Microwave-Promoted Suzuki–Miyaura Cross-Coupling of Aryl Imidazolylsulfonates in Water

José F. Cívicos,^a Diego A. Alonso,^{a,*} and Carmen Nájera^{a,*}

^a Departamento de Química Orgánica and Instituto de Síntesis Orgánica (ISO), Facultad de Ciencias, Universidad de Alicante, Apartado 99, 03080 Alicante, Spain
 Fax: (+34)-96-590-3549; e-mail: diego.alonso@ua.es or cnajera@ua.es

Received: April 26, 2012; Revised: June 14, 2012; Published online: September 28, 2012

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201200364.

Abstract: Aryl imidazol-1-ylsulfonates are efficiently cross-coupled with potassium aryl- and alkenyltri-fluoroborates in neat water under microwave heating (40 W, 110 °C) using 0.5 mol% of oxime palladacycle **1a**, hexadecyltrimethyl ammonium bromide (CTAB) as additive, and triethylamine as base. Under these simple phosphane-free reaction conditions a wide

array of biaryl, stilbene and styrene derivatives has been prepared in good to high yields and with high regio- and diastereoselectivities in only 30 min.

Keywords: microwave chemistry; palladacycles; potassium organotrifluoroborates; Suzuki–Miyaura reaction; water

Introduction

In the past several decades, the Suzuki-Miyaura cross-coupling has become one of the most useful tools to construct carbon-carbon bonds in both laboratory and industry.^[1] Although aryl and alkenyl halides are most commonly employed as the electrophilic partner in the Suzuki reaction, much effort has been directed to search for alternative electrophiles. Oxygen-based electrophiles are particularly attractive partners in cross-coupling reactions due to their high stability and the ubiquitous presence of the O-based starting materials both in nature and in synthetic systems. Phenolic derivatives offer a valuable alternative given that phenols are typically inexpensive and read-ily available materials.^[2,3] The Suzuki–Miyaura crosscoupling reaction of enols, phenols, and hydroxylated arenes usually involves their transformation into triflates due to the superior performance of these derivatives as electrophilic partners.^[4] However, triflates are substrates with limited stability, so recent studies have focused on the development of less common phenol-based electrophiles,^[5] such as mesylates,^[6] to-sylates,^[6e,7] ethers,^[8] esters,^[6c,9] carbamates,^[10] carbon-ates,^[10b] phosphonium salts,^[11] phosphoramides and phosphates,^[12] N,N-dialkyl O-sulfamates,^[6f,10b,f,13] and borates^[14] since these substrates are usually more robust and allow functionalization by regioselective C-H activation and directed ortho metalation processes.^[10a,13a,15] With the exception of aryl mesylates and

tosylates, these electrophiles are typically unreactive towards Pd catalysis, with phosphane-derived nickel complexes, such as $NiCl_2(PCy_3)_2$ being the most active catalysts, usually working in organic or aqueous solvents (Scheme 1). Very recently, aryl imidazolylsulfonates have been demonstrated as efficient electrophilic coupling partners in the Suzuki reaction with arylboronic acids employing bidentate phosphane ligands, such as 1,1'-bis(diphenylphosphino)-farrocene (dppf) and 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene



Scheme 1. Suzuki coupling of phenol-derived electrophiles.

WILEY 2771

(BINAP), under high catalyst loadings (5–10 mol% Pd).^[16,17]

In our group, we have disclosed a phosphane-free oxime-palladacycle^[18,19]-catalyzed Suzuki reaction of aryl imidazolylsulfonates with aryl- and alkenylboronic acids and potassium trifluoroborates in aqueous methanol, a reaction which can be performed using conventional or microwave heating, under low loading conditions (1 mol% Pd).^[20] In this work, the lack of efficiency in the Suzuki coupling under aqueous conditions of other C–O electrophiles, such as carbonates, carbamates, phosphates, and *N*,*N*-dialkylsulfamates, was also demonstrated.

Despite the significant advances in the pool of available electrophiles and their Suzuki cross-coupling, much effort remains to generalize the transformation. To date, no examples of Pd- or Ni-catalyzed C–O activation in water have been reported (Scheme 1).^[21] In this work, we present the first Suzuki–Miyaura coupling of aryl imidazolylsulfamates with potassium aryl- and alkenyltrifluoroborates using oxime palladacycle **1a** as precatalyst in water under microwave irradiation and phosphane-free conditions.

