C), 33.6 (2C), 37.2 (6C), 41.0 (6C), 56.9 (2C), 112.3 (2C), 119.0 (2C), 138.5 (2C). MALDI-TOF mass spectrum: *m*/*z* 404.5 $[M]^+$.

***N*-(1-Adamantylmethyl)aniline (IV)** was synthesized from 0.25 mmol (41 mg) of amine **Ia** and 0.25 mmol (39 mg) of bromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 49 mg (82%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.61 s (6H) 1.65–1.79 m (6H), 2.03 br.s (3H), 2.81 d (2H, ^3J = 5.7 Hz), 3.68 br.s (1H), 6.63 d (2H, ^3J = 8.0 Hz), 6.67 t (1H, ^3J = 7.5 Hz), 7.17 t (2H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 33.8 (1C), 37.0 (3C), 40.7 (3C), 56.2 (1C), 112.5 (2C), 116.6 (1C), 129.1 (2C), 149.2 (1C). MALDI-TOF mass spectrum: *m*/*z* 241.2 $[M]^+$.

***N*,*N*′-Bis(1-adamantylmethyl)benzene-1,4-diamine (IIIa).** *a*. Compound **IIIa** was synthesized from 0.3 mmol (50 mg) of amine **Ia** and 0.1 mmol (24 mg) of *p*-dibromobenzene in the presence of 5 mg (9 mol %) of $Pd(dba)_2$, 5 mg (18 mol %) of 2-(di-*tert*-butylphosphino)biphenyl, and 37 mg (4 equiv) of sodium *tert*-butoxide in 1 ml of anhydrous dioxane.

b. The reaction was carried out with the same amounts of amine **Ia** and *p*-dibromobenzene in the presence of 5 mg (8 mol %) of $Pd(dba)_2$ and 6 mg (16 mol %) of DavePHOS. The products isolated in the two experiments were combined and subjected to chromatography using petroleum ether–methylene chloride (4:1) as eluent. Yield 40 mg (50%), colorless crystalline powder, mp 230–232°C. ^{1}H NMR spectrum (before chromatographic purification), δ, ppm: 1.57 br.s (12H) 1.62–1.76 m (12H), 1.98 br.s (6H), 2.71 d (4H, ^3J = 6.2 Hz), 3.20 t (2H, ^3J = 6.2 Hz), 6.54 s (4H). ^{13}C NMR spectrum (before chromatographic purification), δ_C, ppm: 28.4 (6C), 33.7 (2C), 37.1 (6C), 40.8 (6C), 58.0 (2C), 114.5 (4C), 141.4 (2C). ^{1}H NMR spectrum (after chromatographic purification), δ, ppm: 1.58 br.s (12H) 1.62–1.76 m (12H), 1.99 br.s (6H), 2.75 br.s (4H), 6.52 br.s (4H). MALDI-TOF mass spectrum: *m*/*z* 404.3260 $[M]^+$. $C_{28}H_{40}N_2$. Calculated: *M* 404.3191.

***N*,*N*′-Bis(1-adamantylmethyl)benzene-1,3-diamine (IIIb).** *a*. Compound **IIIb** was synthesized from 0.75 mmol (124 mg) of amine **Ia** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 5 mg (5 mol %) of DavePHOS, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane.

b. The reaction was carried out with the same amounts of amine **Ia** and *m*-dibromobenzene in the presence of 14 mg (10 mol %) of $Pd(dba)_2$ and 10 mg (10 mol %) of DavePHOS. The products isolated in the two experiments were combined and subjected to chromatography using petroleum ether–methylene chloride (2:1, 1:1) as eluent. Yield 50 mg (25%), colorless crystalline powder, mp 168–170°C. ^{1}H NMR spectrum, δ, ppm: 1.58 br.s (12H) 1.62–1.76 m (12H), 2.00 br.s (6H), 2.77 s (4H), 3.55 br.s (2H), 5.88 t (1H, ^4J = 2.0 Hz), 5.97 d.d (2H, ^3J = 7.9, ^4J = 2.0 Hz), 6.94 t (1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.4 (6C), 33.8 (2C), 37.1 (6C), 40.7 (6C), 56.3 (2C), 96.7 (1C), 102.1 (2C), 129.8 (1C), 150.4 (2C). MALDI-TOF mass spectrum: *m*/*z* 404.3174 $[M]^+$. $C_{28}H_{40}N_2$. Calculated: *M* 404.3191. Elution with petroleum ether–methylene chloride (4:1) gave a mixture of monoamino derivative **IIe**, reduction product **IV**, and adamantane-1-carbaldehyde.

***N*-[α-(1-Adamantyl)benzyl]-4-chloroaniline (Va)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (48 mg) of *p*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 57 mg (65%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.46–1.75 m (12H), 2.00 br.s (3H), 3.83 s (1H), 4.40 br.s (1H), 6.41 d (2H, ^3J = 8.8 Hz), 6.98 d (2H, ^3J = 8.8 Hz), 7.21–7.31 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 36.4 (1C), 36.8 (3C), 39.2 (3C), 68.0 (1C), 114.1 (2C), 121.3 (1C), 126.9 (1C), 127.6 (2C), 128.5 (2C), 128.7 (2C), 139.7 (1C), 146.3 (1C). MALDI-TOF mass spec-

trum: *m*/*z* 351.1778 $[M]^+$. $C_{23}H_{26}ClN$. Calculated: *M* 351.1754.

