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Use of a bulky phosphine of weak σ-donicity with palladium as a versatile and highly-active catalytic system: allylation and arylation coupling reactions at 10^{-1}–10^{-4} mol% catalyst loadings of ferrocenyl bis(difurylphosphine)/Pd

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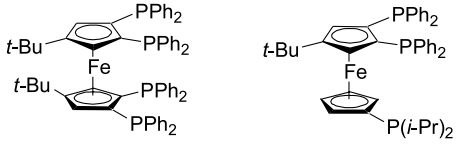
Abstract—Carbon–carbon(sp^2–sp^2 and sp^1–sp^2) and carbon–nitrogen (nucleophilic allylation) coupling processes are promoted by a catalytic system containing $[PdCl(\eta^3\text{–}C_3H_5)]_2$ with the new ferrocenyl bis(difurylphosphine) 1,1′-bis[di(5-methyl-2-furyl)phosphino] ferrocene, $Fc[P(Fu^{Me})_2]_2$. Starting from aryl bromides or allylic acetates this versatile catalyst system may be used at low palladium loadings (10^{-1}–10^{-4} mol%) in some Heck, Suzuki, Sonogashira and allylic amination reactions to give cross-coupled products in excellent yield. Remarkably high activity is obtained in allylic substitution reactions, providing a significant impetus for the development of bulky phosphines possessing weak σ-donicity for this particular reaction.

1. Introduction

Palladium-catalysed carbon–carbon and carbon–heteroatom bond formations represent important catalytic processes with extensive scope in contemporary synthetic chemistry. The progress made since the late 1960's, following the seminal studies by Heck, Sonogashira, Suzuki, Tsuji and others,[1] provides a variety of protocols for the production of organic building blocks of prodigious interest in material science, medicine or agronomy. Some practical problems exist, which will require addressing for these reactions to move from academic laboratories to industrial processes.[2] Indeed, until very recently reported catalytic systems were most often used at 1–10 mol% palladium loadings at best, which is non-efficient in terms of turnover number and sometimes of turnover frequency. Concomitantly, such high catalyst loadings impose financial constraints on scaling up reactions, or at least in problems associated with catalyst removal. The necessity to provide catalytic systems minimising the consumption of expensive transition-metals can be fulfilled through the synthesis of accessible, efficient and inexpensive ligands. The new bis(difurylphosphino)-ferrocene ligand **1** presented herein was developed following this objective, and pertains to a family of highly efficient catalytic auxiliaries based on ferrocenyl poly-phosphines, which we have synthesized (**2a** and **2b** Scheme 1).[3–6]



$Fc(P)_4{}^tBu$, **2a** $Fc(P)_2{}^tBu(P^iPr)$, **2b**

Scheme 1.

Keywords: Catalysis; Palladium; Ferrocenylphosphine; Furyl; Allylic substitution; Cross-coupling; Ligand effect.
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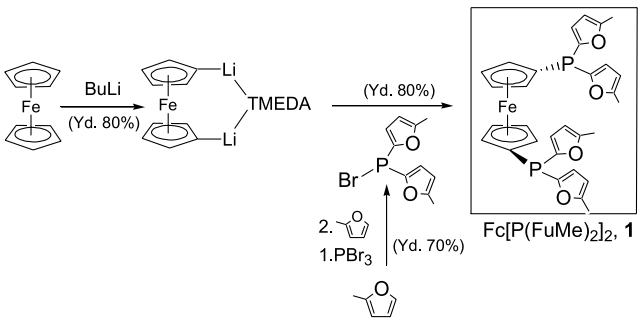
2. Results and discussion

2.1. Preparation and characterization of the ligand 1,1′-bis[di(5-methyl-2-furyl)phosphino]ferrocene

A literature survey from the last 20 years concerning palladium-catalysed cross-coupling reactions clearly shows that much progress in this field was accomplished from the synthesis/identification of efficient auxiliary ligands. Such species not only allowed a wide range of synthetic advances but moreover, provided interesting mechanistic investigations. Amongst these auxiliaries, bulky phosphines with high σ-donicity emerged as powerful ligands.[7–15] Their efficiency was initially surprising since strong σ-donor ligands would not be expected to facilitate the crucial transmetalation[16] and reductive elimination steps,[17] but rather would be assumed to be powerful inhibitors. These results indicated the importance associated with the often rate-limiting oxidative-addition step, particularly with substrates containing strong carbon-halide bonds. Additionally, the success of bulky phosphines has been suggested to be derived from the ability of these ligands to promote geometrically driven coordinative unsaturation and palladium reactivity (mainly due to steric hindrance[2,18,19] and/or cone/bite angle[20]). These geometric features appear to be important to transmetalation[2] and reductive elimination[21] steps, when utilising strongly electron-donating ligands. Finally, investigations on ligands exhibiting both pronounced electronic and steric properties, contribute to synthetic advances, as well as to mechanistic understanding.

