Palladium-Catalyzed Suzuki Cross-Coupling Reactions in Ambient Temperature Ionic Liquids: Evidence for the Importance of Palladium Imidazolylidene Complexes

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Received July 30, 2003

Palladium-catalyzed Suzuki cross-coupling reactions have been conducted in a range of ambient temperature ionic liquids. The ionic liquids give excellent reactivities for bromoarenes in addition to easy product isolation. The preferred reaction conditions are explored and the effect of changing the ionic liquid components is investigated. The in situ formation of mixed phosphine/imidazolylidene palladium complexes is demonstrated in all of the catalytically active solutions, but in none of the inactive solutions. Formation of 1,3-dialkyl-2-arylimidazolium salts is demonstrated, but it is also shown that these salts can act as a source of arene for the reaction; that is, both reductive elimination and oxidative addition of 1,3-dialkyl-2-arylimidazolium salts from/to the palladium are occurring. The implications of this for the use of ionic liquids as solvents for Suzuki reactions are discussed.

Introduction

The application of ionic liquids as solvents for transition metal catalysis is an area of intense current interest,[1] and a wide range of processes are under investigation. These solvents provide attractive alternatives to many volatile molecular solvents and potential nonaqueous polar phases for the isolation of catalysts in biphasic systems. Ionic liquids are generally considered to be noncoordinating solvents with little interaction with solute catalysts. However, the study of how the ionic liquids can interact with solute catalysts to affect their reactivity is in its infancy.[2]

Palladium-centered catalysis in ionic liquids has had particular attention.[3] The first reported example of a palladium-catalyzed coupling reaction in an ionic liquid was the Heck reaction in phosphonium- and ammonium-based ionic liquids.[4] The products were readily distilled from the ionic liquid, permitting successive catalytic runs, each affording comparable activity. Our work in this area has concentrated on the Suzuki reaction in imidazolium-based ionic liquids.[5] The Suzuki cross-coupling reaction is one of the most powerful methodologies for the generation of new carbon−carbon bonds, particularly in the synthesis of biaryls. The traditional Suzuki reaction, however, suffers from a number of disadvantages that limit its application.[6] The traditional catalyst systems often suffer from low activities, and to achieve satisfactory results, high reaction temperatures, high catalyst concentrations, and prolonged reaction times are required. Catalyst decomposition often prevents repeat catalytic runs and decreases reactivity. Despite recent advances,[7] to date no general solution to these problems has been reported. After initial observations that, under the appropriate conditions, $[C_4C_1im][BF_4]$ {where $[C_4C_1im]^+$ is the 1-butyl-3-methylimidazolium ion} is an excellent solvent for the $(PPh_3)_4Pd$-catalyzed Suzuki reaction, with no catalyst decomposition,[5a] the coupling of iodoarenes supported on Wang resin with a variety of aryl boronic acids was also shown under similar conditions.[8] We subsequently demonstrated that palladium imidazolylidene (often referred to as N-heterocyclic carbene, NHC) complexes can spontaneously form under these reaction conditions.[5b]

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10.1021/om034075y CCC: $25.00
Publication on Web 11/11/2003

Scheme 1. Suzuki Reaction of Bromobenzene Tolylboronic Acid

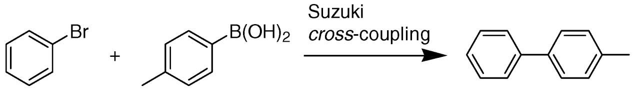

Table 1. Suzuki Cross-Coupling of Bromobenzene and Tolylboronic Acid in $[C_4C_1im][BF_4]$ and Conventional Molecular Solvents

entry	solvent	catalyst loading (mol %)	time	yield[a] (%)	TON h^{-1}	homo[b] (%)
1	$[C_4C_1im][BF_4]$	1.2	3 h	92.4		2.3
2	$[C_4C_1im][BF_4]$	1.2	10 min	68.2	171	2.1
3	$[C_4C_1im][BF_4]$ (uninitiated)	1.2	3 h	28.7	3	4.6
4	toluene	3	6 h	89.8		6.6
5	toluene	3	20 min	13.4	13	6.5
6	dioxane	3	6 h	87.5		4.9
7	dioxane	3	20 min	28.6	29	5.2

[a] Isolated yield. [b] Yield of homocoupled product, 4,4′-dimethylbiphenyl.

However, this does not necessarily mean that these complexes are involved in the Suzuki reaction itself. For instance, Suzuki coupling has been reported in the tetradecyltrihexylphosphonium chloride ionic liquid,[9] which cannot form NHC complexes. To explore this possibility further, in this paper we report that, in a survey of several different imidazolium-based ionic liquids, such NHC complexes are always found when the reaction is successful and not when the reaction is unsuccessful. Further to this, we reveal the reductive elimination of 1-butyl-3-methyl-2-phenylimidazolium from an, as yet, undetected NHC/phenyl palladium complex.

Results and Discussion

In our initial investigations of the Suzuki reaction in ionic liquids the reactions were unreliable, sometimes giving excellent yields with no catalyst decomposition and others giving poor yields with extensive catalyst decomposition. Care was required to ensure that the optimum reaction conditions were achieved, particularly with respect to the need to activate the reaction system first. It was this that gave rise to our original suspicions that a new solution species was being formed. Hence, we will describe in detail the conditions for the reactions to proceed, to shed light on the palladium chemistry that is occurring.

To ensure that we could differentiate between the cross-coupling and homocoupling products, the most studied reaction was that of 4-bromobenzene and tolylboronic acid. This leaves aryl–aryl$_{(phosphine)}$ scrambling as the only other possible source of 4-methylbiphenyl, but the contribution to the yield from this route would be insignificant due to the low phosphine concentration employed. To establish a benchmark, the Suzuki reaction was examined in toluene and dioxane (Table 1). Extensive catalyst decomposition was observed in all reactions in these solvents, evident by the darkening of the reaction mixture and deposition of a black solid. In the toluene reaction, the $Pd(PPh_3)_4$ was only partially dissolved in the toluene phase of the two-component solvent mixture, 2:1 toluene/water. Two conditions were used: one in which the reaction had gone to completion, to reveal final achievable yields; and one where the reaction was terminated before completion, so that the number of turnovers per hour was observed (TON h^{-1}). When suitably initiated (see below), the reaction in $[C_4C_1im][BF_4]$ afforded higher yields in shorter reaction times with a lower catalyst loading than in either toluene or dioxane. Also, the amount of homocoupling was greatly reduced in the ionic liquid reactions.