***N*-[α-(1-Adamantyl)benzyl]-3-chloroaniline (Vb)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (48 mg) of *m*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 66 mg (75%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.46–1.74 m (12H), 2.00 br.s (3H), 3.86 s (1H), 4.47 br.s (1H), 6.36 d.d.d (1H, ^3J = 8.4, ^4J = 2.2, 0.7 Hz), 6.50 t (1H, ^4J = 2.0 Hz), 6.55 d.d.d (1H, ^3J = 7.9, ^4J = 1.9, 0.8 Hz), 6.95 t (1H, ^3J = 8.0 Hz), 7.22–7.32 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 36.4 (1C), 36.8 (3C), 39.2 (3C), 67.7 (1C), 111.2 (1C), 112.9 (1C), 116.6 (1C), 126.9 (1C), 127.7 (2C), 128.5 (2C), 129.9 (1C), 134.7 (1C), 139.5 (1C), 148.9 (1C). MALDI-TOF mass spectrum: *m*/*z* 351.1805 $[M]^+$. $C_{23}H_{26}ClN$. Calculated: *M* 351.1754.

***N*-[α-(1-Adamantyl)benzyl]-2-chloroaniline (Vc)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (48 mg) of *o*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 35 mg (40%) (after chromatography, petroleum ether–methylene chloride, 4:1). Colorless crystalline powder, mp 176–178°C. ^{1}H NMR spectrum, δ, ppm: 1.50–1.82 m (12H), 2.01 br.s (3H), 3.91 d (1H, ^3J = 6.4), 5.13 d (1H, ^3J = 6.3 Hz), 6.33 d (1H, ^3J = 8.2 Hz), 6.50 t.d (1H, ^3J = 7.6, ^4J = 1.4 Hz), 6.89 t (1H, ^3J = 7.8 Hz), 7.20 d.d (1H, ^3J = 7.8, ^4J = 1.4 Hz), 7.21–7.31 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.4 (3C), 36.6 (1C), 36.9 (3C), 39.3 (3C), 67.8 (1C), 112.0 (1C), 116.5 (1C), 119.2 (1C), 126.9 (1C), 127.5 (1C), 127.6 (2C), 128.6 (2C), 128.7 (1C), 139.5 (1C), 143.4 (1C). MALDI-TOF mass spectrum: *m*/*z* 351.1772 $[M]^+$. $C_{23}H_{26}ClN$. Calculated: *M* 351.1754. Elution with petroleum ether–methylene chloride (2:1) gave 11 mg (18%) of 1-adamantyl phenyl ketone. ^{1}H NMR spectrum, δ, ppm: 1.68–1.78 m (6H), 2.00 br.s (6H), 2.06 br.s (3H), 7.35–7.45 m (3H), 7.53 d.d (2H, ^3J = 8.2, ^4J = 1.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.1 (3C), 36.5 (3C), 39.1 (3C), 46.9 (1C), 127.1 (2C), 127.9 (2C), 130.1 (1C), 139.6 (1C), 210.2 (1C).

***N*-[α-(1-Adamantyl)benzyl]-4-bromoaniline (Vd)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 59 mg (60%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.48–1.78 m (12H), 2.00 br.s (3H), 3.83 d (1H, ^3J = 6.4 Hz), 4.39 d (1H, ^3J = 6.4 Hz), 6.37 d (2H, ^3J = 8.8 Hz), 7.11 d (2H, ^3J = 8.8 Hz), 7.21–7.31 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.3 (3C), 36.4 (1C), 36.8 (3C), 39.1 (3C), 67.9 (1C), 108.3 (1C), 114.6 (2C), 126.9 (1C), 127.6 (2C), 128.5 (2C), 131.6 (2C), 139.6 (1C), 146.7 (1C). MALDI-TOF mass spectrum: *m*/*z* 395.2 $[M]^+$.

***N*-[α-(1-Adamantyl)benzyl]-3-bromoaniline (Ve)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 37 mg (37%) (after chromatography; petroleum ether–methylene chloride, 4:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.45–1.80 m (12H), 1.99 br.s (3H), 3.84 d (1H, ^3J = 5.8 Hz), 4.41 d (1H, ^3J = 5.7 Hz), 6.37 d.d (1H, ^3J = 8.4, ^4J = 1.7 Hz), 6.65–6.70 m (2H), 6.86 t (1H, ^3J = 8.0 Hz), 7.20–7.30 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.4 (3C), 36.6 (1C), 36.9 (3C), 39.2 (3C), 67.7 (1C), 111.5 (1C), 115.9 (1C), 119.6 (1C), 123.0 (1C), 127.0 (1C), 127.7 (2C), 128.5 (2C), 130.3 (1C), 139.5 (1C), 149.1 (1C). MALDI-TOF mass spectrum: *m*/*z* 395.1271 $[M]^+$. $C_{23}H_{26}BrN$. Calculated: *M* 395.1249. Elution with the same solvent system gave 7 mg (12%) of 1-adamantyl phenyl ketone.

***N*-[α-(1-Adamantyl)benzyl]-2-bromoaniline (Vf)** was synthesized from 0.25 mmol (61 mg) of amine **Ib** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 40 mg (40%) (after chromatography; petroleum ether–methylene chloride, 4:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.47–1.80 m (12H), 2.01 br.s (3H), 3.91 d (1H, ^3J = 6.4 Hz), 5.16 d (1H, ^3J = 6.4 Hz), 6.30 d.d (1H, ^3J = 8.1, ^4J = 1.0 Hz), 6.43 t.d (1H, ^3J = 7.6, ^4J = 1.4 Hz), 6.92 t.d (1H, ^3J = 7.8, ^4J = 1.0 Hz), 7.21–7.31 m (5H), 7.36 d.d (1H, ^3J = 8.0, ^4J = 1.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 28.4 (3C), 36.7 (1C), 36.9 (3C), 39.3 (3C), 68.0 (1C), 110.1 (1C), 112.1 (1C), 117.1 (1C), 126.9 (1C), 127.7 (2C), 128.2 (1C), 128.6 (2C), 132.0 (1C), 139.4 (1C), 144.3 (1C). MALDI-TOF mass spectrum: *m*/*z* 395.1261 $[M]^+$. $C_{23}H_{26}BrN$. Calculated: *M* 395.1249. Elution

with the same solvent system gave 7 mg (12%) of 1-adamantyl phenyl ketone.