As a consequence of the complexity in the prediction of a rate-limiting step,[20] it did not appear unreasonable to us to test, in more depth, a range of cross-coupling reactions using a comparatively 'forgotten' strongly electron-withdrawing bulky phosphine ligand.[22] We choose to build a weakly σ-donor phosphine on the robustness of the ferrocenic backbone.[3] Ferrocenic phosphines with phosphorus bearing heterocyclic substituents[23] are notably less developed than the corresponding ferrocenyl diphosphines bearing aryl or alkyl substituents.[14,24–26] Nevertheless, the new ligand 1,1′-bis[di(5-methyl-2-furyl)phosphino]ferrocene, **1**, is obtained pure in 80% isolated yield from reaction of lithiated ferrocene with the bis(5-methyl-2-furyl)bromophosphine $BrP(Fu^{Me})_2$ (Scheme 2). Compound **1** was isolated in pure form on a 10 g scale, as a crystalline orange powder, insensitive to air and moisture, easy to handle and crystallise. This synthesis is different to that previously reported for the parent compound: 1,1′-bis[di(-2-furyl)-phosphino]ferrocene, available by reaction of bis(dichlorophosphino)ferrocene with 2-lithiofuran.[23]



Scheme 2.

Table 1 summarizes some of the ^{31}P NMR chemical shifts recorded for ferrocenyl heteroannular diphosphines, including the data for **1**, which displays a noticeable high-field signal. The electronic difference expected between the phosphorus atoms of **1** and the related ferrocenyl diphosphines incorporating aryl or alkyl substituents was confirmed. Evidence concerning the intrinsic low Lewis-basicity of phosphorus bearing 2-furyl substituents have been collected and reported.[27]

Table 1. ^{31}P NMR chemical shifts for ferrocenyl heteroannular diphosphines

$Fe[\eta_5\text{-}C_5H_4(PR_2)]_2$	^{31}P NMR (ppm)/solvent
R = *t*-Bu	27.1[14]/C_6D_6
R = *i*-Pr	−0.2[25]/C_6D_6
R = Cy	−9.7[26]/$CDCl_3$
R = Ph	−17.2[28]/$CDCl_3$
R = Menthyl	−24.1[25]/$CDCl_3$
	−25.2[25]/C_6D_6
R = 5-Me-2-furyl	−63.8/$CDCl_3$
R = 2-Furyl	−64.9[23]/$CDCl_3$

The molecular structure of $Fc[P(Fu^{Me})_2]_2$ shows that in the solid state the cyclopentadienyl rings adopt an eclipsed conformation (Fig. 1). In contrast to dppf (dppf = 1,1′-bis[diphenylphosphino]ferrocene), for which the phosphorus atoms point away from each other (C_{p1}–CNT1–CNT2–C_{p2} torsion angle 180°, antiperiplanar staggered conformation), in **1** a 72° only torsion angle is observed for C_{p1}–CNT1–CNT2–C_{p2} (synclinal eclipsed).[29] We did not detect any noticeable ordered crystalline arrangement or hydrogen bonding, which would explain such a geometry. Bond angles and distances are within the expected values.

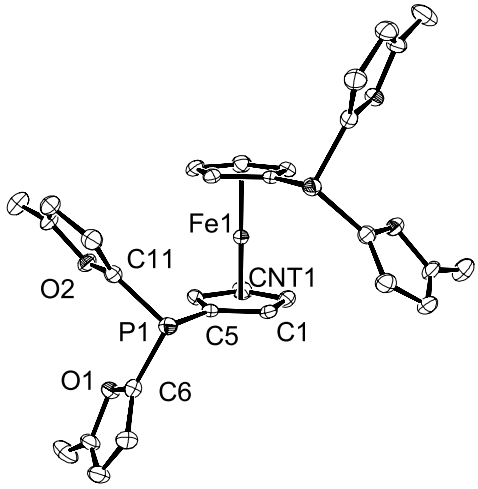


Figure 1. Molecular structure of **1**. Selected bond lengths (Å) and angles (°): Fe(1)–CNT(1) 1.655(2), P(1)–C(5) 1.812(2), P(1)–C(6) 1.804(2), P(1)–C(11) 1.803(2), O(1)–C(6) 1.385(3), O(2)–C(11) 1.385(3), CNT(1)–Fe(1)–CNT(2) 178.18(14), C(11)–P(1)–C(5) 103.80(10), C(11)–P(1)–C(6) 102.77(10), O(1)–C(6)–P(1) 121.77(16), O(2)–C(11)–P(1) 103.80(10).

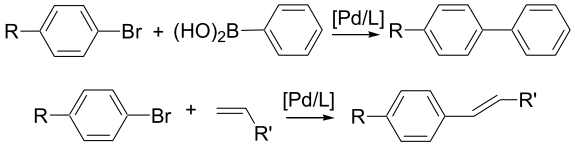
2.2. Catalytic results in 'Suzuki', 'Heck' and 'Sonogashira' cross-coupling reactions

