A Convenient and Efficient Synthesis of Polyphenylmono-, -di-, and -triaminobenzenes

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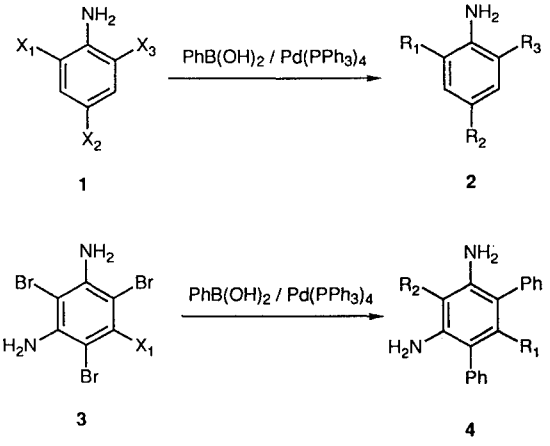
A new convenient and efficient synthesis of polyphenylmono- and -diaminobenzenes by the palladium(0)-catalyzed cross-coupling reaction of polyhalomono- and -diaminobenzenes with phenylboronic acid is described. A synthesis of 2,4-diphenyl-1,3,5-triaminobenzene is also reported.

Polyphenylmono-, -di-, and -triaminobenzenes are an interesting family of compounds because of their unique structures. However, in spite of their simple structures, their convenient syntheses have not yet been established. For example, 2,4,6-triphenylaniline has been prepared in four steps from benzaldehyde and acetophenone. Hence, the total yield is not high (39%),[1] and use of highly toxic anhydrous hydrofluoric acid is required in the second step. Quite recently, we found that a variety of polyphenylmono- and -diaminobenzenes can be conveniently and efficiently prepared by the palladium(0)-catalyzed cross-coupling reaction of polybromomono- or -diaminobenzenes with phenylboronic acid in high yields. For example, 2,4,6-triphenylaniline was obtained in a 95% yield from commercially available tribromoaniline and phenylboronic acid. The palladium-catalyzed cross-coupling reaction of polyarylboronic acids with haloarenes is known as the Suzuki reaction[2] and has been widely used for arylation of a variety of compounds.[3] Herein we report the convenient and efficient synthesis of polyphenylmono- and -diaminobenzenes. A synthesis of 2,4-diphenyl-1,3,5-triaminobenzene (**6**) from 3,5-diamino-1-nitrobenzene is also reported.

Some polybromoanilines (**1aBr, 1cBr,** and **1eBr**) are commercially available. The other polybromoanilines (**1bBr** and **1dBr**) and polybromodiaminobenzenes (**3aBr** and **3bBr**) employed in this study could be easily obtained by treating the corresponding amines and diamines with benzyltrimethylammonium tribromide (Table 1).[4] In all cases pure or almost pure polybromo compounds were obtained in high yields (78–97%) after the standard work-up. On the other hand, polyiodoanilines (**1aI** and **1dI**) were prepared by treating the corresponding amines with benzyltrimethylammonium dichloroiodate (BTMA · ICl_2).[7] Their yields (58–70%), however, were lower than in the case of bromination.

Phenylation of the polyhalomono- and -diaminobenzenes was carried out by treating them with excess amounts of phenylboronic acid in a benzene–ethanol–water mixture containing Na_2CO_3 in the presence of $Pd(PPh_3)_4$ at reflux temperature for 24 h under a nitrogen atmosphere (Scheme 1) (Table 2). The products were isolated by column chromatography (**2a–e** and **4b**) or by column chromatography and subsequent recrystallization (**4a**).

