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A new improved catalyst for the palladium-catalyzed amination of aryl chlorides

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Abstract

The catalytic amination of aryl chlorides is an interesting subject for the fine chemical industry due to the importance of anilines as building blocks for pharmaceuticals, agrochemicals and new materials. Here we report the application of our recently developed di(1-adamantyl)alkylphosphines for the palladium-catalyzed amination of non-activated aryl chlorides. In general, excellent yields of amination products are obtained using 0.5 mol% of palladium(II)acetate and 1 mol% of di(1-adamantyl)-*n*-butylphosphine (**12**) in toluene at 120 °C. Remarkable results are obtained for the coupling of hindered amines with sterically congested aryl chlorides. Comparing the new catalyst system with previously reported best palladium catalysts we found in all cases improved yields of amination products in the presence of our ligands.

Keywords: Palladium; Homogeneous catalysis; Amination; Aryl chlorides; Anilines

1. Introduction

Aromatic amines constitute important substructures in natural products as well as in industrially produced bulk and fine chemicals [1]. Until the mid-1990s the preparation of N-substituted anilines in general involved nitration of arenes with subsequent reduction of the nitro group. Here the directing influence of functional groups attached to the arene had to be considered, so often auxiliary groups had to be implemented in the overall procedure. In addition the subsequent monoalkylation of anilines is often a severe problem because of favored further alkylations resulting in large amounts of tertiary amines and ammonium salts. The reductive amination of carbonyl compounds is probably the best way to avoid these problems, but some important substituents as aryl or *tert*-butyl cannot be introduced by this method.

The copper-mediated Ullmann substitution [2] is one way to circumvent these restrictions, but high temperatures have to be applied for this coupling reaction. The methodology has been improved by developing a copper-mediated coupling of N-nucleophiles with arylboronic acids instead of aryl halides [3]. Reaction conditions are much milder in this case. However, an additional step forming the arylboronic acid from an aryl halide is required.

As a consequence of these problems, interest in palladium-catalyzed C–N coupling reaction has grown constantly during the last few years [4]. The original methodology for the coupling of tin amides [5] has been improved especially by the groups of Buchwald and Hartwig (Buchwald–Hartwig amination) [6,7]. Hence a variety of primary and secondary amines can

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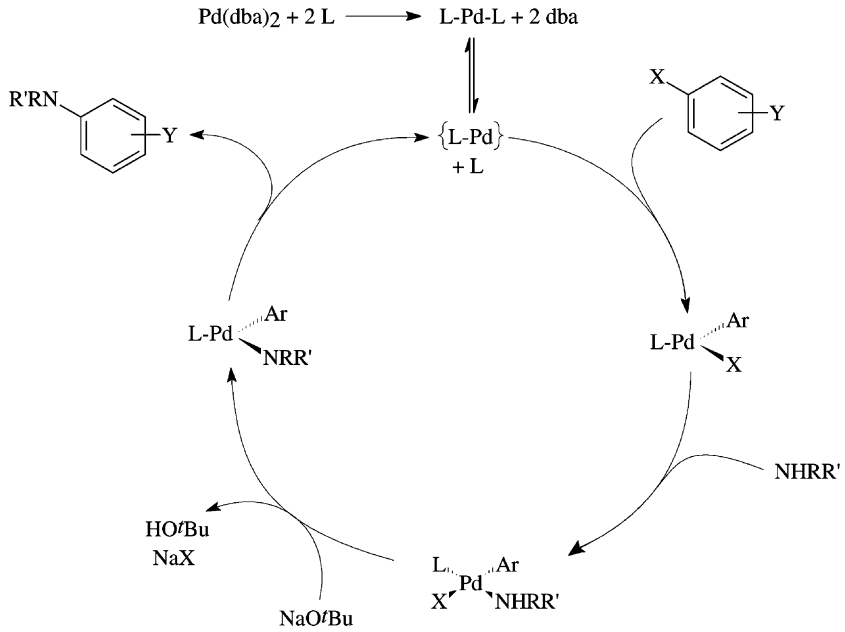
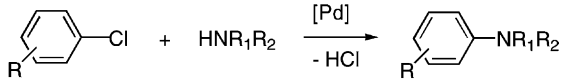


Scheme 1. Proposed mechanism of aryl-X amination.

now be used as substrates for the palladium-catalyzed coupling of different aryl halides in the presence of stoichiometric amounts of a strong base.

