Tetrahedron 65 (2009) 1500–1503

Contents lists available at ScienceDirect

Tetrahedron

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

Copper(I)-catalyzed S-arylation of thiols with activated aryl chlorides on water

María Teresa Herrero, Raul SanMartin *, Esther Domínguez *

Kimika Organikoa II Saila, Zientzia eta Teknologia Fakultatea, Euskal Herriko Unibertsitatea, PO Box 644, 48080 Bilbao, Spain

ARTICLE INFO

Article history:
Received 14 October 2008
Received in revised form 10 November 2008
Accepted 20 November 2008
Available online 27 November 2008

ABSTRACT

Copper chloride-catalyzed S-arylation of arenethiols is effected with activated aryl chlorides in neat water by using ethylenediamine as the pair ligand/base. This convenient, environmentally more friendly procedure for the coupling of aryl chlorides allows the arylation between sterically demanding coupling partners.

1. Introduction

C(aryl)–S bonds are present in a large number of molecules with interest as pharmaceuticals and as useful polymeric materials. For this reason the development of efficient S-arylation methods is a subject of interest in organic chemistry.[1,2] Unfortunately, traditional methods for the formation of diaryl sulfides often require more than stoichiometric amounts of metals and harsh reaction conditions. For example, coupling of thiolates with aryl halides involves the use of polar solvents such as toxic HMPA at high temperatures (around 200 °C), and reduction of aryl sulfones and sulfoxides requires strong reducing agents such as DIBALH or LAH.[3] On the other hand, modern transition-metal-catalyzed cross-coupling reactions of aryl halides with thiols enable the synthesis of aryl sulfides in good yields under milder reaction conditions.[4] Despite the early work of Migita and co-workers,[5] catalytic methods for the S-arylation of thiols have not received much attention compared with metal-catalyzed formation of *N*-aryl or *O*-aryl bonds until very recent times. In this context, C–S bond formation reactions catalyzed by transition metals such as palladium,[6] nickel,[7] cobalt,[8] iron[9] or copper[10] have been reported during the last years. Nevertheless, the development of Cu-catalyzed methods for arylation of thiols is still attractive owing to the advantages of copper over other metals, like its price and minor toxicity.

In this sense, metal-catalyzed processes in green media are interesting not only from an economical perspective but also because of its more limited environmental impact, an aspect of the synthetic procedures that cannot be overlooked nowadays. In fact, over the last years the increasing worldwide public interest in environmental issues had led to a change in chemical research strategies concerning the development of sustainable protocols and the use of nontoxic chemicals, renewable reagents and environmentally friendly solvents.[11]

Considering the lack of green chemical methods to synthesize aryl thioethers and their considerable interest, our group developed an efficient protocol for the copper chloride-catalyzed S-arylation of aryl thiols with aryl iodides and bromides in water.[10h] Then, in order to further develop the method we decided to extend it to the employment of aryl chlorides as arylating agents because of their wider availability and lower cost. Furthermore, only few examples for metal-catalyzed S-arylation of thiols involving aryl chlorides have been reported.[6c,j,10c,12]

2. Results and discussion

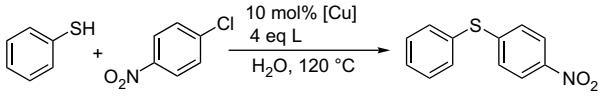
Initially, we studied the reaction of thiophenol **1a** and phenyl chloride **2a** under conditions reported for S-arylation of thiols with aryl iodides.[10h] However, the corresponding coupling product **3a** was not detected in the reaction mixture, even when reaction time was prolonged to 72 h. Negligible yields were also obtained when other copper sources (CuI, Cu_2O, Cu, Cu/Cu_2O, $Cu(OAc)_2$, $Cu(OTf)_2$), amines (ethylendiamine, DABCO, TMEDA, DMEDA, D-glucosamine, urea) or combinations of diamines and different bases (K_2CO_3, $CsCO_3$, KOH, K_3PO_4) were employed.