Results and Discussion

Initially, we investigated the microwave-promoted Suzuki coupling of naphthalen-1-yl 1H-imidazole-1sulfonate (2aa, 1 equiv.) with phenylboronic acid (1.5 equiv.) catalyzed by palladacycle **1a** (1 mol% Pd) at 110°C in water. A first base optimization study,^[22] which was performed in the presence of the surfactant polyoxyethanyl- α -tocopheryl sebacate (PTS) (4a, 15% w/w),^[23] showed triethylamine (TEA) as the most effective base, affording 5a in a 56% isolated yield (Scheme 2). Under these conditions, a subsequent surfactant study^[22] using other non-ionic [polyoxyethylene lauryl ether (Brij 35, 4b), 4-(1,1,3,3-tetramethylbutyl)phenylpolyethylene glycol (Triton X100, 4c), and macrogol (25)-cetostearyl ether (Cremophor A25, 4d)], as well as ionic [hexadecyltrimethylammonium bromide (CTAB, 4e) and tetrabutylammonium bromide (TBAB, 4f)] additives, did not improve this result, affording 5a in much lower yields than for 4a (7-39%).[22]

Next, an exhaustive nucleophile/surfactant screening^[22] was carried out for the microwave-promoted ar-



Scheme 2. Suzuki coupling of 2aa with $PhB(OH)_2$ in water. Reaction conditions study

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

ylation of **2aa** in the presence of TEA as base using different boron nucleophiles **3** and surfactants **4** (Table 1). As shown in entries 1–4 for the best results, the Suzuki cross-coupling of the imidazolylsulfonate **2aa** afforded compound **5a** in good to excellent yields (53–91%) irrespective of the electrophile used, potassium phenyltrifluoroborate and CTAB (**4e**) being the match combination (Table 1, entry 4). The cross-coupling reaction was not so effective when it was carried out with conventional heating at 110 °C for 24 h, yielding compound **5a** in a 38% isolated yield (entry 6).

Regarding the catalyst, a 66% yield of compound **5a** was obtained under the optimized reaction conditions when oxime palladacycle **1b** (1 mol% Pd) was employed (Table 1, entry 7). Other Pd sources such as $Pd(OAc)_2$ and $Pd_2(dba)_3$ were much less effective as shown in entries 8–10. Phosphane-derived nickel complexes, such as $NiCl_2(PCy_3)_2$ have been demonstrated

 Table 1. Suzuki coupling of 2 in water. Reaction conditions study.



PhBX_n (3): PhB(OH)₂; PhBF₃K; PhB[OC(Me₂)]₂; PhB(OCOCH₂)₂NMe

surfactant: PTS (4a); Brij 35 (4b); Triton X100 (4c); Cremophor A25
(4d); (1-hexadecyl)trimethyl ammonium bromide (CTAB, 4e); TBAB (4f)

Entry	2	X _n	Pd catalyst	4	Yield [%] ^[a]
1	2aa	(OH) ₂	1a	4a	56
2	2aa	$[OC(Me_2)]_2$	1a	4e	76
3	2aa	$(OCOCH_2)_2NMe$	1a	4c	53
4	2aa	F ₃ K	1a	4e	91
5	2aa	$(OH)_2$	1a	4e	39
6	2aa	F ₃ K	1a	4e	38 ^[b]
7	2aa	F ₃ K	1b	4e	66
8	2aa	F ₃ K	$Pd(OAc)_2$	4e	33
9	2aa	F ₃ K	$Pd(OAc)_2^{[c]}$	4e	40
10	2aa	F ₃ K	$Pd_2(dba)_3$	4e	< 5
11	2aa	F ₃ K	_[d]	4e	< 5
12	2ab	F ₃ K	1a	4e	< 5
13	2ac	F ₃ K	1a	4e	< 5
14	2ad	F ₃ K	1a	4e	< 5
15	2ae	F ₃ K	1a	4e	< 5
16	2af	F ₃ K	1a	4e	<5

^[a] Isolated yield after flash chromatography.

