Palladium and copper-catalysed arylation reactions in the presence of water, with a focus on carbon–heteroatom bond formation†

Mónica Carril, Raul SanMartin* and Esther Domínguez*

Received 20th November 2007
First published as an Advance Article on the web 8th January 2008
DOI: 10.1039/b709565c

Palladium and copper-catalysed arylation of amines, alcohols and thiols, powerful tools for the construction of C–N, C–O and C–S bonds, are typically carried out in organic (and often toxic) solvents. Therefore the use of such a sustainable, benign solvent as water in this context has gained growing attention. This *tutorial review* presents the most recent advances dealing with palladium and copper-catalysed carbon–heteroatom bond formation performed in total or partial aqueous media. The particular and distinctive features of water which are apparently responsible for the acceleration and greater chemoselectivity of the aqueous protocols will also be discussed.

1. Introduction

Over the last century, palladium and copper-catalysed arylation reactions have proved to be a tool of paramount usefulness for the construction of new carbon–heteroatom bonds and, as such, have found increasing utility in industrial processes.[1,2] Given the relevance of these types of reactions, the design of more sustainable protocols, which avoid the toxic and hazardous organic solvents typically used to perform such transformations, is considered of high practical value. This aim is in connection with the emerging field of green chemistry, which aims to reduce the negative impact that chemical activity currently has on the environment. Indeed, the prevention of waste, achievable by means of renewable reagents and benign solvents, is among the most relevant principles that rule green chemistry. Additionally, the use of substances which minimise potential hazards during manipulation is highly encouraged.[3]

In this context, water is regarded as the most benign and safe solvent. Indeed, although historically water has been deliberately excluded from organic reactions, during recent years it has emerged as a highly desirable solvent for organic transformations in terms of cost, safety, availability and environmental concerns.[4–6] In this respect, it must be pointed out that water does not merely act as a solvent but also influences the course of the reaction, as will be discussed in the following section.[7]

2. Role of water

The addition of either catalytic or stoichiometric amounts of water to a significant number of organic reactions has proved to positively affect the reaction outcome, in terms of improved yield, increased reaction rate and better regio-, diastereo- and enantioselectivities, compared to the corresponding anhydrous reaction conditions. In this context, acceleration of organic transformations is one of the most commonly observed effects derived from the addition of water.[7,8]

On the one hand, some authors have ascribed these beneficial effects to hydrophobic interactions between water and organic molecules. Such interactions, which rise from the immiscibility of organic compounds in water, would bring organic substances closer allowing them to react more efficiently, due to the more intimate contact of the substrates with the reagents provoked by the interaction of nonpolar regions of the reactants, a negligible phenomenon in comparison with

---

Zientzia eta Teknologia Fakultatea, Euskal Herriko Unibertsitatea, P.O. Box 644, 48080 Bilbao, Spain. E-mail: raul.sanmartin@ehu.es; Fax: (+ 34) 94 601 27 48; Tel: (+ 34) 94 601 54 35

† Dedicated to Professor Yus on the occasion of his 60th birthday.

Mónica Carril received her PhD degree from University of the Basque Country under the supervision of Dr. SanMartin and Prof. Domínguez in 2006, working with palladium and copper-catalysed arylation reactions in aqueous media and their application to the synthesis of Oxcarbazepine and other pharmaceutically appealing compounds. She has recently moved to the RWTH in Aachen (Germany) for a postdoctoral stay under the supervision of Prof. C. Bolm.

Raul SanMartin is an Associate Professor with tenure at the University of the Basque Country. He obtained his PhD in 1997 then, granted a Doctorate Extraordinary Award, he joined Professor Timothy C. Gallagher's group as a postdoctoral researcher, and was appointed associate professor in 2000. His research interests deal mainly with the development of new catalytic systems for arylation and heteroarylation reactions applying sustainability criteria.

other steric and electronic effects in most organic solvents.[8,9] However, comparative assays performed under solvent-free conditions have shown that the improved contact between the organic reactants, alone, does not account for the better results obtained when using water and suggest the presence of additional interactions, such as hydrogen-type bonds.

On the other hand, Sharpless and co-workers recently reported substantial acceleration of certain types of reactions when performed in neat water, giving rise to a field they described as "on-water" chemistry.[10] Thus, its main principle claims that organic compounds which do not dissolve in water are forced to remain on its surface so that the reaction takes place in the organic/aqueous interface, through small portions of organic solutes that dissolve in the aqueous layer. They noticed that, in this type of system, heterogeneity was essential to observe acceleration but they also realised that heterogeneity, as such, was not the reason for the increase in the reaction rates. In this context, they suggested that hydrogen bond-type interactions were mostly responsible for the observed acceleration phenomena, rather than the aforementioned hydrophobic interactions. In fact, very recent theoretical studies, carried out by Jung and Marcus, support this hypothesis.[11] These authors studied the behaviour of water molecules in an oil/water interface and they concluded that the accelerating effect of water rests on the ability of those water molecules in the interface to form hydrogen bonds with the transition state of the organic reaction, easier than with the reactants.

Additionally, in the particular case of transition metal-catalysed reactions, water molecules may alter the structure of the catalytic complexes by means of chelation with the transition metal through the oxygen atoms in the water molecule. Such chelating may lead to more active catalysts than those formed in the absence of water.[12] Nevertheless, even if none of the aforementioned beneficial effects (acceleration, chemoselectivity or enhanced catalyst activity) is observed, the use of water as the solvent is still highly advantageous in the context of green chemistry, due to its benign properties and availability.

In the following sections, of the transition metal-catalysed coupling reactions performed in the presence of water, either as an additive or as the solvent, we have focused our interest on copper and palladium-catalysed carbon–heteroatom bond formation reactions. Therefore, in this review we intend to describe all the examples reported thus far on aqueous copper and palladium-catalysed *N*-, *O*- and *S*-arylation processes.