Despite this unsatisfactory outcome, we decided to test the methodology in the coupling of activated aryl chlorides. Indeed, the presence of electron-withdrawing substituents in the aryl ring could possibly facilitate the otherwise troublesome oxidative addition step. As an additional measure, water was degassed in order to avoid undesirable side-reactions like disulfide formation. We found that previously reported conditions worked quiet well for the S-arylation of thiophenol **1a** with 4-nitrophenylchloride **2a** (Table 1, entry 1). Aiming at an improvement of the latter results, we screened a variety of amine ligands using 10 mol % CuCl as the copper source (Table 1, entries 2–9; Fig. 1).[13] It was observed that the best yields were obtained when ethylenediamine (EDA) or tetramethylethylenediamine (TMEDA), amines of quite different

* Corresponding authors. Tel.: +34 94 601 5435; fax: +34 94 601 2748.
E-mail address: raul.sanmartin@ehu.es (R. SanMartin).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.11.062

Table 1
Screening of the reaction conditions[a,b]



1a **2a** **3a**

Entry	[Cu]	Ligand	Yield[c] (%)
1	CuCl	I	65
2	CuCl	II	80
3	CuCl	III	85
4	CuCl	IV	90
5	CuCl	V	60
6	CuCl	VI	60
7	CuCl	VII	70
8	CuCl	VIII[d]	22
9	CuCl	IX	19
10	CuI	IV	88
11	Cu_2O	IV	50
12	Cu	IV	58
13	Cu/Cu_2O	IV	80
14	$Cu(OAc)_2$	IV	48
15	$Cu(OTf)_2$	IV	80

[a] Reaction conditions: 0.5 mmol PhSH, 1 mmol ArCl, 10 mol % [Cu], 2 mmol L, 6.5 mL of H_2O, 120 °C.
[b] H_2O was degassed.
[c] Yield of isolated product.
[d] Cs_2CO_3 (2 mmol) was added to D-glucosamine hydrochloride.

basicity, was employed. These comparable results are in agreement with the hypothesis that, unlike other coordinating and structural properties, the basicity of the amine does not have a determining role in the process.

We then examined the effect of the copper source on the coupling reactions (Table 1, entries 4, 10–15).[6c,j,12] Cu(I), Cu(II) and Cu(0) demonstrated the ability to catalyze the reaction, thus suggesting common oxidation states in the catalytic cycle,[14] but Cu(I) salts were found to be superior.

To expand the scope of the reaction, a number of aryl thiols and activated aryl chlorides were employed. As can be seen in Table 2, a number of diaryl sulfides **3** were obtained in moderate to good yields. It should be pointed out the similar or higher yields obtained for some already known sulfides, which had been also prepared from aryl iodides and bromides (entries 1-3).[10d,e,h] Nevertheless, longer reaction times were required when using chlorides as arylating agents.

Interestingly, the present procedure was shown to work particularly well in the coupling of partners bearing sterically demanding *ortho*-substituents such as acetyl and nitro groups or a fused benzene ring. In fact, the coupling of thiols **1** with *o*-chloroacetophenone **2b**, 2-nitro-4-trifluoromethyl-chlorobenzene **2c** and 2-chloro-5-trifluoromethylacetophenone **2d** was found to proceed in good to excellent yields (entries 2, 6, 10 and 3, 16 and 4,

