Tetrahedron 65 (2009) 1951–1956

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Direct synthesis of primary arylamines via *C–N* cross-coupling of aryl bromides and triflates with amides

M. Romero, Y. Harrak, J. Basset, J.A. Orúe, M.D. Pujol *

Laboratori de Química Farmacèutica (Unitat associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, Av. Diagonal 643, E-08028 Barcelona, Spain

ARTICLE INFO

Article history:
Received 3 December 2008
Accepted 7 January 2009
Available online 14 January 2009

Keywords:
Arylamination
Coupling
Palladium catalyst
Primary amines
Nucleophilic amides

ABSTRACT

Aryl halides and triflates are coupled with primary amides to give the corresponding arylamines in the presence of a palladium catalyst, a suitable ligand, and a base. The catalyst system performs well for a large number of different substrates at 100–150 °C without solvent, and with low catalyst levels (0.12 mol % Pd). Nicotinamide might be useful as a nitrogen source in the Pd-catalyzed amination reaction.

1. Introduction

N-Arylamines are important compounds, particularly in pharmaceutical research and also as intermediates for organic synthesis.[1] For this reason significant efforts have gone into the development of new methods for their preparation.

In spite of its apparent simplicity the preparation of primary arylamines is some times difficult. The classical protocols for aryl amination involve several steps and are often incompatible with several functional groups and are also limited to determined aromatic compounds. In the classical reactions, the most direct formation of *N*-aryl compounds requires copper salts as the catalyst (Ullmann-type conditions) and usually needs drastic reaction conditions.[2–4]

In the last decade, several research groups such as Buchwald and co-workers[5–8] and Hartwig and co-workers[9–12] reported the palladium-catalyzed coupling of aryl halides with several amino-derivatives. Buchwald and co-workers described the synthesis of *N*-arylamines from aryl benzenesulfonates.[13,14] It is noteworthy that significant progress in palladium-catalyzed amination reactions has been achieved by the research groups of Buchwald and Hartwig, showing good conditions and the tolerance for determined substrates.

In general, some experimental reactions proceed efficiently with determined conditions (catalyst, ligand, base, and temperature) for a specific substrate, but often limitations are found when applying to other substrates, or in other cases where the catalyst system or the ligand is excessively expensive, no commercial available or with difficult manipulation.

Reports from several research groups on the palladium-catalyzed cross-coupling of aryl halides with *N*-derivatives have furnished interesting results but have revealed the need to find new conditions for the preparation of primary arylamines. Several times this aryl amination protocol does not provide direct entry to primary arylamines.

Recently, Gooben and co-workers[15] present new reaction conditions for the coupling of aryl chlorides with primary or secondary amines using air- and water-stable naphtho quinone imidazolin-2-ylidene-palladium(0) as catalyst and KOH as a base.

In the past decade, Buchwald and co-workers[16] have been employed commercial available benzophenone imine as ammonia equivalent for the preparation of primary anilines. This method needs an additional acidic hydrolysis or hydrogenolysis for yielding the primary aniline. This work describes the utility of benzophenone imine for the preparation of primary amines under different conditions according to the starting material, showing the lack of a general protocol.

Moreover, Buchwald and Huang[17] and Hartwig and co-workers[18] have described separately the use of $LiN(SiMe_3)_2$/LiHMDS as a system ammonia equivalent for the Pd-catalyzed coupling of aryl halides. Later, Hartwig and co-workers[19] reported that zinc bis(hexamethyldisilazide) is an ammonia surrogate for the amination of aryl halides better than lithium bis(trimethylsilyl)amide ($LiN(SiMe_3)_2$), but the reaction needs of several additives. Recently,

* Corresponding author. Fax: +34 93 4035941.
E-mail address: mdpujol@ub.edu (M.D. Pujol).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.01.033

Weigand and co-workers[20] reported the use of amine resins as amino group sources in palladium-catalyzed amination of aryl halides. This method served for the preparation of primary anilines only from aryl halides containing electron-withdrawing groups. Copper derivatives[21] have been known to catalyze the amination of bromopyridines under several conditions or the synthesis of primary arylamines using amidine hydrochlorides.[22] Also the use of ammonia as a nucleophile has been reported by several authors but these methods for the synthesis of primary arylamines might not be technically safe and simple (special material, high pressure and high temperature, and limited applications).[23]

2. Results and discussion

This work intends to conversion of aryl bromides or triflates to desired primary anilines using palladium catalyst. Aryl bromides are readily available, more reactive than aryl chlorides, and more stable than aryl iodides. The conditions used for the N-arylation of several substrates were Pd[P(*o*-tolyl)$_3$]$_2$Cl$_2$, chelating ligand 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), and cesium carbonate as the base under argon atmosphere without solvent (Fig. 1).