Initiation of Palladium/Phosphine Catalysts in Ionic Liquids. While studying the solubility of $Pd(PPh_3)_4$ in $[C_4C_1im][BF_4]$, it was observed that only in the presence of a halogenoarene and a source of halide ion at 110 °C with vigorous stirring for 1 h under an inert atmosphere did the complex dissolve completely to give a catalytically active solution. Failure to perform this initiation led to low yielding reactions with unreacted halogenoarene remaining and obvious catalyst decomposition. Extensive catalyst decomposition also occurred when this initiation of $Pd(PPh_3)_4$ was attempted under air, and the subsequent Suzuki reaction afforded only a poor yield of the cross-coupled product. However, once the $Pd(PPh_3)_4$ complex had been initiated in the $[C_4C_1im][BF_4]$, the Suzuki reaction could be performed under air with no detrimental effects. The initiation of the ionic liquid solution was clearly generating an air-stable solute species from the unstable $Pd(PPh_3)_4$.

After preparation of the catalyst solution, the mixture was allowed to cool to room temperature and aqueous sodium carbonate and arylboronic acid were added, before heating the reaction mixture once again to 110 °C. Attempts to perform the reaction with other bases commonly used for the Suzuki reaction (i.e., sodium acetate, tetrabutylammonium fluoride, and sodium hydroxide) led only to recovery of unreacted starting material. Similarly, no reaction was observed in the absence of water.

Performing the Suzuki reaction in this way significantly boosted the yield of the cross-coupled product, enhanced reaction rates, and prevented catalyst decomposition (Table 1). For example, the reaction of bromobenzene with tolylboronic acid afforded a 92.4% yield after 3 h compared to 29.6% with the uninitiated $Pd(PPh_3)_4$ suspension in $[C_4C_1im][BF_4]$. Attempts to repeat the reaction using the mixture remaining after a reaction with the uninitiated catalyst led to no cross-coupling and recovery of starting materials, indicating the decomposition of the palladium to an inactive form.

The results were independent of the nature of the added halide and of its counterion; that is, $[C_4C_1im]Cl$ gave the same results as NaCl and NaBr. Decomposition of the catalyst was observed when less than 4 equiv with respect to Pd of halide was used. However, in the presence of a very large excess of halide (1 equiv to the 4-bromobenzene) the Suzuki reaction afforded no 4-methylbiphenyl or biphenyl, and unreacted 4-bromotoluene was recovered, although no palladium precipitation was observed. This suggests that although some halide is required to form the catalytic species, too much leads to the formation of unreactive palladium halide complexes. The addition of 10 equiv (12 mol %) was

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subsequently employed in the reactions, as it affords good yields and was practically convenient.

To study any palladium-containing species formed in the initiation, the concentration of the palladium was maximized. Two experiments were conducted under conditions similar to those used in the catalytic reactions, but with approximately 7 times the typical concentration of $Pd(PPh_3)_4$ employed, leading to a saturated solution. In the first experiment, after heating at 110 °C with vigorous stirring for 1 h under N_2, an orange suspension in a yellow−orange solution similar to that observed after the initiation process in catalytic reactions was formed. The mixture was separated, and the ^{31}P NMR of the yellow−orange filtrate revealed the presence of two signals, at 23.3 ppm {$[PPh_4]^+$} and −5.5 ppm {PPh_3} in approximately equal intensities. Addition of water to the filtrate resulted in further precipitation of an orange solid. This was collected and washed with water and diethyl ether. The ^{31}P NMR spectra in $CDCl_3$ were identical for both orange solids, with signals for $OPPh_3$ {29.8 ppm}, $PhPd(PPh_3)_2Br$ {24.2 ppm}, $(PPh_3)_2PdCl_2$ {23.9 ppm}, $(PPh_3)_2PdBr_2$ {22.6 ppm}, and PPh_3 {−4.8 ppm}. All three of these palladium-containing species are in oxidation state 2 and, therefore, are stable to air.

In the second experiment this part of the initiation was followed by the addition of aqueous Na_2CO_3 and further heating of the mixture for 10 min at 110 °C. On completion, the mixture was filtered and ^{31}P NMR analysis of the filtrate revealed new signals arising from $[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$ {where C_4C_1imy is the 1-butyl-3-methylimidazolylidene ligand, 22.9 ppm} and $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$ {21.8 ppm} as well as those due to $OPPh_3$ and PPh_3 ppm. This time no signal arising from other palladium-containing species nor $[PPh_4]^+$ was seen. These assignments were confirmed by ESI-MS analysis of the solution, which indicated the presence of both $[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$ {803 Da} and $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$ {849 Da}.

Attempts to repeat these experiments in the absence of added halide salts yielded an intractable black solid and solutions with ^{31}P NMR signals at 23.2 ppm {$[PPh_4]^+$} and 5.7 ppm {PPh_3} in a ratio of 6:1. All attempts to detect palladium/phosphine- and palladium/NHC-containing species in this case, by either ^{31}P NMR or ESI-MS, were unsuccessful.

To ensure that the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Cl or Br) complexes were formed from the products of the first step of the initiation {$PhPd(PPh_3)_2Br$, $(PPh_3)_2PdCl_2$, and $(PPh_3)_2PdBr_2$}, rather than in competition with them, separate suspensions of $PhPd(PPh_3)_2Br$ and $(PPh_3)_2PdCl_2$, both with added NaCl, were heated in $[C_4C_1im][BF_4]$ at 110 °C for 1 h, leading to solutions whose ^{31}P NMR spectra and ESI-MS clearly showed the formation of $[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$ and in the case of $PhPd(PPh_3)_2Br$ also $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$.

Variation of the Palladium Source. Given that both $PhPd(PPh_3)_2Br$ and $(PPh_3)_2PdCl_2$ as well as $Pd(PPh_3)_4$ gave rise to the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complexes, we tried a range of possible palladium sources for the catalyst. $Pd(PPh_3)_4$ was the original catalyst employed in the discovery of the Suzuki reaction.[6] Although it exhibits poor activity and stability in comparison with recent developments and is air sensitive and difficult to handle, it remains a popular source of palladium in C−C coupling reactions. Comparable Suzuki results were obtained using another palladium(0) source, $Pd_2(dba)_3$ (where dba is dibenzylideneacetone), with 4 equiv of PPh_3 (Table 3, entry 2).