Originally, tri-*o*-tolylphosphine was used as ligand in these protocols. However, this phosphine has the drawback of concomitant reductive dehalogenation of the aryl halide. As an improvement, chelating bisphosphine ligands, BINAP [8] and DPPF [9], have been introduced for second generation catalysts. For amination reactions using acyclic secondary amines ferrocenyl phosphines were especially successful [10].

The general mechanism of the palladium-catalyzed amination of aryl halides is believed to follow a classical cross-coupling route involving oxidative addition of the aryl halide to Pd(0), coordination and deprotonation of the amine, followed by reductive elimination (Scheme 1). Instead of reductive elimination, β-hydride elimination from the palladium amide complex under liberation of the corresponding imine may occur as a side reaction especially in the case of electron-rich arenes, resulting in reductive dehalogenation of the aryl halide [11]. Investigations by Mann and Hartwig [12] suggest that anionic palladium *tert*-butoxide species may be active intermediates in the catalytic cycle.

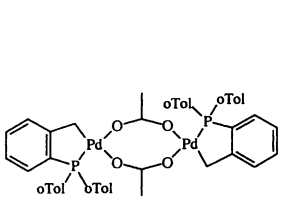


Scheme 2. Catalytic amination of chloroarenes.

Using economically attractive aryl chlorides as substrates (Scheme 2) the oxidative addition to the palladium catalyst requires much harsher reaction conditions compared to reactions of the corresponding aryl bromides or iodides [13]. This is a consequence of the experimental bond dissociation energies found to be 402, 339, and 272 kJ mol^{-1} (298 K) for chloro-, bromo-, and iodobenzene, respectively, [16b] and this trend is seen again in the grading of temperatures needed for catalysis. Table 1 summarizes the efforts which have been made to activate the relatively inert aryl chlorides. Originally, our group suggested the use of palladacycle **1**[1] at higher temperatures, while the group of Wolfe and Buchwald [15] developed a nickel catalyst systems based on DPPF (**2**) or 1,10-phenanthroline as ligand.

[1] For other palladium-catalyzed coupling reactions with **1** see [14].

Table 1
Overview of palladium-catalyzed aminations of aryl chlorides



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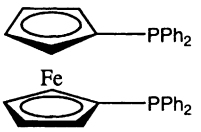

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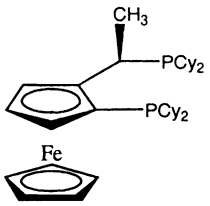

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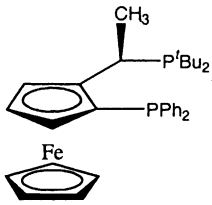

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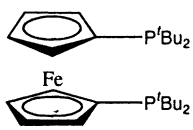

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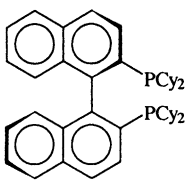

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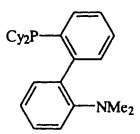

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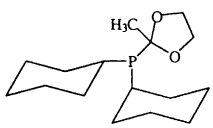

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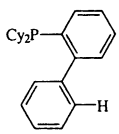

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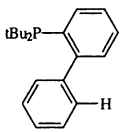

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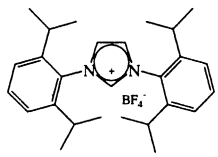