***N*,*N′*-Bis[α-(1-adamantyl)benzyl]benzene-1,4-diamine (VIa)** was synthesized from 0.75 mmol (182 mg) of amine **Ib** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 16 mg (16 mol %) of DavePHOS, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 23 mg (17%) (after chromatography; petroleum ether–methylene chloride, 2:1), colorless oily substance. ^{1}H NMR spectrum (after chromatography), δ, ppm: 1.50–1.76 m (24H), 1.93 br.s (6H), 3.70 br.s (4H), 6.25 br.s (4H), 7.18 br.s (10H). ^{13}C NMR spectrum (after chromatography), δ_C, ppm: 28.5 (6C), 37.0 (6C), 39.3 (6C), 126.5 (2C), 127.4 br.s (4C), 128.7 (4C) (signals from 12 carbon atoms were not observed). MALDI-TOF mass spectrum: *m*/*z* 556.2 $[M]^+$. Elution with petroleum ether–methylene chloride (4:1) gave 15 mg (19%) of *N*-[α-(1-adamantyl)benzyl]-aniline (**VII**), 8 mg (13%) of 1-adamantyl phenyl ketone, and 8 mg (6%) of diamination product **VIb**.

***N*,*N′*-Bis[α-(1-adamantyl)benzyl]benzene-1,3-diamine (VIb)** was synthesized from 0.75 mmol (182 mg) of amine **Ib** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 16 mg (16 mol %) of DavePHOS, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 88 mg (63%) (after chromatography; petroleum ether–methylene chloride, 4:1, 2:1). Light brown crystals, mp 100–102°C. ^{1}H NMR spectrum, δ, ppm (mixture of two diastereoisomers): 1.40–1.72 m (48H), 1.98 br.s (12H), 3.69 br.s (2H), 3.77 s (2H), 4.13 br.s (4H), 5.61 br.s (1H), 5.73 br.s (1H), 5.80 d.d (2H, ^3J = 8.0, ^4J = 0.9 Hz), 5.82 d.d (2H, ^3J = 8.0, ^4J = 0.8 Hz), 6.73 t (1H, ^3J = 8.0 Hz), 6.75 t (1H, ^3J = 8.0 Hz), 7.15–7.32 m (20H). ^{13}C NMR spectrum, δ_C, ppm (mixture of two diastereoisomers): 28.4 (12C), 36.5 (4C), 36.9 (12C), 39.1 (6C), 39.2 (6C), 67.6 (2C), 68.0 (2C), 97.6 (1C), 98.2 (1C), 102.8 (2C), 103.1 (2C), 126.4 (2C), 126.5 (2C), 127.4 (8C), 128.5 (4C), 128.7 (4C), 129.3 (1C), 129.4 (1C), 140.6 (2C), 140.7 (2C), 148.9 (2C), 149.0 (2C). MALDI-TOF mass spectrum: *m*/*z* 556.3880 $[M]^+$. $C_{40}H_{48}N_2$. Calculated: *M* 556.3817. Elution with petroleum ether–methylene chloride (4:1) gave 5 mg (6%) of reduction product **VII**.

***N*,*N′*-Bis[α-(1-adamantyl)benzyl]benzene-1,2-diamine (VIc)** was synthesized from 0.75 mmol (182 mg) of amine **Ib** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 16 mg (16 mol %) of DavePHOS, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 36 mg (26%) (after chromatography; petroleum ether–methylene chloride, 4:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm (mixture of two diastereoisomers): 1.48–1.80 m (48H), 2.05 br.s (12H), 3.93 s (2H), 3.94 s (2H), 4.23 br.s (4H), 6.28-6.36 m (4H), 6.41–6.47 m (4H), 7.20–7.25 m (4H), 7.28–7.35 m (16H). ^{13}C NMR spectrum, δ_C, ppm (mixture of two diastereoisomers): 28.6 (12C), 36.5 (4C), 37.1 (12C), 39.6 (12C), 68.0 (4C), 112.8 (2C), 113.1 (2C), 118.5 (4C), 126.7 (4C), 127.6 (8C), 128.5 (4C), 128.6 (4C), 137.0 (2C), 137.1 (2C), 140.1 (2C), 140.2 (2C). MALDI-TOF mass spectrum: *m*/*z* 556.3 $[M]^+$. Elution with the same solvent system gave 20 mg (25%) of reduction product **VII** [14]. ^{1}H NMR spectrum, δ, ppm: 1.48–1.80 m (12H), 2.02 br.s (3H), 3.91 s (1H), 4.34 br.s (1H), 6.52 d (2H, ^3J = 7.7 Hz), 6.60 t (1H, ^3J = 7.3 Hz), 7.06 t (2H, ^3J = 7.9 Hz), 7.20–7.34 m (5H). ^{13}C NMR spectrum, δ_C, ppm: 28.4 (3C), 36.5 (1C), 36.9 (3C), 39.2 (3C), 67.9 (1C), 113.1 (2C), 116.7 (1C), 126.7 (1C), 127.6 (2C), 128.7 (2C), 129.0 (2C), 140.0 (1C), 147.9 (1C). MALDI-TOF mass spectrum: *m*/*z* 317.2100 $[M]^+$. $C_{23}H_{27}N$. Calculated: *M* 317.2143. Elution with petroleum ether–methylene chloride (2:1) gave 11 mg (18%) of 1-adamantyl phenyl ketone.

