Dalton Transactions

Cite this: *Dalton Trans.*, 2011, **40**, 9229

www.rsc.org/dalton

PAPER

Synthesis of biphenyl-based arsine ligands by Suzuki–Miyaura coupling and their application to Pd-catalyzed arsination†

Paula M. Uberman, Mario N. Lanteri, Sol C. Parajón Puenzo and Sandra E. Martín*

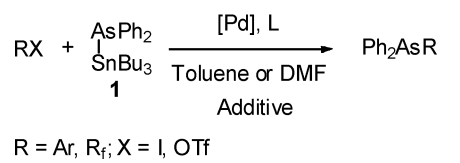
Received 7th February 2011, Accepted 8th June 2011
DOI: 10.1039/c1dt10207a

A versatile and efficient approach for the synthesis of new biphenyl-based arsine ligands, by a Pd-catalyzed arsination to introduce the -$AsPh_2$ moiety, and then a Suzuki–Miyaura cross-coupling for biaryl construction is reported. By Pd-catalyzed arsination with *n*-$Bu_3SnAsPh_2$ (**1**), (2-bromophenyl)diphenylarsine (**2**, 83%) was obtained. The Suzuki–Miyaura reaction between the bromoarsine **2** and aryl boronic acids bearing different substituents provided biarylarsine ligands (80–99%). The efficiency of catalysts derived from the new biarylarsine ligands was evaluated in the Pd-catalyzed arsination with perfluoroalkyl iodides (R_fI). Outstanding activities of catalysts derived from Pd/methoxybiarylarsine ligands were found in this coupling reaction affording perfluoroalkyl arsines in very good yields (57–100%).

Introduction

In metal-catalyzed reactions tertiary phosphines constitute the group of ligands most widely used; however tertiary arsines are gaining particular attention as ligands. The efficiency of such reactions largely depends on the fine electronic and structural properties of the ligands, and even with well-designed phosphine ligands, unsatisfactory results may still be observed. As an option, the coordinating ability of the ligands can be tuned through the donor atom. Arsines have been shown to be excellent supporting ligands and there are several examples where arsine complexes give more active or selective catalysts than phosphines in transition metal-catalyzed organic reactions, including Stille[1] and Suzuki–Miyaura[2] coupling processes, Negishi reactions,[3] Heck and related reactions,[4] cross-coupling with arylsilanols,[5] hydroformylation of terminal alkenes,[6] hydrosilylations,[7] carbonylations[8] and polymerizations.[9] Some other examples of Pd-catalyzed reactions, where arsines have been determined to be particularly useful ligands, have also been reported.[10]

However, arsine ligands, to a large extent, have not yet been developed, probably mainly due to the lack of readily available As-containing precursor compounds. The development of new methods to obtain arsines is thus increasingly recognized as central in the synthesis of new ligands. Accordingly, we have developed a versatile methodology that allows for C–As bond formation through a cross-coupling Pd-catalyzed reaction of different electrophiles with arsine stannane *n*-$Bu_3SnAsPh_2$ (**1**) in one-pot two-step reactions (Scheme 1).[11,12] This methodology allowed the synthesis of functionalized arsines and arsine ligands.



Scheme 1 Pd-catalyzed arsination.

Over the past few years, there has been a growing interest in the synthesis and application of biphenyl-based monophosphine ligands, first introduced by Buchwald.[13] A family of these ligands has been developed and shown to have applications in numerous Pd-catalyzed coupling processes.[14] For the synthesis of such phosphines, a one-pot protocol was used involving the addition of an aryl-Grignard to an *in situ* generated benzyne, followed by trapping of the resulting biaryl–metal intermediate with a chlorophosphine[13d,15] or the directed *ortho*-lithiation of suitable substrates.[14b] However, the biaryl architecture of monophosphines has also been constructed using the Suzuki–Miyaura coupling reaction,[16] including aryl phosphine oxides[17] or phosphines,[18] and the asymmetric coupling of phosphonate naphthylboronic acid.[19]

Recently, we reported the synthesis of a novel biphenylarsine ligand biphenyl-2-yldiphenylarsine (**L1**, Fig. 1) by the efficient Pd-catalyzed arsination with stannane *n*-$Bu_3SnAsPh_2$ (**1**) and 2-iodobiphenyl, as well as the preliminary investigation of its

INFIQC, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, 5000, Córdoba, Argentina. E-mail: martins@fcq.unc.edu; Fax: +54 351 4333030 Int. 151; Tel: +54 351 4334170/73

† Electronic supplementary information (ESI) available: experimental procedures and full spectroscopic data for all new compounds. See DOI: 10.1039/c1dt10207a

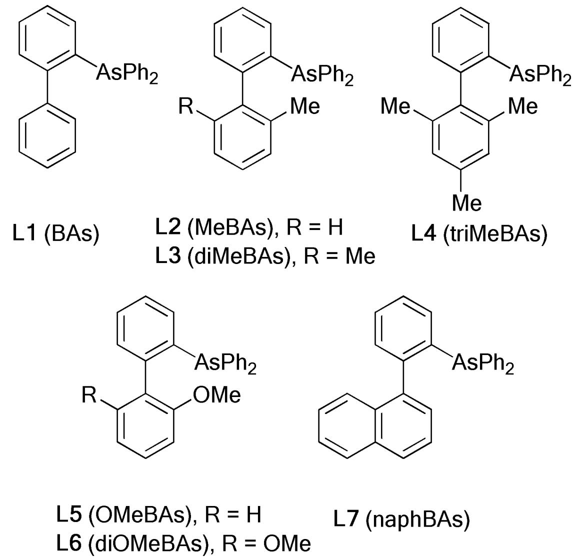


Fig. 1 Biphenyl-based arsine ligands.

