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Highly Efficient Palladium-Catalyzed Arsination. Synthesis of a Biphenyl Arsine Ligand and Its Application to Obtain Perfluoroalkylarsines

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An efficient one-pot, two-step Pd-catalyzed arsination with *n*-$Bu_3SnAsPh_2$ (**1**) and sterically hindered aryl iodides (ArI) with different functional groups is reported. The cross-coupling reactions of this stannane with ArI afforded the functionalized triarylarsines in very good isolated yields (71−88%). By using this methodology, a biphenyl arsine ligand, $AsPh_2$(bph), was achieved, and its use as ligand in the Pd-catalyzed arsination with R_fI to obtain perfluoroalkylarsines is also reported. In this reaction, the activity of a variety of phosphine and arsine ligands was investigated. The new biphenyl arsine ligand $AsPh_2$(bph) proved to be the best one for the arsination reaction with R_fI.

Introduction

The chemistry of organoarsines has been extensively developed and their use in organic synthesis arouses much interest.[1] However, organoarsine compounds are also known as ligands in transition metal complexes, many of which have been used in metal-catalyzed reactions. Recently, novel metal complexes of arsine ligands with Pt, Pd, and other metals have been reported.[2]

Although tertiary phosphines constitute the group of ligands most widely used in transition metal chemistry, mainly due to their versatile tuning abilities via steric and electronic properties,[3] arsines are drawing particular attention as ligands in metal-catalyzed reactions. 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; therefore, novel types of ligands are generally required.

Arsines have been reported to be ligands more suitable than phosphines in several transition-metal-catalyzed organic reactions, such as Stille[4] and Suzuki−Miyaura[5] cross-coupling reactions, Negishi reactions,[6] cross-coupling with arylsilanols,[7] Heck reactions,[8] hydroformylation of terminal alkenes,[9] hydrosilylation,[10] carbonylation,[11] or polymerization.[12]

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Some other examples of Pd-catalyzed reactions, where arsines have been determined to be particularly useful ligands, have also been reported.[13]

Currently, the development of new methods to obtain organoarsines is increasingly recognized as central in the synthesis of new ligands. The classic methods for preparing tertiary arsines involve the reaction of organolithium or organomagnesium reagents with haloarsines, reactions incompatible with many functional groups.[14] A further method implies the reaction of aryl halides with Ph_2AsM (M = Li, Na, K) prepared *in situ*, usually in liquid ammonia.[15] Triarylarsines were also obtained by the photostimulated reactions of Ph_2As^- ions with aryl halides by the $S_{RN}1$ mechanism in liquid ammonia; however, a scrambling of products was observed.[16] Moreover, a synthesis of arsine sulfonic acids from 4-fluorobenzenesulfonate with $AsPh_2K$ was described.[17]

The first Ni-catalyzed arsination was reported by Shibasaki and co-workers for the synthesis of BINAs and BINAPAs ligands, by reaction of BINOL ditriflate with Ph_2AsH.[18] Moreover, a Pd-catalyzed arsination of aryl triflates to achieve functionalized arsines was recently reported.[2f,19] The catalytic reaction proceeded by a Pd-Ar/As-Ph exchange with triphenylarsine as the arsinating agent, yielding no more than 51% yield of triarylarsines after 4−5 days.

Additionally, we have developed a versatile methodology that allows for C−heteroatom bond formation through a cross-coupling Pd-catalyzed reaction of different electrophiles with organoheteroatom stannanes R_3SnZPh_n (Z = P, Se) in a one-pot, two-step reaction.[20] Following the same methodology, we have also performed a few examples of As−C bond formation by the Pd-catalyzed reaction of aryl iodides and triflates with n-$Bu_3SnAsPh_2$.[20c,21]

We have also reported the Pd-catalyzed cross-coupling reaction of organoheteroatom stannanes containing elements of groups 15 (P, As) and 16 (Se) with perfluoroalkyl iodides (R_fI).[22] With this methodology, new types of potential perfluoroalkylphosphine, perfluoroalkylarsine, and perfluoroalkylselenide Ph_nZR_f (n = 2, Z = P, As; n = 1, Z = Se) ligands were obtained.