To evaluate the ligand properties in cross-coupling reactions systematically, we first tested the performance of **1** in Suzuki–Miyaura cross-coupling reactions using the activated substrate 4-bromoacetophenone with phenylboronic acid, following previously reported procedures.[3] The reaction of aryl halide (10 mmol), aryl boronic acid (20 mmol) at 130 °C during 20 h in dry xylene or DMF, under argon, affords the corresponding products in presence of palladium/phosphine catalysts and K_2CO_3. Surprisingly, regarding the low basicity of phosphorus, a high turnover number (TON) of 100,000 with a complete conversion was obtained in presence of 10^{-3} mol% catalyst (Table 2, entry 1), a result equivalent to that obtained with the more electron-rich tetraphosphine **2a** under identical conditions.[3] A conversion of 18% is obtained in the presence of 10^{-4} mol% catalyst (TON 180,000, entry 2) after 20 h. Nevertheless, this facile coupling-reaction is to be used as a guide and not as a stern benchmark to screen new Pd-catalysts.[9] We tested a more demanding substrate, the deactivated and electron-rich organohalide, 4-bromoanisole. Complete conversion was obtained in the presence of 10^{-2} mol% catalyst (TON 10,000, entry 3), but disappointingly a lower concentration produces no cross-coupled product (entry 4). Under identical conditions the tetraphosphine **2a** facilitated a TON of 77,000, in the presence of 10^{-3} mol% catalyst.[3]

The preliminary experiments on the Heck alkenylation reaction were conducted using 4-bromoanisole with *n*-butyl acrylate without addition of tetraalkyl ammonium salts, which are often used to delay palladium black formation. Here, excellent conversions were obtained in the presence of 10^{-1} and 10^{-2} mol% catalyst (entries 5–6, TON 10,000), but lowering the concentration inhibits completely the reaction. At this stage, the results obtained without any further optimization,[30] that meet the definition of high-turnover catalysts (HTC) proposed by Farina[2] (a catalyst that can lead to quantitative conversion of starting materials at a load of 0.1 mol% or less), however did not completely satisfy our activity criteria for the Suzuki–Miyaura cross-coupling and Heck alkenylation reaction.

We next, compared the activity of **1** in the Sonogashira arylation of phenylacetylene with the activated and deactivated substrates: 4-bromoacetophenone and 4-bromoanisole, respectively. Using 4-bromoacetophenone in the presence of 10^{-4} mol% catalyst, a TON of 920,000, among the highest reported,[4,31] was obtained (Table 3, entry 10). 4-Bromoanisole, as expected was quantitatively converted (at 10^{-1} mol% catalyst concentration) at a lower TON of 1000. Note that under the same reactions conditions (i.e., using K_2CO_3 as base and 10^{-1} mol% catalyst) the absence of ligand lead to no conversion.[31] In the presence of a large excess of PPh_3, 5% conversion was observed, 3% with P(*o*-tol)$_3$ and 50% maximum using an excess of 1,4-bis(diphenylphosphino)butane (dppb). With a more demanding substrate such as an activated aryl chloride: 4-chloroacetophenone; no coupling product was obtained, even at 0.4 mol% catalyst loading, whereas under the same

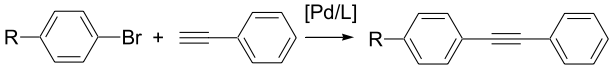
Table 2. Suzuki and Heck reactions catalysed by the Fc[P(Fu^{Me})$_2$]$_2$/palladium system



Entry	Aryl bromide	Aryl boronic acid or alkene	Ratio substrate/catalyst	Yield%
1	4-MeCOC$_6$H$_4$Br	PhB(OH)$_2$	100,000	100
2			1,000,000	18
3	4-MeOC$_6$H$_4$Br	PhB(OH)$_2$	10,000	100
4			100,000	0
5	4-MeOC$_6$H$_4$Br	^{n}BuOCOCH=CH$_2$	1000	100
6			10,000	99
7			100,000	0

Conditions: catalyst [PdCl(η^3–C$_3$H$_5$)]$_2$/**1**: ½. Suzuki: ArBr 1 equiv, ArB(OH)$_2$ 2 equiv, K_2CO_3 2 equiv, 20 h, 130 °C, xylene. Heck: ArBr 1 equiv, alkene 2 equiv, K_2CO_3 2 equiv, 20 h, 130 °C, dimethylformamide (DMF).

Table 3. Sonogashira reaction catalysed by the Fc[P(Fu^{Me})$_2$]$_2$/palladium system



Entry	Aryl halide	Alkyne	Ratio substrate/catalyst	Yield%
8	4-MeCOC$_6$H$_4$Br	PhC≡CH	10,000	100
9			100,000	100
10			1,000,000	92
11	4-MeOC$_6$H$_4$Br	PhC≡CH	250	100
12			1000	100
13			10,000	Traces

Conditions: catalyst [PdCl(η^3-C$_3$H$_5$)]$_2$/**1**: ½. ArBr 1 equiv, alkyne 2 equiv, K_2CO_3 2 equiv, CuI 0.05 equiv, 20 h, 130 °C, DMF.

reactions conditions the triphosphine ligand **2b** leaded to 82% conversion.[4]

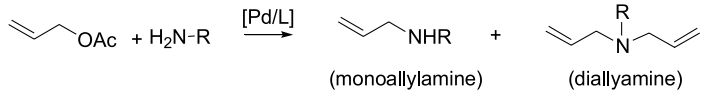
In the reactions conducted with **1**, very high TONs were obtained when activated substrates were used, and comparatively disappointing results were observed from more demanding aryl halides. From these results in C–C cross-coupling reactions, several conclusive trends, which are discussed in Section 2.4, led us to focus our further catalytic investigations on the allylic amination reaction.