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Entry	Author	R	R_1/R_2 (amine)	Catalyst system and additives	Yield (%)	TON
1	Beller (1997) [14]	4-CF_3	Me, Ph	**1**, LiBr	60	60
2	Beller (1997) [14]	4-CF_3	Piperidine	**1**, LiBr	98	98
3	Buchwald (1997) [15]	4-Me	Me, Ph	$Ni(COD)_2$, 2 **2**	80	40
4	Buchwald (1997) [15]	4-CN	Morpholine	$Ni(COD)_2$, 2 **2**	86	43
5	Buchwald (1997) [15]	4-CN	Morpholine	$Ni(COD)_2$, 1,10-phen	82	41
6	Reddy and Tanaka (1997) [17]	4-CN	Me, Ph	$Pd(PCy_3)_2Cl_2$	82	41
7	Reddy and Tanaka (1997) [17]	4-CN	Hexyl, hexyl	$Pd(PCy_3)_2Cl_2$	23	12
8	Yamamoto (1998) [18]	H	Ph, *p*-tolyl	$Pd(OAc)_2$/4 P^tBu_3	99	3960
9	Hartwig (1998) [19]	4-Me	Bu, H	$Pd_2(dba)_3$/1.5 **3**	87	87
10	Hartwig (1998) [19]	4-Me	Bu, H	$Pd_2(dba)_3$/1.5 **4**	89	89
11	Hartwig (1998) [19]	4-Me	Ph, H	$Pd(dba)_2$/1.5 **4**	92	92
12	Hartwig (1998) [19]	3-MeO	Morpholine	$Pd(OAc)_2$/1.5 **5**	81	81
13	Buchwald (1998) [20]	4-CO_2Me	Hexyl, H	$Pd(dba)_2$/1.5 **6**	83	83
14	Buchwald (1998) [20]	4-Me	Bu, Bu	$Pd(dba)_2$/1.5 **7**	95	1900
15	Buchwald (1998) [20]	4-MeO	Bu, Bu	$Pd(dba)_2$/1.5 **7**	90	90
16	Buchwald (1998) [20]	4-MeO	Me, Ph	$Pd(dba)_2$/1.5 **7**	95	95
17	Guram (1999) [21]	3,5-Me_2	Morpholine	$Pd(OAc)_2$/3 **8**	92	46
18	Guram (1999) [21]	2-MeO	Octyl	$Pd(OAc)_2$/3 **8**	83	42
19	Buchwald (1999) [22]	4-Me	Morpholine	$Pd(OAc)_2$/2 **9**	89	1780
20	Buchwald (1999) [22]	4-MeO	Morpholine	$Pd(OAc)_2$/2 **10**	90	45
21	Hartwig (2000) [23]	4-Me	Hexyl, H	$Pd(dba)_2$/**11**	40	20
22	Hartwig (2000) [23]	4-MeO	Morpholine	$Pd(dba)_2$/**11**	96	96

As reviewed by Grushin and Alper [16] bulky basic phosphines act as efficient ligands for chloroarene activation reactions. Hence tricyclohexylphosphine [17] and especially tri-*tert*-butylphosphine [18] proved to be successful for the coupling of activated and non-activated aryl chlorides and amines. Later on, both Hartwig and Buchwald applied chelating bulky basic phosphines in the amination of deactivated chloroarenes successfully. While Hamann and Hartwig [19] used the ferrocenyl ligands **3**, **4**, and **5**, Buchwald and coworkers [20] applied the BINAP analog **6** and the aminophosphine **7** as ligands. A

similar, non-chelating aryldicyclohexylphosphine ligand **8** [21], and the non-chelating ligands **9** and **10** [22] have been applied successfully too. Very recently, a carbene ligand generated in situ from imidazolium salt **11** [23] was also shown to be suitable for aryl chloride amination. These latter results are partly in contradiction to the former opinion [24] that chelating ligands are crucial for the success of aryl amination reactions.

2. Results and discussion

Recently, we have developed improved procedures for Heck [25] and Suzuki [26] reactions of aryl chlorides making use of our novel ligand di(1-adamantyl)-*n*-butylphosphine (**12**). Until now in the presence of **12** the highest turnover numbers (TON) for the catalytic activation of non-activated aryl chlorides were achieved, e.g. the Suzuki reaction of 4-chlorotoluene proceeds with TON up to 17.400 (yield of 4-methylbiphenyl: 87%). Due to the excellent performance of di(1-adamantyl)-*n*-butylphosphine as ligand we were interested in the amination of aryl chlorides in the presence of diadamantylalkylphosphines. In this paper, we describe the results obtained in the amination of chloroarenes using palladium catalysts in the presence of **12** and **13** (Fig. 1).

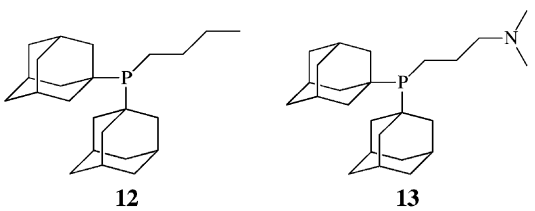
As shown in Table 2 primary aliphatic and aromatic as well as secondary aliphatic amines can be coupled to a variety of aryl chlorides. In general, good to excellent yields are obtained in the presence of 0.5 mol% of palladium(II)acetate and 1 mol% of **12** in toluene at 120 °C. While the reaction time has not been optimized, we have found that in some cases the reaction is nearly complete after 4 h.