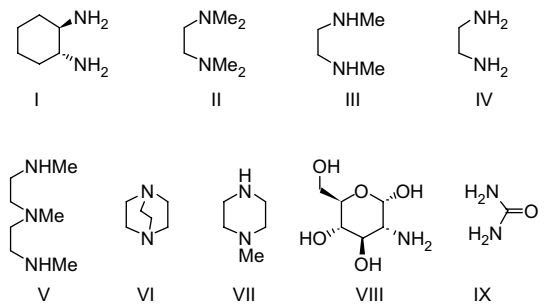
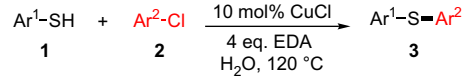
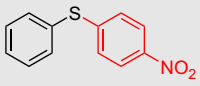
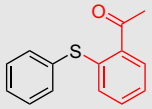
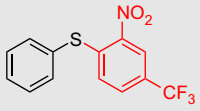
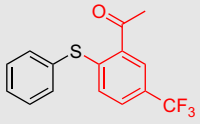
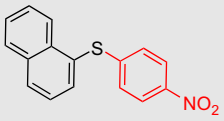
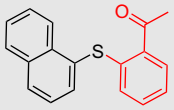
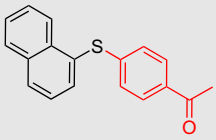
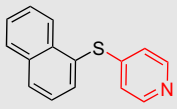
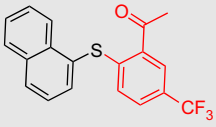
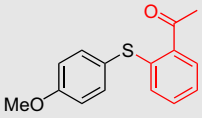
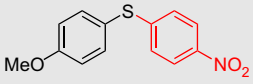
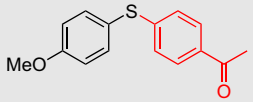
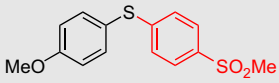
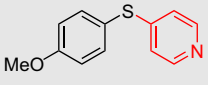


Figure 1. Ligands employed for the S-arylation assays.

Table 2
Coupling of aryl chlorides with aryl thiols[a,b]

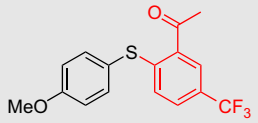
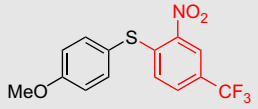


1 **2** **3**

Entry	Product	**3** (%)
1		**3a** (90)[c]
2		**3b** (95)[c]
3		**3c** (97)[c]
4		**3d** (92)[c]
5		**3e** (65)[d]
6		**3f** (95)[c]
7		**3g** (23)[c]
8		**3h** (85)[c]
9		**3i** (70)[c]
10		**3j** (70)[c]
11		**3k** (77)[c]
12		**3l** (39)[d]
13		**3m** (50)[c]
14		**3n** (65)[c]

(*continued on next page*)

Table 2 (*continued*)

Entry	Product	**3** (%)
15		**3o** (70)[c]
16		**3p** (95)[d]

[a] Reaction conditions: 0.5 mmol PhSH, 1 mmol ArCl, 10% CuCl, 2 mmol EDA, 6.5 mL H_2O, 120 °C.
[b] H_2O was degassed.
[c] Yield of isolated product.
[d] Determined by ^1H NMR on the basis of the amount of starting Ar^1SH. Bis-(ethylene glycol) dimethyl ether was used as internal standard.

9, 15, respectively). Surprisingly, the reactions with *p*-chloroacetophenone **2e**, however, afforded the corresponding diaryl sulfides **3** only in moderate yields (entries 7 and 12). In contrast, when a highly electron-withdrawing nitro group was the substituent in *para* position excellent yields were achieved (entries 1, 5 and 11). Similarly, the employment of *p*-chloropyridine provided the corresponding diaryl sulfides in good yields (entries 8 and 14).

3. Conclusion

In summary, we have reported a practical, environmentally more friendly procedure for the copper-catalyzed S-arylation of thiols with activated chlorides on water that proceeds in good yields. The protocol, although limited to the coupling of aryl chlorides substituted with electron-withdrawing groups, is of potentially practical utility because of the low cost and availability of aryl chlorides and the advantages associated to the use of water.