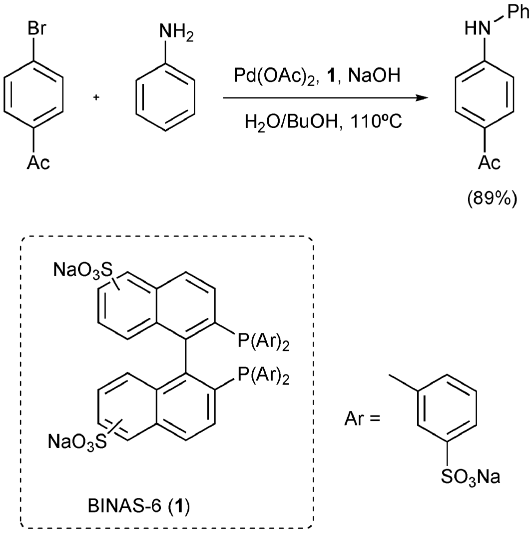
3. Carbon–heteroatom bond formation

Transition metal-catalysed carbon–heteroatom bond formation constitutes a powerful transformation with important applications in the synthesis of valuable frameworks. Of the metals reported to accomplish these types of transformations, palladium and copper have greatly contributed to the development of methodologies for the construction of C–N, C–O and C–S linkages, through *N*-, *O*- and *S*-arylation reactions, respectively. The mechanism generally accepted for these kinds of reactions involves several steps: oxidative addition of either the aryl halide or the nucleophile to the active catalyst, followed by transmetalation and final reductive elimination of the product. Significant research has been done on the mechanism of arylation reactions, particularly in the case of those catalysed by palladium, but its discussion is beyond the aim of this review.[13,14]

3.1 C–N bond formation

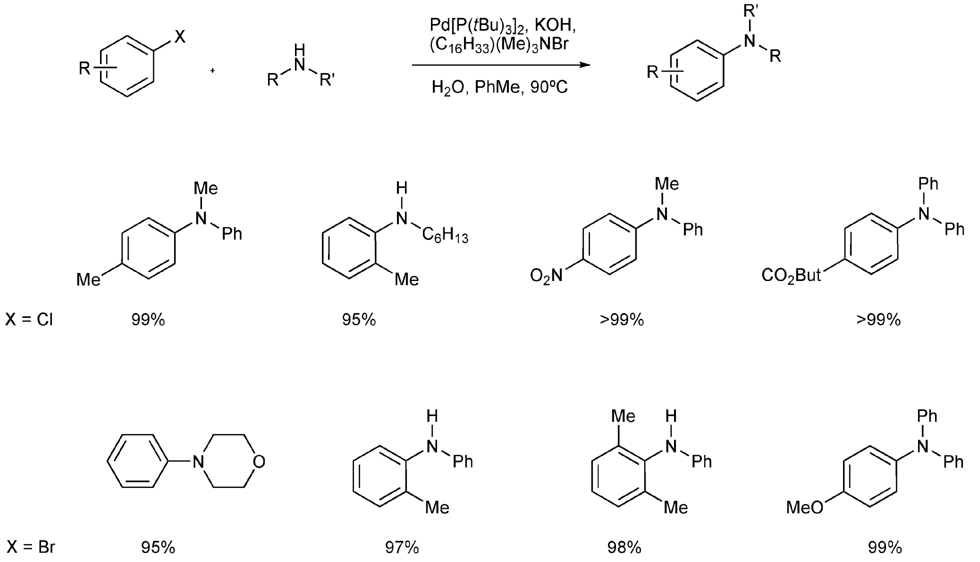
The metal catalysed reaction between a nitrogen-nucleophile, such as an amine or amide, and an aryl halide to assemble a new C–N linkage is also known as *N*-arylation reaction. All the examples reported so far in the presence of water are either copper- or palladium-catalysed and they will be discussed in the following sections.

3.1.1 Palladium-catalysed C–N bond formation. Initially, the first examples reported on palladium-catalysed *N*-arylation were performed in biphasic organic/aqueous systems. Boche and co-workers used this strategy employing the water-soluble ligand BINAS-6 **1**, which is a six-fold sulfonated BINAP derivative. These authors used a combination of $Pd(OAc)_2$ and BINAS-6 as the catalytic system, and NaOH as the base in a mixture of water and butan-2-ol for the *N*-arylation of aniline with 4-bromoacetophenone [eqn (1)]. After the reaction, the catalyst remained in the aqueous phase and the products were recovered by separation of the organic layer. Neither assays performed in neat water nor the addition of emulsifying ammonium salts or toluene as co-solvent provided improved yields. The use of a homogeneous water–methanol mixture instead of the water–butanol biphasic system also led to excellent results. Even so, after completion of the reaction, the products had to be extracted with an organic solvent, for which the use of butanol was considered desirable from an environmental point of view since no extraction was required.[15]



(1)

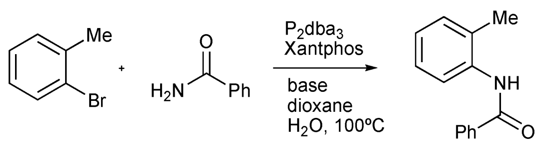
In connection with this work, Hartwig and co-workers demonstrated that not only NaOH but also KOH could efficiently promote the palladium-catalysed arylation of a wide range of amines with aryl chlorides and bromides in a partially aqueous system. Indeed, they showed that the results obtained employing hydroxides as bases were comparable to those observed when using NaO^tBu, which is one of the most common and effective bases for palladium-catalysed *N*-arylation reactions. The conditions developed by Hartwig's research group involved the use of commercially available $Pd[P(^tBu)_3]_2$ as the catalyst, an aqueous solution of an inexpensive alkali metal hydroxide (preferably KOH) and toluene as the organic co-solvent. Unlike the aforementioned protocol reported by Boche, Hartwig's system required the presence of an ammonium salt, cetyltrimethylammonium bromide, as a phase transfer catalyst in order to improve the solubility of the base and deliver the desired products in good yields [eqn (2)].[16]