Table 2 shows that, although phenylation of the polyiodo compounds gives the corresponding coupled products in relatively low yields (40–65%), phenylation of the polybromo compounds proceeds smoothly to give the corresponding coupled products in satisfactorily high yields



1	X_1	X_2	X_3
aBr	Br	Br	H
aI	I	I	H
bBr	Br	Br	*t*-Bu
cBr	Br	H	Br
dBr	Br	*t*-Bu	Br
dI	I	*t*-Bu	I
eBr	Br	Br	Br

2	R_1	R_2	R_3
a	Ph	Ph	H
b	Ph	Ph	*t*-Bu
c	Ph	H	Ph
d	Ph	*t*-Bu	Ph
e	Ph	Ph	Ph

3	X_1
aBr	H
bBr	NO_2

4	R_1	R_2
a	H	Ph
b	NO_2	Br

Scheme 1

(67–95%). Since, in the halogenation of the amino compounds by BTMA · Br_3 or BTMA · ICl_2, bromination gives higher yields than iodination, and in the subsequent phenylation, the bromo compounds give higher yields than the iodo compounds, the bromination and phenylation route is superior to the iodination and phenylation route for the syntheses of polyphenylmono- and -diaminobenzenes.

In the phenylation of **3bBr**, a somewhat different result was observed. This compound carries three bromo atoms

Table 1. Compounds **1** and **3** Prepared

Substrate	Halogenation Reagent (mol equiv)	Reaction Conditions		Product	Isolated yield (%)	mp (°C)[a] (solvent)	^{1}H NMR ($CDCl_3$) δ
		Temp. (°C)	Time (h)				
2-*tert*-butylaniline	BTMA · Br_3 (2.5)	r.t.	2	**1bBr**	97[b]	brownish red oil	1.40 (s, *t*-Bu, 9H), 4.4 (br s, NH_2, 2H), 7.27 (d, J = 2.4 Hz, arom, 1H), 7.47 (d, J = 2.4 Hz, arom, 1H)
4-*tert*-butylaniline	BTMA · Br_3 (2.5)	r.t.	2	**1dBr**	96[b]	brownish red oil[5]	1.25 (s, *t*-Bu, 9H), 4.39 (br s, NH_2, 2H), 7.37 (s, arom, 2H)
4-*tert*-butylaniline	BTMA · ICl_2 (2.5)	reflux	7	**1dI**	58[c]	brownish red oil	1.23 (s, *t*-Bu, 9H), 4.46 (s, NH_2, 2H), 7.61 (s, arom, 2H)
1,3-phenylenediamine	BTMA · Br_3 (3.5)	reflux	5	**3aBr**	78[b]	159–160 (benzene–hexane) (Lit.[6] mp 158 °C)	4.51 (s, NH_2, 4H), 7.44 (s, arom, 1H)
3,5-diaminonitrobenzene	BTMA · Br_3 (3.5)	reflux	24	**3bBr**	92[b]	188–191 (benzene)	4.82 (s, NH_2, 4H)

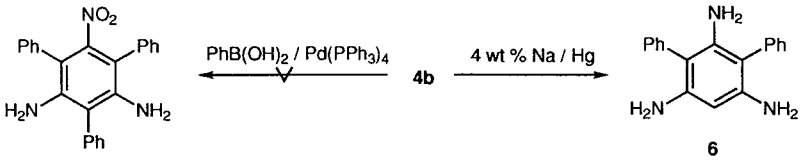
[a] For solid product, the melting point is shown.
[b] Yield after standard workup.
[c] Yield after standard workup followed by recrystallization.

Table 2. Compounds **2** and **4** Prepared[a,b]

Substrate	$PhB(OH)_2$ (mol equiv)	Product	Isolated yield (%)	mp (°C) (solvent)	Column Chromatography (eluant)
1aBr	3.0	**2a**	90[c]	75–77 (hexane)	benzene
1aI	3.0	**2a**	40[c]	76–77 (hexane)	benzene
1bBr	3.0	**2b**	86[c]	100–102 (hexane)	5 : 1 benzene–hexane
1cBr	3.0	**2c**	95[c]	69–71 (hexane)	5 : 1 benzene–hexane
1dBr	3.0	**2d**	94[c]	89–91 (hexane)	5 : 1 benzene–hexane
1dI	3.0	**2d**	65[c]		5 : 1 benzene–hexane
1eBr	4.0	**2e**	95[c]	139–140 (hexane) (Lit.[1] 135–136)	benzene
3aBr	4.0	**4a**	67[d]	231–233 (hexane–benzene)	benzene
3bBr	4.0	**4b**	73[c]	213–216 (hexane–benzene)	benzene

