ACS Catalysis

Research Article

pubs.acs.org/acscatalysis

Palladium-Catalyzed Direct Arylation of Heteroaromatics with Activated Aryl Chlorides Using a Sterically Relieved Ferrocenyl-Diphosphane

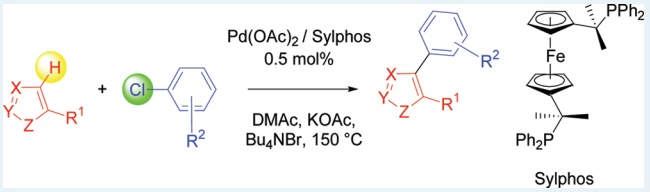
David Roy,[†] Sophal Mom,[‡] Sylviane Royer, Dominique Lucas,[‡] Jean-Cyrille Hierso,*[,‡] and Henri Doucet*[,†]

[†]Institut Sciences Chimiques de Rennes, UMR 6226 CNRS−Université de Rennes "Catalyse et Organométalliques" Campus de Beaulieu, 35042 Rennes, France

[‡]Université de Bourgogne, Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB) UMR-CNRS 6302, 9 avenue Alain Savary 21078 Dijon, France

Supporting Information

ABSTRACT: The palladium-catalyzed direct arylations at C3 or C4 positions of heteroaromatics are known to be more challenging than at C2 or C5 positions. Aryl chlorides are also challenging substrates for direct arylation of heteroaromatics. We observed that in the presence of a palladium-catalyst combining only 0.5 mol % of $Pd(OAc)_2$ with the sterically relieved new ferrocenyl diphosphane **Sylphos**, the direct arylation at C3 or C4 of oxazoles, a benzofuran, an indole, and a pyrazole was found to proceed in moderate to high yields using a variety of electron deficient aryl chlorides. Turnover numbers up to 176 have been obtained with this catalyst. Assessment of the electron-donating properties of **Sylphos** from electrochemical studies and $^1J_{PSe}$ measurement on its selenide derivative indirectly indicated that the influence of steric properties of **Sylphos**—and in particular a less sterically congested environment at phosphorus due to a methylene spacer—are certainly dominant in its catalytic performance.



KEYWORDS: *heteroarenes, aryl chlorides, C−H bond functionalization, palladium, ferrocenylphosphane, ligand design*

The palladium-catalyzed direct arylation of various heteroaromatics via a C−H bond activation using aryl halides has met with great success in recent years.[1−8] However, there are still limitations for these reactions in terms of aryl halide or heteroaromatic tolerance. Especially the use of aryl chlorides has attracted less attention than aryl bromides or iodides. Additionally, in most cases they were successfully employed for the arylation at C2 or C5 of heteroaromatics, as these positions are known to be generally more reactive.[9−23] Up to now, very few examples of palladium-catalyzed direct arylations at C3 or C4 using aryl chlorides have been reported, although aryl groups at these positions are known to be present in several bioactive molecules (Figure 1).[24−29]

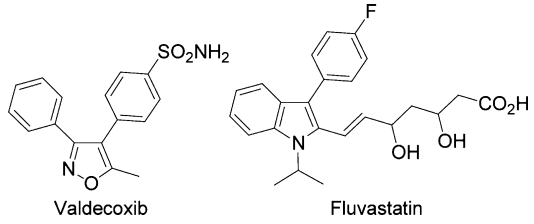


Figure 1. Examples of bioactive heteroaromatics bearing aryl substituents.

Daugulis has reported the C4 arylation of 3,5-dimethylisoxazole with 1-chloronaphthalene in 76% using 5 mol % $Pd(OAc)_2$ associated to 10 mol % of the hindered electron-rich nBuAd$_2$P phosphane.[24] This group has also reported the C3 arylation of indoles with two aryl chlorides using 5 mol % $Pd(OAc)_2$ associated to 10 mol % Cy_2P-o-biphenyl as the catalyst. The coupling products were obtained in 65−92% yields.[25] Coupling of 1-benzyl-5-hexyl-1,2,3-triazole with chlorobenzene was reported by Oshima and co-workers. In the presence of 2.5 mol % $Pd(OAc)_2$ and 5 mol % PCy_3, the C4 arylated triazole was obtained in only 19% yield.[26] Finally, a similar reaction has been reported by Ackermann and co-workers using 4 mol % $Pd(OAc)_2$ associated to 8 mol % PCy_3 and 1-benzyl-5-phenyl-1,2,3-triazole and ethyl 4-chlorobenzoate as the coupling partners. However, the desired coupling product was produced in only 40% yield.[27] Some intramolecular reactions have also been described using furan or thiophene derivatives.[28,29] Therefore, the discovery of a more efficient procedure to couple such heteroarenes with aryl chlorides is highly desirable. Here, we wish to report on our efforts to promote the arylation at C3 or C4 of a set of heteroaromatic derivatives with diverse (hetero)aryl chlorides

Received: February 8, 2012
Revised: March 14, 2012
Published: April 18, 2012

in the presence of a low loading of a palladium-based catalytic system.