In recent years, organofluorine compounds have attracted particular interest for displaying unique reactivities and selectivities and for their promising applications in biological and material science,[23] in particular those containing perfluoroalkyl groups (R_f) becoming increasingly importance. Perfluoroalkyl-substituted phosphines have lately drawn much attention due to their potential application as ligands in organometallic chemistry.[24,25] However, perfluoroalkylarsines have scarcely been mentioned in the literature.[26]

It should be noted that ligands with unusual stereoelectronic properties, such as electron-poor or electroneutral ligands, have been little developed,[27] probably due to the lack of methodologies for introducing electron-withdrawing substituents. For instance, synthetic routes to perfluoroalkylphosphines $R_{3-n}P(R_f)_n$[28] or perfluoroalkylarsines $R_{3-n}As(R_f)_n$[26,29] are not numerous. Consequently, a suitable synthesis for a wide range of this type of ligands remains a challenging task. A convenient route to obtain perfluoroalkylarsines was

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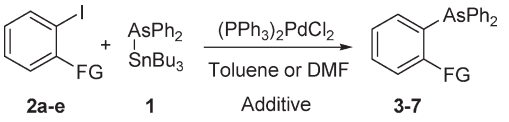
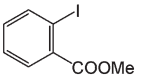
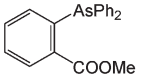
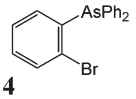
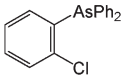
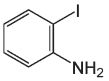
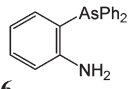
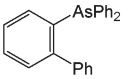
Table 1. Pd-Catalyzed Arsination of *ortho*-Substituted ArI (2a−e) with *n*-$Bu_3SnAsPh_2$ (1) in the Presence of $(PPh_3)_2PdCl_2$[a]



2a-e **1** **3-7**

FG = COOMe (**2a**), Br (**2b**), Cl (**2c**), NH_2 (**2d**), Ph (**2e**)

Entry	Substrate	Conditions	Product	Isolated Yield (%)
1		Toluene (80°C)		75
2		Toluene (80°C), PPh_3		72
3		Toluene (80°C), PPh_3, CuI		71
4		DMF (120°C), PPh_3, CuI		72
5	**2a**	DMF (120°C), PPh_3, CsF	**3**	65
6	 **2b**	Toluene (80°C)	 **4**	83
7	 **2c**	Toluene (80°C)	 **5**	88
8	 **2d**	Toluene (80°C)	 **6**	75
9		Toluene (80°C)		43
10	 **2e**	Toluene (80°C), PPh_3	 **7**	48
11		Toluene (80°C), PPh_3, CuI		71

[a] Reaction conditions: Ph_2As^- anion was prepared in liquid ammonia (300 mL) from $AsPh_3$ (1 mmol) and Na metal (2 mmol); *n*-Bu_3SnCl (1 mmol) was then added. The cross-coupling reaction was carried out with aryl halide (0.7 mmol) and $(PPh_3)_2PdCl_2$ (1.5 mol %), PPh_3 (Pd:L 1:4), CsF (3 equiv), or CuI (Pd:Cu 1:2) for 24 h at 80 °C when toluene was used or at 120 °C with DMF.

recently provided by us via the Pd-catalyzed cross-coupling arsination with R_fI.[22]

Expanding the scope of the Pd-catalyzed arsination to the synthesis of arsine ligands, herein we report on the further use of this reaction for two different purposes. At first, we present the Pd-catalyzed arsination with sterically hindered aryl iodides (ArI) substituted with different functional groups, with an emphasis on the extent of the reaction in terms of synthetic capability. Additionally, an application of this methodology to the synthesis of a biphenyl arsine ligand, $AsPh_2$(bph) (bph = biphenyl), and its use as a ligand in the Pd-catalyzed arsination with R_fI is also reported. Moreover, the activity of a variety of phosphine and arsine ligands in this reaction was investigated.

Results and Discussion

Pd-Catalyzed Arsination with Aryl Iodides. In a previous work, we described for the first time the Pd-catalyzed cross-coupling arsination with the stannane *n*-$Bu_3SnAsPh_2$ (**1**), providing a few examples of the synthesis of Ph_2AsAr (Ar = 1-Naph, 4-$MeOC_6H_4$, and 4-ClC_6H_4).[21] Considering the applications of tertiary arsines as ligands, we extended the studies of Pd-catalyzed arsination to more sterically hindered aryl iodides: *ortho*-substituted ones. Furthermore, we also established that additional common functional groups were compatible under these arsination reaction conditions.

The generation and subsequent use of arsine stannane **1** were in agreement with our procedure previously reported.[21] The Pd-catalyzed cross-coupling reaction of **1** with aryl iodides (**2a−e**) was carried out in a one-pot, two-step procedure. The *in situ* generation of the stannanes eliminates the isolation and purification of tin reagents. The results of the Pd-catalyzed arsination are shown in Table 1.