Because arylation of secondary alkyl amines is one of the most challenging tasks in this type of coupling reaction, we started our investigation with the amination of the relatively inert chlorobenzene with secondary, cyclic amines. Good yields of 76 and 87%, respectively (Table 2, entries 1 and 2) were observed using morpholine and piperidine. Secondary, acyclic amines such as diethylamine and di-*n*-butylamine can also be coupled with chlorobenzene and deactivated chloroarenes giving moderate to good yields (40–72%, entries 3–7). Another challenge in C–N coupling reactions is the efficient synthesis of sterically encumbered amines. We were surprised to find that the tertiary aliphatic, primary amines *tert*-butylamine and 1-adamantylamine react in high yield with 2,6-dimethylchlorobenzene, which is extremely difficult to activate, to give the corresponding anilines (93 and 84%, respectively, entries 8 and 9). Sterically even more congested amines, such as 2,6-dimethylaniline and 2,6-di-*i*-propylaniline can also be coupled with 2-chloro-*m*-xylene in very good yields (87 and 70%, respectively, entries 10 and 13). Amination of *o*-chloroanisole proceeds even more smoothly (100 and 81%, respectively, entries 11 and 12). Also the reaction of 2,6-di-*i*-propylaniline with *o*-chlorofluorobenzene gives a good coupling result (70%, entry 14).

Due to the excellent performance of our palladium catalysts, we wanted to take a closer look at the influence of different ligands on the aminations of 2-chloro-*m*-xylene and *o*-chloroanisole (Fig. 2, Table 3). In fact, our ligand di(1-adamantyl)-*n*-butylphosphine (**12**) proved to be superior in three out of the four investigated reactions. Only in the case of coupling of 2,6-dimethylaniline with 2,6-dimethylchlorobenzene di(1-adamantyl)-3-(*N*,*N*-dimethylamino) propylphosphine (**13**) and tricyclohexylphosphine gave better product yields of bis(2,6-dimethylphenyl) amine.

In aminations of *o*-chloroanisole several ligands give only low to fair yields, while in the presence of di(1-adamantyl)alkylphosphines **12** and **13** as well as P*t*Bu$_3$ and PCy$_3$ good yields can be observed. Comparing conversions and product yields, there seems to be a tendency of reductive dehalogenation becoming an important side reaction going to bulky substrates.

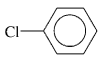
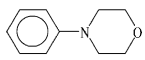
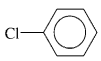
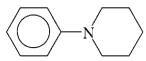
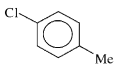
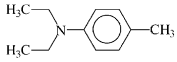
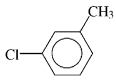
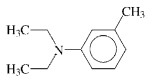
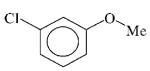
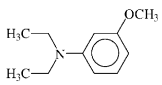
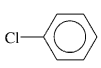
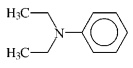
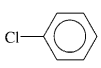
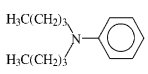
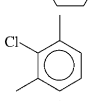
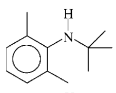
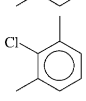
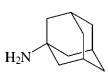
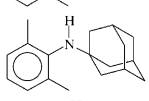
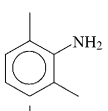
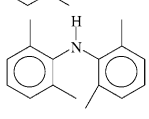
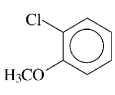
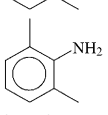
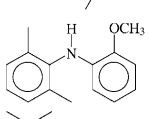
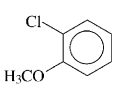
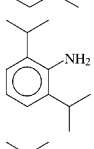
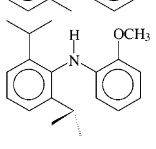
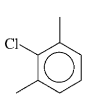
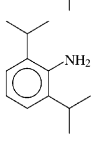
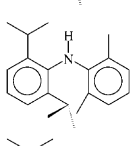
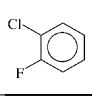
In conclusion, we have shown that di-(1-adamantyl) alkylphosphines lead to efficient palladium catalysts for the amination of aryl chlorides. Non-activated aryl chlorides react with sterically hindered amines in very