This protocol has been developed previously by us for the coupling of aryl bromides or triflates with primary or secondary amines.[24] All the reagents can be weighed in contact with air. Some aryl bromides and triflates were tested in our reaction conditions. The obtained arylamines may be isolated and purified without problems.

Primary anilines were prepared in a one-step palladium-catalyzed amination reaction of aryl bromides with amides, opening a new synthetic route to general preparation of primary anilines (Table 1).

Other procedures reported previously, do not provide direct entry to primary arylamines, and additional steps (protection, cleavage) are necessary for protecting or unmasking or the ammonia surrogate is expensive.[25] Recently, Chang and co-workers reported the use of ammonium salts in Cu-catalyzed amination of aryl halides.[26] We have found that the aryl halides react with nicotinamide in the general conditions indicated before, affording the primary arylamines in a one step (Table 1, entries 2, 5, 6, 8–16, and 20–22). Other amides such as acetamide (Table 1, entries 1 and 4), benzamide (Table 1, entries 3 and 7), isonicotinamide (Table 1, entries 17 and 18) or formamide (Table 1, entry 19) can be used but gave the desired amines in low yield. Coupling of 3-bromopyridine with nicotinamide worked well, providing the 3-aminopyridine in acceptable yield (Table 1, entry 5). Acetamide showed lower reactivity (Table 1, entry 4).

The reactivity of 2-bromopyridine is less than the 3-bromopyridine and gave a mixture of 2-aminopyridine and the intermediate amide (Table 1, entry 6). For 2,6-dibromopyridine, coupling with nicotinamide occurred at the 2-position exclusively (Table 1, entries 8 and 9). Using this procedure, unfortunately, *p*-methoxybromobenzene was not converted to the desired aniline, only the intermediate amide and poor conversion were observed (Table 1, entry 10), but with prolonged time of reaction the yield was increased (Table 1, entry 11) while the methylsulfonyl bromobenzene give a mixture of the expected amine and the corresponding diaryl amine (Table 1, entry 12). The high reactivity of the aryl bromide in the reaction mixture led to the formation of the double arylated amine in 21% yield (Table 1, entry 12). Results demonstrate the expected major reactivity of the bromobenzene containing electron-withdrawing substituents (entries 14 and 15) in comparison with the presence of electron-donating groups (entries 10, 11, and 13).

The 6-amino-[1,4]-benzodioxin was obtained directly from the corresponding electron-rich aryl bromide in moderate yield 65% (Table 1, entry 13). Yields were low for the coupling of isonicotinamide than nicotinamide (compare entry 15 vs 17; entry 16 vs 18).

An *ortho*-substituent on the aryl bromides decreases the coupling yields. Thus the steric hindrance has influence in both electron-rich and electron-deficient aryl halides (compare entry 20 vs 11; and 21 vs 16).

These results demonstrate that Pd-catalyzed aminations using nicotinamide as the ammonia surrogates is a new method for the preparation of primary anilines with interesting yields in one pot reaction. The ease of deprotection is produced in the basic media of the reaction. To determine the relative hydrolysis, the reaction (Table 1, entry 14) was stopped at 45 min, the compounds were separated, and the intermediate arylamide was detected by NMR analysis.[27] After the hydrolysis of the resulting arylamide with Cs_2CO_3 in toluene with open flask gave the *p*-cyanoaniline in quantitative yield improving the hydrolysis process at high temperatures.