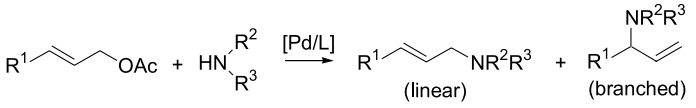
2.3. Catalytic results in 'Tsuji-Trost' allylic amination

Allylamines are important building blocks in modern chemistry and their preparation is a key synthetic and industrial goal.[32] The allylamine fragment is found in many natural products, and can undergo a range of different chemical processes on the C=C bond (functionalization, oxidation, etc.). One of the most attractive and preferred ways to form allylamines is by palladium-catalysed nucleophilic allylic substitution, in the presence of a stabilising ligand, mostly phosphines. In this field, a large number of research groups have mainly focused on the development of chiral catalysts, inducing enantioselectivity in allylic alkylation reactions in general. Some of these complexes have been applied to allylic amination.[32,33] Consequently, even in the achiral form of the reaction, the catalytic systems reported, to date, are generally used at 1–5 mol%. The knowledge related to more efficient catalytic systems in terms of scope and catalyst economy (reduction of the loading of the expensive catalytic metal, of sophisticated ligands and of polluting additives) is very limited, the reported examples being rare.[34–36]

The results obtained in allylic amination with various allylic acetate and amine substrates are summarised in Table 4. To evaluate the scope and limitation of the system Pd/**1**, allyl acetate was reacted with primary and secondary aliphatic and cyclic amines of various steric and nucleophilic features. We were delighted to see that without optimisation procedures our system allowed to reach the best turnover frequencies (TOFs) reported to date, and this at rt, in the absence of base[37] or any additive and in the presence of as little as 0.01 mol% catalyst. A complete conversion was obtained from the primary amine aniline with a satisfactory selectivity of 96% in monoallylaniline (Table 4 entry 14, TOF 10,000 h^{-1}).[38] An excellent 98% conversion was also achieved from the cyclic secondary amine pyrrolidine (entry 15, TOF 4900); we verified the facile access to the product (pure) after classical work-up procedures, with an isolated yield of 88%. Interestingly, only a slightly decreased 85% conversion was obtained with the less nucleophilic cyclic morpholine (entry 16, TOF 4250 h^{-1}) under the same conditions; morpholine can be quantitatively converted in 3 h at rt. The coupling of primary amine benzylamine appeared more difficult and less selective (entry 17, TOF 1825 h^{-1} for a 75% selectivity in monoallylation product). In addition to primary amines and cyclic secondary amines, also more challenging aliphatic secondary amines such as *n*-dioctylamine, can be coupled efficiently. A complete conversion of the sterically demanding diisopropylamine was obtained at 80 °C in the presence of 0.1 mol% catalyst

Table 4. Allylic amination reaction catalysed by the Fc[$P(Fu^{Me})_2$]$_2$**1**/palladium system





Entry	Allylic acetate	Amine	Ratio substrate/catalyst	Reaction conditions	Yield%	Selectivity %
14	Allyl acetate	H_2NPh	10,000	rt,[a] 1 h	100	96/4 (mono/di)
15	Allyl acetate	$-(CH_2)_4HN-$	10,000	rt,[a] 2 h	98	100
16	Allyl acetate	$-[O(CH_2)_4]HN-$	10,000	rt,[a] 2 h	85	100
17	Allyl acetate	H_2NCH_2Ph	10,000	rt,[a] 4 h	73	75/25 (mono/di)
18	Allyl acetate	HN(*n*-octyl)$_2$	1000	rt, 20 h	100	100
19			10,000		45	100
20			100,000		5	100
21	Allyl acetate	HN(*i*-propyl)$_2$	1000	80 °C,[a] 2 h	96	100
22	3-Phenylallyl acetate	$HNEt_2$	1000	rt, 20 h	100	94/6 (lin/brch)
23			10,000		76	94/6
24	3-Phenylallyl acetate	$-(CH_2)_4HN-$	1000	50 °C, 20 h	100	94/6 (lin/brch)
25			10,000		26	94/6
26	3-Phenylallyl acetate	$-[O(CH_2)_4]HN-$	1000	50 °C, 20 h	100	93/7 (lin/brch)
27			10,000		48	93/7
28	*E*-Hex-2-en-1-yl acetate	$HNEt_2$	250	50 °C, 20 h	100	99/1 (lin/brch)
29			1000		76	99/1
30	*E*-Hex-2-en-1-yl acetate	$-(CH_2)_4HN-$	1000	50 °C, 20 h	100	94/6 (lin/brch)
31	*E*-Hex-2-en-1-yl acetate	$-[O(CH_2)_4]HN-$	1000	50 °C, 20 h	98	94/6 (lin/brch)
32	*E*-Hex-2-en-1-yl acetate	HN(*n*-octyl)$_2$	250	50 °C, 20 h	59	100
33			1000		11	100

Conditions: catalyst [$PdCl(\eta^3$-$C_3H_5)]_2$/**1**: ½. No base. Allylic acetate 1 equiv, amine 2 equiv, tetrahydrofuran.
[a] Carried out in toluene. For 100% conversion in 20 h the reaction time was not minimised.

in 2 h (entry 21, TOF 480 h^{-1}),[36] and of the long alkyl chain-bearing dioctylamine at rt after a longer period (entries 18–20, best TOF 250 h^{-1}).