Besides the recognized interest of congested electron-rich monodentate ligands for the activation of aryl chlorides as confirmed by the examples mentioned above with PCy_3, Cy_2P-*o*-biphenyl, and nBuAd$_2$P,[24−27] the usefulness of robust polydentate ferrocenylphosphane as catalytic auxiliaries in [C−H/C−X] direct cross-coupling reactions has been substantiated (Figure 2).[30−33]

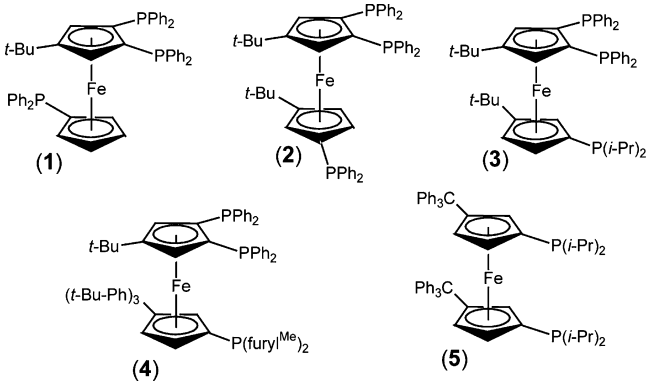


Figure 2. Polydentate ferrocenylphosphane ligands used for [C−H/C−X] direct cross-coupling reactions.

Thus, we initially examined the influence of the nature of several ligands for the reaction of 4-chlorobenzonitrile with 3,5-dimethylisoxazole using DMAc as the solvent, KOAc as the base (Table 1, entries 1−4). These conditions had been previously found operative for the arylation at C2 of pyrroles or thiophenes.[34−37] While use of PPh_3 and dppf (bis-diphenylphosphinoferrocene) as ligands associated to 0.5 mol % Pd(OAc)$_2$ were ineffective (Table 1, entries 1 and 2), ligand **6** (Figure 3) and PCy_3 led to similar yields of 11% and 13%,

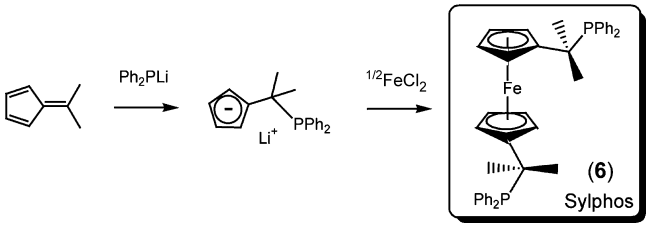
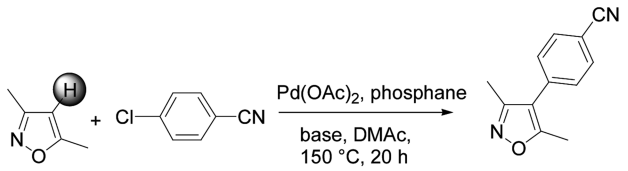


Figure 3. Synthesis of the alkyldiaryl tertiary phosphane **6**.

respectively (Table 1, entries 3 and 4). As air-robust **6** is easier to handle than PCy_3, we decided to explore its potential for such arylation using several conditions. We observed that, in the presence of nBu$_4$NBr as an additive, a higher yield of 48% was obtained (Table 1, entry 5). This additive seems to participate to the stabilization of the active species. It should be noted that, using similar conditions, ligands **1**−**5** (Figure 2) only led to poor conversions of 4-chlorobenzonitrile (7−20%, entries 6−10).[38] Diphosphane **6** (**Sylphos**, Figure 3) in comparison to **1**−**5** is a less congested ligand with a more electron-donating alkyl substituant on phosphorus atom. For designing this phosphane we assumed that the intrinsic

Table 1. Influence of the Reaction Conditions on the Arylation of 3,5-Dimethylisoxazole with 4-Chlorobenzonitrile[a]



entry	phosphane	3,5-dimethylisoxazole (equiv)	base (equiv)	additive	conv (%)
1	PPh_3	2	KOAc (2)	no	0
2	dppf	2	KOAc (2)	no	6
3	PCy_3	2	KOAc (2)	no	13
4	**6**	2	KOAc (2)	no	11
5	**6**	2	KOAc (2)	Bu_4NBr	48
6	**1**	2	KOAc (2)	Bu_4NBr	17
7	**2**	2	KOAc (2)	Bu_4NBr	20
8	**3**	2	KOAc (2)	Bu_4NBr	7
9	**4**	2	KOAc (2)	Bu_4NBr	17
10	**5**	2	KOAc (2)	Bu_4NBr	15
11	**6**	1.1	NaOAc (2)	Bu_4NBr	40
12	**6**	1.1	K_2CO_3 (2)	Bu_4NBr	0
13	**6**	1.1	Cs_2CO_3 (2)	Bu_4NBr	0
14	**6**	2	KOAc (3)	Bu_4NBr	64
15	**6**	2	KOAc (4)	Bu_4NBr	65
16	**6**	1.5	KOAc (3)	Bu_4NBr	72 (65)
17	**6**	1.5	KOAc (3)	Me_4NCl	32
18	**6**	1.5	KOAc (3)	Bu_4NOAc	17
19	**6**	1.5	KOAc (3)	Bu_4NI	0

[a]Conditions: Pd(OAc)$_2$ (0.005 equiv), phosphane (0.005 equiv), 4-chlorobenzonitrile (1 equiv), 3,5-dimethylisoxazole (1.1-2 equiv), base (2−4 equiv), additive (1 equiv), DMAc, 150 °C, 20 h (not optimized), conversion of 4-chlorobenzonitrile (average from several runs); isolated yield of **7** is given in parentheses.