Table 2. Spectral Data for Palladium Complexes Detected in $[C_4C_1im][BF_4]$ and $[C_4C_4im][BF_4]$

complex	^{31}P NMR	ESI$^+$-MS
$PhPd(PPh_3)_2Br$	24.2	707 $[PhPd(PPh_3)_2]^+$
$(PPh_3)_2PdCl_2$	23.9	665 $[Pd(PPh_3)_2Cl]^+$
$(PPh_3)_2PdBr_2$	22.6	709 $[Pd(PPh_3)_2Br]^+$
$[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$	22.9	803 $[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$
$[(PPh_3)_2Pd(C_4C_1imy)Br]^+$	21.8	849 $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$
$[(PPh_3)_2Pd(C_4C_4imy)Cl]^+$	24.8	845 $[(PPh_3)_2Pd(C_4C_4imy)Cl]^+$
$[(PPh_3)_2Pd(C_4C_4imy)Br]^+$	23.0	891 $[(PPh_3)_2Pd(C_4C_4imy)Br]^+$

Table 3. Alternative Palladium/Phosphine Catalytic Systems

entry	palladium source	PPh_3 (equiv with respect to Pd)	yield[a] (%)	TON h^{-1}	homo[b] (%)
1	$Pd(PPh_3)_4$	none	68.2	171	2.1
2	$Pd_2(dba)_3$	4	65.3	163	2.7
3	$Pd(OAc)_2$	4	63.7	159	2.8
4	$PdCl_2$[c]	4	62.2	156	1.7
5a	$(CH_3CN)_2PdCl_2$[c]	4	67.4	169	3.5
5b	2nd run		58.4	146	3.1
5c	3rd run		69.7	174	2.8
5d	4th run		60.1	150	4.2
6	$(CH_3CN)_2PdCl_2$/ $P(3\text{-}C_6H_4SO_3Na)_3$[c]	4	76.3	191	3.5
7	$[C_4C_1im]_2[PdCl_4]$[c]	4	65.8	165	2.9
8	$(PPh_3)_2PdCl_2$[c]	2	66.9	169	1.8

[a] Isolated yields of 4-methylbiphenyl. [b] Yield of homocoupled product, 4,4′-dimethylbiphenyl. [c] No halide additive.

Palladium(II) sources are far less sensitive to the air, are easier to handle, and are relatively inexpensive. Several palladium(II) sources, in the presence of 4 equiv of PPh_3, were also found to afford results comparable to the $Pd(PPh_3)_4$-catalyzed Suzuki reactions in $[C_4C_1im][BF_4]$ (Table 3, entries 3−7). Once again the initiation of the palladium complex in the $[C_4C_1im][BF_4]$ ionic liquid was fundamental to the success of the Suzuki reaction. Attempts to initiate the palladium(II)/4PPh_3 systems in $[C_4C_1im][BF_4]$ with a similar procedure employed for $Pd(PPh_3)_4$ afforded a bright yellow suspension that turned black on heating and showed no Suzuki activity. Further investigation revealed that initiation of these palladium(II) catalysts required the presence of the aqueous Na_2CO_3 from the outset of the initiation as well as the halogenoarene, PPh_3, and halide. This gave a completely colorless solution and achieved Suzuki results comparable to the Pd(0) sources, with no apparent catalyst decomposition. For chloride-containing palladium(II) sources, no halide additive was required (Table 3, entries 4−7).

With the exception of $[C_4C_1im]_2[PdCl_4]$, all of the palladium sources tested were insoluble in $[C_4C_1im][BF_4]$ before the initiation process. It was, therefore, necessary to ensure vigorous mixing and careful delivery of all the palladium to the ionic liquid during the initiation process to prevent catalyst decomposition and leaching into the product. For $[C_4C_1im]_2[PdCl_4]$, its excellent solubility in the ionic liquids circumvented this problem, and at all stages during the initiation process and the Suzuki reaction, the palladium species were fully dissolved.

The ionic $P(3\text{-}C_6H_4SO_3Na)_3$ ligand can also be used to improve the solubility of the palladium complexes during the activation process and so reduce the possibility of decomposition of the palladium before the catalytic solution is achieved. Its use also led to an increase in the yield of 4-methylbiphenyl (Table 3, entry 6).

It was shown (^{31}P NMR and ESI-MS) that when $[C_4C_1im]_2[PdCl_4]$, $PdCl_2$, or $(CH_3CN)_2PdCl_2$ with PPh_3, and $Pd(OAc)_2$ with Cl^- and PPh_3 were added to the ionic liquid without heating, the complex $(PPh_3)_2PdCl_2$ was generated in situ. As described above, addition of bromobenzene and heating of the solution then leads to the formation of $[(PPh_3)_2Pd(C_4C_1imy)Cl]^+$ and $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$. When the full initiation was conducted in the absence of the bromobenzene, no $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$ was observed, confirming that the bromobenzene, presumably via an oxidative addition to a Pd(0) species, must be acting as the source of the bromide ion. This is also in contrast to the studies using $Pd(PPh_3)_4$ (see above), which required the presence of the halogenoarene for successful formation of any imidazolylidene complexes. This suggests that the complexes are initially formed from the Pd(II) species by deprotonation of the imidazolium salt followed by ligand exchange, rather than by oxidative addition of the imidazolium salt directly to a Pd(0) complex.

Repeat Catalytic Runs in $[C_4C_1im][BF_4]$. To confirm that the observation of a colorless solution after the reactions did mean that no catalyst decomposition had occurred and that the catalyst had not produced a new inactive palladium solute, we repeated the reaction. Also, the potential ability to recycle the catalyst solution is one of the most attractive features of this system. This requires the separation of not only the biaryl reaction products but also the inorganic byproducts of the reaction.

Although $[C_4C_1im][BF_4]$ is usually miscible with water in all compositions, addition of Na_2CO_3 (0.28 g) in water (1.25 mL) to $[C_4C_1im][BF_4]$ (2.5 cm^3) leads to a biphasic system below 50 °C. Therefore, the Suzuki reaction mixtures in $[C_4C_1im][BF_4]$ were monophasic at the reaction temperature of 110 °C and biphasic when they had cooled to room temperature. The inorganic salts present in the reaction mixture are preferentially soluble in water and so dissolve in the aqueous layer. This enabled the removal of the salt byproducts generated during the reaction.

Once the biaryl products had been isolated, the aqueous layer of the reaction mixture was separated. The ionic liquid reaction mixture was extracted with successive aliquots of water (20% v/v) until no further phase separation occurred, which was used as an indication that the salt byproducts and excess Na_2CO_3 had been successfully extracted. Then the solution was dried in vacuo for 20 min at 50 °C and was ready for reuse. There was no need to repeat the initiation of the catalyst solution for the repeat reactions.

