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Preparation of 2-arylated-1,4-phenylenediamines by palladium-catalyzed cross-coupling reactions

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Abstract

Protected 2-iodo-1,4-phenylenediamines were converted to the corresponding magnesium derivative by performing an iodine–magnesium exchange. After transmetalation with zinc bromide, a palladium(0)-catalyzed cross-coupling with various aryl iodides and 5-bromo-2-carbethoxyfuran furnished the expected cross-coupling products in 52–79% yield. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Cross-coupling; Palladium; Zinc; Magnesium; Polyfunctional organometallics

1. Introduction

The preparation of polyfunctional aryl- and heteroaryl magnesium reagents obtained by an iodine–magnesium exchange has opened paths to a wide range of functional products using these new functionalized organomagnesium reagents as key intermediates [1,2]. Recently, we have shown that functionalized magnesiated aniline derivatives can be prepared and reacted with various electrophiles [3]. Herein, we wish to report the preparation of 2-magnesiated-1,4-phenylenediamines and their use in cross-coupling reactions with various aryl halides.

2. Results and discussion

2-Iodo-1,4-phenylenediamine (**1**) is readily prepared in two steps from 4-nitroaniline by an iodination (I_2, $AgSO_4$, EtOH, r.t., 1 h; 95% yield) [4] followed by a reduction with $SnCl_2{\cdot}2H_2O$ in concentrated HCl (50 °C, 12 h; 68% yield) [5]. Compound **1** can be converted into the corresponding diimine **2** by treatment with benzaldehyde in toluene in the presence of a catalytic amount of conc. H_2SO_4 and molecular sieves (4 Å) at 120 °C (2 h reaction time). The tetraallylated amine (**3**) is prepared by treatment of **1** with allyl bromide (16 equivalents) in the presence of sodium carbonate (eight equivalents) in DMF (100 °C, 3 h) [6] (Scheme 1).

Preliminary experiments indicate that for both substrates (**2** and **3**), the iodine–magnesium exchange occurs smoothly (THF, −10 °C, 3 h). After transmetalation with CuCN·2LiCl [7], a clean allylation with allyl bromide or ethyl (bromomethyl)acrylate [8] occurs, furnishing the expected products **4** and **5a**–**b** in 81–88% yield (Scheme 2). Having demonstrated that the aminated Grignard reagent can be readily prepared and allylated, we then investigated the transmetalation of the intermediate arylmagnesium compounds to the corresponding organozinc reagents for use in palladium(0) catalyzed cross-coupling with various aryl and heteroaryl iodides [9]. Preliminary results indicate that the iododiimine **2** is the better suited for the performance of Negishi cross-coupling reactions [9]. The best source of palladium(0) was found to be bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$) [10]. Tris-*o*-furyl phosphine (tfp) [11] proved to be an excellent ligand for these cross-coupling reactions [12]. Most cross-coupling reactions were complete within 16 h at r.t. affording the expected products of type **6** in 52–79% yield (Scheme 3 and Table 1).

Various *m*- or *p*-substituted aryl iodides rapidly undergo the expected cross-coupling reaction leading to

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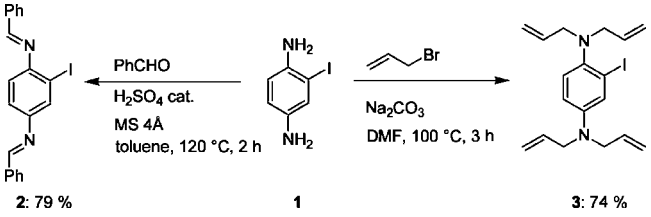
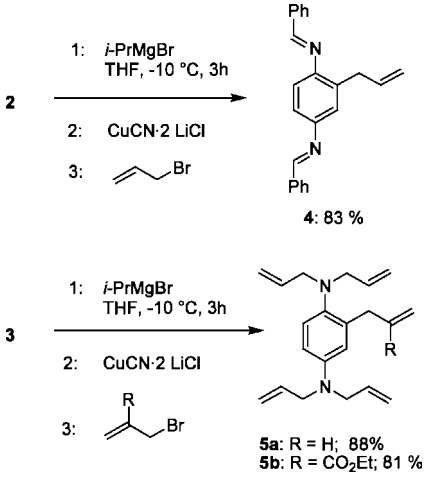
the products **6a**–**f** in satisfactory yield (entries 1–6 of Table 1). Interestingly, the sterically more hindered *o*-methoxyiodobenzene reacts well, leading to **6g** in 74% yield (entry 7). Heterocyclic bromides such as 5-bromo-2-carbethoxyfuran undergo the coupling reaction, furnishing the heterocycle **6h** in 52% yield (entry 8). The resulting protected diamines **4** and **6** can be converted to the free diamines by a rapid treatment with concentrated sulfuric acid in methanol (r.t., 0.5 min) [13], leading to products **9** and **10** in 93–95% yield (Scheme 4).