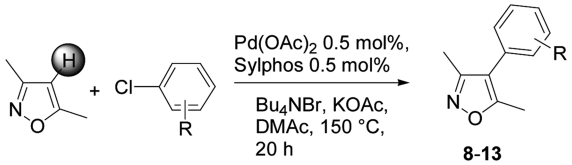
dx.doi.org/10.1021/cs300097v | *ACS Catal.* 2012, 2, 1033−1041

congestion provided by ferrocene backbone might be a limitation to the reaction. Additionally, increasing the donor capacity of phosphanyl groups might also be helpful. Thus, **Sylphos** is obtained in two synthetic steps from 6,6-dimethylfulvene and exhibits a methylene spacer between the two phosphanyl groups and the ferrocene platform. As expected, the features of this novel diphosphane (alkyldiaryl tertiary phosphane) are fairly different from **1**−**5** (triaryl tertiary phosphanes) as it is attested by its ^{31}P NMR chemical shift found at low field 26.1 ppm, compared to δ ranging from −69.3 up to −2.4 ppm for ^{31}P in **1**−**5** polyphosphanes.[30−33,39−41]

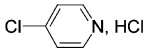
After having found a new ligand suitable for this cross-coupling, the other parameters of the catalytic system were examined for optimization. The nature of the base has also a huge influence on the conversions of 4-chlorobenzonitrile. The presence of NaOAc led to partial conversions of 4-chlorobenzonitrile, while K_2CO_3 or Cs_2CO_3 gave no coupling product (Table 1, entries 11−13). The better performance of acetates as the base is consistent with a concerted metalation deprotonation pathway (CMD).[42,43] The use of 3 equiv of KOAc and of a lower excess of the heteroaromatics allowed to improve the conversion of 4-chlorobenzonitrile to 72% and the corresponding yield in **7** to 65% (Table 1, entry 16). The influence of other additives has been examined: in the presence of 1 equiv of Me_4NCl, nBu_4NOAc, and nBu_4NI, lower conversions of 32%, 17%, and 0% were respectively obtained (Table 1, entries 17−19).

3,5-Dimethylisoxazole was efficiently coupled with six other aryl chlorides in the presence of 0.5 mol % $Pd(OAc)_2$ associated to 0.5 mol % of ferrocenylphosphane **6** and KOAc as the base (Table 2). Selective C4-arylations were observed

Table 2. Direct Arylation of 3,5-Dimethylisoxazole with Aryl Chlorides[a]



8-13

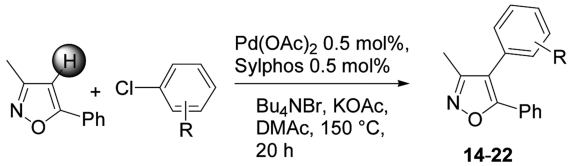
Entry	R or ArCl	Product	Yield (%)
1	4-CHO	**8**	71
2	4-NO_2	**9**	74
3	3-CN	**10**	55
4	3-NO_2	**11**	44
5	2-CN	**12**	70
6		**13**	48

[a]Conditions: $Pd(OAc)_2$ (0.005 equiv), **6** (0.005 equiv), aryl chloride (1 equiv), 3,5-dimethylisoxazole (1.5 equiv), Bu_4NBr (1 equiv), KOAc (3 equiv), 150 °C, 20 h.

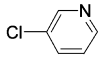
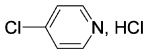
using 4-chlorobenzaldehyde, 3- or 4-chloronitrobenzene, 2- or 3-chlorobenzonitrile, and 4-chloropyridine, resulting in 40−74% yields and 80−148 turnover numbers of the products **8**−**13**. It should be noted that, in the presence of electron-rich aryl chlorides such as 4-chloroanisole or *N*,*N*-dimethyl-4-chloroaniline, no formation of coupling product was detected.