Triflates are not commercially available and therefore it had to be synthesized first.[28] It is important to mention that the procedure for the preparation of aryl triflates is very efficient. The used reaction conditions [Pd[P(*o*-tolyl)$_3$]$_2$Cl$_2$, (BINAP), and cesium carbonate] for the preparation of primary amines were tested previously by us for the amination of aryl triflates,[24] and now extended to other substrates, the new results are summarized in Table 2. The primary arylamines was obtained in moderate to excellent yields (Table 2, entries 1–4). In the preparation of naphthylamine, aryl bromide and aryl triflate gave comparable yield (Table 1, entry 2 vs Table 2, entry 4). While poor-aryl bromides gave best yields than the corresponding triflates, the electron-rich bromides were less effective than the aryl triflate in the amination reaction (Table 1, entry 11 vs Table 2, entry 3). In this paper we showed that the palladium-catalyzed amination of aryl bromides or aryl triflates methodology can be applied to the preparation of aryldiamines.

Attempts to extend our method to diaryl halides or diaryl triflates were successful for benzene derivatives (Table 1, entry 22; Table 2, entries 6 and 7) but we found problems for the pyridine analogues (Table 1, entry 8). The preparation of the diamino-lactona (Table 2, entry 7) is complicated; in this case 44% of the pure isolated diamine was obtained, indicating that the lactone group was compatible with this reaction conditions. We found that the coupling reaction using nicotinamide is effective for the preparation of arylamines and the nicotinamide can be considered as a new and efficient ammonia equivalent not tested in previous palladium-catalyzed *C–N* cross-coupling approaches. Moreover the nicotinamide is a more economical ammonia precursor than other reagents presented previously.

Reactions as in entries 15, 16 (Table 1) and 1, 6 (Table 2) were carried out from 5 g of starting aryl bromide or triflate and the yields were 88, 90, 80, and 53% respectively proving that this methodology can be able for multigram scale. Only 0.12 mol % of palladium catalyst was needed for the formation of the desired arylamines.

Looking at the results obtained in Tables 1 and 2, one can conclude that this methodology is interesting to prepare the desired arylamines or aryldiamines from the corresponding aryl bromides or aryl triflates. Efforts to expand the reaction scope are in progress in our laboratory.

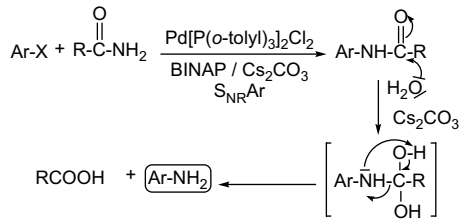
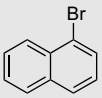
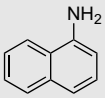
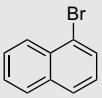
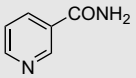
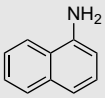
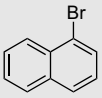
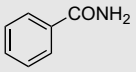
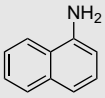
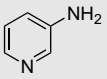
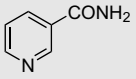
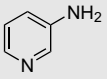
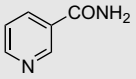
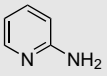
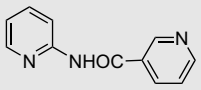
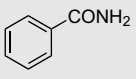
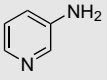
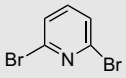
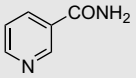
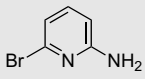
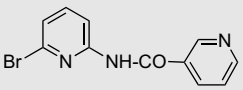
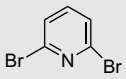
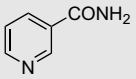
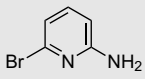
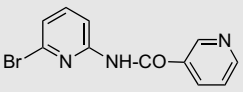
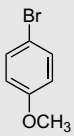
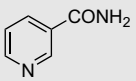
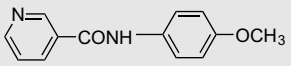
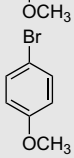
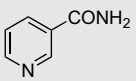
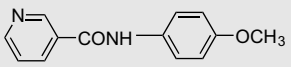
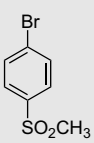
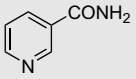
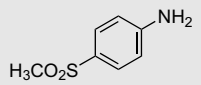
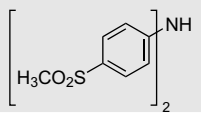