^[b] Reaction performed with conventional heating at 110°C for 24 h.

- [c] Reaction performed in the presence of [HP(t-Bu)₃]BF₄ (2 mol%).
- ^[d] Reaction performed using 1 mol% of NiCl₂(PCy₃)₂.

1a (1 mol% Pd). 4e (15% w/w), TEA, H₂O + RBF₂K 40 W 110 °C 30 min 5 2aa Product Yield [%]^[b] RBF₃K Entry No. BF₃K 1 5a 91 BF₃K 2 5b 85 BF₃K 3 5c 68 5d 55 4 5 60 5e 6 5f 84 7 5g 62

Table 2. Suzuki arylation and alkenylation of 2aa.^[a]

^[a] Reaction conditions: A mixture of **2aa** (0.055 g, 0.2 mmol), RBF₃K (0.3 mmol), Et₃N (0.056 mL, 0.4 mmol), **4e** (0.030 g, 15% w/w in water), **1a** (0.0006 g, 1 mol% Pd) in H₂O (1.7 mL) was heated in air at 110°C for 30 min with the aid of an initial 40 W irradiation.

^[b] Isolated yield after flash chromatography.

as the most effective catalysts to carry out the Suzuki coupling of phenol derivatives in organic solvents.^[6c] However, the coupling between imidazolylsulfonate **2aa** and potassium phenyltrifluoroborate catalyzed by NiCl₂(PCy₃)₂, led to a negligible reaction conversion (Table 1, entry 11). Finally, we also tested the reactivity of the electrophiles **2ab**, **2ac**, **2ad**, **2ae**, and **2af** in the process under the optimized reaction conditions. As depicted in entries 12–16, none of these derivatives showed any reactivity and only starting material was recovered from the crude reaction mixture.^[24,25]

To test the effectiveness of the catalytic system in the Pd-catalyzed Suzuki reaction in water, a range of potassium aryl- and alkenyltrifluoroborates was examined in the coupling with imidazolylsulfonate **2aa** under the optimized reaction conditions (Table 2).

Regarding aryltrifluoroborates, both activated and deactivated nucleophiles afforded the corresponding cross-coupled products in good yields as demonstrated with the coupling of potassium 4-tolyltrifluoroborate and potassium 4-(trifluoromethyl)phenyltrifluoroborate (Table 2, entries 2 and 3). Heterocyclic nucleophiles such as, potassium pyrid-3-yltrifluoroborate and potassium thien-3-yltrifluoroborate were also sub-

mitted to the coupling with naphthalen-1-yl 1*H*-imidazole-1-sulfonate under the optimized reaction conditions. As shown in Table 2, entries 4 and 5, these compounds afforded the corresponding adducts **5d** and **5e** in 55 and 60% isolated yields, respectively. Good yields were also observed for the coupling of **2aa** with potassium *trans*-2-phenylvinylboronic acid (entry 6) and potassium *trans*-1-decen-1-yltrifluoroborate (entry 7), reactions that afforded compounds **5f** and **5g** in 84 and 62% yield, respectively. These reactions were highly regioselective, and no *ipso* coupling was observed, a process often found in Pd-catalyzed alkenylations of aryl chlorides.^[26]

We next extended the substrate scope of the reaction to the arylation and alkenylation of other different aryl imidazolylsulfonates (Table 3). Concerning arylation, electron-rich, electron-poor, sterically hindered, and heterocyclic electrophiles showed good reactivity when coupling with potassium phenyltrifluoroborate, affording the corresponding biphenyl derivatives in good to excellent yields (Table 2, entries 1–4). *ortho*-Cyano-substituted elec-

Table 3. Substrate scope of the Suzuki reaction.



[a] Isolated yield after flash chromatography.
[b] 80 W, 150 °C, 1 h.



Scheme 3. Suzuki coupling of bromo-containing imidazolylsulfonate 2bg in water.

trophile **2be** reacted very efficiently with potassium *p*-toluenetrifluoroborate, producing 2-cyano-4'-methylbiphenyl (**5**I), a key intermediate in the synthesis of angiotensin II receptor antagonists that are used for the treatment of hypertension,^[27] with an 86% yield (Table 3, entry 5).