[a] Reaction conditions: temp. reflux; time 24 h.
[b] For new compounds satisfactory microanalyses were obtained: C ± 0.25, H ± 0.13, N ± 0.25.
[c] Yields after the standard workup followed by column chromatography.
[d] Yield after the standard workup followed by column chromatography and recrystallization.

at the 2, 4, and 6 positions with respect to the nitro group. Phenylation of the compound was carried out using an excess amount (4 mol equiv) of phenylboronic acid in the usual manner. The product isolated was not the desired 3,5-diamino-2,4,6-triphenyl-1-nitrobenzene **(5)**, but 3,5-diamino-4-bromo-2,6-diphenyl-1-nitrobenzene **(4b)** (73 % yield). This reaction was also carried out in dimethoxyethane–water using $Ba(OH)_2$ as base.[8] However, a lower yield (21 %) of **4b** and no formation of **5** were observed. The isolated **4b** was again subjected to the cross-coupling reaction with an excess amount (2 mol equiv) of phenylboronic acid. However, TLC analysis of the reaction mixture indicated no formation of **5**; although the **4b** used was almost completely consumed, the reaction was very complex (the formation of at least six products was observed). This result is very different from the case of **3aBr** where the corresponding triphenylated product **4a** is obtained in 67 % yield. In the case of **4b** the nitro group may deactivate the bromo atom *para* to the nitro group for the palladium(0)-catalyzed cross-coupling reaction. Reduction of **4b** by 4 wt% sodium amalgam in methanol gave 2,4-diphenyl-1,3,5-triaminobenzene **(6)** in 64 % yield (Scheme 2). In contrast to 1,3,5-triaminobenzene which decomposes gradually upon storage, compound **6** was stable even on prolonged storage under ambient conditions.



5 6

Scheme 2

Table 3. IR and ^1H and ^{13}C NMR Data of **2** and **4**

Product	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ	^{13}C NMR ($CDCl_3$/TMS) δ
2a	3450, 3330, 3000, 1610, 1510, 1470, 1340, 1400, 1300, 1260, 1235, 1180, 1160, 900, 830, 785, 770, 745, 700, 630, 590	3.81 (br s, NH_2, 2H), 6.82–7.57 (m, arom, 13H)	115.93, 126.27, 126.35, 127.06, 127.27, 127.81, 128.64, 128.85, 129.08, 131.55, 139.37, 140.94, 142.95
2b	3460, 3360, 3030, 2950, 1600, 1440, 1420, 1320, 1250, 1230, 1065, 1010, 880, 760, 700	1.51 (s, *t*-Bu, 9H), 4.0 (br s, NH_2, 2H), 7.22–7.57 (m, arom, 13H)	29.81, 34.65, 124.90, 126.12, 126.51, 127.16, 127.25, 128.60, 128.83, 129.69, 129.76, 130.53, 133.74, 140.09, 141.29, 141.64
2c	3460, 3430, 3370, 3350, 3050, 3000, 1590, 1490, 1455, 1420, 1300, 1280, 1210, 1070, 1020, 760, 710, 610	3.83 (s, NH_2, 2H), 6.88 (t, J = 7.3 Hz, arom, 1H), 7.12 (d, J = 7.3 Hz, arom, 2H), 7.35 (t, J = 7.3 Hz, arom, 2H), 7.45 (t, J = 7.3 Hz, arom, 4H), 7.51 (d, J = 7.3 Hz, arom, 4H)	118.09, 127.21, 127.88, 128.80, 129.28, 129.71, 139.71, 140.73
2d	3420, 3330, 3040, 2950, 1600, 1460, 1430, 1360, 1240, 885, 780, 725, 700	1.34 (s, *t*-Bu, 9H), 3.7 (br s, NH_2, 2H), 7.18 (s, arom, 2H), 7.37 (t, J = 7.3 Hz, arom, 2H), 7.47 (t, J = 7.3 Hz, arom, 4H), 7.55 (d, J = 7.3 Hz, arom, 4H)	31.59, 34.03, 126.83, 127.14, 127.61, 128.79, 129.39, 138.25, 140.24, 140.90
2e	3460, 3360, 3010, 1600, 1485, 1455, 1425, 1340, 1275, 1250, 1235, 1070, 1025, 895, 790, 780, 765, 740, 705, 635, 590	3.91 (br s, NH_2, 2H), 7.24–7.60 (m, arom, 17H)	126.35, 126.38, 127.39, 128.27, 128.36, 128.67, 128.90, 129.33, 131.02, 139.64, 140.29, 140.81
4a	3450, 3350, 3050, 3000, 1600, 1445, 1425, 1345, 1300, 1240, 1140, 1070, 1030, 890, 800, 770, 750, 705, 590	3.61 (br s, NH_2, 4H), 7.01–7.57 (m, arom, 16H)	113.52, 118.45, 126.51, 127.96, 128.69, 129.33, 129.94, 130.86, 131.40, 136.07, 139.89, 141.13
4b	3450, 3350, 1600, 1530, 1440, 1380, 1300, 700	4.22 (s, NH_2, 4H), 7.32–7.45 (m, arom, 10H)	96.96, 108.88, 128.74, 129.26, 130.25, 132.68, 142.57, 150.78