(2)

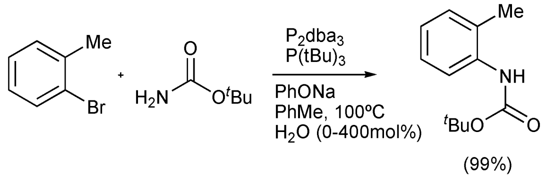
The group of Yin[17] observed, in the course of their research on palladium-catalysed *N*-arylation of heteroarylamines, that the addition of small amounts of water (0.5–1.0 equivalent) to the reaction mixture in some arylation processes had a clearly beneficial effect on the reaction outcome. They explained the improved yields obtained under partially aqueous conditions by a better solubilisation of the inorganic carbonate-type base which would favour the deprotonation step. Additionally, Neumann and co-workers observed that the combination of water and DMF as the solvent system was particularly suitable for the palladium nanoparticle-catalysed *N*-arylation of pyrrolidine.[18]

Taking into account these results and similar ones reported by Buchwald and co-workers[19] in the field of copper-catalysed *N*-arylation of amides, Dallas and Gothelf[20] explored several palladium-catalysed amidation examples and they observed that, when caesium carbonate was the base of choice in combination with both dioxane or toluene as the solvent, the addition of water resulted in a clear improvement of the yields. They studied the effect of the addition of a certain amount of water (from 0 to 400 mol%) to the reaction between benzamide and 2-bromotoluene with $Pd_2(dba)_3$, Xantphos, dioxane and different bases (Cs_2CO_3, NaO^{t}Bu and PhONa), among which Cs_2CO_3 proved to be the one most sensitive to the volume of water. Indeed, for the latter, below 50 mol% of water the yields were particularly low, between 50 and 150 mol% the yields increased up to 90% and over 150 mol% the reaction did not even occur [eqn (3)]. These authors suggested that the impact of water on these reactions was in part due to the improved solubilisation of the base which would facilitate deprotonation of the amide substrate. In addition, they observed that reactions employing more reactive substrates were particularly insensitive to the presence of water [eqn (4)], which is in contrast to the general belief that reactions are mostly hampered by the presence of water.



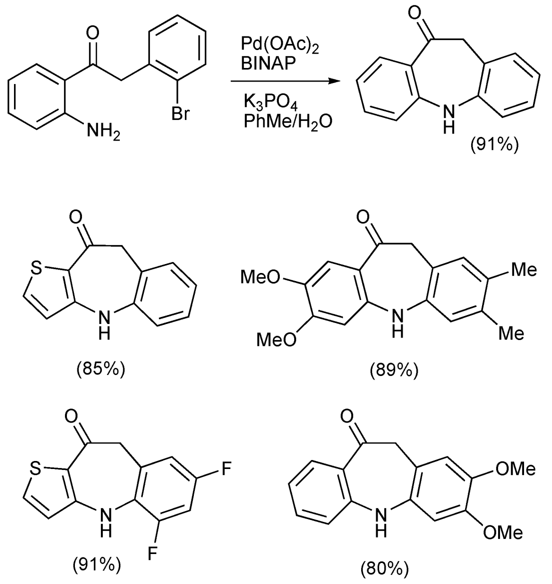
base	H_2O (mol%)	yield (%)
Cs_2CO_3	0-50	<30
	50-150	90
	150-400	0
NaO^{t}Bu	0-50	40-60
	50-400	60-80
PhONa	0-400	70-80

(3)



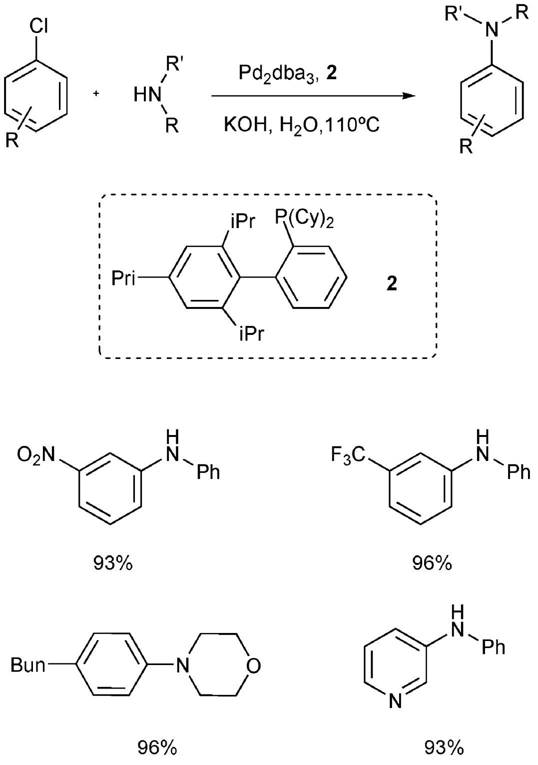
(4)