First, the cross-coupling reaction of aryl iodide **2a** as model substrate was examined. When **2a** was allowed to react with stannane **1** in toluene catalyzed by $(PPh_3)_2PdCl_2$ (1.5 mol %), methyl 2-(diphenylarsino)benzoate (**3**) was obtained in 75% isolated yield within 24 h (entry 1, Table 1). When additional PPh_3[30] was added to the reaction

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mixture, no improved yields were observed (entry 2, Table 1). An important development in Pd-catalyzed cross-coupling reactions involves the use of Cu(I) as cocatalyst, which increased rates and yields.[31] In the presence of CuI, the coupling reaction with stannane **1** and **2a** gave similar yields (entry 3, Table 1). Likewise, when the reaction was carried out in DMF, a more polar and coordinating solvent, the yield of **3** was practically the same as that obtained in toluene (entry 3 vs 4, Table 1). Furthermore, when the reaction was performed in DMF with PPh_3 and CsF as an activator of the organotin reagent,[32] **3** was achieved in lower yield than in the previous reactions (entry 5, Table 1). Thus, the best experimental conditions found for the arsination reaction were those with toluene and no additional ligand or additives.

It should be noticed that the final products of the cross-coupling reaction could be ligands for the catalyst. Although the triarylarsines obtained as products are less σ-donating ligands than PPh_3, they are present in a large extent, and this could be a problem for the scope of the coupling reaction. When we evaluated the effect of a large amount of ligand in Pd-catalyzed arsination, we established that the excess of a good σ-donor ligand affected the coupling reaction, although not to a large extent.[20c]

The reaction of **1** with 1-bromo-2-iodobenzene (**2b**) catalyzed by $(PPh_3)_2PdCl_2$ in toluene afforded (2-bromophenyl)diphenylarsine (**4**) in 83% isolated yield within 24 h (entry 6, Table 1). When 1-chloro-2-iodobenzene (**2c**) was allowed to react under the same experimental conditions, the chloride-containing arsine **5** was also obtained in very good isolated yield (entry 7, Table 1). Bromide and chloride halides did not react under these conditions; thus this selectivity for the arsination allowed further transformation of the remaining halides in the products.

The transformation of 2-iodoaniline (**2d**) to 2-(diphenylarsino)aniline (**6**) was successfully carried out even though the substrate has a strong coordination ability to the Pd center (entry 8, Table 1). The Pd-catalyzed cross-coupling reaction of stannanes with haloarenes substituted with the amino group gave either low yields or no reaction due to the slow-down of the oxidative addition to the Pd(0) produced by the amino group.[33] Moreover, arsine **6** could be regarded as a bidentate [*As,N*] ligand itself.[34]

A remarkable feature of this Pd-catalyzed arsination is that sterically hindered *ortho*-substituted aryl iodides reacted efficiently. In addition, no significant electronic effect was observed since both electron-withdrawing and electron-donating groups showed similar rates and yields of reaction. However, a limitation for the arsination reaction was found; aryl iodide bearing a carboxylic acid group did not react at all, which may probably be due to the fact that this substrate promoted the formation of inactive Pd complex and the catalysis was thus inhibited.[35]

Synthesis of a Biphenyl Arsine Ligand. 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.[36] A family of these ligands have been developed and shown to be excellent ligands for numerous Pd-catalyzed coupling processes, including C−C and C−heteroatom bond-forming reactions.[37] This type of ligand belongs to a class of phosphines with bulky and mainly electron-rich character. Thus, keeping the biphenyl backbone and having in mind that the coordinating ability of the ligands can also be tuned through the donor atom, we aim to obtain a novel biphenyl arsine ligand.

To further develop the methodology above-described, we carried out the Pd-catalyzed arsination with stannane **1** and 2-iodobiphenyl (**2e**), a suitable precursor for the synthesis of a biphenyl arsine ligand. When the Pd-catalyzed arsination was performed in toluene with or without additional PPh_3 (entries 9 and 10, Table 1), the yields of biphenyl-2-yldiphenylarsine (**7**) were only 43% and 48%, respectively. With the addition of CuI the yield improved, and the desired arsine ligand **7**, $AsPh_2$(bph) (bph = biphenyl), was achieved with 71% isolated yield (entry 11, Table 1). With this simple synthetic methodology, we could obtain a new biphenyl arsine ligand.

As a possible mechanistic explanation for the copper effect found, a preliminary transmetalation from the organostannane has been suggested.[31a] However, the copper effect could also be attributed to the ligand association mechanism.[31b,e] In our reaction both mechanistic explanations could be valid.[31b]

Application of the Biphenyl Arsine Ligand. Pd-Catalyzed Arsination with Perfluoroalkyl Iodides. In view of the success of various arsine ligands in Pd-catalyzed Stille reactions,[4] we evaluated the potential of biphenyl-2-yldiphenylarsine ($AsPh_2$(bph), **7**) as a ligand in the cross-coupling reaction of stannane n-$Bu_3SnAsPh_2$ with perfluoroalkyl iodides (R_fI) as electrophiles.