4. Experimental section

4.1. General remarks

All reagents employed in the assays were purchased and used without further purification. The reactions were carried out under argon and water was distilled and degassed. TLC was carried out on silica gel (silica gel 60 F_{254}, Merck), and the spots were located with UV light. Flash chromatography was carried out on SiO_2 (silica gel 60, Merck, 230–400 mesh ASTM). Drying of organic extracts after work-up of reactions was performed over anhydrous Na_2SO_4. IR spectra were recorded on a Perkin–Elmer 1600-FT infrared spectrophotometer as KBr plates or as neat liquids and peaks are reported in cm^{-1}. Melting points were measured in a Büchi apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution in a Bruker AC-300 and chemical shifts are reported in parts per million downfield (d) from Me_4Si. Low and high resolution mass spectra were recorded at the University of Vigo on an VG Autospec M instrument.

4.2. General method for the synthesis of diaryl thiols 3

A screw-capped tube was charged with thiol **1** (0.5 mmol), aryl chloride **2** (1.0 mmol), CuCl (0.05 mmol), ethylenediamine (4.0 mmol) and degassed water (6.5 mL) under nitrogen at room temperature. The reaction mixture was heated to 120 °C for 36 h, allowed to cool to room temperature and the resulting mixture was extracted with CH_2Cl_2 (3×5 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to afford the corresponding compound. All physical data of the known compounds (**3a–c**,[6f,15] **3e**,[10d] **3j–n** [16] and **3p**[6f]) were in agreement with those reported in the literature.

4.2.1. 2-Acetyl-4-trifluoromethylphenyl phenyl sulfide (*3d*)

Yield 136 mg (0.46 mmol), 92%, yellow oil. IR (neat): ν (cm^{-1}) 3064, 1680, 1611, 1334, 1265, 1233, 1177, 1124. ^1H NMR (300 MHz, $CDCl_3$): δ 8.05 (d, J=6.0 Hz, 1H), 7.52–7.57 (m, 2H), 7.26–7.49 (m, 4H), 6.94 (d, J=8.5 Hz, 1H), 2.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.7, 147.9, 135.5, 133.4, 131.7, 130.0, 129.6, 128.1 (q, J=3 Hz), 127.9, 127.3 (q, J=4 Hz), 126.2 (q, J=33 Hz), 123.6 (q, J=272 Hz), 27.9. MS (EI) m/z: 297 (M+1, 15), 296 (M, 100), 282 (15), 281 (77), 261 (29), 253 (10), 234 (10), 233 (46), 205 (45), 202 (12), 184 (55), 183 (15). HRMS (EI): calculated for $C_{15}H_{11}F_3OS$ 296.0483; found 296.0486.

4.2.2. 2-Acetylphenyl naphthyl sulfide (*3f*)

Yield 132 mg (0.47 mmol), 95%, yellow oil. IR (neat): ν (cm^{-1}) 3053, 1671, 1585, 1458, 1432, 1352, 1247, 1131, 1048. ^1H NMR (300 MHz, $CDCl_3$): δ 7.88–7.82 (m, 3H), 7.55–7.50 (m, 3H), 7.23–7.17 (m, 2H), 6.96–6.91 (m, 1H), 2.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.1, 141.9, 134.7, 133.9, 133.1, 132.1, 131.5, 130.6, 129.3, 128.4, 127.8, 127.7, 127.0, 126.6, 124.4, 28.2. MS (EI) m/z: 279 (M+1, 18), 278 (M, 100), 263 (54), 236 (20), 235 (93), 234 (96), 233 (13), 232 (14), 202 (29), 189 (13), 144 (16), 137 (29), 117 (11). HRMS (EI): calculated for $C_{18}H_{14}OS$ 278.0765; found 278.0768.