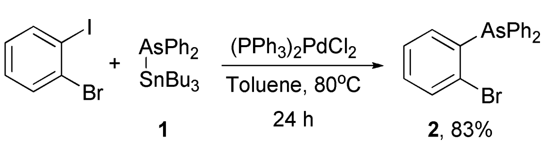
performance as a ligand.[11b] The Pd/**L1**-based catalysts demonstrated significant activity for Pd-catalyzed arsination with perfluoroalkyl iodides (R_fI).[11b] Although the arsine ligand **L1** showed a promising behavior in coupling reactions, its synthetic strategy was limited by the availability of the starting iodobiphenyls.

Our prior results encouraged further fine-tuning of the biphenylarsine ligand **L1** structure and allowed us to investigate the structure-reactivity properties of new biphenylarsine ligands. Herein, we report our studies on the synthesis of a family of biarylarsine ligands (Fig. 1) by an approach, including first the Pd-catalyzed arsination, and then the Suzuki–Miyaura cross-coupling as the key synthetic tool for biaryl construction. Additionally, the activity of new biarylarsine ligands in the Pd-catalyzed arsination with R_fI is also reported.

Results and discussion

Synthesis of arsine precursor

The (2-bromophenyl)diphenylarsine (**2**) was employed as a synthetic intermediate for the synthesis of biarylarsine ligands. The one-pot, two-step reaction of stannane *n*-$Bu_3SnAsPh_2$ (**1**) with 1-bromo-2-iodobenzene catalyzed by $(PPh_3)_2PdCl_2$ in toluene afforded **2** in 83% isolated yield (eqn (1)). The generation and subsequent use of stannane **1** were in agreement with our reported method.[11] For the synthesis of **1** the Ph_2As^- anion was prepared in liquid ammonia from Ph_3As, since by this methodology the anion was obtained more efficiently. The *in situ* generation of the stannane **1** eliminates the isolation and purification of tin reagents.



(1)

Synthesis of biphenylarsine ligands

Due to the particular usefulness of the Suzuki–Miyaura coupling reaction as a method for the formation of C–C bonds,[20] we chose this reaction to build the biaryl structure. To the best of our knowledge this is the first example of the use of aryl halide arsines in this reaction.

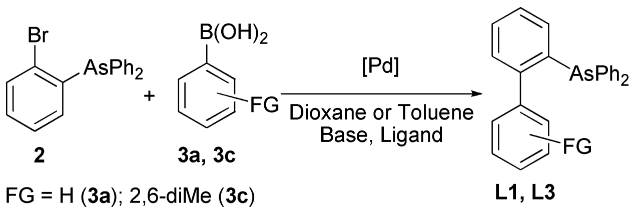
An initial screening was performed to determine the optimum catalyst, ligand, solvent, and base for the reaction between bromoarsine **2** and phenylboronic acid (**3a**). Table 1 summarizes the results obtained. The coupling reaction of arsine **2** with boronic acid **3a** and K_3PO_4 catalyzed by $Pd(OAc)_2$ in dioxane afforded **L1** in 61% yield (entry 1, Table 1). With $Pd(dba)_2$ as a Pd source, a lower yield of **L1** was observed (entry 2, Table 1). The use of Cs_2CO_3 as base decreased the product yield (entry 3, Table 1).

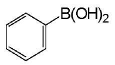
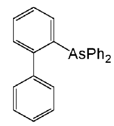
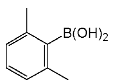
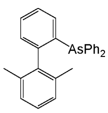
An improvement in the coupling reaction of **2** was observed by using the electron-rich PCy_3 supporting ligand (entry 4, Table 1). However, the less sterically hindered and more available PPh_3 was found to be the most suitable ligand. Excellent yields of biphenylarsine **L1** (98%) were achieved, even though the *ortho*-positioned -$AsPh_2$ moiety in compound **2** is considerably bulky (entry 5, Table 1). It should be noted that the substrate of the coupling reaction could be ligands for the catalyst. Although the triarylarsine **2** is a less σ-donating ligand than phosphines, it is present in a large extent, and this could be a problem for the scope of the coupling reaction. The experimental results showed that despite of the presence of arsine **2** the influence of the supported phosphines ligand could be observed (entries 1 and 5, Table 1). Although we could not discard that the excess of arsine would inhibit the Suzuki–Miyaura coupling, the reaction conversions were high enough.

Thus, the best experimental conditions found for the coupling reaction were those with $Pd(OAc)_2/PPh_3$ and K_3PO_4 as a base and under a nitrogen atmosphere since slightly decreased yields were observed when the reaction was performed in an open system. Following a simple purification procedure under air, biphenylarsine ligand **L1** was isolated in 89% yield. Moreover, **L1** was successfully obtained in two steps starting from 1-bromo-2-iodobenzene with a 74% overall isolated yield. To further explore the efficiency of this catalytic system, the reaction time was decreased to 12 h. However, at this reaction time the conversion of **2** was not complete (entry 6, Table 1). In addition, changing the solvent to toluene slightly decreased the yields of **L1** (entries 7–8, Table 1).