In a previous work, we reported the one-pot, two-step Pd-catalyzed cross-coupling reaction of organoheteroatom stannanes R_3SnZPh_n (Z = P, As, Se) with R_fI to obtain perfluoroalkylphosphines, arsines, and selenides Ph_nZR_f.[22] Optimization studies for the phosphination reaction revealed that the most favorable conditions were $(PPh_3)_2$-$PdCl_2/PPh_3$/CsF in toluene. When the arsination reaction with $C_8F_{17}I$ (**8c**) was carried out under these optimal

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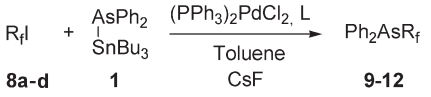
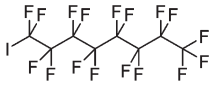
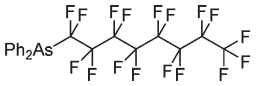
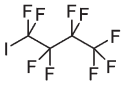
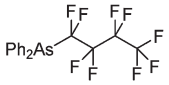
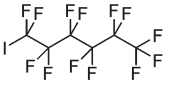
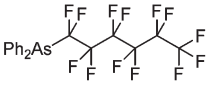
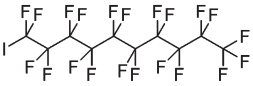
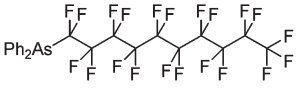
Table 2. Pd-Catalyzed Cross-Coupling Reaction with *n*-$Bu_3SnAsPh_2$ (1) and Perfluoroalkyl Iodides (8a−d) with Different Ligands[a]

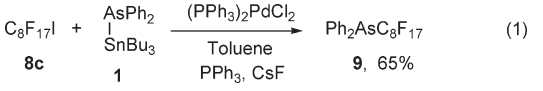


R_fI = C_4F_9I (**8a**), $C_6F_{13}I$ (**8b**), $C_8F_{17}I$ (**8c**), $C_{10}F_{21}I$ (**8d**)

Entry	Substrate	Ligand Pd:L (1:4)	Product	Yield %[b]
1		PPh_3		65[c]
2		-		10
3	 **8c**	$P(2\text{-furyl})_3$	 **9**	<5
4		$P(o\text{-tol})_3$		<5
5		PCy_3		<5
6		$P(t\text{-Bu})_2(bph)$		11
7		$P(t\text{-Bu})_2Me$		80
8		$AsPh_3$		15
9		$AsPh_2(bph)$		87
10	 **8a**	PPh_3	 **10**	47[c]
11		$AsPh_2(bph)$		45
12	 **8b**	PPh_3	 **11**	43[c]
13		$AsPh_2(bph)$		55
14	 **8d**	PPh_3	 **12**	48[c]
15		$AsPh_2(bph)$		78

[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 equiv) for 24 h in toluene at reflux. [b]CG yields. The yields reported represent at least the average of two reactions. [c]Ref 22.

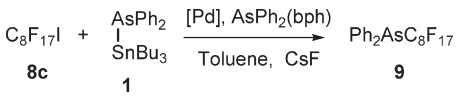
conditions, perfluoroalkyl arsine $Ph_2AsC_8F_{17}$ (**9**) was obtained in 65% yield (eq 1).



The interest of this direct and simple methodology is enhanced by the potential utility of the final products as a new class of ligands. The low reactivity of R_fI could be ascribed to its reluctance to participate in oxidative addition, the first step of the catalytic cycle, where the structure of the ligand has a significant influence. Thus, to evaluate the effectiveness of the $AsPh_2(bph)$ ligand and further improve the Pd-catalyzed arsination with R_fI, we studied the activity of a variety of phosphine and arsine ligands in this reaction, including biphenyl arsine ligand **7**, $AsPh_2(bph)$. We selected $C_8F_{17}I$ (**8c**) as a model substrate; the results of Pd-catalyzed cross-coupling with *n*-$Bu_3SnAsPh_2$ (**1**) are shown in Table 2. It should be noted that in all reactions the conversion of the substrate was complete. The other product achieved, in addition to the cross-coupling one, was the reduced perfluoroalkane (R_fH).