With respect to alkenylations, slightly lower yields were obtained in the coupling reaction of different imidazolylsulfonates **2** with potassium *trans*-2-phenyl-vinyltrifluoroborate and potassium *trans*-1-decen-1-yl-trifluoroborate, which regioselectively led to stilbene derivatives **5m**-**5p** in 55 to 84% isolated yields (Table 3, entries 6–9).

Finally, concerning the Suzuki coupling of halogenated imidazolylsulfonates, the C-Cl bond did not participate in the coupling event as demonstrated in the arylation of *p*-chlorophenyl imidazolylsulfonate (**2bc**) with potassium phenyltrifluoroborate, a reaction that afforded 4-chlorobiphenyl (5j) in a 74% yield (Table 3, entry 3). However, the weaker C-Br bond did react in the process, and the reaction of electrophile 2bg (1 equiv.) with potassium phenyltrifluoroborate $(1.5 \text{ equiv.})^{[28]}$ afforded as a major product 1,1':4',1''-terphenyl (6) in 55% yield, together with a 28% yield of 1,1'-biphenyl-4-yl 1H-imidazole-1-sulfonate (2bh) (Scheme 3). On the other hand, only (E)-4-styrylphenyl 1H-imidazole-1-sulfonate (2bi) was isolated, from the 1a-catalyzed alkenylation of 2bg with potassium trans-2-phenylvinyltrifluoroborate (Scheme 3).^[29]

Conclusions

In conclusion, we have disclosed a general phosphane-free palladium-catalyzed Suzuki cross-coupling reaction of electron-rich, electron-poor, and sterically hindered aryl imidazolylsulfonates with aryl- and alkenylpotassium trifluoroborates using water as solvent under microwave irradiation. This reaction is carried out in the presence of hexadecyltrimethylammonium bromide as additive and is catalyzed by only 1 mol% Pd of bench stable oxime palladacycle **1a**. Further studies to demonstrate the ability of imidazolylsulfonates as electrophiles in cross-coupling reactions in water are underway in the group.

Experimental Section

Typical Procedure for the Suzuki Coupling in Water under MW Irradiation Conditions

A 10-mL MW vessel was charged with 1-naphthalen-1-yl-1H-imidazole-1-sulfonate (2aa) (0.055 g, 0.2 mmol, 1 equiv.), potassium 4-(trifluoromethyl)phenyltrifluoroborate (0.079 g, 0.3 mmol), Et₃N (0.056 mL, 0.4 mmol), CTAB (0.030 g, 15% w/w in water), catalyst **1a** (0.6 mg, 1 mol% Pd), and H_2O (1.7 mL). The vessel was sealed with a pressure lock, and the mixture was heated in air at 110°C for 30 min with the aid of an initial MW irradiation of 40 W in a CEM Discover MW reactor. Then, after cooling to room temperature, the reaction mixture was extracted with EtOAc (3×10 mL), and the organic layers were washed with H_2O (3×10 mL), dried over MgSO₄, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (hexane/EtOAc: 4/1) to afford 5c; yield: 0.033 g (68%); white solid; mp 48–49°C (hexane); R_f 0.34 (hexane). IR (KBr): v=3068, 3045, 1616, 1404, 1323, 1166, 1123, 1069, 1019, 850, 804, 700 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): $\delta_{\rm H} =$ 8.09–7.99 (m, 3 H), 7.90 (d, J = 8.4 Hz, 2 H), 7.72 (d, J =8.4 Hz, 2H), 7.69–7.57 (m, 3H), 7.54 (d, J=8.4 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz): $\delta_{\rm C} = 144.9$, 138.7, 133.8, 131.3, 130.4, 129.5 (q, J = 32.3 Hz), 128.44, 128.39, 127.0, 126.4, 126.0, 125.5, 125.3, 125.2 (q, J=3.3 Hz), 124.4 (q, J=270.5 Hz); MS: m/z (%) = 273 (M^+ + 1, 18), 272 (M^+ , 100), $271 (M^+-1, 23), 251 (15), 203 (50), 202 (54).$

Acknowledgements

Financial support from the MICINN (Projects CTQ2007-62771/BQU, CTQ2010–20387), and Consolider INGENIO 2010 (CSD2007-00006), FEDER, the Generalitat Valenciana (PROMETEO/2009/038), and the University of Alicante is acknowledged.