On the other hand, when arsine **2** was allowed to react with 2,6-dimethylphenylboronic acid (**3c**) under the best above mentioned conditions, a poor conversion to the coupling product **L3** was observed (entry 9, Table 1). With longer reaction times and a higher amount of $Pd(OAc)_2$ the yields did not show a considerable increase. The complexity found in this particular transformation derives from the steric impediment of both the aryl bromide and the boronic acid. The ability to prepare particularly hindered biaryls *via* Suzuki–Miyaura coupling has traditionally proven to be a difficult challenge,[20f] particularly with substrates that contain two or more *ortho*,*ortho′*-substituents.[14c,21] In some cases, the use of certain bases has been reported to improve the reaction outcome.[20f,21a] However, when we used $Ba(OH)_2$ or NaOH in our process, the reaction did not proceed. PCy_3 was also examined

Table 1 Optimization of Suzuki–Miyaura reaction with (2-bromophenyl)diphenylarsine (**2**)[a]



	Boronic acid	Pd/L	Base	Time (h)	Product	Yield (%)[b]
1	 **3a**	$Pd(OAc)_2$	K_3PO_4	24	 **L1**	61
2		$Pd(dba)_2$	K_3PO_4	24		54
3		$Pd(OAc)_2$	Cs_2CO_3	24		50
4		$Pd(OAc)_2/PCy_3$	K_3PO_4	24		73
5		$Pd(OAc)_2/PPh_3$	K_3PO_4	24		98
6		$Pd(OAc)_2/PPh_3$	K_3PO_4	12		89
7[c]		$Pd(OAc)_2/PCy_3$	K_3PO_4	24		82
8[c]		$Pd(OAc)_2/PPh_3$	K_3PO_4	24		84
9	 **3c**	$Pd(OAc)_2/PPh_3$	K_3PO_4	24	 **L3**	24
10[d]		$Pd(OAc)_2/PPh_3$	K_3PO_4	48		61
11[d,e]		$Pd(OAc)_2/PPh_3$	K_3PO_4	48		80
12[d,e]		$Pd(dba)_2/PPh_3$	K_3PO_4	48		70
13[e]		$Pd(dba)_2/(o\text{-bph})PCy_2$[f]	K_3PO_4	24		8
14[e]		$Pd(dba)_2/(o\text{-bph})P^tBu_2$[f]	K_3PO_4	24		16

[a] Reaction conditions: the coupling reaction was carried out with bromoarsine **2** (1 mmol), boronic acid (1,5 equiv), [Pd] (1 mol%), phosphine ligand (Pd : L 1 : 4), base (2 equiv), organic solvent (5 mL) and H_2O (1 mL) at 100 °C under an atmosphere of nitrogen. [b] CG yields. [c] With toluene as solvent. [d] The coupling reaction was carried out with boronic acid **3c** (2 equiv) and an extra 2 equiv of **3c** added after 24 h, and the reaction time increased to 48 h. [e] The coupling reaction was carried out with [Pd] 3 mol%. [f] With Pd : L ratio 1 : 2.

for the reaction of **2** with boronic acid **3c**, while Fu found that this sterically less hindered ligand is more effective than $P(^tBu)_3$ in the coupling of aryl chlorides leading to tri-*ortho*-substituted biaryls.[21e] However, in these conditions our reaction produced a lower yield (40%). The yield of biphenylarsine **L3** was improved with an extra addition of boronic acid **3c** during the reaction and extending the reaction time (entry 10, Table 1). Moreover, the coupling reaction was more efficient when 3 mol% of Pd were employed (entry 11, Table 1). It was also found that by using $Pd(dba)_2$ in the above described conditions the reaction gave similar results (entry 12, Table 1). Catalysts employing electron-rich and bulky (*o*-bph)PCy_2 or (*o*-bph)P^tBu_2 ligands were not effective (entries 13–14, Table 1).

Once we had thoroughly optimized the reaction conditions, the Suzuki–Miyaura coupling with aryl boronic acids bearing different substituents **3b** and **3d–3g** and bromoarsine **2** was carried out. Table 2 shows the results. These reactions gave new biaryl arsine ligands **L2–7** in excellent yields (80–99%). The *ortho*-methyl boronic acid **3b** provided the desired disubstituted biaryl **L2** in 98% yield (entry 2, Table 2). It should be noted that, despite of the considerably bulky -$AsPh_2$ moiety in compound **2** and the boronic acid with two methyl groups in the *ortho* positions, the reaction was successfully carried out (entry 3, Table 2). When the 2,4,6-trimethylphenylboronic acid (**3d**) was allowed to react under the optimized conditions for sterically hindered substrates, a 94% yield of biaryl **L4** was achieved (entry 4, Table 2). The coupling reaction with mono- and dimethoxyphenylboronic acids **3e** and **3f** proceeded smoothly in the presence of 1 mol% $Pd(OAc)_2$ and PPh_3 (entries 5–6, Table 2). In addition, the quantitative transformation of boronic acid **3f** to the tri-substituted biaryl **L6** could be achieved by using 3 mol% of Pd (entry 7, Table 2). The relatively bulky 1-naphthylboronic acid (**3g**) afforded the coupling product **L7** in 80% yields (entry 8, Table 2).

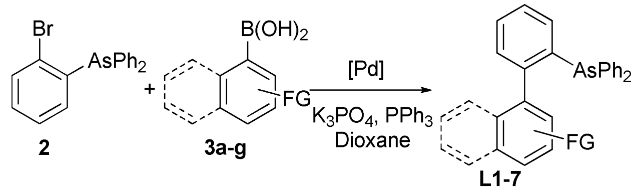
Synthetically a new class of biphenylarsine ligands can be readily prepared in two high-yielding Pd-catalyzed steps from commercially available starting materials (*i.e.*, 1-bromo-2-iodobenzene, $AsPh_3$ and boronic acids). The arsine ligands were obtained as air-stable solids in overall isolated yields of up to 79% .