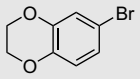
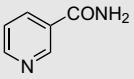
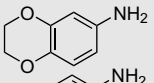
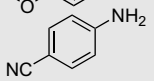
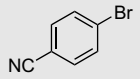
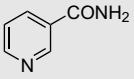
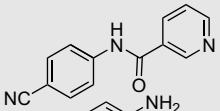
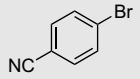
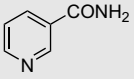
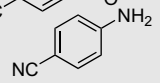
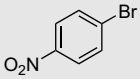
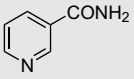
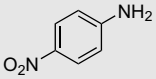
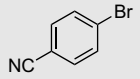
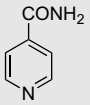
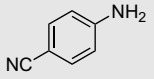
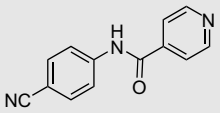
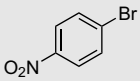
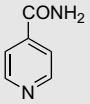
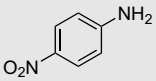
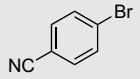
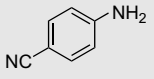
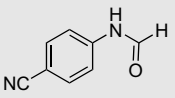
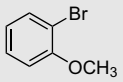
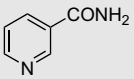
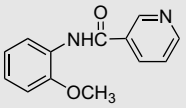
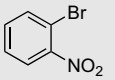
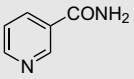
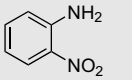
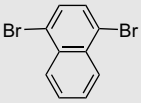
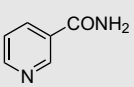
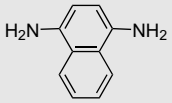
Figure 1. A mechanism for the cross-coupling N-arylation from aryl halides and primary amides.

Table 1
Palladium-catalyzed formation of primary amines from aryl halides

Entry	Ar–X	R^1R^2NH	Time	Product	Yield[a] (%)
1		CH_3CONH_2	2 h		54
2			2 h		75
3			16 h		5
4		CH_3CONH_2	2 h		51
5			2 h		83
6			16 h	 	31 83[27]
7			16 h		12
8			24 h	 	36 52
9			72 h	 	42 24
10			24 h		15[28]
11			72 h		79
12			2 h	 	42 21

(*continued on next page*)

Table 1 (*continued*)

Entry	Ar–X	R^1R^2NH	Time	Product	Yield[a] (%)
13			16 h		65
					10
14			45 min		
					52
15			6 h		88
16			6 h		90
17			24 h		69
					10[29]
18			24 h		71
19		$HCONH_2$	24 h		5
					38
20			72 h		38[30]
21			6 h		56
22			24 h		56

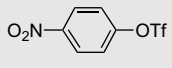
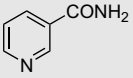
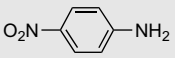
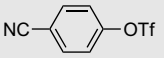
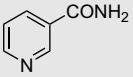
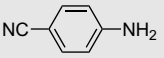
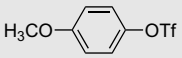
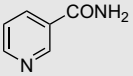
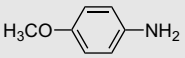
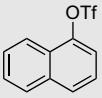
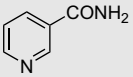
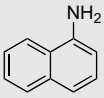
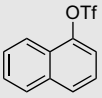
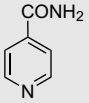
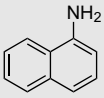
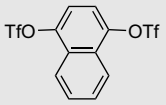
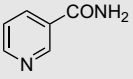
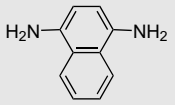
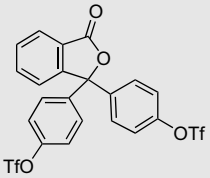
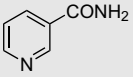
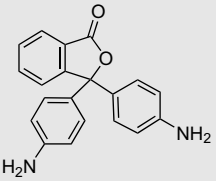
[a] Yields reported correspond to analytically pure isolated compounds (average of two or three runs). $Pd[P(o\text{-tolyl})_3]_2Cl_2$, cesium carbonate, and BINAP(±) were used in all assays. The reactions were conducted at 150 °C.