This new catalytic system was also found to be remarkably active and selective for the more difficult amination of substituted allylic acetates. Using the same pool of amines, we focused our catalytic investigations on coupling reaction of 3-phenylallyl acetate and *E*-hex-2-en-1-yl acetate at 0.1 and 0.01 mol% Pd/**1**, at moderate temperature on a short period of time. Starting from diethyl amine, pyrrolidine and morpholine a complete conversion was obtained from 0.1 mol% catalyst (entries 22, 24 and 26). Lowering the catalyst loading to 0.01 mol% resulted in TONs of 7600, 2600 and 4800, respectively (entries 23, 25 and 27). In each case, good regioselectivity was observed for the linear product (93–94%), especially concerning the primary amine: $HNEt_2$; for which monoallylation occurs exclusively (for primary amines, theoretically five different products could be obtained: linear/branched mono or diallylic product combinations). The selectivity is even higher in linear monoallylamine for the coupling of $HNEt_2$ to the *E*-hex-2-en-1-yl acetate (99%, entries 28, 29). For the cyclic secondary amines these coupling reactions proceeded in >90% yield using as little as 0.1 mol% catalyst (94% selectivity in linear product, entries 30, 31). Finally, only in the course of the addition of dioctylamine, lower TONs and TOFs were observed, since to reach 60% conversion in 20 h at 50 °C, 0.4 mol% catalyst was required (entries 32, 33).

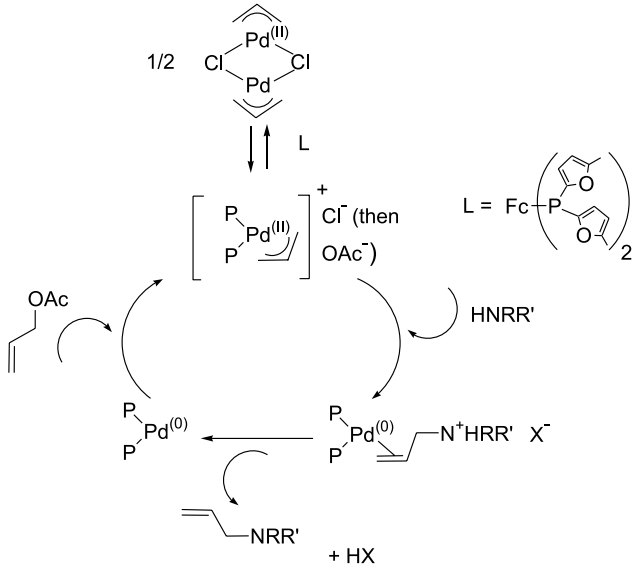
2.4. Discussion

To the best of our knowledge, only a few reports exist on the use of HTC incorporating very poor σ-donating phosphine ligands in Suzuki–Miyaura cross-coupling reactions.[22,39,40] Our experiments from coupling aryl bromide with phenyl boronic acid, confirmed the early investigations by Albisson et al. using a system Pd/triaryl phosphite catalyst system.[39,40] Under the reactions conditions, which are rather close to those used herein (toluene, 110 °C, K_2CO_3 as a base), the authors obtained complete conversion of the activated 4-bromoacetophenone with a turnover number of 10^6, while the complete conversion for the deactivated 4-bromoanisole was obtained at a 10^3 TON. Whereas comparisons between different systems must be treated with some caution, it is worth noting that for the same reactions, we obtained complete conversion from 4-bromoacetophenone with a TON of 10^5 and complete conversion from bromoanisole at 10^4 TON. Under similar conditions, the Pd/**1** catalyst combination shows an order of magnitude weaker activity for the electron-rich substrate and an order of magnitude higher activity for the electron-poor substrate. Our system, as in the Pd/triaryl phosphite combination, exhibits no propensity to couple even electronically-activated aryl chlorides such as 4-chloroacetophenone. A rather simple explanation of this noticeable parallel behaviour could be linked to the subtle changes depending on the substrate of the rate determining-step: thus, for more demanding substrates, the oxidative addition is rate-determining (and severely disfavoured by poor σ-donating ligands). In contrast, for strongly activated substrates (aryl iodides and activated bromides) where the oxidative addition is comparatively facile, the same ligands would multiply the rates of transmetalation and reductive elimination, steps which would become determining.[41] This hypothesis is consistent with the early results from Farina and Krishnan,[16] on the use of trifurylphosphine and triphenylarsine (ligands of weaker basicity compared to PPh_3) in the Stille coupling reaction with substrates capable of undergoing fast oxidative addition (aryl iodides for instance); the Stille coupling of organostannanes being a reaction, for which transmetalation is decisive and possibly rate-determining.[42–44]

Nevertheless, the present tendency in cross-coupling reactions to use the cheaper aryl chlorides (very reluctant to oxidative addition)[45,46] with a view to industrial applications, leaves only a small place to the development of weakly σ-donating ligands,[47] except if other strategies are proposed like the systems developed by Bedford using mixed ligand systems such as bulky σ-acceptor/σ-donor ligands (Pd/{di-*tert*-butylphenyl}phosphite/tricyclohexylphosphine).[48,49]