3. Conclusion

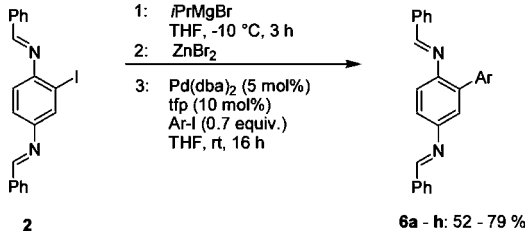
In summary, we have shown that 2-magnesiated-1,4-phenylenediamine derivatives can be transmetalated to the corresponding zinc reagents, which undergo a smooth cross-coupling reaction with various aryl iodides, leading to polyfunctional 1,4-diamines. Efforts to convert several of these products to polyfunctional heterocycles are currently underway in our laboratory.



Scheme 1.



Scheme 2.



Scheme 3.

Table 1
2-Arylated-1,4-phenylenediamines prepared by Pd(0) catalyzed cross-coupling between protected 2-zincated-1,4-phenylenediamine and aryliodides

Entry	Aryl iodide	Product of type **6**	Yield (%)[a]
1	*p*-EtO_2C-C_6H_4I	**6a**: R = CO_2Et	68 %
2	*p*-NC-C_6H_4I	**6b**: R = CN	60 %
3	*p*-Me-C_6H_4I	**6c**: R = Me	71 %
4	*p*-Cl-C_6H_4I	**6d**: R = Cl	62 %
5	*p*-MeO-C_6H_4I	**6e**: R = OMe	79 %
6	*m*-EtO_2C-C_6H_4I	**6f**	62 %
7	*o*-MeO-C_6H_4I	**6g**	74 %
8	EtO_2C-(furan)-Br	**6h**	52 %

[a] Isolated yield of analytically pure products.

4. Experimental

4.1. General considerations

All reactions were carried out under an argon atmosphere. THF was distilled from sodium–benzophenone. Zinc bromide was freshly dried before use for 2 h at 150 °C and less than 0.1 mmHg. Reactions were moni-

tored by gas chromatography (GC) analysis of reaction aliquots. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 (43–60 mesh). 1,4-Phenylenediamine derivatives were purified by solid phase extraction on Varian Bond Elut tubes. The bonded silica sorbent was modified with benzenesulfonic acid for strong cationic exchange (SCX). NMR spectra were recorded on a 300 MHz NMR spectrometer. The ionization method used was electron impact ionization (EI, 70 eV). Elemental analyses were performed by the Microanalytical Service Laboratory of Universität München.

4.2. Preparation of 2-iodo-4-nitroaniline

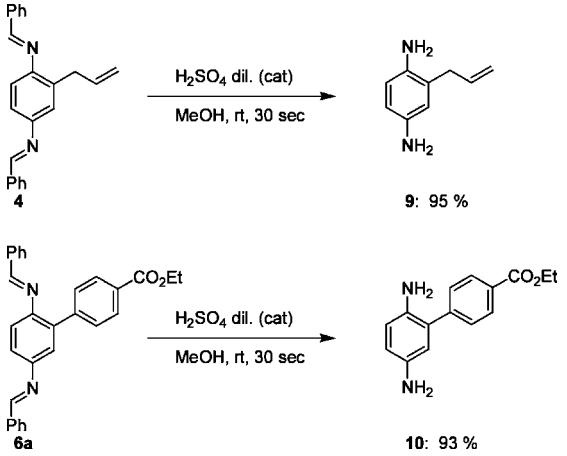
4-Nitroaniline (13.8 g, 100 mmol) was added to a mixture of iodine (25.4 g, 100 mmol) and silver sulfate (31.1 g, 100 mmol) in ethanol (250 ml) and left stirring for 30 min at r.t. The solution was filtered and concentrated in vacuo. The residue was taken up in dichloromethane, and washed with 5% NaOH solution, and water, then dried over $MgSO_4$ and concentrated. The product was found to be of satisfactory purity, and was obtained as a yellow powder. Yield (25.3 g, 95%).