4.2.3. 4-Acetylphenyl naphthyl sulfide (*3g*)

Yield 32 mg (0.12 mmol), 23%, white solid. Mp: 88–90 °C. IR (KBr): ν (cm^{-1}) 3052, 1679, 1396, 1356, 1261, 1093, 816. ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (s, 1H), 7.98–7.86 (m, 5H), 7.54–7.42 (m, 3H), 7.31–7.24 (m, 2H), 2.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.0, 144.7, 134.5, 133.8, 133.3, 132.9, 130.3, 129.4, 129.3, 128.9, 127.8, 127.7, 127.6, 127.0, 126.8, 26.4; MS (EI) m/z: 279 (M+1, 17), 278 (M, 83), 263 (100), 235 (29), 234 (58), 202 (24). HRMS (EI): calculated for $C_{18}H_{14}OS$ 278.0765; found 278.0768.

4.2.4. Naphthyl 4-pyridyl sulfide (*3h*)

Yield 100 mg (0.30 mmol), 85%, white solid. Mp: 82–84 °C. IR (KBr): ν (cm^{-1}) 3032, 1568, 1537, 1405, 1354, 809. ^1H NMR (300 MHz, $CDCl_3$): δ 8.34 (d, J=4.4 Hz, 2H), 8.10 (s, 1H), 7.90–7.81 (m, 3H), 7.59–7.50 (m, 3H), 6.97 (d, J=5.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0, 149.4, 135.0, 133.8, 133.3, 131.0, 129.6, 127.8, 127.4, 126.9, 126.6, 120.9. MS (EI) m/z: 338 (M+1, 20), 337 (M, 100), 336 (53), 204 (12). HRMS (EI): calculated for $C_{15}H_{11}NS$ 237.0612; found 237.0611.

4.2.5. 2-Acetyl-4-trifluoromethylphenyl naphthyl sulfide (*3i*)

Yield 121 mg (0.25 mmol), 70%, yellow oil. IR (neat): ν (cm^{-1}) 3055, 1678, 1610, 1334, 1266, 1234, 1177, 1123, 1049, 817. ^1H NMR (300 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.08 (s, 1H), 7.91–7.83 (m, 3H), 7.59–7.49 (m, 3H), 7.38 (d, J=8.5 Hz, 1H), 6.98 (d, J=8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.6, 147.8, 135.5, 133.9, 133.4, 133.3, 131.4, 129.7, 128.9, 128.1, 128.0, 127.9, 127.8, 127.3, 127.2, 126.8, 126.0 (q, J=33 Hz), 123.6 (q, J=272 Hz), 27.9. MS (EI) m/z: 347 (M+1, 26), 346 (M, 100), 331 (40), 303 (50), 302 (21), 284 (12), 283 (57), 235 (13), 234 (70), 232 (12), 205 (22), 144 (17). HRMS (EI): calculated for $C_{19}H_{13}F_3OS$ 346.0639; found 346.0634.

4.2.6. 2-Acetyl-4-trifluoromethylphenyl 4-methoxyphenyl sulfide (*3o*)

Yield 79 mg (0.24 mmol), 70%, white solid. Mp: 76–78 °C. IR (KBr): ν (cm^{-1}) 2939, 1679, 1611, 1592, 1494, 1463, 1335, 1235, 1123, 1045, 830. ^1H NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.48–7.40 (m, 3H), 6.98 (d, J=8.8 Hz, 2H), 6.90 (d, J=8.5 Hz, 1H), 3.86 (s, 1H), 2.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.7, 160.9, 149.3, 137.4, 132.8, 128.1 (q, J=4 Hz), 127.4 (q, J=4 Hz), 127.3, 125.9 (J=33 Hz), 123.7

(J=272 Hz), 121.9, 115.6, 55.4, 28.0. MS (EI) m/z: 327 (M+1, 17), 326 (M, 100), 311 (42), 296 (10), 268 (35), 240 (11), 239 (17), 203 (13), 171 (20), 124 (37), 121 (12). HRMS (EI): calculated for $C_{16}H_{13}F_3O_2S$ 326.0588; found 326.0581.

Acknowledgements

This research was supported by the University of the Basque Country/Regional Government of Biscay/Basque Government (Projects DIPE 06/10, UNESCO07/08 and GIU06/87/IT-349-07) and the Spanish Ministry of Education and Science (MEC CTQ2007-64501). The authors also thank S. A. Petronor for generous donation of hexane.