In the course of our investigations dealing with the synthesis of the antiepileptic drug Oxcarbazepine (Trileptal®), we observed a similar behaviour to that reported by Dallas and Gothelf when water was added to the palladium-catalysed intramolecular *N*-arylation depicted in eqn (5).[21] In this case, the addition of water provided not only the best yield but also allowed for a shorter reaction time (5 hours) compared to 22 hours under anhydrous conditions. Interestingly, the deoxybenzoin precursor of this cyclisation was achieved by means of a palladium-catalysed intermolecular *C*-arylation of 2′-aminoacetophenone derivative with 1,2-dibromobenzene which also revealed itself to be sensitive to the addition of a certain amount of water. Likewise, it is remarkable that the latter palladium-catalysed reactions proceeded more cleanly in the presence of water than those performed under anhydrous conditions. Furthermore, the partially-aqueous protocol developed for the synthesis of Oxcarbazepine was subsequently applied to differently-substituted substrates efficiently leading to a family of appealing analogues [eqn (5)].[22]



(5)

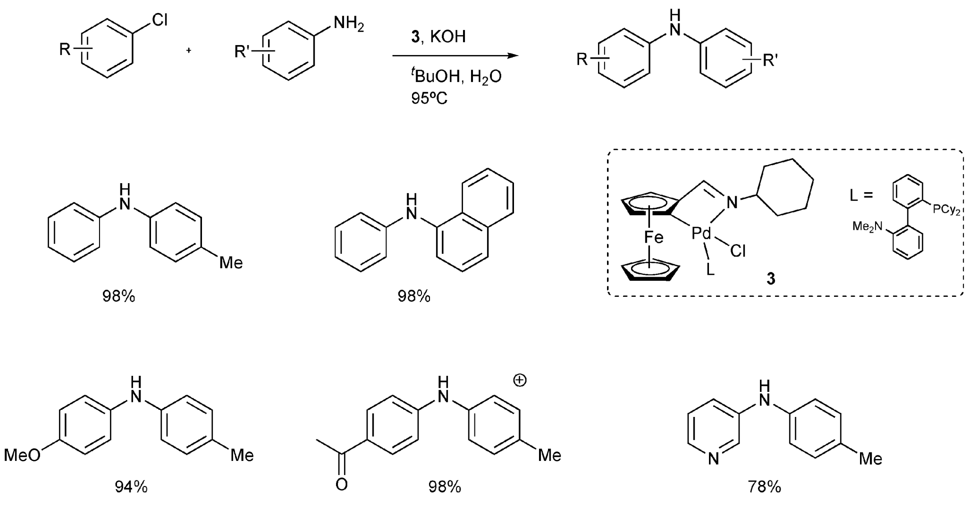
Buchwald and co-workers reported the first palladium-catalysed amination using exclusively water as the solvent, without organic co-solvents and in the absence of any phase transfer catalyst, pointing out that homogeneity is not essential for the success of the reaction. These authors tested the efficacy of ligand **2**, designed by them, in combination of Pd_2dba_3 and KOH as the base to *N*-arylate a wide range of amine derivatives with aryl chlorides, delivering the corresponding *N*-arylated products in excellent yields [eqn (6)]. Additionally, they also presented the first example of aqueous palladium-catalysed amination of an aryl tosylate, but the catalytic system needed to be partially modified.[23]



(6)

Recently, Wu and co-workers prepared cyclopalladated ferrocenylimine complex **3** which was found to successfully aminate aryl chlorides using water as the solvent.[24] The base screening performed on the model reaction between chlorobenzene and *p*-toluidine revealed that KO^{t}Bu was the most effective base affording the corresponding *N*-arylated compound in 98% yield. Since this base in water hydrolyses delivering KOH and ^{t}BuOH, the same reaction was assayed replacing KO^{t}Bu by an equivalent mixture of KOH and ^{t}BuOH, in a similar fashion to the work previously reported by Boche,[15] furnishing the product in exactly the same yield. These optimised reaction conditions, which involved stirring the selected substrates in the presence of palladacycle **3**, KOH as the base, ^{t}BuOH as an additive in water, were successfully applied to a number of aryl chlorides and aryl amines. However, the methodology appeared to be limited when the aryl amine counterpart held functionalities such as hydroxyl, carbonyl or nitro groups. Interestingly, those moieties did not affect the reaction when they were on the aryl chloride [eqn 7)].

3.1.2 Copper-catalysed C–N bond formation. The first examples on copper-catalysed amination in water appeared in the literature as isolated cases, such as the moderately efficient copper-catalysed synthesis of *N*-phenylanthranilic acids in water, reported by Pellón and co-workers.[25] Those preliminary aqueous protocols displayed a restricted scope since they were largely limited by the nature of the substrates, and therefore, water was often replaced by an organic solvent. For instance, Lang and co-workers performed the amination of a bromopyridine derivative using water as the solvent, but ethylene glycol provided far better results.[26] Buchwald and co-workers[19] observed that the addition of small amounts of water to perform the *N*-arylation of amides provided improved yields, but only for a very limited number of substrates. Buchwald and Job carried out a few copper-catalysed selective *N*-arylations of β-amino alcohols in a mixture of DMSO and water. However they realised that ^{i}PrOH provided similar results, so they chose the latter solvent to perform most of their arylation examples.[27] Furthermore, Ma and Xia successfully arylated a number of amino acids with aryl iodides and bromides using CuI as the catalyst and K_2CO_3 as the base, in a mixture of DMF and a small amount of water.[28] Likewise, they elegantly applied their novel protocol to the preparation of the biologically active molecule SB-214857.