The tendencies, discussed above, are somewhat confirmed by the results obtained in Heck alkenylation and Sonogashira cross-coupling reactions. The system Pd/**1** gave a TON of 10^4 for the Heck reaction of the deactivated 4-bromoanisole and *n*-butylacrylate, while the Pd/triarylphosphite system reported by Albisson et al. gave complete conversion[50] at a TON of 440–500 (again for less demanding substrates TONs above 10^6 are reported). Finally, consistent with our hypothesis of the changes of the rate determining-step, depending on the substrate, an extremely high TON of 920,000 (with almost complete conversion) was obtained for 4-bromoacetophenone (facile oxidative addition, the rate-determining step being reductive elimination or transmetalation), while when 4-bromoanisole was used a TON of 10^2 was reached (rate-determining step is thus, oxidative addition). Clearly these hypotheses require further comparative kinetics studies to be confirmed.

To demonstrate the potential and catalytic utility of bulky



Scheme 3.

phosphines of weak σ-donicity we choose to apply the Pd/**1** catalytic system to a reaction where the possible determining-step required an electrophilic metallic transition-state: for instance the palladium-catalysed allylic amination with the nucleophilic attack on the allyl ligand (Scheme 3).[51]

The recent mechanistic studies on allylic amination by Kuhn and Mayr provided meaningful kinetic evidence.[52] Indeed, in this relevant work, the use of various amines (diethylamine, piperidine) and 3-phenylallyl acetate (cinnamyl acetate) in presence of either PPh_3 or the less electron-donor $P(OPh)_3$ conducted to global reaction rates two orders of magnitude higher in favour of $P(OPh)_3$. The excellent results obtained with our system could be rationalized through the catalytic cycle depicted in Scheme 3. Relevant reports discuss the general rate-determining step in the soft nucleophilic allylic substitutions.[51–57] We propose that, as anticipated, that the high TOFs and good TONs reported herein are the result of the ability of the ligand **1** to electronically increase the electrophilicity of the Pd(II)/allyl transient species (accelerating the nucleophilic attack, which seems to be the rate-determining step) and to sterically stabilize the Pd(0) complex resulting from product elimination. This is in agreement with the early work of Åkermark and co-workers.[51]

3. Conclusion

In summary, the synthesis, characterisation and catalytic behaviour of the new bulky ferrocenic ligand of low σ-donicity, 1,1′-bis[di(5-methyl-2-furyl)phosphino]ferrocene **1**, has been reported. In cross-coupling reactions and Heck alkenylation processes starting from aryl bromides, the system using Pd/**1** allows high turnover catalysis ($\leq$0.1 mol% catalyst) since a total conversion is obtained for the model substrates: 4-bromoacetophenone and 4-bromoanisole. However, more demanding substrates (aryl chlorides) are not turned-over in the presence of low concentrations of catalyst. In contrast, the ligand is revealed to be among one of the more efficient auxiliaries for palladium-catalysed allylic substitution processes. Facile and convenient reaction conditions were employed in allylic amination, since most of the screened substitution reactions were conducted: (i) from acetates in the absence of base (neutral conditions);[37] (ii) at 20 or 50 °C temperatures; (iii) in less than 24 h; (iv) in the presence of 0.1–0.01 mol% catalyst. Thus, a subtle combination of electronic and steric properties of the ligand produces a highly active catalyst for allylic amination. In particular, the ligand is expected to substantially enhance the rate of nucleophilic attack on the palladium(II)allyl species. Further studies will address and enlarge the scope of the present system in allylic substitutions.

4. Experimental

4.1. General procedures

All reactions and workup procedures were performed under an inert atmosphere of argon using conventional vacuum-line and glasswork techniques. Solvents were dried and freshly distilled under argon. Reagents were purchased from commercial suppliers. $CDCl_3$ and CD_2Cl_2 degassed and stored over molecular sieves under argon were used for NMR studies. Xylene and DMF analytical grade (98%) were not distilled before use. Potassium carbonate (99+%) was used without drying. Except for the diphosphine ligand and for some of the aryl halides and amines, which were distilled before use, the organic and organometallic products were received from commercial sources, and used without further purification. Flash chromatography was performed on silica gel (230–400 mesh). Elemental analyses, ^{1}H, ^{31}P and ^{13}C NMR were performed in our laboratories (on Bruker 300). The evolution of catalyzed reactions was followed by GC (or GC/MS) and NMR for high boiling point substrates, and by GC for low boiling point substrates. For the X-ray diffraction structure of **1**, data were collected on a Nonius Kappa CDD (Mo Kα) diffractometer at 110 K. The structure was solved by a Patterson search program and refined by full-matrix least-squares methods based on F^2 using SHELX97 with the help of the WinGX program at the 'Université de Bourgogne'.

4.2. Synthesis of 1,1′-bis[di(5-methyl-2-furyl)phosphino] ferrocene, $Fc[P(Fu^{Me})_2]_2$, 1

The starting products $BrP(Fu^{Me})_2$ and $FeCp_2Li_2$-TMEDA were synthesised in high yield following procedures described in the literature.[58,59] To a stirred suspension of 6.78 g (21.61 mmol) of $FeCp_2Li_2$-TMEDA in 60 mL of hexane was added dropwise a solution of 11.8 g (43.22 mmol) $BrP(Fu^{Me})_2$ in 25 mL hexane. After 2 h stirring at rt, 20 mL of degassed water was added. An orange powder was obtained, which was washed three times with hexane and then dried under vacuum. Purification was carried out by dissolution in chloroform and filtration on silica gel. 9.86 g of **1** were obtained (17.30 mmol, yield 80%). The product was recrystallised from a chloroform/hexane mixture.