M.p.: 107 °C. IR (KBr, cm^{-1}): ν 3480 (m), 3373 (s), 1609 (s), 1581 (m), 1491 (s), 1303 (s). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 8.48 (d, $J = 2.4$ Hz, 1H), 7.99 (dd, $J = 2.4$ and 9.2 Hz, 1H) 6.77 (d, $J = 9.2$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 152.9, 139.5, 135.9, 126.1, 112.6, 80.9. MS (EI, 70 eV): 264 (100), 234 (47), 218 (13), 91 (56). Anal. Calc. for $C_6H_5N_2I$: C, 27.29; H, 1.90; N, 10.61. Found: C, 27.08; H, 1.61; N, 10.48%.

4.3. Preparation of 2-iodo-p-phenylenediamine (1)

2-Iodo-4-nitroaniline (8.0 g, 30 mmol) was suspended in concentrated HCl (40 ml) and warmed to 50 °C before slowly adding a solution of $SnCl_2 \cdot 2H_2O$ (25.0 g, 125 mmol) in concentrated HCl (40 ml). The reaction was left for 3 h at this temperature before being cooled to 0 °C on an ice bath and basified with a 50% NaOH solution. The precipitate was filtered and dried in a dessicator, then extracted several times with hot dichloromethane. After concentration, recrystallization from dichloromethane produced the product as yellow crystals. Yield (4.7 g, 68%).

M.p.: 112 °C. IR (KBr, cm^{-1}): ν 3395 (m), 3284 (m), 3183 (m), 1607 (m), 1492 (s). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 8.55 (d, $J = 2.4$ Hz, 1H), 8.04 (dd, $J = 2.4$ and 8.8 Hz, 1H), 6.70 (d, $J = 8.8$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 141.8, 141.4, 127.5, 119.5, 117.9, 86.5. MS (EI, 70 eV): 234 (100), 107 (33), 80 (18), 53 (10). Anal. Calc. for $C_6H_7N_2I$: C, 30.79; H, 3.02; N, 11.97. Found: C, 30.86; H, 2.97; N, 11.85%.



Scheme 4.

4.4. Preparation of 2-iodo-N^1,N^4-di[(E)-phenylmethylidene]-benzene-1,4-diamine (2)

2-Iodo-*p*-phenylenediamine (3.5 g, 15 mmol) was dissolved in dry toluene (15 ml), then benzaldehyde (3.8 g, 36 mmol), H_2SO_4 (conc., a few drops) and molecular sieves (4 Å, 400 mg) were added and the mixture heated to reflux for 2 h. The solution was filtered and concentrated in vacuo, the obtained yellow oil crystallized upon addition of diethyl ether. Recrystallization from ether yielded the product as yellow needles. Yield (4.9 g, 79%).

M.p.: 118 °C. IR (KBr, cm^{-1}): ν 3436 (w), 1622 (s), 1577 (m), 1469 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.36 (s, 1H), 8.24 (s, 1H), 7.90–7.79 (m, 4H), 7.70 (d, $J = 2.1$ Hz, 1H), 7.41–7.36 (m, 6H), 7.17 (dd, $J = 2.1$ and 8.4 Hz, 1H), 6.94 (d, $J = 8.4$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 160.8, 160.7, 151.9, 136.4, 136.3, 132.1, 131.4, 129.5, 129.3, 129.2, 123.0, 118.8, 96.4. MS (EI, 70 eV): 410 (100), 281 (10), 178 (18), 152 (16). Anal. Calc. for $C_{20}H_{15}N_2I$: C, 58.55; H, 3.69; N, 6.83. Found: C, 58.54; H, 3.67; N, 6.75%.