Phenylboronic acid, **1aBr**, **1cBr**, **1eBr**, 1,3-phenylenediamine, and 2- and 4-*tert*-butylanilines were commercially available. 3,5-Diamino-1-nitrobenzene was a gift from Nippon Kayaku Co., Ltd., and used after recrystallization from water. $Pd(PPh_3)_4$,[9] BTMA · Br_3,[4] BTMA · ICl_2,[7] and 2,4-diiodoaniline[7] were obtained by the reported method. Bromo compounds **1bBr**, **1dBr**, **3aBr**, and **3bBr** were obtained by treating the corresponding amines or diamines with BTMA · Br_3 according to the procedure reported for bromination with BTMA · Br_3.[4] Iodo compounds **1aI** and **1dI** were obtained by treating the corresponding amines with BTMA · ICl_2 according to the procedure reported for iodination with BTMA · ICl_2 (Table 1).[7] For column chromatography, silica gel (Wakogel C200) was used. For TLC analyses, Merck silica gel $60F_{254}$ plastic sheets were used. Mps were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were run on a JASCO A202 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a JEOL α-400 spectrometer (400 MHz). Mass spectra were obtained with a JEOL D-400 spectrometer at 70 eV.

2,4-Diphenylaniline (2a); Typical Procdure:

To a solution of 2,4-dibromoaniline **(1aBr)** (0.753 g, 3.00 mmol) in benzene (30 mL) were added a solution of phenylboronic acid (1.10 g, 9.00 mmol) in EtOH (6.0 mL), aq Na_2CO_3 (2 M, 12 mL), and $Pd(PPh_3)_4$ (0.42 g, 0.36 mmol). After the resulting heterogeneous mixture was purged with nitrogen, it was gently refluxed for 24 h with stirring under a nitrogen atmosphere. After cooling to r.t., the organic layer was separated, and the aqueous solution was extracted with Et_2O (2 × 50 mL). The combined organic solution was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (silica gel; benzene) to give **2a**. Recrystallization from hexane gave **2a** as colorless prisms (Tables 2 and 3).

2,4-Diphenyl-1,3,5-triaminobenzene (6):

A solution of **4b** (3.19 g, 8.30 mmol) in dry MeOH (100 mL) was gently refluxed over sodium amalgam (110 g) for 6 h. After the MeOH solution was concentrated to ca. 30 mL under reduced pressure, it was poured into a large excess of ice–water to give a colorless powder, which was collected and chromatographed (silica gel; 2:1, benzene–EtOAc) to give **6** in 64% yield (1.47 g). Recrystallization from benzene–hexane gave **6** as colorless needles with mp 151–153 °C.

^1H NMR ($CDCl_3$/TMS): δ = 3.32 (br s, NH_2, 6H), 5.76 (s, arom, 1H), 7.31–7.48 (m, arom, 10H).

^{13}C NMR ($CDCl_3$/TMS): δ = 92.49, 105.62, 127.40, 129.54, 131.40, 136.14, 142.72, 144.42.

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