References

 a) A. Suzuki, J. Organomet. Chem. 1999, 576, 147; b) N. Miyaura, Top. Curr. Chem. 2002, 219, 11; c) N. Miyaura, A. Suzuki, Chem. Rev. 1995, 95, 2457; d) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, Chem. Rev. 2002, 102, 1359; e) S. Kotha, K. Lahiri, D. Kashinath, Tetrahedron 2002, 58, 9633; f) A. F. Littke, G. C. Fu, Angew. Chem. 2002, 114, 4350; Angew. Chem. Int. Ed. 2002, 41, 4176; g) N. Miyaura, Top. Curr. Chem. 2002, 219, 11; h) F. Bellina, A. Carpita, R. Rossi, Synthesis 2004, 2419; i) U. Christmann, R. Vilar, *Angew. Chem.* 2005, *117*, 370; *Angew. Chem. Int. Ed.* 2005, *44*, 366; j) F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron* 2008, *64*, 3047; k) *Metal-Catalyzed Cross-Coupling Reactions*, Vol. 2, (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, 2004; l) *Modern Arylation Methods*, (Ed.: L. Ackermann), Wiley-VCH, Weinheim, 2009.

- [2] The Chemistry of Phenols, (Ed.: Z. Rappoport), John Wiley & Sons Ltd., Chichester, 2003.
- [3] D. A. Alonso, C. Nájera, I. Pastor, M. Yus, Chem. Eur. J. 2010, 16, 5274.
- [4] a) W. Scott, G. Crisp, J. K. Stille, J. Am. Chem. Soc. 1984, 106, 4630; b) Z. Gilson, R. Larock, Chem. Rev. 2006, 106, 4644.
- [5] For recent reviews on the use of new C–O electrophiles in cross-coupling reactions, see: a) D.-G. Yu, B.-J. Li, Z.-J. Shi, Acc. Chem. Res. 2010, 43, 1486; b) B.-J. Li, D.-G. Yu, C.-L. Sun, Z.-J. Shi, Chem. Eur. J. 2011, 17, 1728.
- [6] For recent examples, see: a) C. M. So, C. P. Lau, F. Y. Kwong, Angew. Chem. 2008, 120, 8179; Angew. Chem. Int. Ed. 2008, 47, 8059; b) D. A. Wilson, C. J. Wilson, B. M. Rosen, V. Percec, Org. Lett. 2008, 10, 4879; c) G. A. Molander, F. Beaumard, Org. Lett. 2010, 12, 4022; d) W. K. Chow, C. M. So, C. P. Lau, F. Y. Kwong, J. Org. Chem. 2010, 75, 5109; e) H. Gao, Y. Li, Y.-G. Zhou, F.-S. Han, Y.-J. Lin, Adv. Synth. Catal. 2011, 353, 309; f) P. Leowanawat, N. Zhang, A.-M. Resmerita, B. M. Rosen, V. Percec, J. Org. Chem. 2011, 76, 9946; g) C. M. So, F. Y. Kwong, Chem. Soc. Rev. 2011, 40, 4963.
- [7] For recent examples, see: a) J. P. Wolfe, H. Tomori, J. P. Sadighi, J. Yin, S. L. Buchwald, J. Org. Chem. 2000, 65, 1158; b) D.-Y. Lee, J. F. Hartwig, Org. Lett. 2005, 7, 1169; c) L. Zhang, T. Meng, J. Wu, J. Org. Chem. 2007, 72, 9346; d) C. M. So, C. P. Lau, A. S. C. Chan, F. Y. Kwong, J. Org. Chem. 2008, 73, 7731.
- [8] a) M. Tobisu, T. Shimasaki, N. Chatani, *Chem. Lett.*2009, 38, 710; b) M. Tobisu, T. Shimasaki, N. Chatani, *Angew. Chem.* 2008, 120, 4944; *Angew. Chem. Int. Ed.*2008, 47, 4866; c) B.-T. Guan, S.-K. Xiang, T. Wu, Z.-P. Sun, B.-Q. Wang, K.-Q. Zhao, Z.-J. Shi, *Chem. Commun.* 2008, 1437; d) J. W. Dankwardt, *Angew. Chem.* 2004, 116, 2482; *Angew. Chem. Int. Ed.* 2004, 43, 2428; e) E. Wenkert, E. L. Michelotti, C. S. Swindell, *J. Am. Chem. Soc.* 1979, 101, 2246.
- [9] a) K. W. Quasdorf, X. Tian, N. K. Garg, J. Am. Chem. Soc. 2008, 130, 14422; b) B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu, Z.-J. Shi, J. Am. Chem. Soc. 2008, 130, 14468; c) Z. Li, S.-L. Zhang, Y. Fu, Q.-X. Guo, L. Liu, J. Am. Chem. Soc. 2009, 131, 8815; d) B.-J. Li, Y.-Z. Li, X.-Y. Lu, J. Liu, B.-T. Guan, Z.-J. Shi, Angew. Chem. 2008, 120, 10278; Angew. Chem. Int. Ed. 2008, 47, 10124; e) L. J. Gooβen, K. Gooβen, C. Stanciu, Angew. Chem. 2009, 121, 3621; Angew. Chem. Int. Ed. 2009, 48, 3569; f) T. Shimasaki, M. Tobisu, N. Chatani, Angew. Chem. 2010, 122, 2991; Angew. Chem. Int. Ed. 2010, 49, 2929; g) C.-L. Sun, Y. Wang, X. Zhou, Z.-H. Wu, B.-J. Li, B.-T. Guan, Z.-J. Shi, Chem. Eur. J. 2010, 16, 5844.
- [10] a) A. Antoft-Finch, T. Blackburn, V. Snieckus, J. Am. Chem. Soc. 2009, 131, 17750; b) K. W. Quasdorf, M. Riener, K. V. Petrova, N. K. Garg, J. Am. Chem. Soc.