3. Experimental section

3.1. General

Melting points were obtained on an MFB-595010M Gallenkamp apparatus in open capillary tubes and are uncorrected. IR spectra were obtained using an FTIR Perkin–Elmer 1600 Infrared Spectrophotometer. Only noteworthy IR absorptions are listed (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 (200 and 50.3 MHz, respectively) or Varian Gemini-300 (300 and 75.5 MHz) Instrument using $CDCl_3$ as solvent with tetramethylsilane as internal standard or $(CD_3)_2CO$. Other ^1H NMR spectra and heterocorrelation ^1H–^{13}C (HMQC and HMBC) experiments were recorded on a Varian VXR-500 (500 MHz). Mass spectra were recorded on a Hewlett-Packard 5988-A. Column chromatography was performed with silica gel (E. Merck, 70–230 mesh). Reactions were monitored by TLC using 0.25 mm silica gel F-254 (E. Merck). Microanalysis was determined on a Carlo Erba-1106 analyzer. All reagents were of commercially quality or were purified before use. Organic solvents were of analytical grade or were purified by standard procedures. All the commercially available reagents used were purchased from *Aldrich Chemical Co.* and were used without previous purification. The catalyst was acquired from *Strem* (Chemicals for Research).

Table 2
Palladium-catalyzed formation of primary amines from triflates

Entry	Ar–X	R^1R^2NH	Time	Product	Yield[a] (%)
1			16 h		80
2			16 h		83
3			72 h		52
4			16 h		76
5			16 h		65
6			16 h		53
7			16 h		44

[a] Yields reported correspond to analytically pure isolated compounds (average of two or three runs). $Pd[P(o\text{-tolyl})_3]_2Cl_2$, cesium carbonate, and BINAP(±) were used in all assays. The reactions were conducted at 150 °C.

3.2. Aryl triflates. General procedure

The starting triflates were prepared by treatment of the corresponding phenol (1 mmol) with triflate anhydride (1.2 mmol) in dichloromethane (10 mL) in the presence of triethylamine (1.2 mmol) at 0 °C. The resulting mixture was stirred at this temperature for 90 min. The reaction was performed under an argon atmosphere. The solvent was removed and the crude of reaction was directly purified by silica gel column chromatography (hexane/ethyl acetate).

3.2.1. 3,3-Bis(4-trifluoromethylsulfonyloxyphenyl)-1(3H)-isobenzofuranone (Table 2, entry 7)

IR (KBr) ν (cm^{-1}): 1560 (C=C), 1425 (S=O), 1210 (Ar–O). ^1H NMR (200 MHz, acetone-d_6) δ (ppm): 7.29 (d, J=8.2 Hz, 4H, *ortho*-phenyl), 7.43 (d, J=8.2 Hz, 4H, *meta*-phenyl), 7.52 (d, J=8 Hz, H-4), 7.61 (t, J=8 Hz, 1H, H-5), 7.78 (t, J=8 Hz, 1H, H-6), 8.00 (d, J=8 Hz, 1H, H-7). ^{13}C NMR (50.3 MHz, acetone-d_6) δ (ppm): 100.2 (C, C-3), 116.8 (CH, C-3′, C-5′ (×2)), 118.6 (C, CF_3 (×2)), 127.2 (CH, C-6), 128.1 (CH, C-4), 129.3 (C, C-7a), 130.2 (CH, C-2′, C-6′ (×2)), 132.1 (CH, C-7), 134.2 (CH, C-5), 138.0 (C, C-1′ (×2)), 153.2 (C, C-4′ (×2)), 158.3 (C, C-6′), 150.1 (CH, C-6), 167.4 (C, CO). Anal. Calcd for $C_{22}H_{12}F_6O_8S_2$: C 45.38%; H 2.09%; F 19.58%. Found: C 45.67%; H 2.34%; F 19.86%.