4.5. Preparation of N^1,N^1,N^4,N^4-tetraallyl-1-iodobenzene-1,4-diamine (3)

2-Iodo-*p*-phenylenediamine (2.6 g, 11 mmol) was dissolved in dry dimethylformamide (100 ml). Allyl bromide (16 ml, 185 mmol) and Na_2CO_3 (9.3 g, 87 mmol) were added and the mixture heated to 100 °C for 3 h. The solution was filtered after cooling to r.t., the filter cake was washed with diethyl ether and the combined organic phases poured into water (200 ml). The water was extracted three times with diethyl ether (3×100 ml), the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The obtained oil was purified by bulb-to-bulb distillation (10^{-2} mbar, 200 °C) to give the product as an orange oil. Yield (3.2 g, 74%).

IR (KBr, cm^{-1}): ν 3077 (w), 2979 (w), 2810 (w), 1596 (s), 1496 (s), 1229 (m), 919 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.09 (d, $J = 3.0$ Hz, 1H), 6.77 (d, $J = 8.7$ Hz, 1H), 6.54 (dd, $J = 3.0$ and 8.7 Hz, 1H), 5.73 (m, 4H), 5.04 (m, 8H), 3.76 (m, 4H), 3.42 (m, 4H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 147.1, 141.4, 135.9, 134.1, 124.6, 123.1, 117.6, 116.8, 113.1, 103.1, 57.4, 53.3. MS (EI, 70 eV): 394 (100), 353 (81), 225 (39), 183 (24), 157 (27), 130 (30). Anal. Calc. for $C_{18}H_{23}N_2I$: C, 54.83; H, 5.88; N, 7.10. Found: C, 54.36; H, 6.24; N, 7.10%.

4.6. General procedure for the preparation of compounds of type **4** and **5**. Preparation of ethyl 2-[2,5-bis(diallylamino)benzyl]acrylate (**5b**)

A dry and argon flushed 10 ml Schlenk-flask, equipped with a magnetic stirrer, was charged with **3** (394 mg, 1 mmol) in dry THF (1 ml) and cooled to −10 °C. *i*PrMgBr (3.3 ml, 0.6 M in THF, 2 mmol) was added slowly. After 1 h the exchange was complete (checked by TLC analysis) and CuCN·2LiCl (1.0 ml, 1 M in THF, 1 mmol) was added slowly. After 30 min ethyl 2-(bromomethyl)acrylate (576 mg, 3 mmol) was added and the reaction mixture allowed to warm to r.t. overnight. The reaction was quenched with NH_4Cl–NH_3 9:1 (3 ml), poured into water (20 ml) and extracted with ether (3 × 40 ml). The combined organic fractions were washed with brine (100 ml), then dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography (pentane–EtOAc 95:5) to yield **5b** as a pale yellow oil (309 mg, 81%).

IR (KBr, cm^{-1}): ν 3078 (w), 2980 (m), 1717 (s), 1607 (m), 1508 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 6.88 (d, $J = 8.7$ Hz, 1H), 6.48 (dd, $J = 3.3$ and 8.7 Hz, 1H), 6.40 (d, $J = 3.3$ Hz, 1H), 6.12 (s, 1H), 5.77–5.71 (m, 4H), 5.24 (s, 1H), 5.11–4.94 (m, 8H), 4.13(q, $J = 7.2$ Hz, 2H), 3.77 (d, $J = 6$ Hz, 4H), 3.64 (s, 2H), 3.36 (d, $J = 6$ Hz, 4H), 1.20 (t, $J = 7.2$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 167.9, 145.9, 141.3, 140.2, 136.7, 136.4, 134.8, 126.9, 125.8, 124.5, 117.0, 116.5, 114.8, 111.4, 60.6, 57.7, 53.4, 33.4, 14.6. MS (EI, 70 eV): 380 (100), 339 (30), 297 (17), 265 (18). Anal. Calc. for $C_{24}H_{32}N_2O_2$: C, 75.75; H, 8.48; N, 7.36. Found: C, 75.94; H, 7.98; N, 6.98%.

The products **4** and **5a** were prepared according to this method.