2009, *131*, 17748; c) L. Xi, B.-J. Li, Z.-H. Wu, X.-Y. Lu, B.-T. Guan, B.-Q. Wang, K.-Q. Zhao, Z.-J. Shi, *Org. Lett.* **2010**, *12*, 884; d) C. Dallaire, I. Kolber, M. Gingras, *Org. Synth.* **2002**, *78*, 42; e) S. Sengupta, M. Leite, D. S. Raslan, C. Quesnelle, V. Snieckus, *J. Org. Chem.* **1992**, *57*, 4066; f) K. W. Quasdorf, A. Antoft-Finch, P. Liu, A. L. Silberstein, A. Komaromi, T. Blackburn, S. D. Ramgren, K. N. Houk, V. Snieckus, N. K. Garg, *J. Am. Chem. Soc.* **2011**, *133*, 6352.

- [11] a) F.-A. Kang, Z. Sui, W. V. Murray, J. Am. Chem. Soc.
 2008, 130, 11300; b) F.-A. Kang, Z. Sui, W. V. Murray, Eur. J. Org. Chem. 2009, 461.
- [12] a) Y.-L. Zhao, Y. Li, Y. Li, L.-X. Gao, F.-S. Han, *Chem. Eur. J.* 2010, *16*, 4991; b) H. Chen, Z. Huang, X. Hu, G. Tang, P. Xu, Y. Zhao, C.-H. Cheng, *J. Org. Chem.* 2011, *76*, 2338; c) J. D. Sellars, P. G. Steel, *Chem. Soc. Rev.* 2011, *40*, 5170.
- [13] a) T. K. Macklin, V. Snieckus, Org. Lett. 2005, 7, 2519;
 b) M. Baghbanzadeh, C. Pilger, C. O. Kappe, J. Org. Chem. 2011, 76, 1507.
- [14] D.-G. Yu, Z.-J. Shi, Angew. Chem. 2011, 123, 7235; Angew. Chem. Int. Ed. 2011, 50, 7097.
- [15] C. E. I. Knappke, A. J. Wangelin, Angew. Chem. 2010, 122, 3648; Angew. Chem. Int. Ed. 2010, 49, 3568.
- [16] J. Albaneze-Walker, R. Raju, J. A. Vance, A. J. Goodman, M. R. Reeder, J. Liao, M. T. Maust, P. A. Irish, P. Espino, D. R. Andrews, *Org. Lett.* **2009**, *11*, 1463.
- [17] For the use of aryl imidazolylsulfonates in other cross-coupling reactions, see: a) Y. Luo, J. Wu, *Organometallics* 2009, 28, 6823; b) S. J. Shirbin, B. A. Boughlton, S. C. Zammit, S. D. Zanatta, S. M. Marcuccio, C. A. Hutton, S. J. Williams, *Tetrahedron Lett.* 2010, 51, 2971; c) L. Ackermann, S. Barfüesser, J. Pospech, *Org. Lett.* 2010, 12, 724.
- [18] Palladacycles: Synthesis Characterization and Applications, (Eds.: J. Dupont, M. Pfeffer), Wiley-VCH, Weinheim, 2008.
- [19] For recent reviews on the use of oxime-palladacycles as precatalysts in cross-coupling reactions, see: a) E. Alacid, D. A. Alonso, L. Botella, C. Nájera, M. C. Pacheco, *Chem. Rec.* 2006, *6*, 117; b) D. A. Alonso, C. Nájera, *Chem. Soc. Rev.* 2010, *39*, 2891.