Similar results were obtained in the presence of 3-phenyl-5-methylisoxazole (Table 3). A range of aryl chlorides was employed, and in all cases the expected 4-arylated isoxazoles

Table 3. Direct Arylation of 3-Phenyl-5-methylisoxazole with Aryl Chlorides[a]



14-22

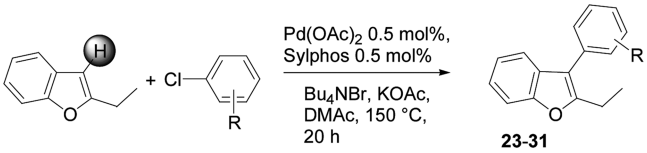
Entry	R or ArCl	Product	Yield (%)
1	4-CN	**14**	73
2	4-NO_2	**15**	72
3	4-CHO	**16**	70
4	4-CF_3	**17**	66
5	3-NO_2	**18**	38
6	2-CN	**19**	39
7	2-CHO	**20**	34
8		**21**	80
9		**22**	78

[a]Conditions: $Pd(OAc)_2$ (0.005 equiv), **6** (0.005 equiv), aryl chloride (1 equiv), 3-phenyl-5-methylisoxazole (1.5 equiv), Bu_4NBr (1 equiv), KOAc (3 equiv), 150 °C, 20 h.

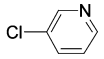
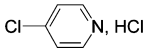
14−**18**, **21**, and **22** were selectively obtained using again 0.5 mol % catalyst. In the presence of 2-chlorobenzaldehyde, a moderate yield in **20** was obtained due to the formation of some side-products (Table 3, entry 7). The use of 2-chlorobenzonitrile led to a moderate yield in **19** due to a only partial conversion of this aryl chloride (Table 3, entry 6).

Under the same optimized reaction conditions, 2-ethylbenzofuran was also found viable substrate for palladium-catalyzed direct arylations with aryl chlorides (Table 4). It is worth mentioning that for coupling of 4-chloronitrobenzene

Table 4. Direct Arylation of 2-Ethylbenzofuran with Aryl Chlorides[b]



23-31

Entry	R or ArCl	Product	Yield (%)
1	4-CN	**23**	56
2	4-NO_2	**24**	70
3	4-NO_2	**24**	75[a]
4	4-CHO	**25**	75
5	4-COMe	**26**	78
6	4-COMe	**26**	0[a]
7	4-CF_3	**27**	44
8	3-NO_2	**28**	61
9	2-CN	**29**	53
10		**30**	44
11		**31**	57

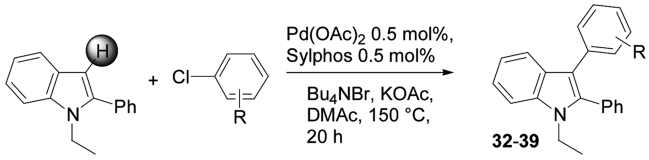
[a]Reaction without nBu_4NBr. [b]Conditions: $Pd(OAc)_2$ (0.005 equiv), **6** (0.005 equiv), aryl chloride (1 equiv), 2-ethylbenzofuran (1.5 equiv), Bu_4NBr (1 equiv), KOAc (3 equiv), 150 °C, 20 h.

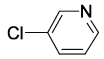
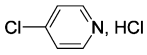
dx.doi.org/10.1021/cs300097v | *ACS Catal.* 2012, 2, 1033−1041

the presence of nBu$_4$NBr is not necessary to get a high yield in **24** (Table 4, entries 2 and 3), while 4-chloroacetophenone was found to be unreactive in the absence of this ammonium salt (Table 4, entries 5 and 6). From 4-chloroacetophenone and 4-chlorobenzaldehyde, **25** and **26** were obtained in 75% and 78% yields, respectively. From 4-trifluoromethylchlorobenzene, a moderate conversion was observed and **27** was isolated in 44% yield (Table 4, entry 7).

1-Ethyl-2-phenylindole was found to be very reactive with 4-chlorobenzonitrile or 4-chloronitrobenzene in the presence of our catalytic system, and the C3 arylated products **32** and **33** were obtained in high yields. It should be noted that with these two aryl chlorides also, comparable yields were obtained with or without addition of nBu$_4$NBr (Table 5, entries 1−4). Lower

Table 5. Direct Arylation of 1-Ethyl-2-phenylindole with Aryl Chlorides[b]



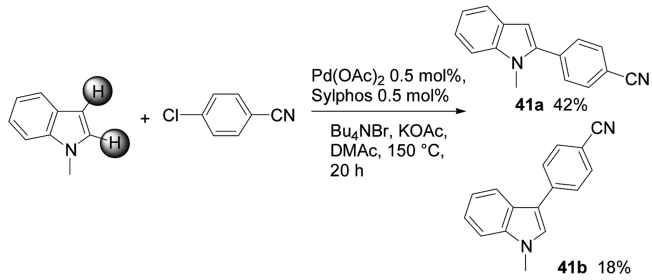
Entry	R or ArCl	Product	Yield (%)
1	4-CN	**32**	88
2	4-CN	**32**	80[a]
3	4-NO_2	**33**	82
4	4-NO_2	**33**	84[a]
5	4-CHO	**34**	31
6	4-CHO	**34**	43[a]
7	4-COMe	**35**	28[a]
8	3-NO_2	**36**	62
9	2-CN	**37**	57
10		**38**	61
11		**39**	71

[a]Reaction without nBu$_4$NBr. [b]Conditions: Pd(OAc)$_2$ (0.005 equiv), **6** (0.005 equiv), aryl chloride (1 equiv), 1-ethyl-2-phenylindole (1.5 equiv), Bu$_4$NBr (1 equiv), KOAc (3 equiv), 150 °C, 20 h.

yields were obtained from 4-chlorobenzaldehyde or 4-chloroacetophenone (Table 5, entries 5−7, 28−43%). Conversely, good yields of 61% and 71% in **38** and **39** were obtained in the presence of 3- or 4-chloropyridines (Table 5, entries 10 and 11).