Evaluation of biphenylarsine ligands. Pd-catalyzed arsination with perfluoroalkyl iodides

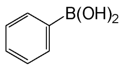
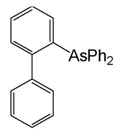
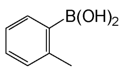
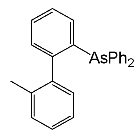
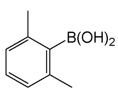
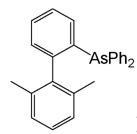
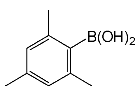
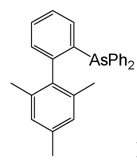
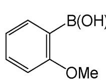
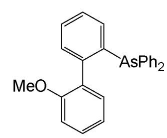
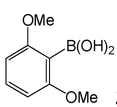
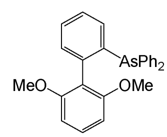
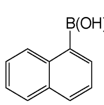
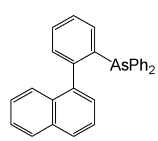
In view of the success of various arsine ligands[1–10] and sterically demanding phosphines[22] as the supporting ligand in Pd-catalyzed Stille reactions, we evaluated in a previous work the effectiveness of **L1** as a ligand in the reaction of stannane $n\text{-}Bu_3SnAsPh_2$ (**1**) with perfluoroalkyl iodides (R_fI).[11b] A variety of phosphine and arsine ligands were screened to improve the low reactivity of R_fI in Pd-catalyzed arsination, which could be ascribed to its reluctance to participate in oxidative addition, where the structure of the ligand has a significant influence. Accordingly, yields of perfluoroalkyl arsines Ph_2AsR_f were highly dependent on the ligand.[11b] It should be noted that ligand **L1** was found to achieve the best results for this transformation. The interest in this simple methodology is further enhanced by evidence in the potential usefulness of Ph_2AsR_f products as a new class of electron-deficient arsine ligands.[9b,12,23]

We evaluated the effect of biphenyl ligand substituents on Pd-catalyzed arsination of perfluoroalkyl iodides (R_fI) with our

Table 2 Suzuki–Miyaura cross-coupling with (2-bromophenyl)diphenylarsine (**2**) and substituted aryl boronic acids **3a–g**[a]

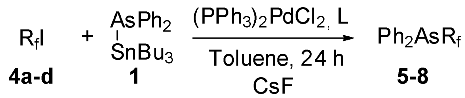


FG = H (**3a**); 2-Me (**3b**); 2,6-diMe (**3c**); 2,4,6-triMe (**3d**); 2-OMe (**3e**); 2,6-diOMe (**3f**); Naph (**3g**)

	Boronic acid	Catalyst (loading)	Time (h)	Product	Yield (%)[c]
1	 **3a**	$Pd(OAc)_2$ (1 mol%)	24	 **L1**	98 (89)
2	 **3b**	$Pd(OAc)_2$ (1 mol%)	24	 **L2**	98 (88)
3[b]	 **3c**	$Pd(OAc)_2$ (3 mol%)	48	 **L3**	80 (71)
4[b]	 **3d**	$Pd(OAc)_2$ (3 mol%)	48	 **L4**	94 (85)
5	 **3e**	$Pd(OAc)_2$ (1 mol%)	24	 **L5**	96 (88)
6	 **3f**	$Pd(OAc)_2$ (1 mol%)	24	 **L6**	83 (74)
7	 **3g**	$Pd(dba)_2$ (3 mol%)	24	 **L7**	99 (95)
8		$Pd(OAc)_2$ (1 mol%)	24		80 (70)

[a] Reaction conditions: the coupling reaction was carried out with **2** (1 mmol), boronic acid (1,5 equiv), [Pd], PPh_3 (Pd : L 1 : 4), K_3PO_4 (2 equiv), dioxane (5 mL) and H_2O (1 mL) at 100 °C for 24 h under atmosphere of nitrogen. [b] With 2 equiv of boronic acid and an extra 2 equiv added after 24 h, for 48 h. [c] GC yields. Isolated yields in branches (average of two or more experiments).

Table 3 Pd-catalyzed arsination with n-$Bu_3SnAsPh_2$ (**1**) and perfluoroalkyl iodides (**4a–d**) with biarylarsine ligands[a,b]

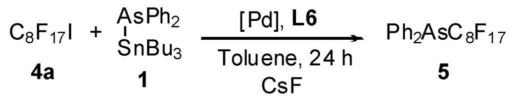


R_fI = $C_8F_{17}I$ (**4a**), C_4F_9I (**4b**), $C_6F_{13}I$ (**4c**), $C_{10}F_{21}I$ (**4d**)

Entry	R_fI	L	Conditions[a,b]	Product	Yield (%)[c]
1		**L2**	—		59
2		**L3**	—		42
3		**L7**	—		45
4		**L5**	—		100 (92)
5	$C_8F_{17}I$	**L6**	—	$Ph_2AsC_8F_{17}$	100
6	**4a**	**L5**	12 h	**5**	93
7		**L5**	25 °C		66
8		**L5**	Pd 5 mol(%)		80
9		**L5**	Pd 2 mol(%)		74
10	C_4F_9I **4b**	**L5**	—	$Ph_2AsC_4F_9$ **6**	57 (43)
11	$C_6F_{13}I$ **4c**	**L5**	—	$Ph_2AsC_6F_{13}$ **7**	63 (50)
12	$C_{10}F_{21}I$ **4d**	**L5**	—	$Ph_2AsC_{10}F_{21}$ **8**	92 (81)

[a] Reaction conditions: the Ph_2As^- anion was prepared in liquid ammonia (300 mL) from $AsPh_3$ (1 mmol) and Na metal (2 mmol); then n-Bu_3SnCl (1 mmol) was added. The cross-coupling reaction was carried out with perfluoroalkyl iodide (0.7 mmol), $(PPh_3)_2PdCl_2$ (10 mol%), ligand (Pd : L 1 : 4) and CsF (3 eq.) for 24 h in toluene at reflux under an atmosphere of nitrogen. [b] When the reaction conditions were modified, details are provided in the table. [c] CG yields. Isolated yields in brackets. The yields reported represent at least the average of two reactions.