***N*-[1-(1-Adamantyl)propyl]-4-chloroaniline (VIIIa)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (48 mg) of *p*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 38 mg (50%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 0.86 t (3H, ^3J = 7.3 Hz), 1.08–1.20 m (1H), 1.50–1.82 m (13H), 1.95 br.s (3H), 2.75 t (1H, ^3J = 10.2 Hz), 3.35 d (1H, ^3J = 9.8 Hz), 6.48 d (2H, ^3J = 8.8 Hz), 7.02 d (2H, ^3J = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.9 (1C), 23.0 (1C), 28.4 (3C), 37.1 (3C), 37.8 (1C), 39.0 (3C), 64.6 (1C), 113.2 (2C), 119.8 (1C), 128.2 (2C), 149.0 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.1694 $[M]^+$. $C_{19}H_{26}ClN$. Calculated: *M* 303.1754.

***N*-[1-(1-Adamantyl)propyl]-3-chloroaniline (VIIIb)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (48 mg) of *m*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane; the mixture was heated for 7 h under

reflux. Yield 40 mg (53%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, ^3J = 7.3 Hz), 1.07–1.19 m (1H), 1.50–1.74 m (12H), 1.75–1.84 m (1H), 1.96 br.s (3H), 2.78 t (1H, ^3J = 10.3 Hz), 3.43 d (1H, ^3J = 9.8 Hz), 6.44 d.d (1H, ^3J = 8.2 , ^4J = 2.2 Hz), 6.52 d (1H, ^3J = 7.8 Hz), 6.55 t (1H, ^3J = 1.9 Hz), 6.98 t (1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.8 (1C), 22.9 (1C), 28.4 (3C), 37.1 (3C), 37.8 (1C), 39.0 (3C), 64.3 (1C), 110.5 (1C), 111.7 (1C), 115.5 (1C), 130.0 (1C), 134.8 (1C), 151.5 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.1778 $[M]^+$. $C_{19}H_{26}ClN$. Calculated: *M* 303.1754.

***N*-[1-(1-Adamantyl)propyl]-2-chloroaniline (VIIIc)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (48 mg) of *o*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 38 mg (50%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, ^3J = 7.0 Hz), 1.15–1.25 m (1H), 1.51–1.80 m (13H), 1.96 br.s (3H), 2.88 t.d (1H, ^3J = 10.3, ^4J = 1.3 Hz), 4.07 d (1H, ^3J = 9.6 Hz), 6.49 t.d (1H, ^3J = 7.9, ^4J = 1.3 Hz), 6.69 d (1H, ^3J = 8.1 Hz), 7.04 t (1H, ^3J = 7.8 Hz), 7.20 t.d (1H, ^3J = 7.8, ^4J = 1.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.7 (1C), 22.8 (1C), 28.4 (3C), 37.1 (3C), 37.8 (1C), 38.9 (3C), 64.6 (1C), 111.4 (1C), 115.6 (1C), 123.1 (1C), 127.5 (1C), 129.0 (1C), 145.8 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.16 $[M]^+$.

***N*-[1-(1-Adamantyl)propyl]-4-bromoaniline (VIIId)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane; the mixture was heated for 7 h under reflux. Yield 41 mg (48%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, ^3J = 7.2 Hz), 1.07–1.19 m (1H), 1.50–1.73 m (12H), 1.74–1.82 m (1H), 1.96 br.s (3H), 2.76 t (1H, ^3J = 9.5 Hz), 3.37 d (1H, ^3J = 9.9 Hz), 6.46 d (2H, ^3J = 8.6 Hz), 7.17 d (2H, ^3J = 8.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.9 (1C), 23.0 (1C), 28.4 (3C), 37.1 (3C), 37.8 (1C), 39.0 (3C), 64.5 (1C), 106.8 (1C), 113.7 (2C), 131.7 (2C), 149.4 (1C). MALDI-TOF mass spectrum: *m*/*z* 347.3 $[M]^+$.

***N*-[1-(1-Adamantyl)propyl]-3-bromoaniline (VIIIe)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 41 mg (48%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, ^3J = 7.3 Hz), 1.08–1.19 m (1H), 1.50–1.74 m (12H), 1.75–1.83 m (1H), 1.97 br.s (3H), 2.79 t.d (1H, ^3J = 10.3, ^4J = 1.2 Hz), 3.41 d (1H, ^3J = 10.0 Hz), 6.48 d.d (1H, ^3J = 8.0, ^4J = 2.0 Hz), 6.67 d (1H, ^3J = 7.9 Hz), 6.72 br.s (1H), 6.94 t (1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.9 (1C), 22.9 (1C), 28.4 (3C), 37.1 (3C), 37.8 (1C), 39.0 (3C), 64.3 (1C), 110.9 (1C), 114.7 (1C), 118.5 (1C), 123.2 (1C), 130.4 (1C), 151.6 (1C). MALDI-TOF mass spectrum: *m*/*z* 347.3 $[M]^+$.

***N*-[1-(1-Adamantyl)propyl]-2-bromoaniline (VIIIf)** was synthesized from 0.25 mmol (48 mg) of amine **Ic** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane; the mixture was heated for 14 h under reflux. Yield 11 mg (13%) (after chromatography; petroleum ether–methylene chloride, 10:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, ^3J = 7.2 Hz), 1.10–1.20 m (1H), 1.50–1.74 m (12H), 1.75–1.85 m (1H), 1.97 br.s (3H), 2.88 t.d (1H, ^3J = 10.3 Hz), 4.11 d (1H, ^3J = 9.5 Hz), 6.44 t (1H, ^3J = 7.5 Hz), 6.67 d (1H, ^3J = 8.3 Hz), 7.09 t (1H, ^3J = 7.5 Hz), 7.38 d (1H, ^3J = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 11.8 (1C), 22.9 (1C), 28.5 (3C), 37.2 (3C), 37.9 (1C), 39.0 (3C), 64.9 (1C), 109.2 (1C), 111.6 (1C), 116.2 (1C), 128.2 (1C), 132.4 (1C), 146.8 (1C). MALDI-TOF mass spectrum: *m*/*z* 347.1302 $[M]^+$. $C_{19}H_{26}BrN$. Calculated: *M* 347.1249. Elution with the same solvent system gave 3 mg (4.5%) of reduction product **X**. Elution with petroleum ether–methylene chloride (2:1) gave 10 mg (21%) of 1-(1-adamantyl)propan-1-one. ^{1}H NMR spectrum, δ, ppm: 0.99 t (3H, ^3J = 7.5 Hz), 1.63–1.76 m (6H), 1.79 br.s (6H), 2.02 br.s (3H), 2.45 q (3H, ^3J = 7.5 Hz).