4.2.1. Spectroscopic and single X-ray characterization of the ligand $Fc[P(Fu^{Me})_2]_2$. ^{1}H NMR ($CDCl_3$, 300.13 MHz, δ in ppm): δ=2.33 (s,12H, ^{Me}Fu); 4.15 and 4.30 (m, 8H, Cp) 5.96 and 6.52 (m, 4H, *H*Fu); ^{31}P {H} NMR ($CDCl_3$, 121.49 MHz): δ=−63.8 (s); ^{13}C {^{1}H} NMR (CD_2Cl_2, 75.47 MHz): δ=12.95 (s, 4C, ^{Me}Fu), 71.02 (d, 4C, $^{2}J_{CP}$=5.4 Hz, CpCH), 73.18 (d, 4C, $^{3}J_{CP}$=17.2 Hz, CpCH), 73.02 (d, 2C, $^{1}J_{CP}$=3.6 Hz, Cp), 105.80 (d, 4C, $^{2}J_{CP}$=5.7 Hz, C=C(O)Me), 119.75 {d, 4C, $^{3}J_{CP}$=21.7 Hz, sp^2 CH=C(O)}, 149.45 (d, 4C, $^{1}J_{CP}$=4.1 Hz, P–C(O)=C), 155.47 (d, 4C, $^{4}J_{CP}$=2.3 Hz, Me–C(O)=C). Anal. Calcd. for $C_{30}H_{28}FeP_2O_4$: C 63.17, H 5.20. Found C 63.05, H 4.95. Crystal data for **1**. $C_{30}H_{28}FeO_4P_2$, M=570.32, orthorhombic, space group *Pbcn*, a=8.1795(2) Å, b=12.9172(4) Å, c=24.9485(9) Å, Z=4, V=2635.96(14) Å^3, D_c=1.437 g/cm^3, Mo Kα radiation (λ=0.71073 Å), μ=0.729 mm^{-1}, crystal dimensions 0.25×0.15×0.05 mm^3, T=110(2) K. From 12136 reflections, 3014 were unique (R_{int}=0.0771). 1956 with $I>2s(I)$ were used in refinement. Data parameters ratio 3014/170, R=0.0404, $R\omega$=0.0761.

4.3. Catalytic reactions procedures

Cross-coupling and Heck reactions were carried out following reported procedures.[3,4] In a typical procedure for allylic amination, with a ratio substrate/catalyst = 10,000, the palladium/ferrocenyl furylphosphine catalyst was prepared by stirring a mixture of the diphosphine **1** (0.04 mmol, 22.8 mg) with $[Pd(\eta\text{-}C_3H_5)Cl]_2$ (0.01 mmol, 3.65 mg) in 10 mL toluene, under argon for 30 min. The same batch of catalyst was used for more than a week without any activity decrease (stable in solution in the fridge under argon). One millilitre of the previously prepared catalyst solution (thus, 0.001 mmol Pd) was added to the mixture of allyl acetate and amine (20 mmol) in solvent. The mixture was stirred at fixed temperature for 1–20 h. Pure products are obtained after addition of water, extraction with organic solvents (ether, dichloromethane), separation, drying of the organic phase ($MgSO_4$), concentration, chromatography on silica gel and possibly distillation for oily compounds.

4.4. ^{1}H NMR characterization of some coupling products

References for some of the cross-coupled products are available.[4,36]

4.4.1. 4-Acetyl-1,1′-biphenyl. ^{1}H NMR ($CDCl_3$): δ 8.0 (d, J=8.5 Hz, 2H), 7.67 (d, J=8.5 Hz, 2H), 7.61 (d, J=7.0 Hz, 2H), 7.45 (dd, J=7.5, 7.0 Hz, 2H), 7.37 (t, J=7.5 Hz, 1H), 2.6 (s, 3H). CAS: 92-91-1.

4.4.2. 4-Methoxy-1,1′-biphenyl. ^{1}H NMR ($CDCl_3$): δ 7.54 (d, J=7.4 Hz, 2H), 7.52 (d, J=8.6 Hz, 2H), 7.40 (dd, J=7.4, 7.2 Hz, 2H), 7.29 (t, J=7.4 Hz, 1H), 6.96 (d, J=8.6 Hz, 2H), 3.82 (s, 3H). CAS: 613-37-6.

4.4.3. *E*-Butyl 4-acetylcinnamate (coupling anisole/butyl acrylate). ^{1}H NMR ($CDCl_3$): δ 7.55 (d, J=16.0 Hz, 1H, ArCH=), 7.37 (d, J=8.7 Hz, 2H, Ar), 6.80 (d, J=8.7 Hz, 2H, Ar), 6.21 (d, J=16.0 Hz, 1H, =$CHCO_2Bu$), 4.12 (t, J=6.6 Hz, 2H, $CO_2CH_2CH_2$), 3.69 (s, 3H, OMe), 1.60 (tt, J=6.8, 6.6 Hz, 2H, $CO_2CH_2CH_2$), 1.33 (qt, J=7.3, 6.8 Hz, 2H, CH_2CH_3), 0.87 (q, J=7.3 Hz, 3H, CH_2CH_3). CAS: 173464-57-8.