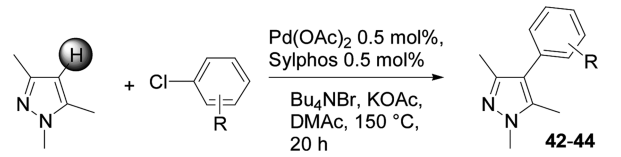
The reactivity and regioselectivity of the arylation of benzofuran and *N*-methylindole with this catalytic system was also examined. From benzofuran and 4-chloronitrobenzene, the C2 arylated product **40** was obtained as the major isomer (ratio C2:C3 = 11:6) in moderate yield (Scheme 1). A similar regioselectivity was observed for the arylation of 1-methylindole, with the formation of **41a** in 61% selectivity and 42% yield (Scheme 2).

Scheme 2



To the best of our knowledge no example of direct intermolecular coupling of aryl chlorides with pyrazoles had been described up to now.[44] Three aryl chlorides have been employed in the presence of [Pd/**Sylphos**], and in all cases very good yields of products were obtained (Table 6, **42**−**44** in 66−78% yield).

Table 6. Direct Arylation of 1,3,5-Trimethylpyrazole with Aryl Chlorides

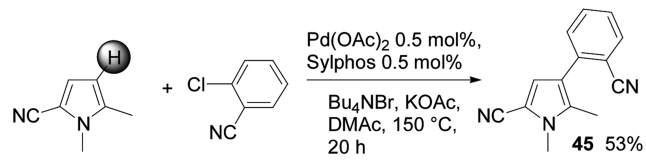


entry	R or ArCl	product	yield (%)
1	4-NO_2	**42**	71
2	4-CHO	**43**	66
3	2-CN	**44**	78

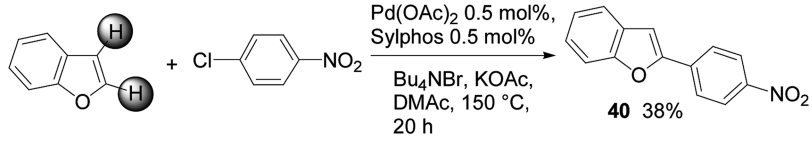
[a]Conditions: Pd(OAc)$_2$ (0.005 equiv), ligand **6** (0.005 equiv), aryl chloride (1 equiv), 1,3,5-trimethylpyrazole (1.5 equiv), Bu$_4$NBr (1 equiv), KOAc (3 equiv), 150 °C, 20 h.

Finally, the regioselectivity of the direct arylation of 1,5-dimethyl-2-pyrrolecarbonitrile with 2-chlorobenzonitrile was examined. The reaction proceed regioselectively at C4 (ratio C3:C4 = 16:84) to give **45** in moderate yield using again 0.5 mol % Pd(OAc)$_2$/**6** as the catalyst (Scheme 3).

Scheme 3



Scheme 1



dx.doi.org/10.1021/cs300097v | *ACS Catal.* 2012, 2, 1033−1041

To better assess the essential features of **Sylphos** in comparison to the other ferrocenyl diphosphane ligands of our library,[45,46] we conducted electrochemical analyses of **Sylphos**, as well as measurement of $^{31}P-^{77}Se$ coupling constant for its diselenide derivative. We compared it to $^{1}J_{P,Se}$ coupling constants for the diselenide derivatives of the ferrocenyl diphosphane **5** (Figure 2), dppf (bis-diphenylphosphino ferrocene), and 1,1′-bis[di(5-methyl-2-furyl)phosphanyl] ferrocene ($Fc[P(Fu^{Me})_2]_2$), which include substituent on phosphorus atoms with different electron-donor properties. A decrease in these $^{1}J_{P,Se}$ coupling constants indicates a decrease in the *s* character of the phosphorus lone-pair orbital, i.e. an electron-donating effect of the phosphanyl group to the selenium atom.[47,48] As benchmark the $^{1}J_{P,Se}$ for triphenylphosphane selenide $Se{=}PPh_3$ and for dppf selenide have been reported to be respectively 730 ± 2 and 736 ± 2 Hz.[47,49] The $^{1}J_{P,Se}$ values we found are reported Figure 4.