The yields obtained were strongly dependent on the ligand L. When the coupling of **1** and **8c** was carried out with CsF

Table 3. Effect of the Pd Source and Pd:L Ratio on the Arsination with *n*-$Bu_3SnAsPh_2$ (1) and $C_8F_{17}I$ (8c)



entry	catalyst	Pd:$AsPh_2$(bph) ratio	product **9** (%)[b]
1	$(PPh_3)_2PdCl_2$	1:4	87
2	$(PPh_3)_2PdCl_2$	1:2	77
3	$Pd_2(dba)_3$	1:4	36
4	$Pd_2(dba)_3$	1:2	66
5	$PdCl_2$	1:4	22
6	$PdCl_2$	1:2	48

[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 $C_8F_{17}I$ (**8c**) (0.7 mmol), [Pd] (10 mol %), $AsPh_2$(bph) ligand, and CsF (3 equiv) for 24 h in toluene at reflux. [b] CG yields. The yields reported represent at least the average of two reactions.

and no additional ligand, only 10% of perfluoroalkyl arsine **9** was achieved (entry 2, Table 2). In this case the reaction was retarded with regard to the reaction with PPh_3 as ligand (entry 1, Table 2), indicating that the presence of ligand facilitated the reaction. In addition, P(2-furyl)$_3$ and P(*o*-tol)$_3$ ligands proved to be less effective than PPh_3 in the coupling reaction (entries 3 and 4, Table 2). These ligands, as well as $AsPh_3$, are believed to enhance Stille couplings by increasing the rate of transmetalation,[30] which could imply that the rate-limiting step in these cases might not be the transmetalation.

Significant progress has been made on the basis of sterically demanding and electron-rich phosphines as the supporting ligand for the Stille cross-coupling.[38] With this possibility in mind, electron-rich PCy_3 and P(*t*-Bu)$_2$Me[39] and bulky P(*t*-Bu)$_2$(bph)[40] were investigated as ligands that might promote oxidative addition by increasing the nucleophilicity of the Pd(0) species or by suitable steric properties. In the presence of PCy_3 or P(*t*-Bu)$_2$(bph) as supporting ligand, the cross-coupling reaction with stannane **1** and perfluoroalkyl iodide **8c** became inefficient (entries 5 and 6, Table 2). However, under the same experimental conditions the coupling reaction with P(*t*-Bu)$_2$Me as ligand affords arsine **9** in 80% yield (entry 7, Table 2). The Pd/P-(*t*-Bu)$_2$Me-based catalyst was employed with success to achieve the Stille couplings of alkenyltin reagents with functionalized alkyl bromides that contain β-hydrogens.[39]

The coordinating ability of $AsPh_3$ was fine-tuned by steric means in biphenyl arsine ligand **7** [$AsPh_3$ vs $AsPh_2$(bph)]. When the arsination reaction of **8c** was carried out with ligand $AsPh_2$(bph), perfluoroalkylarsine **9** was obtained in 87% (entry 9, Table 2). $AsPh_2$(bph) was the most efficient ligand. This result represents a significant advance in the synthesis of new types of potential perfluoroalkylarsine ligands. Although the highest yields were obtained with a bulky, relatively weakly donating $AsPh_2$(bph) ligand, the electron-rich trialkylphosphine P(*t*-Bu)$_2$Me ligand also proved to be an efficient ligand for this catalytic system.

The different activity of the ligands results from the presence of many reaction steps, each of which may contribute to the rate of the reaction. The Stille coupling reactions are generally thought to proceed through a mechanism that involves three distinctive main steps: an oxidative addition of the electrophile to the Pd(0) active catalyst followed by a transmetalation reaction in which the aryl or alkyl group is transferred from the stannane to Pd, yielding a Pd(II) complex; and a reductive elimination to release the product with the concomitant regeneration of the active Pd(0) catalyst. More electron-rich and less bulky ligands facilitate the oxidative addition step, while more bulky and less electron-rich ligands enable the reductive elimination step. In addition, the use of less coordinating ligands allows for the transmetalation step. However, another important component of the mechanism for the Stille coupling is thought to be a predissociation and reduction step in which the Pd(II) source is converted to the more active and coordinatively unsaturated Pd(0) catalyst. This step is enforced by sterically demanding and more electron-rich ligands. Therefore, the relative contribution of steric and electronic effects is a very important matter, particularly for less reactive electrophiles.

For the P(*t*-Bu)$_2$Me ligand, it was determined that the species that undergoes oxidative addition was PdL_2 by a S_N2 process. The efficiency of this ligand in cross-coupling reactions with alkyl electrophiles was associated with a relatively fast oxidative addition.[41] Thus, the improved yields achieved in the coupling reaction of **1** with perfluoroalkyl iodide **8c** with the P(*t*-Bu)$_2$Me ligand could also be related to a facilitated oxidative addition.