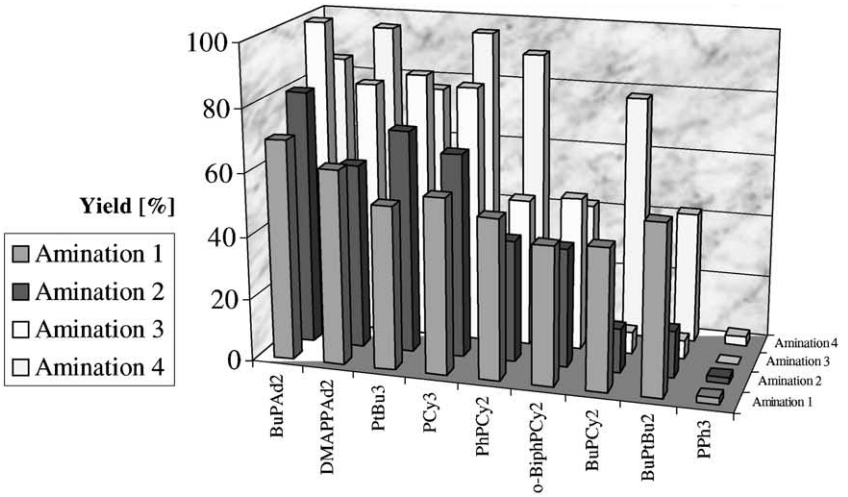
12 **13**

Fig. 1. Di(1-adamantyl)alkylphosphines.

Table 2
Amination of aryl chlorides ($Pd(OAc)_2$/2 *n*-$BuPAd_2$)[a]

Entry	Aryl chloride	Amine	Product	Conversion (%)	Yield (%)	TON
1				100	76	152
2				100	87	174
3[b]				100	40	80
4				100	49	98
5				82	58	116
6				100	44	88
7				100	72	144
8				100	93	186
9				100	84	168
10				100	87	174
11				100	100	200
12				100	81	162
13				100	70	140
14				100	70	140

[a] Reaction conditions: 0.5 mol% $Pd(OAc)_2$, $BuPAd_2$:Pd = 2:1, 5.0 mmol aryl chloride, 6.0 mmol amine, 6 mmol NaO^tBu, 5 ml toluene, 20 h, 120 °C.
[b] 0.1 mol% $Pd(OAc)_2$.



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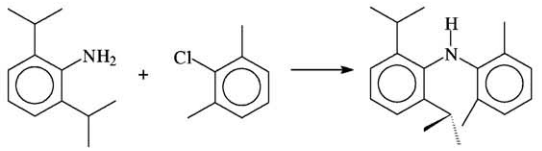

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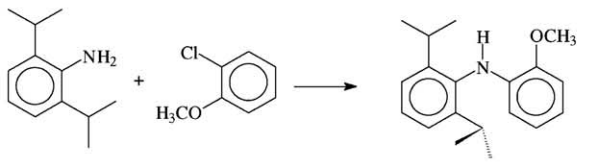

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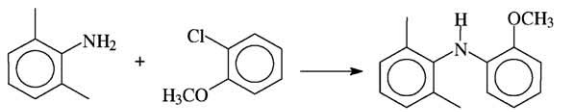

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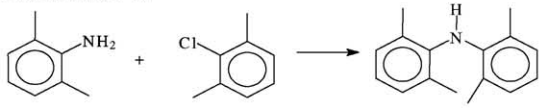

Reaction conditions: 0.5 mol-% $Pd(OAc)_2$, $BuPAd_2$:Pd = 2:1, 5.0 mmol aryl chloride, 6.0 mmol amine, 6 mmol NaO^tBu, 5 ml toluene, 20 h, 120 °C.

Fig. 2. Use of nine phosphine ligands in four different amination reactions of aryl chlorides.