4.6.1. N^1,N^1,N^4,N^4,2-pentaallyl-1-iodobenzene-1,4-diamine (**5a**)

From **3** (394 mg, 1 mmol) and allyl bromide (360 mg, 3 mmol). Purification by flash chromatography (pentane–EtOAc 95:5) yielded **5a** as a colorless oil (270 mg, 88%).

IR (KBr, cm^{-1}): ν 3077 (w), 2978 (w), 1639 (W9, 1607 (m), 1507 (s), 917 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 6.86 (d, $J = 6.0$ Hz, 1H), 6.48–6.43 (m, 2H), 5.79–5.71 (m, 5H), 5.13–4.95 (m, 10H), 3.80–3.77 (m, 5H), 3.40–3.38 (m, 5H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 144.6, 138.7, 137.3, 136.4, 135.0, 133.6, 122.8, 115.6, 115.1, 114.1, 113.0, 109.7, 56.3, 52.0, 34.3. MS (EI, 70 eV): 308 (88), 267 (64), 226 (100), 185 (48), 170 (50), 157 (42), 143 (26), 130 (30). Anal. Calc. for $C_{21}H_{28}N_2$: C, 81.77; H, 9.15; N, 9.08. Found: C, 81.78; H, 9.19; N, 8.96%.

4.6.2. 2-Allyl-N^1,N^4-di[(E)-phenylmethylidene]-benzene-1,4-diamine (**4**)

From **2** (1.23 g, 3 mmol) and allyl bromide (1.08 g, 9 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:5) yielded **4** as a yellow powder (812 mg, 83%).

M.p.: 57 °C. IR (KBr, cm^{-1}): ν 3059 (w), 2874 (w), 1623 (s), 1576 (m), 756 (s), 691 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.44 (s, 1H), 8.35 (s, 1H), 7.86–7.82 (m, 4H), 7.43–7.39 (m, 6H), 7.09 (s, 1H), 7.01 (d, $J = 6.9$ Hz, 2H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 159.8, 159.4, 150.3, 148.9, 137.6, 136.9, 136.7, 135.7, 131.6, 129.2, 122.6, 120.1, 118.8, 116.1, 18.1. MS (EI, 70 eV): 324 (44), 323 (100), 220 (16), 115 (18). Anal. Calc. for $C_{23}H_{20}N_2$: C, 85.15; H, 6.21; N, 8.63. Found: C, 84.75; H, 6.38; N, 8.52%.

4.7. General procedure for the preparation of compounds of type **6**: preparation of ethyl 2′,5′-bis{[(E)-phenylmethylidene]amino}[1,1′-biphenyl]-4-carboxylate (**6a**)

A dry and argon flushed 10 ml Schlenk-flask, equipped with a magnetic stirrer, was charged with **2** (410 mg, 1 mmol) in dry THF (1 ml) and cooled to −10 °C. *i*PrMgBr (3.3 ml, 0.6 M in THF, 2 mmol) was added slowly. After 1 h the exchange was complete (checked by TLC analysis) and $ZnBr_2$ (0.8 ml, 1.5 M in THF, 1.1 mmol) was added. The reaction was allowed to warm to r.t.. Another dry and argon flushed 10 ml Schlenk-flask, equipped with a magnetic stirrer, was charged with $Pd(dba)_2$ (29 mg, 0.05 mmol) and tfp (23 mg, 0.10 mmol) in dry THF (1 ml). After formation of the active catalyst ethyl 4-iodobenzoate (191 mg, 0.7 mmol) was added followed by the zinc reagent. The reaction mixture was stirred at r.t. for 16 h, then quenched with NH_4Cl (2 ml), poured into water (50 ml) and extracted with ether (3 × 40 ml). The combined organic fractions were washed with brine (70 ml), then dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography (pentane–ether–TEA 20:1:2) to yield **6a** as a pale yellow oil (868 mg, 81%).