The enhanced reactivity observed in cross-coupling Pd-catalyzed reactions with catalytic systems that contained an electron-rich and bulky phosphine has been attributed to the formation of unsaturated and reactive monoligated Pd species [PdL], which activated unreactive and sterically hindered aryl chlorides.[42] Therefore, the effectiveness of our sterically demanding ligand $AsPh_2$(bph) could be also the result of the formation of monoligated Pd species, and these species could be responsible for a rapid oxidative addition of the R_fI to the Pd(0) center. Moreover, the weak donicity of the arsine ligand could improve the rate of the transmetalation step.

It is important to notice that the Pd source used to evaluate the behavior of the different ligands was $(PPh_3)_2PdCl_2$. Preliminarily, this Pd source seems to be inappropriate since the PPh_3 present in the catalyst has coordinating properties which could hinder the formation of Pd(II) catalytic active species with other ligands. Strong donor phosphines should substitute PPh_3 in the complexes, but the same could not be true for arsines. Despite that, the experimental results showed that regardless of the presence of PPh_3, the influence of the extra ligand could be noticed; other sources of Pd were considered. In addition, the Pd:L ratio was also investigated. The results of Pd-catalyzed arsination with *n*-$Bu_3SnAsPh_2$ and $C_8F_{17}I$ in the presence of the $AsPh_2$(bph) ligand and different Pd sources and Pd:L ratios are shown in Table 3.

When we examined the Pd:L ratio and the coupling reaction was carried out using $(PPh_3)_2PdCl_2$ and $AsPh_2$(bph) in a Pd:L ratio of 1:2, the yields of the reaction were lower

(38) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704–4734.

(39) The air- and moisture-stable salt [HP(*t*-Bu)$_2$Me]BF_4 was used as ligand instead of P(*t*-Bu)$_2$Me. It is commercially available and furnishes yields similar to phosphine itself. See: Menzel, K.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 3718–3719.

(40) Zim, D.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2413–2415.

(41) Hills, I. D.; Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5749–5752.

(42) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366–374.

than those previously obtained for a Pd:L ratio 1:4; nevertheless the change of the yields was not to a large extent (entries 1 and 2, Table 3).

Additionally, we evaluated $Pd_2(dba)_3$ and $PdCl_2$ as Pd source. Both Pd catalysts with $AsPh_2$(bph) as ligand were less effective than $(PPh_3)_2PdCl_2$ (entries 3−6, Table 3). However, it should be noted that a remarkable improvement in the yields of **9** was found when the cross-coupling reaction was performed with $Pd_2(dba)_3$ or $PdCl_2$ in a Pd:L ratio of 1:2.

Despite the presence of unwanted PPh_3 ligand, the Pd(0) complexes generated from $(PPh_3)_2PdCl_2$ and $AsPh_2$(bph), to which the oxidative addition of R_fI took place, demonstrated to be the most reactive. Therefore, on the basis of this experimental data, $(PPh_3)_2PdCl_2$ was selected as a Pd source for the Pd-catalyzed arsination reaction.

The effectiveness of the biphenyl arsine $AsPh_2$(bph) as ligand was examined in the arsination reaction with other R_fI with perfluoroalkyl chains between four and 10 carbon atoms (**8a**, **8b**, and **8d**) (Table 2). Previously, it was observed that the chain length of the R_fI had nearly no influence on the reactivity in the coupling reaction in the most favorable conditions observed earlier with PPh_3 as ligand (entries 10, 12, and 14, Table 2).[22] However, the chain length had a more significant impact on the yields when the reaction was carried out with ligand $AsPh_2$(bph) (entries 11, 13, and 15, Table 2). With perfluoroalkyl iodide **8a** practically the same results were accomplished with PPh_3 or $AsPh_2$(bph), while the couplings with longer R_f chain length led to progressively increased yields.

Conclusion

We reported an efficient one-pot, two-step Pd-catalyzed arsination with *n*-$Bu_3SnAsPh_2$ and sterically hindered *ortho*-substituted aryl iodides. This methodology has some notable features: (i) the feasibility of a one-pot reaction; (ii) a high-yield preparation method of functionalized triarylarsines; (iii) a high functional group compatibility. This synthesis methodology is further heightened by the potential application of the final products as a new class of ligands in organometallic chemistry.

Particularly, this methodology allowed the synthesis of an arsine ligand. Our newly prepared biphenyl arsine ligand $AsPh_2$(bph) shows a large activity for Pd-catalyzed arsination with R_fI. The improved reactivity observed with the Pd/$AsPh_2$(bph)-based catalysts could be attributed to the formation of unsaturated [PdL] species. Thus, the novel perfluoroalkyldiphenylarsines with perfluoroalkyl chains between four and 10 C atoms are obtained in higher yields than those previously reported. Moreover, the arsine ligand $AsPh_2$(bph) is easy to use, is stable under several conditions, and shows a promising behavior in cross-coupling reactions.