Table 4 Effect of the Pd source and Pd : L ratio on the arsination with n-$Bu_3SnAsPh_2$ (**1**) and $C_8F_{17}I$ (**4a**) with **L6**[a]



Entry	Catalyst	Pd:**L6** ratio	Product **5**(%)[b]
1	$(PPh_3)_2PdCl_2$	1 : 4	100
2	$(PPh_3)_2PdCl_2$	1 : 2	21
3	$Pd_2(dba)_3$	1 : 4	79
4	$Pd_2(dba)_3$	1 : 2	32
5	$Pd(OAc)_2$	1 : 4	13
6	$Pd(OAc)_2$	1 : 2	63
7	$PdCl_2$	1 : 4	5

[a] Reaction conditions: Ph_2As^- anion was prepared in liquid ammonia (300 mL) from $AsPh_3$ (1 mmol) and Na metal (2 mmol); then n-Bu_3SnCl (1 mmol) was added. The cross-coupling reaction was carried out with $C_8F_{17}I$ (**4a**) (0.7 mmol), [Pd] (10 mol%), **L6** and CsF (3 equiv) for 24 h in toluene at reflux under an atmosphere of nitrogen. [b] CG yields. The yields reported represent at least the average of two reactions.

newly prepared ligands **L2–L7**. At first, we selected $C_8F_{17}I$ (**4a**) as a model substrate; the results of the arsination with stannane **1** are shown in Table 3. In all reactions the conversion of the substrate was complete. The only side product achieved, was the reduced perfluoroalkane (R_fH). We have previously shown that arsination reaction with **4a** in the presence of ligand **L1** under the optimized conditions gave perfluoroalkyl arsine $Ph_2AsC_8F_{17}$ (**5**) in 87% yield.[11b]

The arsination reaction of **4a** with arsine-supported ligands **L2**, **L3** and **L7** under the previously optimized conditions provided perfluoroalkyl arsine **5** in lower yields (entries 1–3, Table 3). From these results it appears that the sterically more hindered ligand reduces catalytic efficiency. However, catalysts derived from both biarylarsine ligands with methoxy group **L5** and **L6** led to a highly effective catalytic complex, capable of quantitatively converting **4a** to perfluoroalkyl arsine **5** (entries 4–5, Table 3). Thus, the outstanding activity of the catalysts derived from **L5** and **L6** in the Pd-catalyzed arsination with R_fI compared to **L1** arises from the influence of the methoxy group on the non-arsine-containing aromatic ring of the ligands.

We examined the reaction conditions to extend the catalytic system. We found that, by using a **L5**/Pd catalyst, the reaction time could be reduced by half (entry 6, Table 3). Slightly lower yields were observed with a lower catalyst loading (5 and 2 mol%) or room temperature reaction conditions (entries 7–9, Table 3).

The effectiveness of **L5** was examined in the arsination reaction with other R_fI with perfluoroalkyl chains having four to ten carbon atoms (**4b–c**). It was found that, as the chain length of R_fI increased, the couplings led to progressively improved yields (entries 10–12, Table 3). Moreover, **L5**/Pd catalyst afforded higher yields of perfluoroalkyl arsines **6–8**, compared to those obtained with the non-substituted **L1** (45%, 55% and 78% respectively).[11b]

It is important to note that the Pd source used to evaluate the behavior of the different ligands was $(PPh_3)_2PdCl_2$ on the basis of previous screening.[11b] Despite that, the experimental results showed that regardless of the presence of PPh_3, the influence of the supported arsine ligands could be noticed; other phosphine-free sources of Pd were considered. The results of Pd-catalyzed arsination with **1** and **4a** in the presence of different Pd/**L6** catalysts and Pd : L ratios are shown in Table 4.

When we examined the coupling reaction using $(PPh_3)_2PdCl_2$ and **L6** in a Pd : L ratio 1 : 2 the yields of the reaction were drastically decreased, compared to those previously obtained for a Pd : L ratio 1 : 4 (entries 1 and 2, Table 4). All other Pd catalysts evaluated ($Pd_2(dba)_3$, $Pd(OAc)_2$, $PdCl_2$) with **L6** in Pd : L ratios 1 : 4 and 1 : 2 were less effective than $(PPh_3)_2PdCl_2$ (entries 3–7, Table 4). However, it should be noted that under phosphine-free conditions with $Pd_2(dba)_3$ in a Pd : L ratio of 1 : 4 a 79% yield of perfluoroarsine **5** was obtained (entry 3, Table 4). Despite the presence of an unwanted PPh_3 ligand, the Pd(0) complexes generated from $(PPh_3)_2PdCl_2$ and **L6** demonstrated to be the most reactive.

The efficiency of catalysts derived from biarylphosphine ligands in cross-coupling reactions has been attributed to a combination of factors: (i) electron-donating character; (ii) their steric bulk favoring the formation of the active *monophosphine* complex LPd(0);[24] and (iii) the absence of *ortho* hydrogens which prevents the formation of palladacycles.[25] Therefore, we believe that the ability of our biarylarsine ligands to allow the formation of a reasonable amount of highly reactive LPd species is the key for a successful coupling of the low reactive R_fI, and that monoligated Pd species could be responsible for a rapid oxidative addition of the R_fI to the Pd(0) center.

It should be noted that, although arsines are less bulky and poorer σ-donors or better π-acceptors than the analogous phosphines,[4h] the catalysts derived from Pd-arsine complexes were particularly efficient in this coupling reaction. Moreover, the weak donicity of the arsine ligand could also improve the rate of the transmetalation step.

In addition, experimental and computational studies have established that either a Pd-arene interaction with the *ipso* carbon or a Pd–O interaction with an oxygen atom of the methoxy group on the second aromatic ring stabilizes intermediate complexes, increasing catalyst life time.[14b,26] Taking into account our results, we consider that Pd–O interactions with **L5** and **L6** ligands could contribute to the stability and thus to the efficiency of their catalysts relative to other biarylarsine ligands.