Repeat catalytic runs were performed for the $(CH_3CN)_2PdCl_2/4PPh_3$-catalyzed Suzuki reaction of bromobenzene with tolylboronic acid (Table 3, entries 5a–d). The yields of 4-methylbiphenyl obtained from these repeat runs varied considerably, but this demonstrates that the catalyst is certainly not decomposing nor forming an inactive complex. Although no attempt has been made to optimize the recycling process, it also indicates that with the appropriate optimization of conditions it will be possible to recycle the entire ionic liquid catalyst solution and repeat the reactions.

Table 4. Scope of the Suzuki Reaction in $[C_4C_1im][BF_4]$: Variation of Halogenoarene

entry	X	R	time	yield[a] (%)	TON h^{-1}	homo[b] (%)
1	I	H	10 min	86.7	430	3.4
			3 h	94.9		0
2	Br	H	10 min	93.4	465	2.6
			3 h	94.5		0
3	Cl	H	10 min	1.2[c]	5	1.5
			3 h	1.8[c]		0
4	Br	Cl		17.2[c]	85	4.1
5	Br	C(O)H	10 min	64.8	325	2.2
			3 h	90.6		0
6	Br	$C(O)CH_3$	10 min	67.1	335	3.8
			3 h	95.9		0
7	Br	CH_3	10 min	69.3	345	3.0
			3 h	91.7		0
8	Br	OCH_3	10 min	81.3	401	1.8
			3 h	92.4		0

[a] Isolated yields of cross-coupled product. [b] Homocoupled product yield. [c] Catalyst decomposition and leaching observed.

Variation of Halogenoarene. Since the presence of the halogenoarene was required in the initiation process for the Pd(0) sources, it was important to establish that halogenoarenes other than bromobenzene would allow the catalytic solution to be produced. Hence, a limited investigation of the scope of the Suzuki reaction with a series of electron-rich and -deficient halogenoarenes with phenylboronic acid in $[C_4C_1im][BF_4]$ was undertaken (Table 4). Although the reactivities for all iodo- and bromoarenes are good, chlorobenzene was still inactive even after 3 h, with only a trace of biphenyl being detected, presumably due to homocoupling of the arylboronic acid (Table 4, entry 3). Instantaneous catalyst decomposition occurred on the addition of the chlorobenzene to the ionic liquid solution, and unreacted chlorobenzene was detected after the reaction. Again, this strongly suggests that the route to the stable catalyst is via the initial product of the oxidative addition of the halogenoarene to Pd(0) $\{PhPd(PPh_3)_2X$ $(X = Br$ or $I)\}$, which is facile for bromo- and iodoarenes, but not possible for the chlorobenzene under these conditions.

Interestingly, the rate of reaction for functionalized electron-rich halogenoarenes is considerably faster than the electron-deficient halogenoarenes, as illustrated by the TON h^{-1} for the 10 min reactions of functionalized bromoarenes: $-OCH_3 > -CH_3 > -C(O)CH_3 > -C(O)H$. This is the reverse order of reactivity generally observed in Suzuki reactions, where the most nucleophilic electron-deficient halogenoarenes are the most reactive. We are investigating the effects of ionic liquids on the relative nucleophilicities of both charged and neutral nucleophiles in a separate series of papers.[10]

Variation of the Ionic Liquid. Changing the Cation. Once a set of reaction conditions had been established for the Suzuki reaction in $[C_4C_1im][BF_4]$ and the potential importance of the cation recognized, we investigated the effect of changing the ionic liquid on

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Table 5. Variation of the Cation of $[BF_4]^-$ Ionic Liquids

entry	ionic liquid	yield[a] (%)	TON h^{-1}	homo[b] (%)
1	$[C_4C_4im][BF_4]$	76.5	191	3.7
2	$[C_4C_1im][BF_4]$	68.2	171	2.1
3	$[C_2C_1im][BF_4]$	16.7	42	1.5
4	$[C_4C_1C_1im][BF_4]$	3.5[c]	9	0.2

[a] Isolated yields of 4-methylbiphenyl. [b] Homocoupled product yield. [c] Catalytic solution not formed, with a $Pd(PPh_3)_4$ suspension present in ionic liquid after initiation period and extensive decomposition observed during the Suzuki reaction.

Table 6. Variation of the Anion of the $[C_4C_1im]^+$ Ionic Liquids

entry	ionic liquid	yield[a] (%)	TON h^{-1}	homo[b] (%)
1	$[C_4C_1im][BF_4]$	68.2	171	2.1
2	$[C_4C_1im][OSO_2CF_3]$	69.3	173	4.3
3	$[C_4C_1im][N(SO_2CF_3)_2]$	52.1	129	1.2
4	$[C_4C_1im][PF_6]$[c]	32.4	81	3.9
5	$[C_4C_1im][SbF_6]$[c]	11.2	28	0.9
6	$[C_4C_1im]Cl$	0	0	0

[a] Isolated yields of 4-methylbiphenyl. [b] Homocoupled product yield. [c] Extensive decomposition observed during the Suzuki reaction.

the reaction. The Suzuki reaction was conducted in a series of $[BF_4]^-$ ionic liquids with different cations. The results clearly illustrate two regimes: ionic liquids in which the $Pd(PPh_3)_4$ gives a catalytic solution with high Suzuki reactivity and no catalyst decomposition or leaching, such as $[C_4C_1im][BF_4]$ and $[C_4C_4im][BF_4]$ {where $[C_4C_4im]^+$ is the 1,3-dibutylimidazolium cation} (Table 5, entries 1 and 2); and ionic liquids where the $Pd(PPh_3)_4$ could not be initiated and resulted in poor Suzuki reactivity with extensive catalyst decomposition and leaching, such as $[C_4C_1C_1im][BF_4]$ {where $[C_4C_1C_1im]^+$ is the 1-butyl-2,3-dimethylimidazolium cation} (Table 5, entry 4). For this ionic liquid unreacted bromobenzene was not detected after the reaction period, probably due to consumption by dehalogenation to benzene.

The imidazolium cation has a dramatic effect on the ability of the ionic liquid to form a catalytic solution from the $Pd(PPh_3)_4$ and, therefore, the success of the subsequent Suzuki reaction. Increasing the size of the N-substituent leads to an improved yield of 4-methylbiphenyl from $[C_2C_1im]^+$, to $[C_4C_1im]^+$ and finally $[C_4C_4im]^+$ (Table 5, entries 1−3). Using an ionic liquid that had been methylated at the C-2 position of the imidazolium ring leads to extensive catalyst decomposition and almost no reaction. We attempted to detect the mixed phosphine/NHC palladium complexes by both ^{31}P NMR and ESI-MS in these ionic liquids (see above) and were successful for those ionic liquids that gave a catalytic solution, but not for $[C_4C_1C_1im][BF_4]$, which do not. Clearly the ability to form the $[(PPh_3)_2Pd(imy)X]^+$ (X = Br or Cl) complex is crucial in determining the ability of the ionic liquid to give a successful Suzuki reaction.