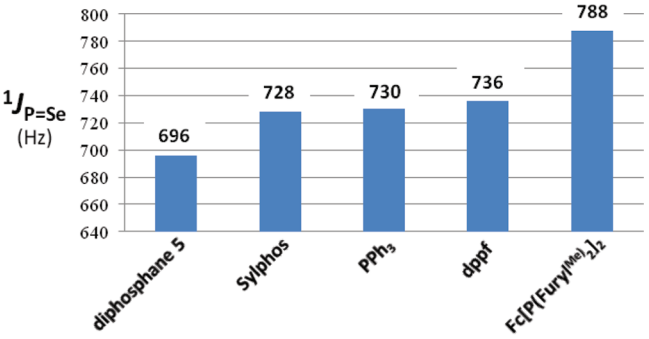


Figure 4. Measurement of $^{31}P-^{77}Se$ coupling constants for diselenide of ferrocenyl diphosphanes and for $Se{=}PPh_3$.

Much to our surprise, according to the $^{1}J_{P,Se}$ values the electron-donating character of phosphanyl groups from **Sylphos** is not strongly marked ($^{1}J_{P,Se}$ = 728 Hz) but is very close to triphenylphosphane ($^{1}J_{P,Se}$ = 730 Hz). It nevertheless does not seem to be superior to the one of diphosphane **5** ($^{1}J_{P,Se}$ = 696 Hz). This was contrasting with our first belief concerning donor-character of **Sylphos** coming from the low-field ^{31}P NMR chemical shift found for **6**.[50] This was confirmed and explained by the observation of the electrochemical behavior of the ferrocenyl diphosphane.

The electrochemical behavior of **Sylphos** was examined in CH_2Cl_2/NBu_4PF_6 (0.2 M) as an electrolytic medium. Figure 5 displays the cyclic voltammogram obtained by exploring the oxidative side for various scan rates (0.05−1 $V{\cdot}s^{-1}$).

Over the whole range of experiments, the response fulfills the characteristics of a reversible system:[51,52] (i) separation between the forward anodic and backward cathodic peak ($\Delta E_p = E_{pa} - E_{pc}$) comprised between 60 and 77 mV, (ii) current peak, i_{pa}, growing proportionally to $v^{1/2}$, (iii) ratio of peak currents close to unity ($0.9 < i_{pc}/i_{pa} < 0.99$). Thus, the behavior of **Sylphos** differs markedly from substituted ferrocenes bearing directly the diphenylphosphino groups on the cyclopentadienyl ring. With these latter, the electron transfer is accompanied by a follow-up reaction which has been proposed to be a dimerization.[53−55] Conversely, at the voltammetric time scale, such a reaction is not observed with **Sylphos**. Interestingly, the half-wave potential of **Sylphos** is shifted negatively by 80 mV compared to ferrocene (see Table 7). In comparison to unsubstituted ferrocene this denotes a clear electrodonating effect (+I) of the groups $-C(Me)_2PPh_2$

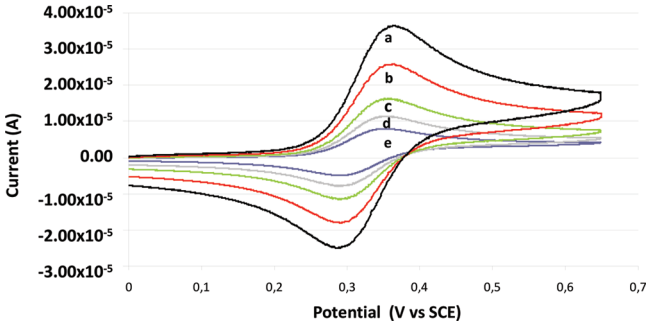


Figure 5. Cyclic voltammogram of **Sylphos** (1 mM in CH_2Cl_2) with 0.2 M nBu_4NPF_6 on a vitreous carbon disk electrode. Scan rate from up to down: (a) 50, (b) 100, (c) 200, (d) 500, and (e) 1000 $mV{\cdot}s^{-1}$.

Table 7. Half-Wave Potential, Peak Separation (Defined as $E_{pa} - E_{pc}$), and Peak Current Ratio (i_{pc}/i_{pa}) for Ferrocene and Sylphos Extracted from the Voltammetric Data at v = 100 $V{\cdot}s^{-1}$

compound	$E_{1/2}$ (V vs SCE)[a]	ΔE_p (mV)	$\lvert i_{pc}/i_{pa}\rvert$
ferrocene	0.40	57	0.99
Sylphos	0.32	60	0.90

[a]Determined as the half sum of E_{pa} and E_{pc}

to the iron redox center. This electron transfer to ferrocene backbone may explain the only weak σ-donating effect predicted from $^{1}J_{P,Se}$ constant for phosphanyl groups of **Sylphos**.