***N*,*N*′-Bis[1-(1-adamantyl)propyl]benzene-1,4-diamine (IXa)** was synthesized from 0.75 mmol (144 mg) of amine **Ic** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 14 mg (9 mol %) of BINAP, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. The diamination product was detected only in the reaction mixture. ^{1}H NMR spectrum: δ 6.42 ppm (C_6H_4). ^{13}C NMR spectrum, δ_C, ppm: 114.0 (4C) and 142.0 (2C) (C_6H_4). MALDI-TOF mass spectrum: *m*/*z* 460.41 $[M]^+$. Chromatographic separation using petroleum ether–methylene chloride (5:1) as eluent gave 17 mg (25%) of reduction product **X**, and

elution with petroleum ether–methylene chloride (2:1) gave 19 mg (40%) of 1-(1-adamantyl)propan-1-one.

***N*,*N′*-Bis[1-(1-adamantyl)propyl]benzene-1,3-diamine (IXb)** was synthesized from 0.75 mmol (144 mg) of amine **Ic** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 14 mg (9 mol %) of BINAP, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 38 mg (33%) (after chromatography; petroleum ether–methylene chloride, 5:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 0.90 t (6H, ^3J = 7.2 Hz), 1.07–1.17 m (2H), 1.53–1.71 m (24H), 1.77 d.q.d (2H, ^3J = 13.2, 6.8, 1.9 Hz), 1.95 br.s (6H), 2.75 t (2H, ^3J = 8.7 Hz), 3.17 d (2H, ^3J = 6.8 Hz), 5.83 s (1H), 5.87 d (2H, ^3J = 8.0 Hz), 6.85 t (1H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.2 (2C), 23.3 (2C), 28.6 (6C), 37.3 (6C), 37.8 (2C), 39.2 (6C), 64.3 (2C), 96.6 and 96.7 (1C), 101.4 (2C), 129.6 (1C), 151.5 (2C). MALDI-TOF mass spectrum: *m*/*z* 460.3738 $[M]^+$. $C_{32}H_{48}N_2$. Calculated: *M* 460.3817. Elution with petroleum ether–methylene chloride, (10:1) gave 16 mg (24%) of reduction product **X**. ^{1}H NMR spectrum, δ, ppm: 0.91 t (3H, ^3J = 7.0 Hz), 1.12–1.18 m (1H), 1.55–1.74 m (12H), 1.77–1.84 d.q.d (1H, ^3J = 14.2 Hz, ^3J = 7.4, 2.5 Hz), 1.97 br.s (3H), 2.83 t (1H, ^3J = 9.5 Hz), 3.32 d (1H, ^3J = 9.0 Hz), 6.57 t (1H, ^3J = 7.4 Hz), 6.59 d (2H, ^3J = 7.8 Hz), 7.11 t (2H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.0 (1C), 23.2 (1C), 28.5 (3C), 37.3 (3C), 37.9 (1C), 39.2 (3C), 64.3 (1C), 112.3 (2C), 115.8 (1C), 129.2 (2C), 150.4 (1C). MALDI-TOF mass spectrum: *m*/*z* 269.2208 $[M]^+$. $C_{19}H_{27}N$. Calculated: *M* 269.2143.

***N*-[2-(1-Adamantyl)-1-methylethyl]-4-chloroaniline (XIa)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (48 mg) of *p*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 67 mg (89%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.14 d (3H, ^3J = 5.4 Hz), 1.23 d.d (1H, ^2J = 14.5, ^3J = 4.0 Hz), 1.30 d.d (1H, ^2J = 14.5, ^3J = 7.2 Hz), 1.54 br.s (6H), 1.57–1.72 m (6H), 1.93 br.s (3H), 3.36 d (1H, ^3J = 7.7 Hz), 3.50–3.59 m (1H), 6.47 d (2H, ^3J = 8.6 Hz), 7.13 d (2H, ^3J = 8.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.1 (1C), 28.6 (3C), 32.5 (1C), 36.9 (3C), 43.0 (3C), 44.2 (1C), 52.7 (1C), 113.8 (2C), 120.9 (1C), 129.0 (2C), 145.8 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.18 $[M]^+$.

***N*-[2-(1-Adamantyl)-1-methylethyl]-3-chloroaniline (XIb)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (48 mg) of *m*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 61 mg (81%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.14 d (3H, ^3J = 5.2 Hz), 1.22–1.31 m (2H), 1.54 br.s (6H), 1.58–1.72 m (6H), 1.94 br.s (3H), 3.44 d (1H, ^3J = 7.7 Hz), 3.52–3.62 m (1H), 6.40 d (1H, ^3J = 8.1 Hz), 6.53 br.s (1H), 6.60 d (1H, ^3J = 7.8 Hz), 7.04 t.d (1H, ^3J = 8.0, ^4J = 1.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.1 (1C), 28.6 (3C), 32.5 (1C), 36.9 (3C), 43.0 (3C), 44.0 (1C), 52.8 (1C), 111.1 (1C), 112.2 (1C), 116.2 (1C), 130.2 (1C), 135.0 (1C), 148.3 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.1778 $[M]^+$. $C_{19}H_{26}ClN$. Calculated: *M* 303.1754.