Table 3
Comparison of different ligands in palladium-catalyzed aminations of aryl chlorides[a]

Phosphine	Amination 1		Amination 2		Amination 3		Amination 4	
	Conversion (%)	Yield (%)	Conversion (%)	Yield (%)	Conversion (%)	Yield (%)	Conversion (%)	Yield (%)
$BuPAd_2$	100	70	100	81	100	100	91	85
$DMAPPAd_2$	100	62	100	59	81	81	100	96
$PtBu_3$	100	52	100	71	86	85	83	77
Pcy_3	100	56	100	65	82	82	100	96
$PhPCy_2$	100	51	89	39	86	47	100	90
o-$BiphPCy_2$	100	44	100	38	65	49	56	42
$BuPCy_2$	100	45	82	14	7	7	88	78
$BuPtBu_2$	100	54	80	15	6	6	42	42
PPh_3	83	2	75	2	0	0	23	3

[a] Reaction conditions: 0.5 mol% $Pd(OAc)_2$, $BuPAd_2$:Pd = 2:1, 5.0 mmol aryl chloride, 6.0 mmol amine, 6 mmol NaO^tBu, 5 ml toluene, 20 h, 120 °C.

good yields to give the corresponding anilines. A comparison of our catalyst with the previously reported best ligands reveals the superiority of our system under the described reaction conditions. Further work using adamantylalkylphosphines in other coupling reactions are currently under way.

3. Experimental section

General procedure. 5.0 mmol aryl chloride, 6.0 mmol amine, 6.0 mmol NaO^tBu, 0.025 mmol Pd catalyst (0.50 mol%) and 0.050 mmol phosphine ligand (1.0 mol%) were dissolved in 5 ml toluene, and the mixture was stirred under argon at 120 °C for 20 h in a pressure tube. The mixture was cooled to room temperature, diluted with dichloromethane and washed with 2% aqueous HCl (three times). The organic layer was dried over $MgSO_4$. After removal of the solvent the desired products were isolated by distillation, crystallization from mixtures of ethanol/acetone or by column chromatography (silicagel, hexane/ethyl acetate). Alternatively, 500 mg diethyleneglycol–di-*n*-butylether were added as an internal standard, and quantitative analysis was done by gas chromatography [27].

Bis(2,6-dimethylphenyl)amine. ^{1}H NMR (400.1 MHz, $CDCl_3$, 297 K): δ = 6.89 (m, H_{ar}, 4H); 6.76 (m, H_{ar}, 2H); 4.66 (s, N*H*, 1H); 1.93 ppm (s, CH_3, 12H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): δ = 142.2 (*C*N); 130.0 (C_{ar}H); 129.2 ($C_{ar}CH_3$); 122.2 (*C*H); 19.6 ppm (*C*H_3). MS (E.I., 70 eV): *m*/*z*: 225 (M^+, 100%); 210 (M^+–CH_3, 25%); 195 (M^+–$2CH_3$, 18%). IR (KBr): ν = 3409.7 s (NH). $C_{16}H_{19}N$ (225.33). Microanalytical results (calc.): C: 85.02% (85.28%); H: 8.56% (8.50%); N: 6.23% (6.22%).

N-2′,6′-Dimethylphenyl-2,6-di-i-propylaniline. ^{1}H NMR (400.1 MHz, $CDCl_3$, 297 K): δ = 7.03 (m, H_{ar}, 3H); 6.84 (m, H_{ar}, 2H); 6.63 (m, H_{ar}, 1H); 4.65 (s, N*H*, 1H); 3.06 (sept., $^3J_{HH}$ = 6.9 Hz, C*H*–$(CH_3)_2$, 2H); 1.88 (s, Ar–CH_3, 6H); 1.02 ppm (d, $^3J_{HH}$ = 6.7 Hz, CH–$(CH_3)_2$, 12H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): δ = 144.6 (*C*N); 143.6 (*C*N); 139.3 ($C_{ar}{}^i$Pr); 130.0 (C_{ar}H); 126.2 ($C_{ar}CH_3$); 125.3 (C_{ar}H); 123.8 (C_{ar}H); 120.1 (C_{ar}H); 28.6 (*C*H–$(CH_3)_2$); 24.0 (CH–(*C*H_3)$_2$); 19.8 ppm ($C_{ar}CH_3$). MS (E.I., 70 eV): *m*/*z*: 281 (M^+, 100%). IR (KBr): ν = 3434.1 s (NH). $C_{20}H_{27}N$ (281.44). Microanalytical results (calc.): C: 85.12% (85.35%); H: 9.66% (9.67%); N: 4.99% (4.98%).