3.3. Amination of aryl halides (Tables 1 and 2). General procedure

A flask was charged with aryl halide or aryl triflate (1 mmol), amide (2 mmol), cesium carbonate (2 mmol), $Pd[P(o\text{-tolyl})_3]_2Cl_2$ (0.12 mol % Pd), and BINAP (0.075 mmol) under argon without addition of solvent (just a drop of toluene was added only in exceptional cases). The flask was hermetically closed, and the mixture was heated at 100–150 °C (after the substrate and all reagents have been added without any period of incubation) with stirring until the starting material has been completely consumed as analyzed by TLC. The mixture was then allowed to cool to room temperature with the flask opened, water was added (15 mL) and was taking up in dichloromethane (15 mL), filtered, and concentrated. The crude product was then purified further by flash chromatography on silica gel, eluting with mixtures of hexane/ethyl acetate. Yields reported correspond to analytically pure isolated compounds.

The spectroscopic data of the known compounds is in full agreement with that obtained from an authentic sample purchased from *Aldrich Chemicals Co*. Combustion analyses were obtained for all new compounds, and for compounds which had been previously reported with limited analysis.

3.3.1. N-(6-Bromopyridin-2-yl)nicotinamide (Table 1, entries 8 and 9)

IR (KBr) ν (cm^{-1}): 3000 (NH), 2912 (C–H), 1674 (C=O). ^1H NMR (200 MHz, acetone-d_6) δ (ppm): 7.45 (d, J=8 Hz, 1H, H-3′), 7.58 (m, 1H, H-5), 7.81 (t, J=8 Hz, H-4′), 8.36 (d, J=8 Hz, 1H, H-5′), 8.46 (m, 1H, H-3), 8.81 (dd, J=1, 6 Hz, 1H, H-6), 9.21 (d, J=1 Hz, 1H, H-2). ^{13}C NMR (50.3 MHz, acetone-d_6) δ (ppm): 110.4 (CH, C-3′), 118.6 (CH, C-5′), 124.2 (CH, C-5), 131.6 (C, C-3), 138.0 (CH, C-4), 140.2 (CH, C-4′), 144.3 (C, C-6′), 150.1 (CH, C-6), 154.8 (CH, C-2), 159.0 (C, C-2′), 166.4 (C, CO). Anal. Calcd for $C_{11}H_8BrON_3$: C 47.51%; H 2.90%; N 15.11%. Found: C 47.86%; H 2.78%; N 14.78%.

3.3.2. N-(4-Cyanophenyl) nicotinamide (Table 1, entry 14)

IR (KBr) ν (cm^{-1}): 3165 (NH), 2928 (C–H), 2230 (CN), 1654 (C=CO). ^1H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.52 (m, 1H, H-5), 7.78 (d, J=8.8 Hz, 2H, H-2′, and H-6′), 8.06 (d, J=8.8 Hz, 2H, H-3′, H-5′),

8.32 (d, J=7 Hz, 1H, H-4), 8.80 (d, J=5 Hz, 1H, H-6), 9.20 (d, J=2.4 Hz, 1H, H-2). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ (ppm): 108.3 (C, C-4′), 120.8 (C, CN), 122.4 (CH, C-2′, C-6′), 125.4 (CH, C-5), 132.4 (C, C-3), 134.9 (CH, C-3′, C-5′), 137.6 (CH, C-4), 145.5 (C, C-1′), 151.1 (CH, C-6), 154.4 (CH, C-2), 166.7 (C, CO). Anal. Calcd for $C_{13}H_9ON_3$: C 69.95%; H 4.06%; N 18.82%. Found: C 70.22%; H 4.42%; N 18.46%.

3.3.3. 3,3-Bis(4-aminophenyl)-1(3H)-isobenzofuranone (Table 2, entry 7)

IR (KBr) ν (cm^{-1}): 3262 (OH), 2922 (C–H), 1600 (C=C), 1261 (Ar–O), 1080 (C–O). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 6.74 (d, J=8 Hz, 4H, *ortho*-amine), 7.02 (d, J=8 Hz, 4H, *meta*-amine), 7.46 (m, 2H, Ar), 7.62 (d, J=7.6 Hz, 1H, H-4), 7.82 (d, J=7.2 Hz, 1H, H-7). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 90.2 (C, C-3), 115.3 (CH, *ortho*-amine (×4)), 119.8 (C, C-1′ (×2)), 120.9 (CH, C-4), 121.4 (CH, C-6), 128.2 (CH, *meta*-amine (×2)), 128.7 (CH, C-7), 130.9 (C, C-7a), 131.6 (CH, C-5), 140.5 (C, C-3a), 144.2 (C, C-4′), 165.8 (C, CO). Anal. Calcd for $C_{20}H_{18}O_2N_2$: C 75.45%; H 5.70%; N 8.80%. Found: C 75.21%; H 5.93%; N 8.42%.