- [20] a) J. F. Cívicos, M. Gholinejad, D. A. Alonso, C. Nájera, *Chem. Lett.* **2011**, 40, 907; b) J. F. Cívicos, D. A. Alonso, C. Nájera, *Eur. J. Org. Chem.* **2011**, 3670–3676.
- [21] For a recent review about cross-coupling and Heck reactions using water as solvent, see: D. A. Alonso, C. Nájera, in: *Science of Synthesis. Water in Organic Synthesis*, (Ed.: S. Kobayashi), George Thieme Verlag, Stuttgart, **2012**, Vol. 2011/7, p 535.
- [22] For the full reaction optimization study, see the Supporting Information.
- [23] For the use of surfactants in cross-coupling reactions in water, see: a) B. H. Lipshutz, S. Ghorai, Aldrichimica Acta 2008, 41, 59; b) B. H. Lipshutz, D. W. Chung, B. Rich, Org. Lett. 2008, 10, 3793; c) B. H. Lipshutz, S. Ghorai, A. R. Abela, R. Moser, T. Nishikata, C. Duplais, A. J. Krasovkiy, J. Org. Chem. 2011, 76, 4379; d) B. H. Lipshutz, S. Ghorai, W. W. Y. Leong, B. R. Taft, J. Org. Chem. 2011, 76, 5061.
- [24] For a recent comparative study about the efficiency of different aryl C–O-based electrophiles in the Ni-cata-

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

lyzed Suzuki cross-coupling with aryl neopentylglycolboronates, see: P. Leowanawat, N. Zhang, V. Percec, J. Org. Chem. **2011**, 77, 1018.

- [25] For a recent comparative study about the efficiency of different aryl C–O-based electrophiles in the Ni-catalyzed Suzuki cross-coupling with potassium heteroarylfluoroborates, see: G. A. Molander, F. Beaumard, Org. Lett. 2010, 12, 4022.
- [26] J. F. Cívicos, D. A. Alonso, C. Nájera, Adv. Synth. Catal. 2011, 353, 1683, and references cited therein.
- [27] a) A. Daugherty, L. Cassis, *Trends Cardiovasc. Med.*2004, 14, 117; b) G. García, M. Rodríguez-Puyol, R.

Alajarín, I. Serrano, P. Sánchez-Alonso, M. Griera, J. J. Vaquero, D. Rodríguez-Puyol, J. Alvarez-Builla, M. L. Díez-Marqués, *J. Med. Chem.* **2009**, *52*, 7220.

- [28] Similar results and selectivities were obtained when the reaction was performed using a larger excess of nucleophile (2.5 equiv.).
- [29] For a Pd-catalyzed Suzuki cross-coupling of 2-bromoand 2-iodo-O-phenylsulfamates with arylboronic acids, see: T. K. Macklin, V. Snieckus, Org. Lett. 2005, 7, 2519.