Conclusions

We have developed a versatile and high-yielding method requiring only two steps to prepare a new family of biarylarsine ligands from commercially available starting materials. On the basis of this development, the properties of these ligands can be varied according to the steric and electronic effects associated with the substituents in the biaryl backbone.

Our newly prepared biphenylarsine ligands show great activity for Pd-catalyzed arsination with R_fI. Specifically, **L5** and **L6** evidence unprecedented activity in this coupling reaction, producing a catalyst system that overcomes mayor limitations of the reaction.

In addition to the high reactivity of catalytic systems based upon biarylarsines **L1**, **L5** and **L6**, these ligands have some notable features: (i) they are crystalline materials, (ii) they are air-stable, and (iii) thermal stable at the reaction conditions (*i.e.* toluene at reflux).

Further tuning of the biarylarsine ligand structure, as well as its applications to other transition-metal catalyzed reactions, is underway.

Experimental

General methods

Gas chromatographic analyses were performed on a gas chromatograph with a flame ionization detector, and equipped with the following columns: HP-1 25 m × 0.20 mm × 0.25 μm column. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were conducted on a high resolution spectrometer Bruker Advance 400, in $CDCl_3$ as solvent. Gas chromatographic/mass spectrometer analyses were carried out on a GC-MS QP 5050 spectrometer equipped with a VF-5ms, 30 m × 0.25 mm × 0.25 μm column. Melting points were performed with an electrical instrument. The HRMS were recorded at the UCR Mass Spectrometry Facility, University of California, USA. The elemental analyses were carried out on an EXETER CE 440 at the UMYMFOR-FCEN, University of Buenos Aires, Argentina.

The $AsPh_3$, PPh_3, (o-bph)PCy_2, (o-bph)P^tBu_2, PCy_3, n-Bu_3SnCl, $(PPh_3)_2PdCl_2$, $Pd(OAc)_2$, $Pd(dba)_2$, CuI, R_fI, $ArB(OH)_2$, K_3PO_4, Cs_2CO_3, $Ba(OH)_2$, NaOH, Na_2SO_4 and ArI were commercially available and used as received. (2-bromophenyl)diphenylarsine (**2**) was prepared as previously reported from the corresponding 2-bromoiodobenzene.[11b] CsF was dried under vacuum at 120 °C. All solvents were analytical grade and distilled before use. Toluene was distilled under nitrogen with Na-benzophenone and dioxane was distilled under nitrogen. All reactions were carried out under atmosphere of nitrogen. Silica gel (0.063–0.200 mm) was used in column chromatography.

General procedure for the preparation of *n*-$Bu_3SnAsPh_2$

A typical procedure involves the formation of Ph_2As^- ions from Ph_3As and Na metal in liquid ammonia, followed by addition of n-Bu_3SnCl to obtain the n-$Bu_3SnAsPh_2$. Into a three-necked, 500 mL, round-bottomed flask equipped with a cold finger condenser charged with dry ice–ethanol, a nitrogen inlet, and a magnetic stirrer, approximately 400 mL of ammonia previously dried with Na metal under nitrogen was condensed. $AsPh_3$ (1.0 mmol) and then 2 equivalents of Na metal (2 mmol) in small pieces were added, with a pause for bleaching between each addition. At 20–30 min from the last addition, Ph_2As^- anion was formed (clear orange-red solution), and n-Bu_3SnCl (1 mmol) was added slowly. The mixture was then stirred for 5 min and the liquid ammonia allowed to evaporate. The evaporation left a white solid residue which was dissolved in dry organic solvent (12 mL). Reagent **1** was formed in almost quantitative yield. This stannane solution without purification was used for the cross-coupling Pd-catalyzed arsinations.

Representative procedure for Pd-catalyzed cross-coupling Suzuki–Miyaura reaction

The following reaction procedure is representative of all cross-coupling Suzuki–Miyaura reactions. Into a Schlenk tube with a Teflon screw-cap septum equipped with a magnetic stirrer and a nitrogen inlet, $Pd(OAc)_2$ (1 mol%, 0.01 mmol), PPh_3 (Pd : L 1 : 4, 0.04 mmol) (2-bromophenyl)diphenylarsine (**2**) (1 mmol), arylboronic acid (**3a–g**) (1.5 mmol), K_3PO_4 (2 mmol) were added, and then dioxane (5 mL) and water (2.5 mL) were added. The reaction mixture was heated for 24 h in an oil bath at 100 °C. The solvent condensation took place on the walls of Schlenk tube. After being cooled to room temperature, the mixture was diluted with water and then extracted three times with CH_2Cl_2 (30 mL each). The biarylarsine product was purified in an open atmosphere by silica-gel column chromatography after being dried with anhydrous Na_2SO_4. These reactions were scaled up to 5 mmol of (2-bromophenyl)diphenylarsine (**2**) at most.

2-Diphenylarsino-2′-methylbiphenyl (L2). Compound **L2** was obtained according to the general procedure. Product **L2** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether) obtaining 0.3488 g of **L2** (88% yield). After crystallization from CH_3CN cubic crystals were obtained (mp 74.3–75.7 °C). ^{1}H NMR ($CDCl_3$): δ 7.42–7.18 (16 H, m); 7.08–7.04 (1 H, m); 6.91 (1 H, d, ^3J = 8 Hz); 2.05 (3 H, s). ^{13}C NMR ($CDCl_3$): δ 147.45; 141.61; 139.95; 139.90; 139.69; 136.03; 134.00; 133.94; 133.84; 130.43; 129.80; 129.62; 128.51; 127.74; 127.57; 125.05; 20.51. NMR 2D (COSY-45) δ_H/δ_C: 2.05/6.91; 2.05/7.09; 2.05/7.23; 6.91/7.09; 6.91/7.26. NMR 2D (HSQC) δ_H/δ_C: 2.05/20.51; 6.90/129.80; 7.04/125.05; 7.23/133.78; 7.38/128.51. MS: m/z (%): 396 (89), 381 (74), 303 (12), 241 (84), 227 (100), 165 (88), 152 (50), 139 (6), 115 (6), 91 (8), 78 (9), 51 (6). HRMS (EI): calcd. for $C_{25}H_{22}As$ 397.0932, found $[M+H]^+$ 397.0937. Elemental analysis (%) calc. for $C_{25}H_{21}As$: C, 75.76; H, 5.34; As, 18.90. Found: C, 75.53; H, 5.28.