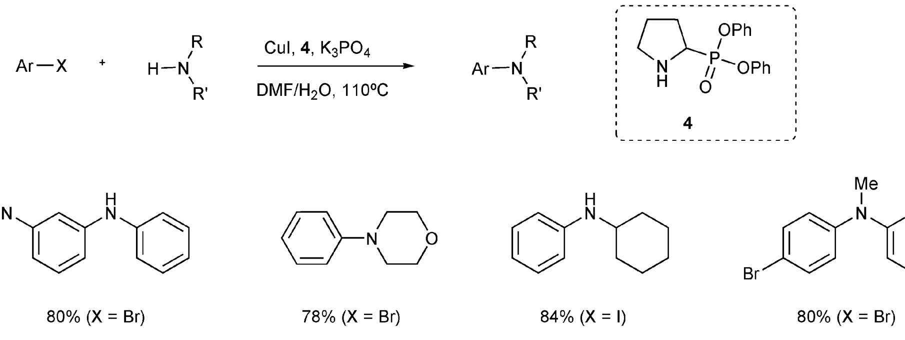


(7)

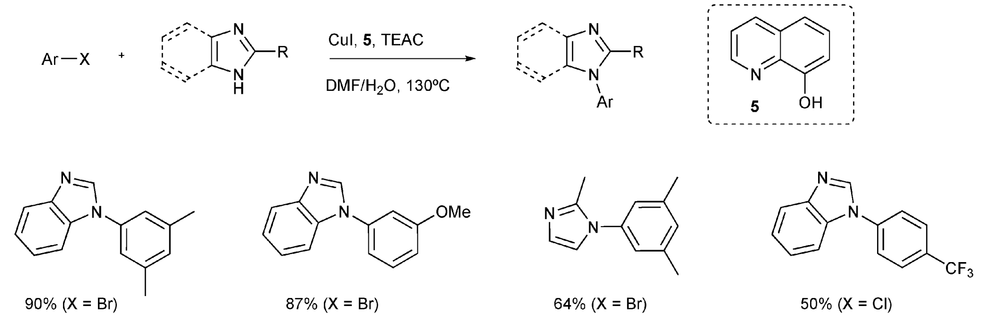
More recently, Fu and co-workers reported that diphenyl pyrrolidine-2-phosphonate **4**, in combination with CuI and K_3PO_4, was an effective ligand for the copper-catalysed arylation of amines.[29] Furthermore, they observed that such an amination process perceptibly benefited from the addition of a small amount of water when DMF was used as the solvent [eqn (8)]. In a parallel fashion, Liu and co-workers developed a protocol for the successful arylation of imidazole derivatives employing CuI and 8-hydroxyquinoline **5** as the catalytic system and triethylammonium carbonate (TEAC) as the base in DMF.[30] In this case, the addition of a small amount of water to the reaction mixture also proved beneficial. This protocol was successfully applied to the amination of aryl iodides and bromides and, to a lesser extent, to aryl chlorides [eqn (9)].9

Twieg and co-workers observed that the *N*-arylation of pyrrolidine with aryl iodides assisted by CuI in *N*,*N*-dimethylaminoethanol (deanol) as the solvent was noticeably affected by the amount of water introduced by the potassium phosphate hydrates employed as base.[31] Indeed, the use of thoroughly dried base led to sluggish reactions, but up to two equivalents of hydration water afforded selective arylations and faster reaction times. Taking these results into account, they decided to explore the use of water as the solvent and deanol as the ligand in their subsequent investigations on the copper-catalysed *N*-arylation of amino acids.[32] This aqueous protocol proved to be suitable for the arylation of not only particularly hydrophilic α- or β-amino acids but also for the selective *N*-arylation of amino alcohols and diamines [eqn (10)].

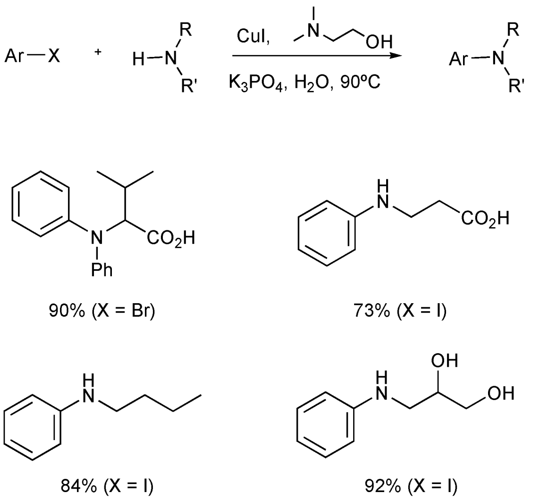
More recently, microwave irradiation has been effectively applied to the copper-catalysed *N*-arylation of a wide range of amine substrates in an aqueous medium. Wan and co-workers observed that bis(cyclohexanone)oxalyldihydrazone (BCO) could behave as an efficient ligand through chelation to



(8)

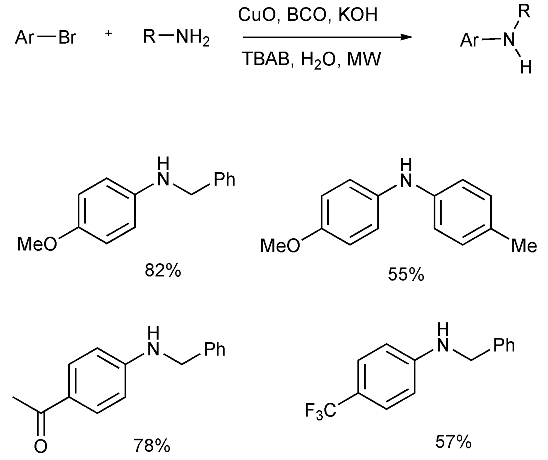


(9)



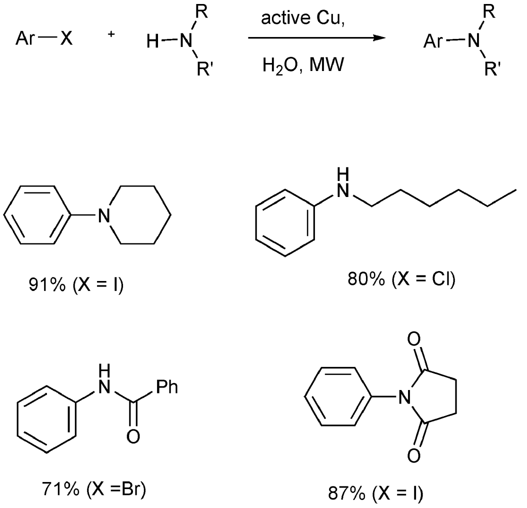
(10)

CuO, in the amination of a broad range of aryl bromides in water as the solvent.[33] The designed aqueous protocol, which additionally required the use of KOH as the base and a phase transfer agent such as TBAB, exhibited a rather general scope allowing for the arylation of alkyl and aryl-substituted primary and secondary amines [eqn (11)].