Supplementary data

^{1}H NMR and ^{13}C NMR spectra of new compounds. This material is available free of charge via ScienceDirect. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.11.062.

References and notes

1. (a) Metzner, P.; Thuillier, A. In *Sulfur Reagents in Organic Synthesis*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Academic: San Diego, CA, 1994; (b) *Organic Sulfur Chemistry: Biochemical Aspects*; Oae, S., Okuyama, T., Eds.; CRC: Boca Raton, FL, 1992; (c) Damani, L. A. *Sulfur-Containing Drugs and Related Compounds—Chemistry, Biochemistry and Toxicology*; Ellis Horwood: Chichester, UK, 1989; Vol. 1, Part A, Chapter 1.
2. (a) Amorati, R.; Fumo, M. G.; Menichetti, S.; Mugnaini, V.; Pedulli, G. F. *J. Org. Chem.* **2006**, *71*, 6325–6332; (b) de Martino, G.; Edler, M. C.; La Regina, G.; Coluccia, A.; Barbera, M. C.; Barrow, D.; Nicholson, R. I.; Chiosis, G.; Brancale, A.; Hamel, E.; Artico, M.; Silvestry, R. *J. Med. Chem.* **2006**, *49*, 947–954; (c) Bley, K. R.; Clark, R. D.; Jahangir, A.; (F. Hoffman-La Roche AG, Switzerland) WO 2005/005394 A2, 2005; [*Chem. Abstr.* **2005**, *142*, 155951]; (d) Alcaraz, M.-L.; Atkinson, S.; Cornwall, P.; Foster, D. M.; Gill, L. A.; Humphries, L. A.; Keegan, P. S.; Kemp, R.; Merifield, E.; Nixon, R. A.; Noble, A. J.; O'Beirne, D.; Patel, Z. M.; Perkins, J.; Rowan, P.; Sadler, P.; Singleton, J. T.; Tornos, J.; Watts, A. J.; Woodland, I. A. *Org. Process Res. Dev.* **2005**, *9*, 555–569; (e) Cai, L.; Chin, F. T.; Pike, V. W.; Toyama, H.; Liow, J. S.; Zoghbi, S. S.; Modell, K.; Briard, E.; Shetty, H. U.; Sinclair, K.; Donohue, S.; Tipre, D.; Kung, M. P.; Dagostin, C.; Widdowson, D. A.; Green, M.; Gao, W.; Herman, M. M.; Ichise, M.; Innis, R. B. *J. Med. Chem.* **2004**, *47*, 2208–2218; (f) Liu, G.; Huth, J. R.; Olejniczak, E. T.; Mendoza, R.; DeVries, P.; Leitza, S.; Reilly, G. F.; Okasinski, G. F.; Fesik, S. W.; Von Geldern, T. W. *J. Med. Chem.* **2001**, *44*, 1202–1210; (g) Liu, G.; Link, J. T.; Pei, Z.; Reilly, E. B.; Leitza, S.; Nguyen, B.; Marsh, K. C.; Okasinski, G. F.; Von Geldern, T. W.; Ormes, M.; Fowler, K.; Gallatin, M. *J. Med. Chem.* **2000**, *43*, 4025–4040; (h) Wang, Y.; Chackalamannil, S.; Hu, Z.; Clader, J. W.; Greenlee, W.; Billard, W.; Binch, H.; Crosby, G.; Ruperto, V.; Duffy, R.; McQuade, R.; Lachowicz, J. E. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2247–2250.
3. (a) Van Bierbeek, A.; Gingras, M. *Tetrahedron Lett.* **1998**, *39*, 6283–6286; (b) Hickman, R. J. S.; Christie, B. J.; Guy, R. W.; White, T. J. *Aust. J. Chem.* **1985**, *38*, 899–904; (c) Lindley, J. *Tetrahedron* **1984**, *40*, 1433–1456; (d) Yamamoto, T.; Sekine, Y. *Can. J. Chem.* **1984**, *62*, 1544–1547.
4. (a) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428; (b) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400–5449; (c) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205–3220.