That $[C_4C_1C_1im][BF_4]$ does not afford the $[(PPh_3)_2Pd(imy)X]^+$ (X = Br or Cl) complex again favors a deprotonation of the $[C_4C_1im]^+$ cation and ligand exchange route to the formation of $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl), since oxidative addition of $[C_4C_1C_1im]^+$ to a Pd(0) complex is, at least, potentially possible.

Changing the Anion. Since the formation of a mixed phosphine/NHC palladium complex was so crucial to the success of the reactions, we initially thought that changing the anion of the 1-butyl-3-methylimidazolium-based ionic liquids would have only a negligible effect on the Suzuki reactivity performed within it. This, however, was proved quite wrong when the reaction of bromobenzene with tolylboronic acid was performed in a series of $[C_4C_1im]^+$ ionic liquids (Table 6).

The results illustrate three regimes. In the first the $Pd(PPh_3)_4$ is initiated to afford a catalytic solution with high Suzuki reactivity and no evident catalyst decomposition {$[C_4C_1im][BF_4]$, $[C_4C_1im][OSO_2CF_3]$, $[C_4C_1im][N(SO_2CF_3)_2]$, Table 6, entries 1−3}. In the second, the $Pd(PPh_3)_4$ could not be initiated and poor Suzuki reactivity resulted, with extensive catalyst decomposition and leaching {$[C_4C_1im][PF_6]$, $[C_4C_1im][SbF_6]$, Table 6, entries 4 and 5}. The catalytic solution was not afforded in these ionic liquids even after prolonged heating at 110 °C for 6 h under N_2, and extensive catalyst decomposition was observed during the Suzuki reaction. Finally, in $[C_4C_1im]Cl$ a solution was formed, but no Suzuki reaction occurred and unreacted product was recovered

It has been shown that the basicity of the anions of ionic liquids can affect the electrophilicity of transition metal centers.[2] The greater the basicity of the anion, the stronger is its interaction with the metal center and the slower the reaction. However, this cannot be the only explanation here. Mass spectral analysis of the solution in $[C_4C_1im]Cl$ revealed peaks derived from $[C_4C_1im]_2[PdCl_4]$, which is inactive in the Suzuki reaction, as the only palladium-containing species. For the other ionic liquids, those with poorly basic ions ($[PF_6]^-$ and $[SbF_6]^-$) fail to lead to a stable palladium solution. In these cases all attempts to find the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complex met with failure. However, moderately basic ions ($[BF_4]^-$, $[CF_3SO_3]^-$, and $[(CF_3SO_2)_2N]^-$) give successful Suzuki reactions, and the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complex could be detected in all cases. Clearly, the anions are playing an important role in the formation of the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complex, but, as yet, we do not know what this is.

The only other example of a clearly demonstrated anion effect in the formation of imidazolylidene complexes that we are aware of is from iridium chemistry.[11] Here, when a bromide salt is used as the source of the imidazolylidene, the "normal" C-2 binding site is bound to the metal, and when the poorly basic $[SbF_6]^-$ ion is the counterion of the salt, the imidazolylidene binds through the C-4(5) position. The intermediate $[BF_4]^-$ ion leads to a mixture of products. This may suggest that the basic counterion in some way activates the C-2 proton (perhaps through hydrogen bonding[12]). However, it should be noted that we have added halide salts to all of our reactions.

Detection of 2-Arylimidazolium Cations in Ionic Liquids. Although the identification of $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) in the $[C_4C_1im][BF_4]$ ionic liquid

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raises the possibility of the involvement of NHC complexes in the Suzuki reaction in imidazolium-based ionic liquids, it in no way demonstrates it. This would, perhaps, be best achieved by the unequivocal identification of a palladium complex containing an NHC ligand and preferably both the coupling partners, or at least one of them. We have not been able to achieve this. However, the ESI-MS investigations into the formation of $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) in the $[C_4C_1im][BF_4]$ ionic liquid also revealed the presence of a signal attributable to 1-butyl-2-phenyl-3-methylimidazolium cations $\{[C_4C_1(C_6H_5)im]^+\}$. Furthermore, $[C_4C_1(C_6H_5)im]^+$ cations were also produced from the independently prepared $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complex in $[C_4C_1im][BF_4]$ under similar conditions. In this case, the mass spectra of the solution of $[(PPh_3)_2Pd(C_4C_1imy)Cl][BF_4]$ in $[C_4C_1im][BF_4]$ with added phenyl bromide did not reveal the signal until it had been heated for 1 h (cf. the initiation of the reactions above). Reinspection of the original ESI-MS spectra of the ionic liquids used for the Suzuki reactions after extraction of the products also showed the presence of 2-arylimidazolium cations. However, we should note that all attempts to quantify the amount of the 2-arylimidazolium cations generated were unsuccessful. The 2-arylimidazolium cations could not be isolated from the ionic liquids, and analytical techniques such as ion chromatography and LC-MS were ineffective.

The most plausible explanation of the formation of $[C_4C_1(C_6H_5)im]^+$ cations under these conditions is that they have been reductively eliminated from a palladium complex with both an imidazolylidene and a phenyl ligand. The reductive elimination of 2-arylimidazolium cations from platinum, palladium, and nickel imidazolylidene complexes has been reported in molecular solvents.[13,14] This strongly suggests that an as yet undetected species plays an important role in establishing the reaction system and may be part of the catalytic cycle. The formation of 1,3-bis(2,6-diisopropylphenyl)-2-phenylimidazolium chloride by reductive elimination from $[(^iPrimy)Pd(PPh_3)(Ph)Cl]$ {where (^iPrimy) = 1,3-bis(2,6-diisopropylphenyl)imidazolylidene} has recently been observed.[15] It is likely that our undetected species is closely related to this. To achieve such a phenyl-containing species from a solution of $[(PPh_3)_2Pd(C_4C_1imy)X][BF_4]$ (X = Br or Cl) and phenyl bromide in $[C_4C_1im][BF_4]$, the $[(PPh_3)_2Pd(C_4C_1imy)X]^+$ (X = Br or Cl) complex would first need to be reduced. This could be a base-catalyzed phosphine reduction mechanism similar to that observed for palladium(II) phosphine complexes.[6] This is supported by the appearance of $OPPh_3$ in the ^{31}P NMR after heating a solution of $[(PPh_3)_2Pd(C_4C_1imy)X][BF_4]$ (X = Br or Cl) in $[C_4C_1im][BF_4]$ with an aqueous solution of Na_2CO_3. Signals corresponding to $OPPh_3$ were also observed in the ESI-MS at this stage, although these were always observed to some extent with palladium phosphine complexes under our ESI-MS conditions. Alternatively, the reduction could be via reductive elimination of 1-butyl-2-halogeno-3-methylimidazolium cations, but no evidence for these species has yet been observed in any of our spectra.