(11)

In connection with this work, Yadav and co-workers developed a general protocol for the amination of aryl halides under microwave irradiation using active copper in the absence of base [eqn (12)].[34] Reactions were performed either in water or solvent-free and the results so obtained were compared with those observed when the same reactions were carried out using oil-bath conventional heating. Interestingly, in all the cases, reactions in water provided better yields than solvent-free reactions and those under standard heating. Recently, Larhed and co-workers reported on a microwave-enhanced racemisation-free arylation of amino acids and amino acid esters in water.[35] The designed protocol, based on the use of CuI as the catalyst, afforded moderate to good yields of target *N*-arylated amino acids, but required a significant excess of aryl bromide and a KI-saturated aqueous solution as the reaction medium in order to achieve very high temperatures (185 °C).

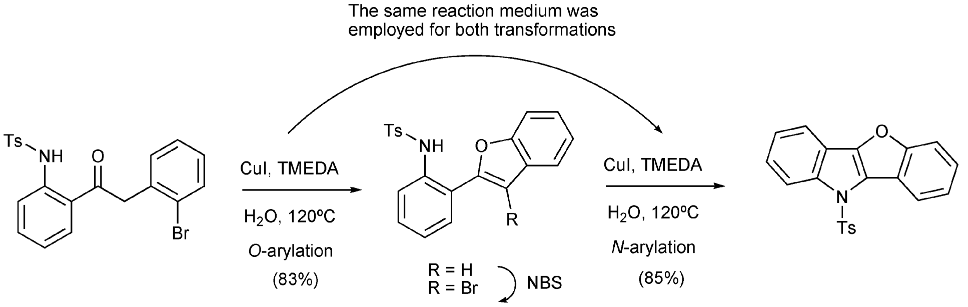


(12)

In our research group, we have recently reported a novel green approach to the benzofuroindole framework based on a final intramolecular amidation of a bromobenzofuran moiety, in the presence of a catalytic amount of CuI and DMEDA or TMEDA as the ligand/base, in only water as the solvent.[36] Furthermore, our methodology afforded the target benzofuroindole in comparatively better yields than those provided by copper and palladium-catalysed standard procedures in anhydrous conditions. Additionally, the aqueous reaction medium containing the catalyst was successfully recycled and employed to accomplish two different arylation processes: firstly, an *O*-arylation to furnish the benzofuran moiety, a transformation that will be discussed in detail within the next section, and secondly, the *N*-arylation to eventually deliver target benzofuroindole [eqn (13)].

3.2 C–O bond formation

The metal catalysed reaction between a hydroxylated compound and an aryl halide to construct a new C–O linkage is often called *O*-arylation. The examples of C–O bond

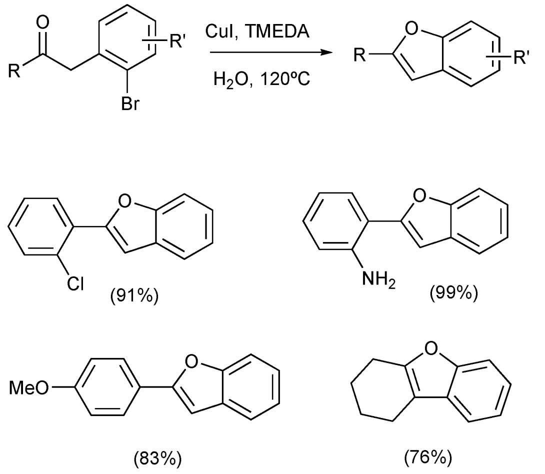


(13)

formation in the presence of water either as an additive or as the solvent are scarce and thus far restricted to the use of copper catalysts.

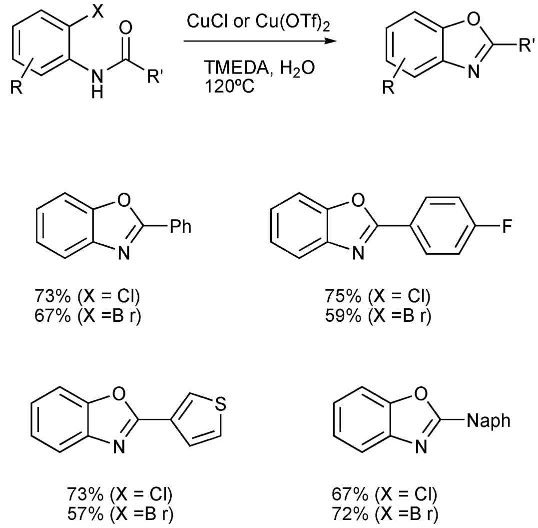
As mentioned in the previous section, Twieg and co-workers developed a copper-catalysed arylation of pyrrolidine using deanol as the solvent in the presence of water introduced in the system as hydration molecules delivered by the base, $K_3PO_4 \cdot nH_2O$.[31] However, in the optimisation process of those reaction conditions, during the ligand/solvent screening of β-hydroxylated tertiary amines, they observed that depending on the hydroxyl derivative, a competing *O*-arylation of the hydroxyl moiety of the solvent took place in moderate yields, instead of the desired *N*-arylation of pyrrolidine. They also observed that, when using deanol, the aryl ether byproduct formation was influenced by the amount of water present in the system, being suppressed by high concentrations of water.