5. (a) Kosugi, M.; Ogata, T.; Terada, M.; Sano, H.; Migita, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3657–3658; (b) Migita, T.; Shimizu, T.; Asami, Y.; Shiobara, J.; Kato, Y.; Kosugi, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1385–1389.
6. (a) Itoh, T.; Mashe, T. *Org. Lett.* **2007**, *9*, 3687–3689; (b) Barbieri, R. S.; Bellato, C. R.; Dias, A. K. C.; Massabni, A. C. *Catal. Lett.* **2006**, *109*, 171–174; (c) Fernandez-Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. *Chem.—Eur. J.* **2006**, *12*, 7782–7796; (d) Vicente, J.; Abad, J. A.; Lopez-Nicolas, R. M. *Tetrahedron Lett.* **2005**, *46*, 5839–5840; (e) Mispelaere-Canivet, C.; Spindler, J.-F.; Perrio, S.; Beslin, P. *Tetrahedron* **2005**, *61*, 5253–5259; (f) Itoh, T.; Mase, T. *Org. Lett.* **2004**, *6*, 4587–4590; (g) Fernandez Rodrıguez, M. A.; Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 2180–2181; (h) Murata, M.; Buchwald, S. L. *Tetrahedron* **2004**, *60*, 7397–7403; (i) Schopfer, U.; Schlapbach, A. *Tetrahedron* **2001**, *57*, 3069–3073; (j) Li, G. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513–1516; (k) Dickens, M. J.; Gilday, J. P.; Mowlem, T. J.; Widdowson, D. A. *Tetrahedron* **1991**, *47*, 8621–8634; (l) Ishiyama, T.; Mori, M.; Suzuki, A.; Miyaura, N. *J. Organomet. Chem.* **1996**, *525*, 225–231; (m) Zheng, N.; McWilliams, J. C.; Fleitz, F. J.; Armstrong, J. D.; Volante, R. P. *J. Org. Chem.* **1998**, *63*, 9606–9607; (n) Mann, G.; Baranano, D.; Hartwig, J. F.; Rheingold, A. L.; Guzei, I. A. *J. Am. Chem. Soc.* **1998**, *120*, 9205–9219.
7. (a) Jammi, S.; Barua, P.; Rout, L.; Saha, P.; Punniyamurthy, T. *Tetrahedron Lett.* **2008**, *49*, 1484–1487; (b) Saxena, A.; Kumar, A.; Mozumdar, S. *Appl. Catal., A.* **2007**, *317*, 210–215; (c) Zhang, Y.; Ngeow, K. C.; Ying, J. Y. *Org. Lett.* **2007**, *9*, 3495–3498; (d) Yatsumonji, Y.; Okada, O.; Tsubouchi, A.; Takeda, T. *Tetrahedron* **2006**, *62*, 9981–9987; (e) Cristau, H. J.; Chabaud, B.; Chene, A.; Christol, H. *Síntesis* **1981**, 892–894; (f) Millois, C.; Diaz, P. *Org. Lett.* **2000**, *2*, 1705–1708; (g) Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 6895–6903; (h) Takagi, K. *Chem. Lett.* **1987**, 2221–2224.
8. Wong, Y.-C.; Jayanth, T. T.; Cheng, C.-H. *Org. Lett.* **2006**, *8*, 5613–5616.
9. Correa, A.; Carril, M.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 2880–2883.