IR (KBr, cm^{-1}): ν 3430 (br), 1712 (w), 1622 (s), 1576 (m), 755 (m), 691 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.33 (s, 1H), 8.21 (s, 1H), 7.88–7.84 (m, 2H), 7.80–7.76

(m, 2H), 7.68 (d, $J = 2.1$ Hz, 1H), 7.38–7.22 (m, 1H), 7.15 (dd, $J = 2.1$ and 8.4 Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 2.43 (q, $J = 7.2$ Hz, 2H), 0.93 (t, $J = 7.3$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 189.3, 160.8, 160.7, 151.8, 136.3, 132.0, 130.9, 130.0, 129.5, 129.3, 127.9, 127.4, 123.0, 118.8, 46.7, 11.9. MS (EI, 70 eV): 432 (100), 355 (48), 327 (47), 281 (13), 254 (22), 77 (9). HRMS: Calc. for $C_{29}H_{24}N_2O_2$: 432.1838. Found: 432.1851%.

The products **6b**–**h** were prepared according to this method.

*4.7.1. 2′,5′-Bis{[(E)-phenylmethylidene]amino}[1,1′-biphenyl]-4-carbonitrile (**6b**)*

From **2** (410 mg, 1 mmol) and 4-iodobenzonitrile (160 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6b** as a yellow oil (162 mg, 60%).

IR (KBr, cm^{-1}): ν 3407 (m), 2960 (m), 2225 (m), 1618 (s), 1603 (s), 1495 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.35 (s, 1H), 8.31 (s, 1H), 7.63–7.61 (m, 2H), 7.54 (d, $J = 9$ Hz, 2H), 7.41 (d, $J = 9$ Hz, 2H), 7.33–7.24 (m, 6H), 7.18–7.16 (m, 5H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 155.4, 145.5, 144.0, 141.1, 137.9, 135.8, 134.8, 130.1, 129.9, 127.7, 126.9, 126.2, 118.0, 113.1, 109.1. MS (EI, 70 eV): 386 (83), 296 (9), 154 (17), 133 (30), 91 (100). HRMS Calc. for $C_{27}H_{19}N_3$: 385.1579. Found: 385.1568%.

*4.7.2. 4′-Methyl-N²,N²-bis[(E)-phenylmethylidene]-[1,1′-biphenyl]2,5-diamine (**6c**)*

From **2** (410 mg, 1 mmol) and 4-iodo-1-methylbenzene (153 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6c** as a yellow oil (188 mg, 71%).

IR (KBr, cm^{-1}): ν 3419 (br), 3026 (w), 2960 (s), 1594 (m), 1495 (s), 1451 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.32 (s, 1H), 8.30 (s, 1H), 7.64–7.63 (m, 2H), 7.35–7.04 (m, 12H), 6.86 (d, $J = 8.4$ Hz, 1H), 6.56 (d, $J = 2.7$ Hz, 1H), 6.40 (dd, $J = 2.7$ and 8.4 Hz, 1H), 2.28 (s, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 156.6, 130.5, 129.1, 128.9, 128.9, 128.7, 128.6, 127.7, 127.3, 121.3, 119.3, 115.6, 113.1, 35.3. MS (EI, 70 eV): 375 (45), 281 (11), 253 (8), 207 (100). HRMS Calc. for $C_{27}H_{22}N_2$: 374.1783. Found: 374.1799%.

*4.7.3. 4′-Chloro-N²,N²-bis[(E)-phenylmethylidene]-[1,1′-biphenyl]2,5-diamine (**6d**)*

From **2** (410 mg, 1 mmol) and 1-chlor 4-iodobenzene (167 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6d** as a yellow oil (170 mg, 62%).

IR (KBr, cm^{-1}): ν 3436 (br), 2869 (w), 1619 (s), 1577 (m), 1494 (m), 1473 (m), 1450 (m), 688 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.43 (s, 1H), 8.39 (s, 1H), 7.82–7.80 (m, 2H), 7.70–7.67 (m, 2H), 7.39–7.12 (m, 12H), 7.03 (d, $J = 8.4$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 160.1, 150.4, 147.8, 138.2, 136.8, 136.7, 135.8, 133.5, 132.0, 129.3, 129.0, 123.2, 122.3, 121.6, 120.0. MS (EI, 70 eV): 394 (21), 317 (25), 207 (100), 191 (9), 133 (8). Anal. Calc. for $C_{26}H_{19}N_2Cl$: C, 79.08; H, 4.85; N, 7.09. Found: C, 78.90; H, 5.19; N, 6.94%.