In our research group we have paid particular attention to copper-catalysed *O*-arylation of enolate-type substrates, generated *in situ* from the corresponding carbonyl derivatives. In this context, we have developed an efficient methodology involving the use of 8.5 mol% of a simple commercially-available copper salt and a stoichiometric amount of a 1,2-diamine derivative acting both as the ligand and as the base in an aqueous solution free of organic co-solvents. Among the obvious benefits derived from the use of water, it must be pointed out that our protocol allowed in a number of cases for the recovery of the aqueous solution with the catalyst dissolved in it, and further re-utilisation. Such a general method has been effectively applied to the straightforward synthesis of benzo[*b*]furans through a selective intramolecular copper-catalysed *O*-arylation of conveniently substituted ketone derivatives, employing CuI and TMEDA [eqn (14)].[37] The same protocol was successfully applied in the aforementioned synthesis of the benzofuroindole skeleton to achieve the benzofuran moiety comprised in that skeleton [eqn (13)].[36]



(14)

Recently, we have employed this strategy to generate benzo[*d*]oxazoles through a related intramolecular *O*-arylation of adequately substituted *o*′-haloanilides, in the presence of either CuCl or $Cu(OTf)_2$ and TMEDA as the ligand/base.[38] It must be pointed out that, when *o*′-chloroanilides were submitted to the optimised reaction conditions the corresponding benzo[*d*]oxazoles were obtained in moderate to good yields, often higher than those observed when starting from the corresponding bromo analogues [eqn (15)]. These results are of particular interest since existing examples of copper-catalysed arylation of aryl chlorides are rather scarce and they are still regarded as challenging arylating partners.



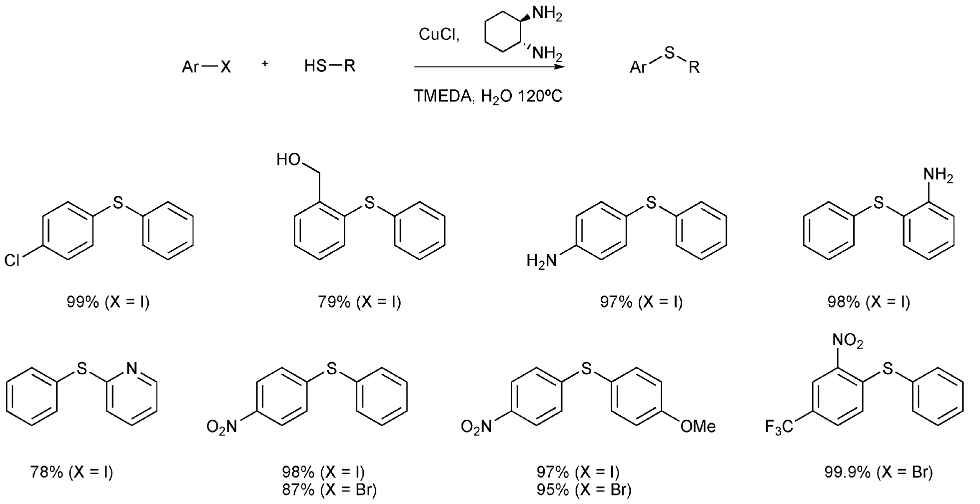
(15)

3.3 C–S bond formation

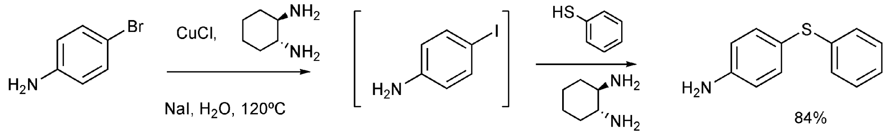
The metal catalysed reaction between a thiol moiety and an aryl halide to construct a new C–S linkage is often known as *S*-arylation. To the best of our knowledge, thus far there has been only one reported example of *S*-arylation in water as the solvent. Indeed, this absolute lack of an aqueous protocol for arylation of thiol derivatives encouraged us to extend the methodology that we had already effectively applied to *N*- and *O*-arylations, to the arylation of thiophenol substrates. We found that the combination of CuCl with *trans*-1,2-diaminocyclohexane was particularly effective for the *S*-arylation of thiophenol derivatives with both aryl iodides and bromides [eqn (16)].[39] Indeed, a wide range of aryl iodides were coupled in good to excellent yields, even in the presence of free amino and hydroxyl groups. However, the use of aryl bromides was largely limited to those bearing electron-withdrawing substituents. In order to overcome this limitation, we carried out one example of one-pot Br–I exchange followed by *S*-arylation of the *in situ* generated aryl iodide [eqn (17)].

4. Conclusion

Water has proved to be a desirable reaction medium not only from an environmental, safety or economical point of view but also due to the greater chemoselectivity and faster reaction times observed compared to those often provided by non-aqueous procedures. It must be pointed out that the role of water seems to be different depending on the type of reaction under study, and probably a combination of the already mentioned hydrophobic, hydrogen-bond interaction and chelating effects should be considered. For instance, some authors suggest that in the particular case of transition metal-catalysed arylations, water acts as a solubilising agent for inorganic



(16)



(17)

bases. However, most of the results obtained during our research allowed us to conclude something else. Indeed, as has been shown in this tutorial review, we observed that some organic bases in aqueous medium were far better than inorganic ones. This fact could be understood if it is taken into account that in the system we studied the organic substrates were not dissolved in water and could not interact with the water-soluble catalyst unless first deprotonated and converted into ionic species. This deprotonation step could only happen when the base was also organic and both substrate and base were in the same organic phase. Certainly a better understanding of the whole field is still needed, but the number of arylation reactions performed either in partially or fully aqueous media is continuously increasing, and will undoubtedly develop further in the next few years, especially for the less explored *O*- and *S*-arylation processes, allowing for a greater knowledge of the role that water plays in these types of reactions.