N-2′-Fluorophenyl-2,6-di-i-propylaniline. ^{1}H NMR (400.1 MHz, $CDCl_3$, 297 K). δ = 7.66 (m, H_{ar}, 2H); 7.43 (m, H_{ar}, 1H); 7.21 (m, H_{ar}, 1H); 7.00 (m, H_{ar}, 1H); 6.62 (m, H_{ar}, 1H); 5.74 (m, H_{ar}, 1H); 4.27 (s, N*H*, 1H); 3.61 (m, C*H*–$(CH_3)_2$, 2H); 1.55 ppm (m, CH_3, 12H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): δ = 151.7 (d, $^1J_{CF}$ = 238.4 Hz, *C*F); 148.3 (*C*N), 137.1 (d, $^2J_{CF}$ = 10.5 Hz, *C*N), 134.8 ($C_{ar}{}^i$Pr); 128.2 (C_{ar}H), 125.0 (d, $^4J_{CF}$ = 2.9 Hz, C_{ar}H), 124.5 (C_{ar}H), 117.7 (d, $^3J_{CF}$ = 6.7 Hz, C_{ar}H), 115.2 (d, $^2J_{CF}$ = 18.1 Hz, C_{ar}H), 113.8 (d, $^3J_{CF}$ = 2.8 Hz, C_{ar}H); 28.8 (*C*H–$(CH_3)_2$); 24.4 ppm (*C*H_3). ^{19}F NMR

(235.4 MHz, $CDCl_3$, 297 K): $\delta = -136.8$. MS (E.I., 70 eV): *m/z*: 271 (M^+, 100%); 256 (M^+–CH_3, 49%). IR (KBr): $\nu = 3433.0$ s (NH). $C_{18}H_{21}FN$ (271.38). Microanalytical results (calc.): C: 79.67% (79.67%); H: 8.26% (8.17%); N: 5.33% (5.16%).

N-2′-Anisyl-2,6-di-i-propylaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 7.70$–7.45 (m, H_{ar}, 3H); 7.20 (m, H_{ar}, 1H); 7.05 (m, H_{ar}, 2H); 6.50 (m, H_{ar}, 1H); 6.02 (s, N*H*, 1H); 4.31 (s, O*CH*$_3$, 3H); 3.54 (sept., $^3J_{HH} = 6.9$ Hz, C*H*–$(CH_3)_2$, 2H); 1.52 ppm (d, $^3J_{HH} = 6.9$ Hz, CH–(*CH*$_3$)$_2$, 12H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta =$ 148.1, 146.8 ($C_{ar}O$, $C_{ar}{}^i$Pr); 138.4 (*C*N); 135.9 (*C*N); 127.6 ($C_{ar}H$); 124.2 ($C_{ar}H$); 121.7 ($C_{ar}H$); 117.3 ($C_{ar}H$); 111.5 ($C_{ar}H$); 110.3 ($C_{ar}H$); 56.2 (O*CH*$_3$); 28.7 (*C*H–$(CH_3)_2$); 24.4 ppm (CH–(*C*H$_3$)$_2$). MS (E.I., 70 eV): *m/z*: 283 (M^+, 100%). IR (KBr): $\nu = 3424.7$ s (NH). $C_{19}H_{25}NO$ (283.41).

N-2′-Anisyl-2,6-dimethylaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 7.10$–6.94 (m, H_{ar}, 3H); 6.76 (m, H_{ar}, 1H); 6.61 (m, H_{ar}, 2H); 6.05 (m, H_{ar}, 1H); 5.21 (s, N*H*, 1H); 3.84 (s, O*CH*$_3$, 3H); 2.11 ppm (s, C*CH*$_3$, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta = 147.2$ ($C_{ar}O$), 138.9 (*C*N), 136.6, 136.5 (*C*N, *C*CH3), 128.9 ($C_{ar}H$), 126.2 ($C_{ar}H$), 121.6 ($C_{ar}H$), 117.8 ($C_{ar}H$), 111.5 ($C_{ar}H$), 110.3 ($C_{ar}H$), 56.1 (O*CH*$_3$); 18.7 ppm (C*CH*$_3$). MS (E.I., 70 eV): *m/z*: 227 (M^+, 100%). IR (KBr): $\nu = 3388.1$ s (NH). $C_{15}H_{17}NO$ (227.31). Microanalytical results (calc.): C: 79.20% (79.26%); H: 7.49% (7.54%); N: 6.22% (6.16%).