While the formation of 2-arylimidazolium salts supports the proposal that NHC complexes are key to the stability and reactivity of palladium catalysts in the Suzuki reaction, it also raises a number of questions. The formation of the 2-arylimidazolium cations could be catalytic. Thus, the consumption of the phenyl halide and the imidazolium cation of the ionic liquid to afford the 2-arylimidazolium cation could compete with the Suzuki reaction. This would be expected to result in a lowering of the yield of cross-coupled product and the eventual destruction of the ionic liquid solvent. However, the high yields of the Suzuki reactions that we observe in the ionic liquids, together with the long-term stability of the reaction solution, suggest that none of this is happening.

Palladium/Phosphine-Catalyzed Coupling of 2-Arylimidazolium Salts in $[C_4C_1im][BF_4]$. The apparent inconsistency of high Suzuki yields and the concomitant formation of 2-arylimidazolium cations was further investigated. For example, the reaction of bromobenzene with tolylboronic acid, catalyzed by 1.2 mol % $(PPh_3)_4Pd$ in $[C_4C_1im][BF_4]$ with 12 mol % $[C_4C_1im]Cl$, gave a 92.4% yield of 4-methylbiphenyl after 3 h at 110 °C (Table 1). No unreacted bromobenzene was detected after the reaction period. The mass balance was largely attributed to the formation of biphenyl (2.3%) originating from homocoupling, with the remaining 5.3% being attributed to all other experimental losses.

Since reductive elimination and oxidative addition are elementary reversible processes, the oxidative addition of the 2-arylimidazolium cation back onto a palladium(0) species was possible. The oxidative addition of 2-arylimidazolium cations to palladium(0) complexes was examined under catalytic Suzuki conditions with the independently prepared $[C_4C_1(C_6H_5)im][BF_4]$ salt. Palladium-catalyzed coupling reactions involving aryl moieties from charged species are not uncommon, and a number of recent examples have been reported, including aryl- and alkenyliodonium,[16] aryltrifluoroborates,[17] and aryldiazonium salts.[18] The $[C_4C_1(C_6H_5)im][BF_4]$ salt (0.380 mmol, 0.5 equiv) was added to a suspension of $(PPh_3)_2PdCl_2$ (9.22 μmol, 1.2 mol %) in $[C_4C_1im][BF_4]$ (1.6 cm^3) with PPh_3 (18.5 μmol, 2.4 mol %) and NaCl (93.6 μmol, 12 mol %). Under normal reaction conditions the aryl halide is required and, therefore, 4-bromotoluene (0.382 mmol, 0.5 equiv) was added to the mixture. The initiation was performed in the usual manner by the addition of the Na_2CO_3 (1.52 mmol, 2 equiv) in water (0.8 mL) and subsequent heating at 110 °C for 1 h under N_2 to obtain a colorless solution. The tolylboronic acid (0.837 mmol, 1.1 equiv) was added, and the mixture was then heated at 110 °C for 20 min. Isolation and analysis of the products revealed the presence of both 4−4′-dimethylbiphenyl (0.325 mmol, 42.6%) and 4-methylbiphenyl (0.110 mmol, 14.4%). The 4−4′-dimethylbiphenyl originated from the

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Suzuki cross-coupling of the 4-bromotoluene and the tolylboronic acid. Since homocoupling was not previously observed, it is unlikely to contribute greatly to the 4−4′-dimethylbiphenyl yield. The source of 4-methylbiphenyl was the coupling of the phenyl moiety derived from $[C_4C_1(C_6H_5)im]^+$ with the tolylboronic acid. Hence, oxidative addition of the 2-arylimidazolium cations to palladium(0) complexes can occur under the conditions of our reactions to give a species that is capable of cross-coupling with the boronic acid. The reversibility of the reductive elimination/oxidative addition reactions of the 2-arylimidazolium cations can account for the high Suzuki yields despite their in situ formation during catalytic reactions. Thus, the amount of 2-arylimidazolium cations generated in situ during catalytic reactions in the ionic liquids was not a concern, as the aryl moiety was still available for coupling. The resultant palladium complex from the oxidative addition of the 2-arylimidazolium cation also regenerated the mixed phosphine/NHC palladium complex.

Imidazolylidene Ligand Scrambling Affects. Although the formation of $[C_4C_1(C_6H_5)im]^+$ does not affect the yields of the Suzuki reactions in ionic liquids, it provides a potential mechanism for the exchange of the imidazolylidene ligand with that derived from the ionic liquid cation. To investigate this, we used a solution of $[(PPh_3)_2Pd(C_4C_1imy)Br][BF_4]$ in $[C_2C_1im][BF_4]$. The $[(PPh_3)_2Pd(C_4C_1imy)Br]^+$ was initiated in $[C_2C_1im][BF_4]$ as before and the ESI-MS recorded. At this stage no palladium-containing species with C_2C_1imy ligands were observed. However, once the reaction had been completed, the ESI-MS revealed both the complexes $\{[(PPh_3)_2Pd(C_4C_1imy)Br]^+\}$ and $\{[(PPh_3)_2Pd(C_2C_1imy)Br]^+\}$ as well as both of the possible 2-arylimidazolium cations. Hence, ligand scrambling in these systems does indeed occur. This has important implications when wishing to derive the potential benefits of the use of NHC complexes in ionic liquids. Ultimately, since it is in such excess, it is the ionic liquid cation that will determine which imidazolylidene will be the dominant ligand in the system and, as such, will determine the reactivity of the solution. Hence, we are seeking to develop ionic liquids that will combine the positive catalytic effects of the bulky, basic imidazolylidenes with providing salts that are liquid at useful temperatures.

Conclusions

Suzuki reactions of bromo- and iodoarenes can be performed in imidazolium-based ionic liquids with both increased reactivities and catalyst stabilities, when compared to the same reactions in conventional molecular solvents. A successful Suzuki reaction in the ionic liquids requires the prior initiation of the catalytic system in the ionic liquid to afford a catalytic solution. The generation of a successful catalytic solution was found to be highly dependent upon both the cation and the anion of the ionic liquid. Both palladium(0) and palladium(II) compounds can be used as sources of palladium for the catalyst, with ionic liquid-soluble palladium(II) salts being the preferred form.