***N*-[2-(1-Adamantyl)-1-methylethyl]-2-chloroaniline (XIc)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (48 mg) of *o*-bromochlorobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 62 mg (82%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.18 d (3H, ^3J = 6.1 Hz), 1.30 d.d (1H, ^2J = 14.6, ^3J = 3.7 Hz), 1.40 d.d (1H, ^2J = 14.6, ^3J = 7.5 Hz), 1.57 br.s (6H), 1.58–1.72 m (6H), 1.94 br.s (3H), 3.59–3.68 m (1H), 4.10 d (1H, ^3J = 7.4 Hz), 6.57 t (1H, ^3J = 7.6 Hz), 6.67 d (1H, ^3J = 8.1 Hz), 7.13 t (1H, ^3J = 7.3 Hz), 7.24 d (1H, ^3J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.1 (1C), 28.6 (3C), 32.5 (1C), 36.9 (3C), 43.0 (3C), 43.8 (1C), 52.7 (1C), 111.1 (1C), 116.1 (1C), 118.8 (1C), 127.7 (1C), 129.2 (1C), 143.0 (1C). MALDI-TOF mass spectrum: *m*/*z* 303.12 $[M]^+$.

***N*-[2-(1-Adamantyl)-1-methylethyl]-4-bromoaniline (XId)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 65 mg (75%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, ^3J = 6.1 Hz), 1.18 d.d (1H, ^2J = 14.5, ^3J = 4.0 Hz), 1.25 d.d (1H, ^2J = 14.5, ^3J = 7.0 Hz), 1.50 br.s (6H), 1.53–1.69 m (6H), 1.89 br.s (3H), 3.42 d (1H, ^3J = 7.6 Hz), 3.45–3.55 m (1H), 6.39 d (2H, ^3J = 8.9 Hz), 7.18 d (2H, ^3J = 8.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.0 (1C), 28.5 (3C), 32.4 (1C), 36.8 (3C), 42.9 (3C), 44.0 (1C), 52.6 (1C), 107.6 (1C), 114.2 (2C), 131.8 (2C), 146.1 (1C). MALDI-TOF mass spectrum: *m*/*z* 345.0 $[M - H_2]^+$.

***N*-[2-(1-Adamantyl)-1-methylethyl]-3-bromoaniline (XIe)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 58 mg (67%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.14 d (3H, ^3J = 6.1 Hz), 1.21–1.32 m (2H), 1.55 br.s (6H), 1.57–1.74 m (6H), 1.94 br.s (3H), 3.44 d (1H, ^3J = 7.5 Hz), 3.52–3.62 m (1H), 6.45 d (1H, ^3J = 8.1 Hz), 6.68 br.s (1H), 6.75 d (1H, ^3J = 7.6 Hz), 6.98 t (1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.0 (1C), 28.6 (3C), 32.5 (1C), 36.9 (3C), 43.0 (3C), 44.0 (1C), 52.8 (1C), 111.5 (1C), 115.1 (1C), 119.1 (1C), 123.3 (1C), 130.5 (1C), 148.5 (1C). MALDI-TOF mass spectrum: *m*/*z* 345.0 $[M - H_2]^+$.

***N*-[2-(1-Adamantyl)-1-methylethyl]-2-bromoaniline (XIf)** was synthesized from 0.25 mmol (48 mg) of amine **Id** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 37 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 56 mg (65%), light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.18 d (3H, ^3J = 6.3 Hz), 1.31 d.d (1H, ^2J = 14.5 Hz, ^3J = 3.2 Hz), 1.40 d.d (1H, ^2J = 14.5 Hz, ^3J = 7.8 Hz), 1.57 br.s (6H), 1.58–1.71 m (6H), 1.94 br.s (3H), 3.57–3.68 m (1H), 4.12 d (1H, ^3J = 7.1 Hz), 6.50 t (1H, ^3J = 7.6 Hz), 6.63 d (1H, ^3J = 8.1 Hz), 7.17 t (1H, ^3J = 7.7 Hz), 7.40 d (1H, ^3J = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.1 (1C), 28.6 (3C), 32.5 (1C), 37.0 (3C), 43.0 (3C), 44.1 (1C), 52.8 (1C), 109.7 (1C), 111.2 (1C), 116.7 (1C), 128.4 (1C), 132.5 (1C), 143.9 (1C). MALDI-TOF mass spectrum: *m*/*z* 347.3 $[M]^+$.

***N*,*N*′-Bis[2-(1-adamantyl)-1-methylethyl]benzene-1,4-diamine (XIIa)** was synthesized from 0.75 mmol (144 mg) of amine **Id** and 0.25 mmol (59 mg) of *p*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 16 mg (16 mol %) of DavePHOS, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Compound **XIIa** separated from the reaction mixture as colorless crystals. Yield 32 mg (28%). ^{1}H NMR spectrum, δ, ppm: 1.12 t (6H, ^3J = 6.0 Hz), 1.17 d.d (2H, ^2J = 14.1, ^3J = 4.1 Hz), 1.31 d.d (2H, ^2J = 14.1, ^3J = 6.3 Hz), 1.55 br.s (12H), 1.57–1.71 m (12H), 1.92 br.s (6H), 2.87 br.s (2H), 3.47 br.s (2H), 6.49 s (4H). ^{13}C NMR spectrum, δ_C, ppm: 23.6 (2C), 28.7 (6C), 32.5 (2C), 37.0 (6C), 43.1 (6C), 45.3 (2C), 52.9 (2C), 115.3 (4C), 139.4 (2C). MALDI-TOF mass spectrum: *m*/*z* 460.35 $[M]^+$. By chromatography (petroleum ether–methylene chloride, 5:1 to 2:1) we isolated 9 mg (13%) of reduction product **XIII**.