Literature reports have dealt with correlations between the oxidation potentials of 1,1′-disubstituted ferrocenes and the Hammet parameters (σ_p) for the substituents on the cyclopentadienyl rings.[56] All available potential data for this family of compounds have been compiled resulting in the following empirical relation:

$$E_L(\text{vs SHE}) = {}^1/_2[E_{1/2}(\text{vs SCE}) + 0.25]$$

$$\text{and } E_L = 0.45\sigma_p + 0.36$$

Operating these equations on **Sylphos** leads to E_L = 0.28 V and σ_p = −0.18, setting the $-C(Me)_2PPh_2$ group as a medium donor to ferrocene to be compared to σ_p = −0.15 for $-C(Me)_2H$, and σ_p = −0.20 for $-C(Me)_3$.[57]

The electrochemical behavior of **Sylphos** mainly confirms that the presence of the spacer induces noticeable difference in this diphosphane in comparison to other 1,1′-ferrocenyl diphosphanes. The expected electron-donating properties of methylene groups, or more generally $-C(Me)_2PPh_2$, are efficiently transferred to ferrocene plateform. This observation is fully consistent with the only moderate σ-donating properties of phosphorus in **Sylphos** as deduced from $^{1}J_{PSe}$ in its selenide derivative. Therefore, regarding the catalytic performances of this diphosphane, its steric features—and in particular a less sterically congested environment at phosphorus due to the methylene spacer—seems to be dominant and essential.

The reported ligand was designed for three main reasons: (i) releasing steric effects from ferrocene backbone on the phosphorus but keeping its beneficial steric protection for general robustness of the phosphine—*with the view to experience a better activity in direct arylation*, (ii) changing triarylP(III) for alkyldiaryl(PIII) donors benefiting from inductive donor influence from two methyl groups—*with the view to experience*

dx.doi.org/10.1021/cs300097v | *ACS Catal.* 2012, 2, 1033−1041

a better activity in aryl chloride activation—in keeping air stability, (iii) two-step straightforward synthesis in several grams scale of an air-insensitive diphosphine.

We demonstrated that the electron-donating effect of this ligand is negligible compared to PPh_3 (see $J_{P=Se}$ *coupling* constants), and thus steric releasing is crucial in the present reactions. Electrochemistry indicates that the expected inductive donating effects from the methyl groups of the spacer are mostly transferred to the ferrocene backbone.

To conclude, we reported here conditions for the palladium-catalyzed direct arylation of a range of heteroaromatic derivatives with electron-deficient aryl chlorides. As low as 0.5 mol % of $Pd(OAc)_2$-diphosphane **6** as the catalyst associated to $KOAc/Bu_4NBr$ promotes the arylation, and turnover numbers up to 176 have been obtained. To our knowledge, this protocol employs a lower catalyst loading than any previously reported direct C3 or C4 arylation procedure. This protocol has proved to be tolerant to a variety of functional groups on aryl chloride such as formyl, acetyl, nitrile, nitro, or trifluoromethyl in para, meta, or ortho positions. Moreover, it is economically and environmentally attractive as the major wastes are AcOH/KCl instead of metallic salts when organometallic coupling procedures are used (Suzuki, Negishi, or Stille couplings). To achieve such direct arylation, a new sterically relieved air-stable ferrocenyldiphosphane, **Sylphos**, has been designed which proved to be superior to a variety of mono- and diphosphane ligands tested for these couplings. Assessment of the electron-donating properties of **Sylphos** from electrochemical studies and $^1J_{PSe}$ measurement of its selenide derivative indicated that the influence of steric properties of **Sylphos** were certainly dominant over electronic features in its catalytic performances.

EXPERIMENTAL SECTION

General. The reactions were carried out in oven-dried glassware (115 °C) under argon atmosphere using Schlenk and vacuum-line techniques. $FeCl_2$ from a commercial source was used (Aldrich anhydrous beads, 99.9%, <100 ppm H_2O). All catalytic reactions were performed in Schlenk tubes under argon atmosphere. *N,N*-Dimethylacetamide (DMAc) was of analytical grade and was not distilled before use. Potassium acetate (purity = 99%+) was used. Commercial aryl chlorides and heteroaromatic derivatives were used without purification. Flash chromatography was performed on silica gel (230−400 mesh). ^1H NMR (500, 400, or 300 MHz), ^{31}P NMR (202.46 MHz), ^{13}C NMR (125, 100, or 75 MHz), ^{13}C *J* modulation APT, and ^{13}C-dept 135 NMR experiments were performed in our laboratories (on Bruker equipment) in $CDCl_3$ at 298 K. Chemical shifts (δ) are reported in parts per million relative to $CDCl_3$ (^1H: δ = 7.26 ppm and ^{13}C: δ = 77.0 ppm). The exact mass was measured on a Bruker MicrOTOF Q system. Syntheses of ligands **1**−**5** have been previously reported.[30−33,41]