In all successfully initiated solutions the mixed phosphine/NHC complexes $[(PPh_3)_2Pd(C_xC_yimy)X]^+$ ($X = Br$ or Cl) were formed, and they were not detected in any solution where the catalysis was unsuccessful. This strongly suggests that these complexes are crucial to the catalytic process. Cations that cannot give rise to stable mixed $[(PPh_3)_2Pd(C_xC_yimy)X]^+$ ($X = Br$ or Cl) complexes give ionic liquids in which the Suzuki reactions are unsuccessful. The same is true for anions, but at this stage we do not know the role that they play in the formation of the complexes.

The need to add a source of halide to the reaction mixture suggests that one of the key intermediates to the $\{[(PPh_3)_2Pd(C_xC_yimy)X]^+$ ($X = Br$ or Cl) complex requires its presence. Such a species could be $(PPh_3)_2PdX_2$ ($X = Br$ or Cl) or a halide-bridged dimeric species similar to those detected in the formation of other NHC complexes in ionic liquids.[19] Although there is no conclusive evidence, the observations to date suggest that the $[(PPh_3)_2Pd(C_xC_yimy)X]^+$ ($X = Br$ or Cl) complex is more likely to be formed from acid−base chemistry with a Pd(II) complex rather than oxidative addition to Pd(0).

Imidazolylidene ligands are already having a huge impact on catalytic chemistry.[20] Their chemistry with palladium has been extensively investigated,[21] and the use of palladium NHC complexes as catalysts for Suzuki and other cross-coupling reactions is well known.[22] Their complexes with palladium, using bulky imidazolylidenes, have recently been used successfully for Suzuki reactions of chloroarenes, and the effect of changing the substitution on the ligand was demonstrated.[23] Clearly, this offers the opportunity to investigate the development of ionic liquids that will be capable of giving a system in which chloroarenes will be reactive. However, it will be necessary to find an ionic liquid that is capable of both producing an imidazolylidene that gives a complex active for chloroarenes and being liquid at an accessible temperature.

The tetradecyltrihexylphosphonium chloride ionic liquid has already been shown to act as a solvent for the coupling of chloroarenes (albeit activated).[9] If it was acting simply as a noncoordinating solvent, this is difficult to explain. However, the results reported here, together with the well-known phosphine/arene scrambling in many Suzuki systems,[6] suggest that it could be acting as a source of alkylphosphines ligands. These are just the kind of complexes that have recently proved so successful in Suzuki reactions of chloroarenes.[7]

The mixed phosphine/NHC nature of the complex gives this system a further synthetic flexibility, in that the phosphine can be changed. The use of bulky, electron-rich phosphines to enhance the reactivity of palladium catalysts has become an area of much interest.[7] The stability offered by our ionic liquid system offers the possibility of easier handling of these highly active catalysts. Further to this, it has been suggested

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that mixed phosphine/NHC palladium complexes are even more active in C−C coupling and cross-coupling reactions.[24] We are continuing to study this system with the aim of finding a combination that will offer a stable, recyclable catalyst system for the activation of chloroarenes.

Experimental Section

General Procedures. Unless otherwise stated, all materials were used as obtained without further purification. Acetonitrile, CH_2Cl_2, toluene, and ethyl acetate were distilled from CaH_2, and toluene from Na/benzophenone. $Pd(PPh_3)_4$,[25] $(CH_3CN)_2PdCl_2$,[26] and $[C_4C_1im]_2[PdCl_4]$[27] are known compounds and were prepared using literature procedures. The ionic liquids were prepared using methodologies that we have previously described.[28]

GC analyses were performed with a Hitachi 163 gas chromatograph using a 2 m × 3 mm carbowax column. GC−MS was performed on a HP5890 Series II with a HP5MS capillary column and 1 mol min^{-1} flow rate.

Synthesis of $[C_4C_1(C_6H_5)im][BF_4]$. A flask containing a stirred solution of 1-butyl-2-phenylimidazole (7.17 g, 35.80 mmol, 1 equiv) in CH_2Cl_2 (75 cm^3) was cooled in an dry ice/acetone bath under N_2, and a solution of $[(CH_3)_3O][BF_4]$ (5.30 g, 35.81 mmol, 1 equiv) in CH_2Cl_2 (50 cm^3) was added dropwise. The colorless solution was stirred for a further 24 h under N_2, quenched with water (3 × 30 cm^3), and dried in vacuo. The yellow-tinted viscous liquid was washed with ethyl acetate (3 × 20 cm^3) and diethyl ether (3 × 20 cm^3), then dried in vacuo to afford $[C_4C_1(C_6H_5)im][BF_4]$ (10.80 g, 100%) as a pale straw yellow viscous liquid; ν_{max}(neat)/cm^{-1} 3639, 3560, 3147, 2963, 1583, 1516, 1246, 1074, and 834; δ_H (270 MHz, $CDCl_3$)/ppm 7.88 (2H, AB quartet, $^3J_{A-B} = 2.0$ Hz, $2NCH$), 7.81−7.65 (5H, m, C_6H_5), 3.99 (2H, t, $^3J = 7.3$ Hz, $NCH_2(CH_2)_2CH_3$), 3.67 (3H, s, NCH_3), 1.63 (2H, quintet, $^3J = 7.3$ Hz, $NCH_2CH_2CH_2CH_3$), 1.14 (2H, sextet, $^3J = 7.4$ Hz, $N(CH_2)_2CH_2CH_3$), and 0.73 (3H, t, $^3J = 7.3$ Hz, $N(CH_2)_3CH_3$); δ_C (68 MHz, $CDCl_3$)/ppm 144.01 (s, N_2C), 133.32 (s, *p*-C_6H_5), 130.47 and 129.49 (s, *o*- and *m*-C_6H_5), 123.44 (s, *ipso*-C_6H_5), 121.74 and 121.35 (s, $2NCH$), 47.84 (s, $NCH_2(CH_2)_2CH_3$), 35.42 (s, NCH_3), 31.00 (s, $NCH_2CH_2CH_2CH_3$), 18.58 (s, $N(CH_2)_2CH_2CH_3$), and 13.00 (s, $N(CH_2)_3CH_3$); *m*/*z* (FAB^+) 515 ($[(C_4C_1(C_6H_5)im)_2BF_4]^+$, 19%) and 215 ($[C_4C_1(C_6H_5)im]^+$, 100%); *m*/*z* ($FAB^-$) 87 ($[BF_4]^-$, 94%) and 19 ($F^-$, 100).