10. (a) Sperotto, E.; van Klink, G. P. M.; de Vries, J. G.; van Koten, G. *J. Org. Chem.* **2008**, *73*, 5625–5628; (b) Carril, M.; SanMartin, R.; Domínguez, E. *Chem. Soc. Rev.* **2008**, *37*, 639–647; (c) Buranaprasertsuk, P.; Chang, J. W. W.; Chavasin, W.; Hong Chan, P. W. *Tetrahedron Lett.* **2008**, *49*, 2023–2025; (d) Rout, L.; Saha, P.; Jammi, S.; Punniyamurthy, T. *Eur. J. Org. Chem.* **2008**, 640–643; (e) Rout, L.; Sen, T. K.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 5583–5586; (f) Lv, X.; Bao, W. *J. Org. Chem.* **2007**, *72*, 3863–3867; (g) Zhang, H.; Cao, W.; Ma, D. *Synth. Commun.* **2007**, *37*, 25–35; (h) Carril, M.; SanMartin, R.; Dominguez, E.; Tellitu, I. *Chem.—Eur. J.* **2007**, *13*, 5100–5105; (i) Verma, A. K.; Singh, J.; Chaudhary, R. *Tetrahedron Lett.* **2007**, *48*, 7199–7202; (j) Ranu, B. C.; Saba, A.; Jana, R. *Adv. Synth. Catal.* **2007**, *349*, 2690–2696; (k) Chen, Y.-J.; Chen, H.-H. *Org. Lett.* **2006**, *8*, 5609–5612; (l) Zhu, D.; Xu, L.; Wu, F.; Wan, B. *Tetrahedron Lett.* **2006**, *47*, 5781–5784; (m) Deng, W.; Zou, Y.; Wang, V.; Liu, L.; Guo, Q.-X. *Synlett* **2004**, 1254–1258; (n) Bates, C. G.; Saejueng, P.; Doherty, M. Q.; Venkataraman, D. *Org. Lett.* **2004**, *6*, 5005–5008; (o) Wu, Y.-J.; He, H. *Synlett* **2003**, 1789–1790; (p) Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2002**, *4*, 4309–4312; (q) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803–2806; (r) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517–3520; (s) Palomo, C.; Oiarbide, M.; Lopez, R.; Gomez-Bengoa, E. *Tetrahedron Lett.* **2000**, *41*, 1283–1286; (t) Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019–2022.
11. Poliakoff, M.; Fitzpatrick, J. M.; Farren, T. R.; Anastas, P. T. *Science* **2002**, *297*, 807–810.
12. (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176–4211; (b) Li, G. Y. *J. Org. Chem.* **2001**, *66*, 8677–8681; (c) For a recent copper-catalyzed intramolecular O-arylation of chloroarene moieties, see: Barbero, N.; Carril, M.; SanMartin, R.; Domínguez, E. *Tetrahedron* **2007**, *63*, 10425–10432.
13. In our previous research it was observed that the concentration played a critical role in the reaction and 13 mL water mmol^{-1} was concluded to be the optimal value. Thus, 13 mL mmol^{-1} was the concentration employed for all the assays.
14. For a revision on the mechanism of copper-catalyzed cross-coupling reactions, see: Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; See also Ref. 4b.
15. (a) Creed, T.; Leardini, R.; McNab, H.; Nanni, D.; Nicolson, I. S.; Reed, D. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1079–1085; (b) See Ref. 10h.
16. (a) Ueda, I.; Sato, Y.; Maeno, S.; Umio, S. *Chem. Pharm. Bull.* **1975**, *23*, 2223–2231; (b) Sawyer, J. S.; Schmittling, E. A.; Palkowitz, J. A.; Smith, W. J., III. *J. Org. Chem.* **1998**, *63*, 6338–6343; (c) Gorczynski, M. J.; Leal, R. M.; Mooberry, S. L.; Bushweller, J. H.; Brown, M. L. *Bioorg. Med. Chem.* **2004**, *12*, 1029–1036; (d) Brown, M. G. *J. Chem. Phys.* **1960**, *33*, 1881–1882; (e) Pathak, A. K.; Pathak, V.; Seitz, L. E.; Suling, W. J.; Reynols, R. C. *J. Med. Chem.* **2004**, *47*, 273–276.