4.4.4. 4-(2-Phenylethynyl)acetophenone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J=8.1 Hz, 2H), 7.59 (d, J=8.1 Hz, 2H), 7.53 (m, 2H), 7.35 (m, 3H), 2.58 (s, 3H). CAS: 1942-31-0.

4.4.5. (4-Methoxyphenyl)phenylacetylene. ^{1}H NMR ($CDCl_3$): δ 7.50–7.48 (m, 2H), 7.45 (d, J=8.8 Hz, 2H), 7.32 (m, 3H), 6.86 (d, J=8.8 Hz, 2H), 3.80 (s, 3H). CAS: 7380-78-1.

4.4.6. Allyldioctylamine. ^{1}H NMR δ 5.78 (ddt, 1H, J=16.9, 10.1, 6.6 Hz), 5.06 (d, 1H, J=16.9 Hz), 5.00 (d, 1H, J=10.1 Hz), 3.00 (d, 2H, J=6.6 Hz), 2.5 (t, 4H, J=6.8 Hz), 1.15–1.43 (m, 24H), 0.8 (t, 6H, J=6.3 Hz).

4.4.7. *N*-3-Phenylallylmorpholine. ^{1}H NMR δ 7.35–7.15 (m, 5H), 6.45 (d, 1H, J=16.4 Hz), 6.18 (dt, 1H, J=16.4, 6.8 Hz), 3.65 (t, 4H, J=4.6 Hz), 3.08 (d, 2H, J=6.8 Hz), 2.40 (t, 4H, J=4.6 Hz); ^{13}C NMR δ 136.8, 133.4, 128.6, 127.6, 126.4, 126.1, 67.0. *N*-1-Phenylallylmorpholine was not isolated in pure form. Partial ^{1}H NMR spectra was obtained from the mixture: δ 5.15 (d, 1H, J=17.2 Hz), 5.01 (d, 1H, J=9.9 Hz).

4.4.8. *N*-3-Phenylallylpyrrolidine. ^{1}H NMR δ 7.30–7.10 (m, 5H), 6.50 (d, 1H, J=16.0 Hz), 6.20 (dt, 1H, J=16.0, 6.5 Hz), 3.20 (d, 2H, J=6.5 Hz), 2.50 (t, 4H, J=6.5 Hz), 1.80 (m, 4H); ^{13}C NMR δ 136.8, 133.4, 128.6, 127.6, 126.4, 126.1, 67.0. *N*-1-Phenylallylpyrrolidine was not isolated in pure form. Partial ^{1}H NMR spectra was obtained from the mixture: δ 5.10 (d, 1H, J=17.4 Hz), 5.05 (d, 1H, J=10.0 Hz).

4.4.9. *E*-1-(2-Hexenyl)diethylamine. ^{1}H NMR δ 5.59 (dt, 1H, J=15.4, 6.3 Hz), 5.43 (dt, 1H, J=15.4, 6.6 Hz), 3.11 (d, 2H, J=6.3 Hz), 2.58 (q, 4H, J=7.1 Hz), 1.96 (td, 2H, J=7.3, 6.6 Hz), 1.33 (tq, 2H, J=7.3, 7.3 Hz), 1.02 (t, 6H, J=7.1 Hz), 1.33 (t, 3H, J=7.3 Hz).

4.4.10. *E*-1-(2-Hexenyl)morpholine. ^{1}H NMR δ 5.47 (dt, 1H, J=15.4, 6.3 Hz), 5.35 (dt, 1H, J=15.4, 6.0 Hz), 3.60 (t, 4H, J=4.4 Hz), 2.80 (d, 2H, J=6.3 Hz), 2.31 (d, 4H, J=4.4 Hz), 1.90 (td, 2H, J=7.3, 6.3 Hz), 1.28 (tq, 2H, J=7.3, 7.3 Hz), 0.77 (t, 3H, J=7.3 Hz). 3-(1-Hexenyl) morpholine was not isolated in pure form. Partial ^{1}H NMR spectra was obtained from the mixture: δ 5.15 (dd, 1H, J=17.2, 1.5 Hz), 5.05 (dd, 1H, J=10.0, 1.5 Hz).

4.4.11. *E*-1-(2-Hexenyl)pyrrolidine. ^{1}H NMR δ 5.57 (dt, 1H, J=15.4, 5.8 Hz), 5.45 (dt, 1H, J=15.4, 6.1 Hz), 3.10 (m, 6H), 2.60 (m, 4H), 1.90 (td, 2H, J=7.3, 6.1 Hz), 1.28 (tq, 2H, J=7.3, 7.3 Hz), 0.80 (t, 3H, J=7.3 Hz). 3-(1-Hexenyl)pyrrolidine was not isolated in pure form. Partial ^{1}H NMR spectra was obtained from the mixture: δ 5.15 (dd, 1H, J=17.2, 1.5 Hz), 5.05 (dd, 1H, J=10.0, 1.5 Hz).

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