Acknowledgements

Financial support for this work was provided by the *Ministerio de Ciencia y Tecnología* (CTQ2007-60614/BQU), and the *Departament d'Universitats, Recerca i Societat de la Informació de la Generalitat de Catalunya,* Spain (2005-SGR-00180). One of us (J.B.) acknowledges the *Generalitat de Catalunya* for the doctoral fellowship.

References and notes

1. Oshiro, Y.; Sato, S.; Kurahashi, N.; Tanaka, T.; Kikuchi, T.; Tottori, K.; Uwahodo, Y.; Nishi, T. *J. Med. Chem.* **1998**, *41*, 658–667.
2. Wiingarten, H. *J. Org. Chem.* **1964**, *29*, 977–978.
3. Paine, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 1496–1502.
4. Shirota, Y.; Kobata, T.; Noma, N. *Chem. Lett.* **1989**, 1145–1148.
5. Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215–7216.
6. Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264–1267.
7. Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *52*, 7525–7546.
8. (a) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144–1157; (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 6043–6048; (c) Ikawa, T.; Barder, T. E.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 13001–13007.
9. Mann, G.; Hartwig, J. F.; Driver, M. S.; Fernández-Rivas, C. *J. Am. Chem. Soc.* **1998**, *120*, 827–828.
10. Hartwig, J. F. *Synlett* **1996**, 329–340.
11. Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217–7218.
12. Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067.
13. (a) Ahman, J.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6363–6366; (b) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653–6655.
14. Wolfe, J. P.; Ahman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6367–6370.
15. Gooben, L. J.; Paetzold, J.; Briel, O.; Rivas-Nass, A.; Karch, R.; Kayser, B. *Synlett* **2005**, 275–278.
16. Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 10251–10252.
17. Buchwald, S. L.; Huang, X. *Org. Lett.* **2001**, *3*, 3417–3419.
18. Lee, S.; Jorgensen, M.; Hartwig, J. F. *Org. Lett.* **2001**, *3*, 2729–2732.
19. Lee, D.-Y.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1169–1172.
20. Weigand, K.; Pelka, S. *Org. Lett.* **2002**, *4*, 4689–4692.
21. (a) Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164–5173 and references cited therein; (b) Lang, F.; Zewge, D.; Houpis, I. N.; Volante, R. P. *Tetrahedron Lett.* **2001**, *42*, 3251–3254; (c) Jiang, D.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2007**, *72*, 672–674; (d) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42* 5400–5449.
22. Gao, X.; Fu, H.; Qiao, R.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2008**, *73*, 6864–6866.
23. (a) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10028–10029; (b) Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354–10355.
24. (a) Harrak, Y.; Romero, M.; Constans, P.; Pujol, M. D. *Lett. Org. Chem.* **2006**, *3*, 29–35; (b) Romero, M.; Harrak, Y.; Basset, J.; Ginet, L.; Constans, P.; Pujol, M. D. *Tetrahedron* **2006**, *62*, 9010–9016.
25. (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805–818; (b) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125–146.
26. Kim, J.; Chang, S. *Chem. Commun.* **2008**, 3052–3054.
27. Blanco, M. M.; Levin, G. J.; Schapira, C. B.; Perillo, I. *Heterocycles* **2002**, *57*, 1881–1890.
28. Chen, B.; Jiao, K.; Song, H. *Huaxue Xuebao* **1986**, *44*, 417–420; *CAN* **1986**, *106*, 67059.
29. Yoshikawa, M.; Motoshima, K.; Fujimoto, K.; Tai, A.; Kakuta, H.; Sasaki, K. *Bioorg. Med. Chem.* **2008**, *16*, 6027–6033.
30. Correa, A.; Elmore, S.; Bolm, C. *Chem.—Eur. J.* **2008**, *14*, 3527–3529.