*4.7.4. 4′-Methoxy-N²,N²-bis[(E)-phenylmethylidene]-[1,1′-biphenyl]2,5-diamine (**6e**)*

From **2** (410 mg, 1 mmol) and 4-iodoanisol (164 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6e** as a yellow oil (215 mg, 79%).

IR (KBr, cm^{-1}): ν 3430 (br), 3058 (w), 2957 (w), 1624 (s), 1578 (m), 1493 (m), 1451 (m), 1250 (m), 754 (s), 692 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.44 (s, 1H), 8.29 (s, 1H), 7.81–7.79 (m, 2H), 7.60–7.57 (m, 2H), 7.36–6.75 (m, 13H), 3.51 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 160.1, 160.0, 132.0, 131.7, 129.3, 129.2, 129.0, 128.9, 128.7, 123.8, 122.3, 121.8, 120.7, 119.7, 111.1, 55.9. MS (EI, 70 eV): 390 (100), 359 (71), 284 (77), 181 (36), 139 (24). HRMS Calc. for $C_{27}H_{22}N_2O$: 390.1732. Found: 390.1718%.

*4.7.5. Ethyl 2′,5′-bis{[(E)-phenylmethylidene]amino}-[1,1′-biphenyl]-3-carboxylate (**6f**)*

From **2** (410 mg, 1 mmol) and ethyl 4-iodobenzoate (191 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6f** as a yellow oil (188 mg, 62%).

IR (KBr, cm^{-1}): ν 3414 (br), 3060 (w), 2870 (w), 1714 (s), 1623 (s), 1578 (m), 1365 (s), 1270 (s), 692 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.46 (s, 1H), 8.40 (s, 1H), 8.21 (s, 1H), 7.92 (d, $J = 7.8$ Hz, 1H), 7.84–7.67 (m, 5H), 7.38–7.30 (m, 8H), 7.20 (dd, $J = 2.1$ and 8.1 Hz, 1H), 7.06 (d, $J = 8.1$ Hz, 1H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.19 (t, $J = 7.1$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 167.1, 160.4, 150.5, 147.9, 139.8, 136.8, 136.6, 136.0, 135.1, 131.9, 131.7, 130.9, 129.2, 128.7, 128.6, 127.3, 121.8, 61.3, 14.7. MS (EI, 70 eV): 432 (15), 147 (13), 197 (13), 133 (17), 123 (24), 109 (43), 95 (70), 83 (58), 55 (100). HRMS Calc. for $C_{29}H_{24}N_2O_2$: 432.1838. Found: 432.1847%.

*4.7.6. 2′-Methoxy-N²,N²-bis[(E)-phenylmethylidene]-[1,1′-biphenyl]2,5-diamine (**6g**)*

From **2** (410 mg, 1 mmol) and 2-iodoanisol (164 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6g** as a yellow oil (200 mg, 74%).

IR (KBr, cm^{-1}): ν 3429 (br), 2957 (w), 1623 (s), 1600 (m), 1577 (m), 1492 (m), 1452 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.44 (s, 1H), 8.29 (s, 1H), 7.81–7.79 (m, 2H), 7.60–7.57 (m, 2H), 7.36–6.75 (m, 13H), 3.51 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 160.1, 160.0, 132.0, 131.7, 129.3, 129.2, 129.0, 128.9, 128.7, 123.8,

122.3, 121.8, 120.7, 119.7, 111.1, 55.9. MS (EI, 70 eV): 390 (100), 359 (71), 284 (77), 181 (36), 139 (24). HRMS Calc. for $C_{27}H_{22}N_2O$: 390.1732. Found: 390.1748%.

4.7.7. Ethyl 5-(2,5-bis{[(E)-phenylmethylidene]amino}-phenyl-2-furoate (6h)

From **2** (410 mg, 1 mmol) and ethyl 5-iodo-2-furoate (153 mg, 0.7 mmol). Purification by flash chromatography (pentane–ether–TEA 20:1:2) yielded **6g** as a yellow oil (153 mg, 52%).