Further tuning of the biphenyl arsine ligand $AsPh_2$(bph) structure, as well as its applications to other transition-metal-catalyzed reactions, is currently underway.

Experimental Section

General Considerations. Gas chromatographic analyses were performed on a gas chromatograph with a flame ionization detector, equipped with the following column: 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 Bruker Advance 400 high-resolution spectrometer, in $CDCl_3$ as solvent. Gas chromatographic/mass spectrometer analyses were carried out on a GC/MS QP 5050 spectrometer equipped with a VF-5 ms, 30 m × 0.25 mm × 0.25 μm column. Melting points were obtained with an electrical instrument. The HRMS were recorded at UCR Mass Spectrometry Facility, University of California.

$AsPh_3$, PPh_3, P(*t*-Bu)$_2$bph, P(*o*-tolyl)$_3$, P(2-furyl)$_3$, PCy_3, [HP(*t*-Bu)$_2$Me]BF_4, *n*-Bu_3SnCl, $(PPh_3)_2PdCl_2$, CuI, R_fI, and ArI were commercially available and used as received. Methyl 2-(iodo)benzoate (**2a**) was prepared as previously reported from the corresponding acid.[43] CsF was dried under vacuum at 120 °C. All solvents were analytical grade and distilled before use. Toluene was distilled under nitrogen from Na-benzophenone. DMF was stored under molecular sieves and then distilled under reduced pressure with bubbling of nitrogen. All reactions were carried out under an atmosphere of nitrogen. Silica gel (0.063−0.200 mm) was used in column chromatography.

General Procedure for Pd-Catalyzed Cross-Coupling Arsination. The following procedure of the reaction of *n*-$Bu_3SnAsPh_2$ (**1**) with 2-iodobiphenyl (**2e**) is representative of all cross-coupling reactions. Into a three-necked, 500 mL, round-bottomed flask equipped with a coldfinger condenser charged with dry ice/ethanol, a nitrogen inlet, and a magnetic stirrer, approximately 300 mL of ammonia previously dried with Na metal under nitrogen was condensed. $AsPh_3$ (1.0 mmol) and then 2 equiv of Na metal (2 mmol) in small pieces were added, with a pause for bleaching between each addition. At 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 then stirred for 5 min and the liquid ammonia allowed to evaporate. The evaporation left a white solid residue, which was dissolved in dry toluene (12 mL). This solution was added via cannula and syringe into a Schlenk tube. In the tube, $(PPh_3)_2PdCl_2$ (1.5 mol %, 0.0105 mmol), PPh_3 (Pd:L 1:4, 0.042 mmol), CuI (Pd:Cu 1:2, 0.021 mmol), **2e** (0.7 mmol), and toluene (3 mL) were added. When the solution of **1** was added, the reaction mixture turned deep brown. The reaction mixture was heated for 24 h in an oil bath at 80 °C. Water was added to the cool reaction mixture and then extracted three times with CH_2Cl_2 (30 mL each). The crude reaction mixture was treated with aqueous KF (ca. 2 equiv) to eliminate *n*-Bu_3SnI.[44] After drying with anhydrous $MgSO_4$, product **7** was purified by silica gel column chromatography (petroleum ether) to give a white solid (mp 55.9−57.1 °C), yielding 71% of the product.

The products were characterized by ^{1}H NMR, ^{13}C NMR, GC-MS, and HRMS. All the spectroscopic data agreed with those previously reported for compounds **9**, **10**, **11**, and **12**.[22]

Methyl 2-(Diphenylarsino)benzoate (3).[45] Compound **3** was obtained according to the general procedure. Product **3** was isolated from the reaction mixture by silica gel column chromatography (petroleum ether/ethyl acetate gradient, 90:10 → 70:30) and recrystallized from methanol to give **3** as a white solid, mp 90−91 °C (lit. mp 92 °C),[45] yielding 75% of the isolated product. ^{1}H NMR ($CDCl_3$): δ 8.12−8.05 (1 H, m); 7.41−7.24 (12 H, m); 7.08−7.03 (1 H, m); 3.75 (3 H, s). ^{13}C NMR ($CDCl_3$): δ 167.56; 143.38; 140.82; 134.62; 133.82; 132.31; 130.82; 128.59; 128.29; 128.18; 51.99. MS: *m*/*z* (%): 365 (3), 364 (10), 288 (16), 287 (100), 257 (23), 227 (15), 210 (6), 165 (13), 152 (17), 151 (13), 105 (4), 77 (13), 51 (7). HRMS (EI): calcd for $C_{20}H_{17}AsO_2$ 364.0444, found $[M]^+$ 364.0435.