N-1′-Adamantyl-2,6-dimethylaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 6.93$ (m, H_{ar}, 2H); 6.83 (m, H_{ar}, 1H); 3.85 (s, N*H*, 1H); 2.33 (s, C*H*$_3$, 6H); 1.95 (m, $C_{alk}H$, 3H); 1.75 (m, C*H*$_2$, 6H); 1.53 ppm (m, C*H*$_2$, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta = 135.2$ (*C*CH_3); 129.0 ($C_{ar}H$); 124.1 ($C_{ar}H$); 44.2 (*C*H$_2$); 36.7 (*C*H$_2$); 30.5 (*C*H); 21.2 ppm (*C*H$_3$). MS (E.I., 70 eV): *m/z*: 255 (M^+, 100%). IR (KBr): $\nu = 3377.3$ s (NH). $C_{18}H_{25}N$ (255.40). Microanalytical results (calc.): C: 84.37% (84.65%); H: 10.20% (9.87%); N: 5.55% (5.48%).

N-tert-Butyl-2,6-dimethylaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 7.41$ (m, H_{ar}, 2H); 7.28 (m, H_{ar}, 1H); 3.13 (s, N*H*, 1H); 2.73 (s, $C_{ar}CH_3$, 6H); 1.60 ppm (s, C–$(CH_3)_3$, 9H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta = 144.4$ ($C_{ar}N$), 135.2 ($C_{ar}CH_3$); 129.0 ($C_{ar}H$), 123.7 ($C_{ar}H$); 55.7 (*C*–$(CH_3)_2$); 31.6 (C–(*C*H$_3$)$_2$), 20.8 ppm ($C_{ar}CH_3$). MS (E.I., 70 eV): *m/z*: 177 (M^+, 35%); 162 (M^+–CH_3, 65%); 121 (M^+–C_4H_8, 100%). IR (KBr): $\nu =$ 3381.1 s (NH). $C_{12}H_{19}N$ (177.29). Microanalytical results (calc.): C: 81.05% (81.30%); H: 11.03% (10.80%); N: 7.59% (7.90%).

N,N-Diethyl-4-methylaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 7.22$ (m, H_{ar}, 2H); 6.82 (m, H_{ar}, 2H); 3.50 (m, C*H*$_2$, 4H); 2.44 (s, $C_{ar}CH_3$, 3H); 1.33 ppm (m, CH_2CH_3, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta = 146.5$ ($C_{ar}N$); 130.4 ($C_{ar}H$); 125.4 ($C_{ar}CH_3$); 113.2 ($C_{ar}H$); 45.2 (*C*H$_2$); 20.8 ($C_{ar}CH_3$); 13.2 ppm (CH_2CH_3). MS (E.I., 70 eV): *m/z*: 163 (M^+, 50%); 148 (M^+–CH_3, 100%). $C_{11}H_{17}N$ (163.26). Microanalytical results (calc.): C: 80.51% (80.93%); H: 10.33% (10.50%); N: 8.38% (8.58%).

N,N-Diethyl-3-methoxyaniline. ^1H NMR (400.1 MHz, $CDCl_3$, 297 K): $\delta = 7.45$ (m, H_{ar}, 1H); 6.67 (m, H_{ar}, 1H); 6.58 (m, H_{ar}, 2H); 4.12 (s, O*CH*$_3$, 3H); 3.68 (m, C*H*$_2$, 4H); 1.51 ppm (m, CH_2CH_3, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$, 297 K): $\delta = 161.5$ ($C_{ar}O$); 149.7 ($C_{ar}N$); 130.4 ($C_{ar}H$), 105.6 ($C_{ar}H$); 100.6 ($C_{ar}H$); 98.9 ($C_{ar}H$); 55.5 (O*CH*$_3$); 44.9 (*C*H$_2$); 13.1 ppm (CH_2CH_3). MS (E.I., 70 eV): *m/z*: 179 (M^+, 43%), 164 (M^+–CH_3, 100%). $C_{11}H_{17}NO$ (179.26). Microanalytical results (calc.): C: 73.48% (73.70%); H: 9.35% (9.56%).

Acknowledgements

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