2-Diphenylarsino-2′,6′-dimethylbiphenyl (L3). Compound **L3** was obtained according to the general procedure. Product **L3** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether), yielding 0.2914 g of the product (71% yields). After crystallization from CH_3CN cubic crystals were obtained (mp 92.5–93.3 °C). ^{1}H NMR ($CDCl_3$): δ 7.39–7.36 (1 H, m); 7.29–7.22 (13 H, m); 7.09 (1H, d, ^3J = 7.6); 6.87 (2 H, s); 2.33 (3 H, s); 1.77 (6 H, s). ^{13}C NMR ($CDCl_3$): δ 146.60; 141.35; 139.89; 139.72; 136.39; 134.27; 133.80; 129.22; 129.05; 128.50; 128.22; 127.51; 127.34; 127.10; 20.77. NMR 2D (COSY-45) δ_H/δ_C: 1/6.82; 7.04/7.19; 7.11/7.40; 7.29/7.40. NMR 2D (HSQC) δ_H/δ_C: 1.79/20.77; 7.03/127.10; 7.10/129.22; 7.19/127.47; 7.24/133.76; 7.38/129.05. NMR 2D (HMBC) δ_H/δ_C: 1.79/127.10; 1.79/136.39; 1.79/141.35; 7.04/20.77. MS: m/z (%): 410 (77), 395 (60), 317 (8), 255 (31), 241 (100), 227 (17), 179 (37), 165 (64), 152 (32), 91 (14), 77 (14), 51 (12). HRMS (EI): calcd. for $C_{26}H_{24}As$ 411.1088, found $[M - H]^+$ 411.1099. Elemental analysis (%) calc. for $C_{26}H_{23}As$: C, 76.09; H, 5.65; As, 18.26. Found: C, 75.75; H, 5.72.

2-Diphenylarsino-2′,4′,6′-trimethylbiphenyl (L4). Compound **L4** was obtained according to the general procedure. Product **L4** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether), yielding 0.3607 g of the product (85% yield). After crystallization from CH_3CN needle-shaped crystals were obtained (mp 118.9–119.5 °C). ^{1}H NMR ($CDCl_3$): δ 7.39–7.36 (1 H, m); 7.29–7.22 (13 H, m); 7.10–7.08 (1H, d, ^3J = 7.6); 6.87 (2 H, s); 2.33 (3 H, s); 1.77 (6 H, s). ^{13}C NMR ($CDCl_3$): δ 146.72; 140.05; 139.87; 138.55; 137.00; 136.17; 134.29; 133.77; 129.52; 129.03; 128.48; 128.18; 127.91; 127.25; 21.22; 20.70. NMR 2D (COSY-45) δ_H/δ_C: 1.77/2.33; 1.77/6.87; 2.33/6.87; 7.09/7.39; 7.26/7.09; 7.27/7.38. NMR 2D (HSQC) δ_H/δ_C: 1.77/20.70; 2.33/21.22; 6.87/127.91; 7.09/129.52; 7.26/127.25; 7.38/129.03. NMR 2D (HMBC) δ_H/δ_C: 1.77/127.91; 1.77/136.17; 1.77/138.55; 2.33/127.91; 2.33/137.00; 6.87/127.91; 6.87/138.55; 7.09/127.25; 7.09/140.05; 7.38/134.29. MS: m/z (%): 425 (29), 424 (84), 410 (18), 409 (75), 270 (19), 269 (37), 255 (100), 227 (13), 194 (22), 193 (27), 179 (44), 178 (31), 165 (22), 152 (20), 91 (9). HRMS (EI): calcd. for $C_{27}H_{26}As$ 425.1245, found $[M - H]^+$ 425.1235. Elemental Analysis (%) calc. for $C_{27}H_{25}As$: C, 76.41; H, 5.94; As, 17.65. Found: C, 76.15; H, 6.02.

2-Diphenylarsino-2′-methoxybiphenyl (L5). Compound **L5** was obtained according to the general procedure. Product **L5** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether), yielding 0.3629 g (88% yield) of the product as an amorphous white solid (mp 87.6–89 °C). ^{1}H NMR ($CDCl_3$): δ 7.38 (1 H, td; ^3J = 7.5 Hz; ^4J = 1.4 Hz); 7.32–7.16 (14 H, m); 7.09 (1 H, dd, ^3J = 7.5 Hz; ^4J = 1.6 Hz); 6.91 (1 H, td, ^3J = 7.4 Hz; ^4J = 1.0 Hz); 6.82 (1 H, d, ^3J = 8 Hz); 3.40 (3 H, s). ^{13}C NMR ($CDCl_3$): δ 156.58; 144.66; 140.96; 140.29; 140.10; 134.20; 133.74; 131.45; 130.99; 130.21; 129.09; 128.53; 128.44; 128.35; 128.06; 127.94; 127.49; 120.10; 110.26; 54.80. NMR 2D (COSY-45) δ_H/δ_C: 3.40/6.83; 6.82/7.30; 6.91/7.08; 6.91/7.30; 7.10/7.30. NMR 2D (HSQC) δ_H/δ_C: 3.40/54.8; 6.82/110.27; 6.91/120.10; 7.08/131.45. NMR 2D (HMBC) δ_H/δ_C: 3.40/156.58; 6.82/120.1; 7.09/156.59. MS: m/z (%): 412 (9), 382 (30), 381 (100), 303 (6), 257 (24), 243 (11), 228 (10), 227 (23), 213 (13), 168 (11), 152 (16), 151 (9), 139 (9), 78 (4), 51 (5). HRMS (EI): calcd. for $C_{25}H_{22}AsO$ 413.0881, found $[M - H]^+$ 413.0888. Elemental analysis (%) calc. for $C_{25}H_{21}AsO$: C, 72.82; H, 5.13; As, 18.17; O, 3.88. Found: C, 72.95; H, 5.35.