***N*,*N*′-Bis[2-(1-adamantyl)-1-methylethyl]benzene-1,3-diamine (XIIb)** was synthesized from 0.75 mmol (144 mg) of amine **Id** and 0.25 mmol (59 mg) of *m*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 14 mg (9 mol %) of BINAP, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 58 mg (50%) (after chromatography; petroleum ether–methylene chloride, 1:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.17 d (6H, ^3J = 6.2 Hz), 1.21 d.d (2H, ^2J = 14.4, ^3J = 3.9 Hz), 1.34 d.d (2H, ^2J = 14.4, ^3J = 6.8 Hz), 1.58 br.s (12H), 1.59–1.71 m (12H), 1.94 br.s (6H), 3.26 br.s (2H), 3.54–3.64 m (2H), 5.79 br.s (1H), 5.92 d (2H, ^3J = 7.9), 6.95 t (two very closely located triplets, 1H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.5 (1C), 23.6 (1C), 28.7 (6C), 32.5 (2C), 37.0 (6C), 43.1 (6C), 44.0 (2C), 53.0 (2C), 97.1 and 97.3 (1C), 102.3 (1C), 102.4 (1C), 129.9 (1C), 148.4 (2C). MALDI-TOF mass spectrum: *m*/*z* 460.3790 $[M]^+$. $C_{32}H_{48}N_2$. Calculated: *M* 460.3817. Elution with petroleum ether–methylene chloride (5:1) gave 16 mg (23%) of compound **XIII**.

***N*,*N*′-Bis[2-(1-adamantyl)-1-methylethyl]benzene-1,2-diamine (XIIc)** was synthesized from 0.75 mmol (144 mg) of amine **Id** and 0.25 mmol (59 mg) of *o*-dibromobenzene in the presence of 12 mg (8 mol %) of $Pd(dba)_2$, 16 mg (16 mol %) of DavePHOS, and 72 mg (3 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield 41 mg (35%) (after chromatography; petroleum ether–methylene chloride, 2:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.18 d (6H, ^3J = 5.6 Hz), 1.24–1.33 m (2H), 1.37–1.46 m (2H), 1.58 br.s (12H), 1.60–1.72 m (12H), 1.94 br.s (6H), 3.04 br.s (2H), 3.52–3.62 m (2H), 6.71 br.s (2H), 6.76 br.s (2H). ^{13}C NMR spectrum, δ_C, ppm: 23.1 (1C), 23.5 (1C), 28.7 (6C), 32.5 (1C), 32.6 (1C), 37.0 (6C), 43.1 (6C), 43.8 (1C), 44.2 (1C), 53.0 (1C), 53.1 (1C), 112.0 (1C), 113.1 (1C), 118.2 (1C), 118.6 (1C), 136.4 (1C), 136.7 (1C). MALDI-TOF mass spectrum: *m*/*z* 460.34 $[M]^+$. Elution with petroleum ether–methylene chloride (5:1) gave 22 mg (32%) of reduction product **XIII**. ^{1}H NMR spectrum, δ, ppm: 1.15 d (3H, ^3J = 7.0 Hz), 1.22 d.d (1H, ^2J = 14.4, ^3J = 4.2 Hz), 1.31 d.d (1H, ^2J = 14.4, ^3J = 7.2 Hz), 1.55 br.s (6H), 1.57–1.70 m (6H), 1.92 br.s (3H), 3.33 br.s (1H), 3.55–3.65 m (1H), 6.55 d (2H, ^3J = 8.5 Hz), 6.64 t (1H, ^3J = 7.0 Hz), 7.15 t (2H, ^3J = 7.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.3 (1C), 28.7 (3C), 32.6 (1C), 37.0 (3C), 43.1 (3C), 44.1 (1C), 53.0 (1C), 112.9 (2C), 116.5 (1C), 129.3 (2C) (signal from

one quaternary carbon atom was not observed). MALDI-TOF mass spectrum: *m*/*z* 269.2140 $[M]^+$. $C_{19}H_{27}N$. Calculated: *M* 269.2143.

***N*,*N*′-Bis[1-(1-adamantylmethyl)propyl]benzene-1,2-diamine (XIV)** was synthesized from 0.3 mmol (62 mg) of amine **Ie** and 0.1 mmol (24 mg) of *o*-dibromobenzene in the presence of 5 mg (9 mol %) of $Pd(dba)_2$, 4.5 mg (11 mol %) of DavePHOS, and 37 mg (4 equiv) of sodium *tert*-butoxide in 1 ml of anhydrous dioxane. Yield 11 mg (22%) (after chromatography; petroleum ether–methylene chloride, 4:1), colorless oily substance. ^{1}H NMR spectrum, δ, ppm (two diastereoisomers): 0.88 t (6H, ^3J = 7.5 Hz), 1.12–1.70 m (32H), 1.91 br.s (6H), 3.08 br.s (2H), 3.28–3.40 m (2H), 6.60–6.67 m (2H), 6.71–6.76 m (2H). ^{13}C NMR spectrum, δ_C, ppm (two diastereoisomers): 9.7 (1C), 9.8 (1C), 28.2 (1C), 28.7 (6C), 29.0 (1C), 32.5 (2C), 37.0 (6C), 43.1 (6C), 49.2 (1C), 49.4 (1C), 50.0 (1C), 50.2 (1C), 111.7 (1C), 112.6 (1C), 118.0 (1C), 118.3 (1C), 136.3 (1C), 136.6 (1C). MALDI-TOF mass spectrum: *m*/*z* 488.4117 $[M]^+$. $C_{34}H_{52}N_2$. Calculated: *M* 488.4130. Elution with the same solvent system gave 6 mg (21%) of reduction product **XV**. ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, ^3J = 7.2), 1.12–1.70 m (16H), 1.91 br.s (3H), 3.08 br.s (1H), 3.30–3.40 m (1H), 6.53 d (2H, ^3J = 8.5 Hz), 6.61 t (1H, ^3J = 7.2 Hz) 7.15 t (2H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.9 (1C), 28.7 (3C), 29.7 (1C), 32.5 (1C), 37.0 (3C), 43.1 (1C), 49.3 (1C), 50.0 (1C), 112.7 (2C), 116.2 (1C), 129.2 (2C), 147.5 (1C). MALDI-TOF mass spectrum: *m*/*z* 283.26 $[M]^+$.