IR (KBr, cm^{-1}): ν 3421 (br), 1711 (s), 1624 (s), 1578 (m), 1495 (m), 1300 (s), 1208 (m), 1141 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.50 (s, 1H), 8.38 (s, 1H), 7.88–7.84 (m, 4H), 7.45–7.39 (m, 6H), 7.19–7.13 (m, 3H), 6.96 (d, $J = 9$ Hz, 1H), 4.30 (q, $J = 7.2$ Hz, 2H), 1.29 (t, $J = 7.2$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 192.8, 160.8, 160.5, 155.1, 150.4, 147.6, 143.7, 136.5, 132.1, 131.9, 129.1, 129.0, 123.1, 119.6, 118.6, 114.1, 61.3, 14.8. MS (EI, 70 eV): 422 (12), 281 (13), 207 (100), 191 (11), 133 (8), 96 (9). HRMS Calc. for $C_{27}H_{22}N_2O_3$: 422.1630. Found: 422.1647%.

4.8. General procedure for the deprotection of N-phenylmethyleneamine derivatives. Preparation of 2-allyl-1,4-phenylenediamine (9)

2-Allyl-N^1,N^4-di[(*E*)-phenylmethylidene]-benzene-1,4-diamine (324 mg, 1 mmol) was dissolved in methanol (10 ml) and a few drops of a 2 M sulfuric acid were added. The solution immediately became deep red, then decolorized within 30 s. The solution was concentrated in vacuo. The product was purified by cation exchange extraction on a Varian bond elute SCX column. The SCX column was conditioned with 10% acetic acid in methanol, then the product was applied with methanol and the column washed with methanol and acetonitrile. For the elution of the product 10% ammonia in methanol was employed. The product was obtained after concentration of the latter fractions. Yield (140 mg, 95%).

IR (KBr, cm^{-1}): ν 3338 (br), 1620 (m), 1506 (s), 1453 (m). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 6.48–6.38 (m, 3H), 5.90–5.79 (m, 1H), 5.05–4.97 (m, 2H), 3.18–3.15 (m, 6H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 139.2, 137.4, 136.4, 126.2, 118.2, 117.8, 116.4. MS (EI, 70 eV): 148 (100), 133 (47), 121 (24), 77 (15). HRMS Calc. for $C_9H_{12}N_2$: 148.1000. Found: 148.1003%.

Also product **10** was deprotected according to this method.

4.8.1. Ethyl 2′,5′-diamino(1,1′-biphenyl)-4-carboxylate (10)

From **6a** (100 mg, 0.23 mmol). Purification by Varian bond elute SCX column yielded **10** as a yellow oil (54 mg, 93%).

IR (KBr, cm^{-1}): ν 3348 (br), 2981 (w), 1708 (s), 1608 (s), 1513 (m), 1498 (s), 1284 (s), 1103 (s). ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.00 (dd, $J = 2.1$ and 6.6 Hz, 2H), 7.43 (dd, $J = 2.1$ and 6.6 Hz, 2H), 6.58–6.46 (m, 3H), 4.3 (q, $J = 7.2$ Hz, 2H), 3.16 (br, 4H), 1.42 (t, $J = 7.2$ Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 166.9, 144.9, 139.1, 130.3, 129.5, 128.2, 117.9, 117.3, 61.4, 14.7. MS (EI, 70 eV): 256 (100), 228 (82), 211 (6), 183 (49), 154 (9), 91 (22). HRMS Calc. for $C_{15}H_{16}N_2O_2$: 256.1212. Found: 256.1208%.

4.9. General procedure for the deprotection of N,N-diallylamine derivatives: preparation of 2-allyl-1,4-phenylenediamine (9)

In a dry and argon flushed flask $Pd(PPh_3)_4$ (23 mg, 0.02 mmol) and *N*,*N*′-dimethylbarbituric acid (936 mg, 6 mmol) was mixed before adding N^1,N^1,N^4,N^4-tetraallyl-1-allylbenzene-1,4-diamine (150 mg, 0.5 mmol) in dry degassed dichloromethane (3 ml). The suspension was warmed to 35 °C and left for 2 h. After cooling to r.t. the dichloromethane was distilled off and the residue taken up in diethyl ether, then washed with $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, concentrated and purified on a SCX column as described above. Yield (63 mg, 85%).

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