Representative Palladium(0)/Phosphine Suzuki Reaction in $[C_4C_1im][BF_4]$. A suspension of $Pd(PPh_3)_4$ (11.5 mg, 0.00996 mmol, 1.2 mol %) in thoroughly degassed and dried $[C_4C_1im][BF_4]$ (1.6 cm^3) in the presence of 4-bromotoluene (142 mg (0.102 cm^3), 0.830 mmol, 1 equiv) and NaCl (5.80 mg, 0.01 mmol, 12 mol %) was heated at 110 °C under N_2 with vigorous stirring until a yellow-orange solution resulted. The solution was allowed to cool to room temperature, and a solution of Na_2CO_3 (176 mg, 1.66 mmol, 2 equiv) in water (0.80 mL) and phenylboronic acid (111 mg, 0.913 mmol, 1.1 equiv) was added. The flask was heated in an oil bath thermostatically controlled at 110 °C and was vigorously stirred for 10 min under N_2. On completion the flask was immediately cooled in a dry ice/acetone bath, then extracted with hexane (4 × 15 cm^3). The combined extracts were washed with brine (3 × 15 mL) and water (3 × 15 mL), then filtered through a short pad of silica with copious amounts of hexane. The hexane was removed, and the product was dried in vacuo to afford 4-methylbiphenyl (96.6 mg, 69.3%) as a white crystalline solid. (Product separation could also be achieved by sublimation or precipitation by the addition of water. However, the reproducibility of this method proved to be greater, and so it was more suitable for the measurements made here.)

Representative Palladium(II)/Phosphine Suzuki Reaction in $[C_4C_1im][BF_4]$. Into a flask, charged with $(PPh_3)_2PdCl_2$ (6.52 mg. 0.00930 mmol, 1.2 mol %), NaCl (5.39 mg, 0.0930 mmol, 12 mol %), PPh_3 (4.87 mg, 0.0186 mmol, 2.8 mol %), and thoroughly degassed and dried $[C_4C_1im][BF_4]$ (1.6 cm^3), a solution of Na_2CO_3 (164 mg, 1.55 mmol, 2 equiv) in deoxygenated water (0.8 mL) was injected. Bromobezene (0.1217 mg (0.0816 cm^3), 0.775 mmol, 1 equiv) was then injected and the mixture heated at 110 °C with vigorous stirring under N_2 until a completely colorless solution resulted. The solution was allowed to cool to room temperature, and tolylboronic acid (116 mg, 0.853 mmol, 1.1 equiv) was added. The solution was then heated in an oil bath thermostatically controlled at 110 °C for 20 min with vigorous stirring under N_2. On completion, the flask was immediately cooled in an acetone/solid CO_2 bath and water (2 mL) was added. The mixture was extracted with ether (4 × 15 cm^3) and washed with brine (3 × 15 mL) and water (3 × 15 mL), then filtered through a short pad of silica with copious amounts of hexane. The hexane was removed, and the product was dried in vacuo to afford 4-methylbiphenyl (87.0 mg, 66.9%) as a white crystalline solid.

Representative Palladium(0)/Phosphine Suzuki Reaction in Toluene. Under N_2, 4-bromotoluene (475 mg, 2.78 mmol, 1 equiv), phenylboronic acid (373 mg, 3.06 mmol, 1.1 equiv), and a deoxygenated solution of Na_2CO_3 (589 mg, 5.56 mmol, 2.1 equiv) in H_2O (2.5 mL) was added to a suspension of $Pd(PPh_3)_4$ (96.3 mg, 0.0833 mmol, 3 mol %) in freshly distilled toluene (5 cm^3). The mixture was heated at reflux (110 °C) for 6 h with vigorous stirring under N_2. On completion the flask was removed from the oil bath and placed in an acetone/dry ice bath. The product was extracted with hexane (4 × 10 cm^3) and washed with brine (3 × 10 mL) and water (3 × 10 mL). The combined extracts were then filtered through a pad of silica and dried in vacuo to afford 4-methylbiphenyl (408 mg, 87.3%) as a colorless crystalline solid.

Characterization of 4-Methylbiphenyl. R_f (TLC, SiO_2, hexane) 0.26; t_R (GC−MS, HP5MS capillary, col temp 150 °C, carrier flow 25.7 mL) 7.08 min; mp 48.5−50.5 °C (lit., 49 50 °C, from ethanol); δ_H (270 MHz, $CDCl_3$)/ppm 7.70−7.65 (2H, m, 3′-H), 7.62−7.56 (2H, m, 3-H), 7.55−7.47 (2H, m, 2′-H), 7.44−7.37 (1H, m, 4′-H), 7.36−7.30 (2H, m, 2-H) and 2.38 (3H, s, 4-CH_3); δ_C (68 MHz, $CDCl_3$)/ppm 141.14 (1C, s, 1′-C), 138.33 (1C, s, 1-C), 136.95 (1C, s, 4-C), 129.45 (4C, s, 3′-C; 3-C), 128.68 (1C, s, 4′-C), 126.93 (4C, s, 2-C; 2′-C) and 21.05 (1C, s, 4-CH_3); ν_{max} (KBr)/cm^{-1} 3032, 1487, 1402, 1377, 824, 754, and 689; *m*/*z* (EI), 168 (M^+, 100%), 152 (15), 115 (7), 91 (5), and 84 (8).

Characterization of 4,4′-Dimethylbiphenyl. R_f (TLC, SiO_2, hexane) 0.28; t_R (GC−MS, HP5MS capillary, col temp 150 °C, carrier flow 25.7 mL) 7.72 min; mp 116−117 °C (lit., 115−117, from water); δ_H (270 MHz, $CDCl_3$)/ppm 7.68 (4H, d, $J = 7$ Hz, 3′-H; 2-H), 7.42 (4H, d, $J = 7$ Hz, 3-H; 2′-H) and 2.69 (6H, s, 4-CH_3); δ_C (68 MHz, $CDCl_3$)/ppm 138.23 (1C, s, 1′-C), 136.55 (1C, s, 1-C), 129.38 (4C, s, 3′-C; 2-C), 126.72 (4C, s, 3-C; 2′-C), and 20.98 (2C, s, 4-CH_3); ν_{max} (KBr)/cm^{-1} 3021, 1501, 1113, 1005, 803, and 502; *m*/*z* (EI) 182 (M^+, 100%), 167 ($-CH_3$, 48), 152 (10), 89 (8), 76 (5), 63 (3), and 51 (2).

OM034075Y

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