***N*^{1}-(1-Adamantylmethyl)-*N*^{3}-[2-(1-adamantyl)-1-methylethyl]benzene-1,3-diamine (XVI)** was synthesized from 0.3 mmol (50 mg) of amine **Ia** and 0.3 mmol (71 mg) of *m*-dibromobenzene in the presence of 7 mg (4 mol %) of $Pd(dba)_2$, 8.5 mg (4.5 mol %) of BINAP, and 50 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield of compound **IIe** 40% (in the reaction mixture). Compound **IIe** was then brought (without isolation) into reaction with 0.25 mmol (48 mg) of amine **Id** in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 40 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Chromatographic separation using petroleum ether–methylene chloride (1:1) as eluent gave 18 mg (35%) of compound **XVI** as a colorless oily substance. ^{1}H NMR spectrum, δ, ppm: 1.15 d (3H, ^3J = 6.2 Hz), 1.20 d.d (1H, ^2J = 14.4, ^3J = 4.2 Hz), 3.01 d.d (1H, ^2J = 14.4, ^3J = 7.2 Hz), 1.56 s (6H), 1.57 s (6H), 1.58–1.76 m (12H), 1.92 br.s (3H), 1.99 br.s (3H), 2.76 s (2H), 3.40 br.s (2H), 3.54–3.63 m (1H), 5.83 br.s (1H), 5.92 d (1H, ^3J = 8.0 Hz), 5.96 d.d (1H, ^3J = 7.4, ^4J = 1.2 Hz), 6.93 t (1H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 23.5 (1C), 28.4 (3C), 28.7 (3C), 32.5 (1C), 33.7 (1C), 37.0 (3C), 37.1 (3C), 40.7 (3C), 43.1 (3C), 44.0 (1C), 53.0 (1C), 56.3 (1C), 97.0 (1C), 102.0 (1C), 102.5 (1C), 129.9 (1C), 148.4 (1C), 150.4 (1C). MALDI-TOF mass spectrum, *m*/*z*: 432.3464 $[M]^+$, 428.36 (base peak) $[M - 2H_2]^+$. $C_{30}H_{44}N_2$. Calculated: *M* 432.3504.

***N*^{1}-[α-(1-Adamantyl)benzyl]-*N*^{3}-[2-(1-adamantyl)-1-methylethyl]benzene-1,3-diamine (XVII)** was synthesized from 0.3 mmol (72 mg) of amine **Ib** and 0.3 mmol (71 mg) of *m*-dibromobenzene in the presence of 7 mg (4 mol %) of $Pd(dba)_2$, 8.5 mg (4.5 mol %) of BINAP, and 50 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Yield of compound **Ve** 52% (in the reaction mixture). Compound **Ve** was then brought (without isolation) into reaction with 0.25 mmol (48 mg) of amine **Ib** in the presence of 5.5 mg (4 mol %) of $Pd(dba)_2$, 7 mg (4.5 mol %) of BINAP, and 40 mg (1.5 equiv) of sodium *tert*-butoxide in 2.5 ml of anhydrous dioxane. Chromatographic separation using petroleum ether–methylene chloride (1:1) as eluent gave 39 mg (49%) of compound **XVII** as a colorless oily substance. ^{1}H NMR spectrum, δ, ppm (two diastereoisomers): 0.96 d (3H, ^3J = 6.7 Hz), 1.08 d (3H, ^3J = 6.2 Hz), 0.94–1.21 m (4H), 1.46 br.s (12H), 1.51 br.s (12H), 1.55–1.72 m (24H), 1.91 br.s (6H), 1.97 br.s (6H), 3.32–3.45 m (2H), 3.84 s (1H), 3.86 s (1H), 5.65 br.s (1H), 5.67 br.s (1H), 5.82 d (2H, ^3J = 7.7 Hz), 5.85 d (1H, ^3J = 7.5 Hz), 5.87 d (1H, ^3J = 7.5 Hz), 6.81 t (2H, ^3J = 7.9 Hz), 7.17 t (1H, ^3J = 8.4 Hz), 7.18 t (1H, ^3J = 8.4 Hz), 7.23–7.27 m (8H) (signals from the NH protons were not assigned unambiguously). ^{13}C NMR spectrum, δ_C, ppm: 23.3 (1C), 23.5 (1C), 28.4 (6C), 28.7 (6C), 34.7 (2C), 36.5 (2C), 36.9 (6C), 37.0 (6C), 39.3 (6C), 42.9 (3C), 43.0 (3C), 43.9 (1C), 44.0 (1C), 52.9 (1C), 53.0 (1C), 68.0 (1C), 68.1 (1C), 97.4 (1C), 97.6 (1C), 102.6 (1C), 102.7 (3C), 126.6 (2C), 127.5 (4C), 128.7 (4C), 129.6 (2C), 140.7 (1C), 140.8 (1C), 148.2 (2C), 149.1 (1C), 149.2 (1C). MALDI-TOF mass spectrum, *m*/*z*: 508.3894 $[M]^+$, 504.34 (base peak) $[M - 2H_2]^+$. $C_{36}H_{48}N_2$. Calculated: *M* 508.3817.

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