(2-Bromophenyl)diphenylarsine (4).[46] Compound **4** was obtained according to the general procedure. Product **4** was isolated from the reaction mixture by silica gel column chromatography (petroleum ether) and recrystallized from pentanes to give **4** as a white solid, mp 100−101 °C (lit. mp 101.5−103.5 °C),[46]

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yielding 83% of the isolated product. ^{1}H NMR ($CDCl_3$): δ 7.64−7.62 (1 H, m); 7.41−7.36 (10 H, m); 7.24−7.21 (2 H, m); 6.92−6.90 (1 H, m). ^{13}C NMR ($CDCl_3$): δ 141.85; 138.88; 134.88; 133.93; 132.78; 130.28; 128.91; 128.78; 127.63. MS: *m*/*z* (%) 386 (23), 384 (21), 232 (41); 230 (41), 229 (10), 228 (16), 227 (86), 152 (100), 151 (69), 126 (5), 77 (13), 51 (9). HRMS (EI): calcd for $C_{18}H_{15}AsBr$ 384.9568, found $[M - H]^+$ 384.9569.

(2-Chlorophenyl)diphenylarsine (5).[47] Compound **5** was obtained according to the general procedure. Product **5** was isolated from the reaction mixture by silica gel column chromatography (petroleum ether) to give **5** as a white solid, mp 86−87 °C, yielding 88% of the isolated product. ^{1}H NMR ($CDCl_3$): δ 7.36−7.20 (12 H, m); 7.10−7.09 (1 H, m); 6.86−6.84 (1 H, m). ^{13}C NMR ($CDCl_3$): δ 139.67; 139.52; 138.56; 134.65; 133.98; 130.17; 129.42; 128.93; 128.83; 127.12. MS: *m*/*z* (%) 342 (2), 340 (4), 263 (5), 227 (12), 188 (10), 186 (18), 154 (7), 152 (100), 151 (22), 101 (6), 77 (9), 51 (6). HRMS (EI): calcd for $C_{18}H_{15}AsCl$ 341.0071, found $[M - H]^+$ 341.0077.

2-(Diphenylarsino)benzenamine (6).[34a] Compound **6** was obtained according to the general procedure. Product **6** was isolated from the reaction mixture by silica gel column chromatography (petroleum ether/dichloromethane gradient, 90:10 → 60:40) as a pale yellow solid, mp 82−83 °C (lit. mp 81.5−83 °C),[34a] yielding 75% of the isolated product. ^{1}H NMR ($CDCl_3$): δ 7.38−7.32 (10 H, m); 7.19−7.15 (1 H, t, ^3J = 8 Hz); 6.85−6.82 (1 H, dd, ^3J = 7.6 Hz, ^4J = 1.2 Hz); 6.71−6.69 (2 H, m); 3.88 (2 H, s br). ^{13}C NMR ($CDCl_3$): δ 149.39; 137.69; 134.52; 133.81; 130.09; 128.84; 128.68; 123.09; 119.20; 115.68. MS: *m*/*z* (%): 321 (10), 244 (12), 243 (78), 242 (100), 227 (16), 207 (9), 169 (51), 168 (29), 167 (41), 166(34), 152 (22); 151 (11), 139 (8), 78 (10), 51 (7). HRMS (EI): calcd for $C_{18}H_{17}AsN$ 322.0571, found $[M - H]^+$ 322.0578.

Biphenyl-2-yldiphenylarsine (7).[47] Compound **7** was obtained according to the general procedure. Product **7** was isolated from the reaction mixture by silica gel column chromatography (petroleum ether). After extensive drying with a vacuum pump, compound **7** was obtained as a white solid, mp 56−57 °C, yielding 71% of the isolated product. ^{1}H NMR ($CDCl_3$): δ 7.47−7.19 (19 H, m). ^{13}C NMR ($CDCl_3$): δ 148.12; 142.23; 140.21; 138.74; 134.30; 133.94; 129.85; 129.64; 128.63; 128.57; 128.32; 127.80; 127.54; 127.32. MS: *m*/*z* (%) 383 (13), 382 (44), 230 (6), 229 (17), 228 (72), 227 (100), 153 (9), 152 (53), 151 (9), 115 (2), 78 (3), 51 (3). HRMS (EI): calcd for $C_{24}H_{20}As$ 383.0775, found $[M - H]^+$ 383.0784.

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