2-Diphenylarsino-2′,6′-dimethoxybiphenyl (L6). Compound **L6** was obtained according to the general procedure. Product **L6** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether), yielding 0.4203 g of the product (95% yield). After crystallization from CH_3CN cubic crystals were obtained (mp 133.0–133.8 °C). ^{1}H NMR ($CDCl_3$): δ 7.41–7.39 (1 H, m); 7.29–7.22 (13 H, m); 7.18–7.16 (1 H, m); 6.53 (2 H, d, ^3J = 8.8 Hz); 3.46 (6 H, s). ^{13}C NMR ($CDCl_3$): δ 157.83; 140.80; 140.63; 133.97; 133.74; 130.81; 129.20; 128.45; 128.24; 127.83; 127.37; 119.30; 103.57; 55.39. NMR 2D (COSY-45) δ_H/δ_C: 3.46/6.52; 3.46/7.26; 6.52/7.28; 7.17/7.25; 7.17/7.40; 7.25/7.40. NMR 2D (HSQC) δ_H/δ_C: 3.46/55.39; 6.56/103.57; 7.17/133.97; 7.40/129.20. MS: m/z (%): 442 (8), 411 (100), 396 (8), 273 (8), 257 (8), 227 (12), 214 (10), 152 (7), 77 (5), 51 (6). HRMS (EI): calcd. for $C_{26}H_{24}AsO_2$ 443.0987, found $[M - H]^+$ 443.0998. Elemental analysis (%) calc. for $C_{26}H_{23}AsO_2$: C, 70.59; H, 5.24; As, 16.94; O, 7.23. Found: C, 70.65; H, 5.13.

1-(2-Diphenylarsinophenyl)naphthalene (L7). Compound **L7** was obtained according to the general procedure. Product **L7** was isolated from the reaction mixture by silica-gel column chromatography (petroleum ether), obtaining 0.3026 g of the product (70% yield). After extensive drying with a vacuum pump, **L7** was obtained as an amorphous white solid (mp 50–53 °C). ^{1}H NMR ($CDCl_3$): δ 7.87–7.81 (2 H, m); 7.46–7.10 (20 H, m). ^{13}C NMR ($CDCl_3$): δ 145.99; 140.67; 140.30; 139.98; 139.57; 133.99; 133.76; 133.72; 133.35; 132.35; 130.62; 128.51; 128.36; 128.26; 128.20; 128.06; 127.89; 127.86; 127.81; 126.38; 125.83; 125.66; 124.68. MS: m/z (%): 433 (15), 432 (51), 354 (10), 279 (14), 278 (45), 277 (100), 202 (75), 177 (14). HRMS (EI): calcd. for $C_{28}H_{22}As$ 433.0932, found $[M - H]^+$ 433.0918. Elemental Analysis (%) calc. for $C_{28}H_{21}As$: C, 77.78; H, 4.90; As, 17.33. Found: C, 77.86; H, 4.72.

Representative procedure for Pd-catalyzed arsination reaction with *n*-$Bu_3SnAsPh_2$ and perfluoroalkyl iodides (R_fI)

The following reaction procedure of *n*-$Bu_3SnAsPh_2$ (**1**) with perfluorooctyl iodide (**4a**) is representative of all these reactions. Into a three-necked, 500 mL, round-bottomed flask equipped with a cold finger condenser charged with dry ice–ethanol, a nitrogen inlet, and a magnetic stirrer, approximately 400 mL of ammonia previously dried with Na metal under nitrogen was condensed. The $AsPh_3$ (1.0 mmol) was added followed by 2 equivalents of Na metal (2 mmol) in small pieces, waiting for bleaching between each addition. After 20–30 min of the last addition, Ph_2As^- anion was formed (clear orange-red solution), and *n*-Bu_3SnCl (1 mmol) was added slowly. The mixture was stirred for 5 min and the liquid ammonia was then allowed to evaporate. Evaporation left a solid white residue which was dissolved in dry toluene (12 mL). This solution was added *via* cannula and syringe into a Schlenk tube. In the tube, CsF (3 eq.) was previously dried under vacuum at 120 °C for 3 h; after cooling the tube at room temperature, $(PPh_3)_2PdCl_2$ (10 mol%), ligand (40 mol%), substrate **4a** (0.7 mmol) and toluene (3 mL) were added. When the solution of stannane **1** was added, the reaction mixture turned deep brown. The reaction mixture was heated for 24 h in an oil bath at reflux. Water was added to the cooled reaction mixture and then extracted three times with CH_2Cl_2 (30 mL each). After being dried with anhydrous Na_2SO_4, product **5** was quantified by CG using the internal standard method.

The products were characterized by ^{1}H NMR, ^{13}C NMR, GC-MS and HRMS. All these spectroscopic data agreed with those previously reported for compounds **L1**[11b] and **5–8**.[12a]

Acknowledgements

This work was supported by ACC, CONICET, FONCYT and SECYT. P.M.U. and M.N.L. gratefully acknowledges CONICET for fellowships.

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