Acknowledgements

This research was supported by the University of the Basque Country (GIU06/87), the Regional Government of Bizkay (DIPE06/10) and the Spanish Ministry of Education and Science (MEC CTQ2004-03706/BQU). M.C. thanks the University of the Basque Country (UPV/EHU) for a postdoctoral scholarship.

References

1 B. Schlummer and U. Scholz, *Adv. Synth. Catal.*, 2004, **346**, 1599.
2 S. L. Buchwald, C. Mauger, G. Mignani and U. Scholz, *Adv. Synth. Catal.*, 2006, **348**, 23.
3 M. Poliakoff, J. M. Fitzpatrick, T. R. Farren and P. T. Anastas, *Science*, 2002, **297**, 807.
4 C.-J. Li, *Chem. Rev.*, 1993, **93**, 2023.
5 C.-J. Li, *Chem. Rev.*, 2005, **105**, 3095.
6 C.-J. Li and L. Chen, *Chem. Soc. Rev.*, 2006, **35**, 68.
7 J. E. Klijn and J. B. F. N. Engberts, *Nature*, 2005, **435**, 746.
8 C. M. Kleiner and P. R. Schreiner, *Chem. Commun.*, 2006, 4315.
9 M. C. Pirrung, *Chem.–Eur. J.*, 2006, **12**, 1312.
10 S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2005, **44**, 3275.
11 Y. Jung and R. A. Marcus, *J. Am. Chem. Soc.*, 2007, **129**, 5492.
12 S. Ribe and P. Wipf, *Chem. Commun.*, 2001, 299.
13 S. V. Ley and W. A. Thomas, *Angew. Chem., Int. Ed.*, 2003, **42**, 5400.
14 A. R. Muci and S. L. Buchwald, *Top. Curr. Chem.*, 2002, **219**, 131.
15 G. Wüllner, H. Jänsch, S. Kannenberg, F. Schubert and G. Boche, *Chem. Commun.*, 1998, 1509.
16 R. Kuwano, M. Utsunomiya and J. F. Hartwig, *J. Org. Chem.*, 2002, **67**, 6479.
17 J. Yin, M. M. Zhao, M. A. Huffman and J. M. McNamara, *Org. Lett.*, 2002, **4**, 3481.
18 V. Kogan, Z. Aizenshtat, R. Popovitz-Biro and R. Neumann, *Org. Lett.*, 2002, **4**, 3529.
19 A. Klapars, X. Huang and S. L. Buchwald, *J. Am. Chem. Soc.*, 2002, **124**, 7421.
20 A. S. Dallas and K. V. Gothelf, *J. Org. Chem.*, 2005, **70**, 3321.
21 M. Carril, R. SanMartin, F. Churruca, I. Tellitu and E. Domínguez, *Org. Lett.*, 2005, **7**, 4787.
22 M. Carril, R. SanMartin, E. Domínguez and I. Tellitu, *Tetrahedron*, 2007, **63**, 690.
23 X. Huang, K. W. Anderson, D. Zim, L. Jiang, A. Klapars and S. L. Buchwald, *J. Am. Chem. Soc.*, 2003, **125**, 6653.
24 C. Xu, J.-F. Gong and Y.-J. Wu, *Tetrahedron Lett.*, 2007, **48**, 1619.
25 R. F. Pellón, R. Carrasco and L. Rodes, *Synth. Commun.*, 1993, **23**, 1447.
26 F. Lang, D. Zewge, I. N. Houpis and R. P. Volante, *Tetrahedron Lett.*, 2001, **42**, 3251.
27 G. E. Job and S. L. Buchwald, *Org. Lett.*, 2002, **4**, 3703.
28 D. Ma and C. Xia, *Org. Lett.*, 2001, **3**, 2583.
29 H. Rao, H. Fu, Y. Jiang and Y. Zhao, *J. Org. Chem.*, 2005, **70**, 8107.
30 L. Liu, M. Frohn, N. Xi, C. Dominguez, R. Hungate and P. J. Reider, *J. Org. Chem.*, 2005, **70**, 10135.

31 Z. Lu, R. J. Twieg and S. D. Huang, *Tetrahedron Lett.*, 2003, **44**, 6289.
32 Z. Lu and R. J. Twieg, *Tetrahedron Lett.*, 2005, **46**, 2997.
33 X. Zhu, Y. Ma, L. Su, H. Song, G. Chen, D. Liang and Y. Wan, *Synthesis*, 2006, 3955.
34 L. D. S. Yadav, B. S. Yadav and V. K. Rai, *Synthesis*, 2006, 1868.
35 S. Röttger, P. J. R. Sjöberg and M. Larhed, *J. Comb. Chem.*, 2007, **9**, 204.
36 M. Carril, R. SanMartin, E. Domínguez and I. Tellitu, *Green Chem.*, 2007, **9**, 219.
37 M. Carril, R. SanMartin, I. Tellitu and E. Domínguez, *Org. Lett.*, 2006, **8**, 1467.
38 N. Barbero, M. Carril, R. SanMartin and E. Domínguez, *Tetrahedron*, 2007, **63**, 10425–10432.
39 M. Carril, R. SanMartin, E. Domínguez and I. Tellitu, *Chem.–Eur. J.*, 2007, **13**, 5100.