Synthesis of Sylphos (6). To a stirred solution of Ph_2PH (5 mL, 28.7 mmol) in Et_2O (30 mL) at −80 °C was added *n*BuLi (18 mL, 1.6 M in hexane, 28.7 mmmol), and after 20 min stirring a solution of 6,6-dimethylfulvene (3 g, 28.7 mmol) in 20 mL THF at −40 °C. The reaction mixture was stirred for 2 h at room temperature, and the resulting solution of functionalized cyclopentadienyl lithium salt was used to pursue the synthesis. To a stirred suspension of $FeCl_2$ (1.81 g, 14.3 mmol) in 30 mL of THF was added dropwise at −40 °C the above-prepared solution. After it was stirred for 1 h at room temperature, the reaction mixture was evapored under vacuum, and the residue was refluxed in 100 mL of toluene for 20 h. The reaction mixture was cooled and dried under vacuum. The crude product was purified by colomn chromatography under an argon atmosphere (silica gel, column height = 30 cm, column diameter = 5.5 cm, using a 4:1 toluene/heptane mixture). A 3.56 g portion (39% yield) of the desired product **6** were obtained after crystallization from hot ethanol. The solubilized product is more air-sensitive on a silica column than ferrocenyl polyphosphanes **1**−**5**, and consequently, the chromatography fractions should be rapidly handled. Anal. calcd for $C_{40}H_{40}FeP_2$·EtOH (684.5): C, 73.65; H,6.72. Found: C, 73.95; H, 6.89. Exact mass (EI): *m*/*z* (%) 638.19499, (100) $[M]^+$, 638.19598. ^1H NMR: δ = 1.46 (d, $^3J_{PH}$ = 7.5 Hz, 12H, CH_3), 3.78 (m, 8H, H−Cp), 7.07−7.15 (m, 12H, *m*-Ph and *p*-Ph), 7.52 (m, 8H, *o*-Ph). $^{13}C\{^1H\}$: δ = 27.22 (d, $^2J_{PC}$ = 18.9 Hz, $C(CH_3)_2PPh_2$), 35.58 (d, $^1J_{PC}$ = 18.9 Hz, $C(CH_3)_2PPh_2$), 67.17 (m, 3,4-Fc), 67.43 (m, 2,5-Fc), 95.50 (d, $^2J_{PC}$ = 8.7 Hz, 1-Fc), 127.59 (d, $^3J_{PC}$ = 7.55 Hz, *m*-Ph), 128.73 (s, *p*-Ph), 135.23 (d, J_{PC} = 20.12 Hz, *o*-Ph), 135.79 (d, $^1J_{PC}$ = 20.12 Hz, *ipso*-Ph). $^{31}P\{^1H\}$ NMR: δ = 26.08 (s, PPh_2).

Electrochemical Experiments. The supporting electrolyte (tetrabutylammonium hexafluorophosphate) was degassed under vacuum before use and then solubilized at a concentration of 0.2 M. For cyclic voltammetry experiments, the concentration of the ligand was set at 10^{-3} M. Voltammetry was carried out in a standard three-electrode cell using an Autolab PGSTAT302N potentiostat under argon overpressure. The reference electrode was a saturated calomel electrode (SCE) separated from the solution by a sintered glass disk. The auxiliary electrode was a platinum wire. For all voltammetric measurements, the working electrode was a glassy carbon disk (diameter = 1 mm).

General Catalytic Procedure. As a typical experiment, the reaction of the aryl chloride (1 mmol), heteroaryl derivative (1.5 mmol), KOAc (0.294 g, 3 mmol), and nBu_4NBr (0.322 g, 1 mmol, see tables) at 150 °C over 20 h in DMAc (3 mL) in the presence of $Pd(OAc)_2$ (1.12 mg, 0.005 mmol) and ligand **6** (3.2 mg, 0.005 mmol) under argon affords the coupling product after evaporation and purification on silica gel.

4-(3,5-Dimethylisoxazol-4-yl)-benzonitrile (7).[58] 4-Chlorobenzonitrile (0.138 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **7** in 65% (0.129 g) yield.

4-(3,5-Dimethylisoxazol-4-yl)-benzaldehyde (8).[58] 4-Chlorobenzaldehyde (0.141 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **8** in 71% (0.143 g) yield.

3,5-Dimethyl-4-(4-nitrophenyl)-isoxazole (9).[58] 4-Chloronitrobenzene (0.158 g, 1 mmol), and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **9** in 74% (0.161 g) yield.

3-(3,5-Dimethylisoxazol-4-yl)-benzonitrile (10). 3-Chlorobenzonitrile (0.138 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **10** in 55% (0.109 g) yield.

^1H NMR (300 MHz, $CDCl_3$) δ = 2.26 (s, 3 H), 2.41 (s, 3 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.54 (s, 1 H), 7.59 (t, *J* = 7.7 Hz, 1 H), 7.65 (d, *J* = 7.6 Hz, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 10.6, 11.5, 113.1, 114.8, 118.3, 129.7, 131.0, 131.9, 132.3, 133.3, 158.1, 165.9. Elemental analysis calcd (%) for $C_{12}H_{10}N_2O$: (198.22) C 72.71, H 5.08. Found: C 72.54, H 4.97.

3,5-Dimethyl-4-(3-nitrophenyl)-isoxazole (11).[58] 3-Chloronitrobenzene (0.158 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **11** in 44% (0.096 g) yield.

2-(3,5-Dimethylisoxazol-4-yl)-benzonitrile (12).[58] 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **12** in 70% (0.139 g) yield.

dx.doi.org/10.1021/cs300097v | *ACS Catal.* 2012, 2, 1033−1041

4-(3,5-Dimethylisoxazol-4-yl)-pyridine (13). 4-Chloropyridine hydrochloride (0.150 g, 1 mmol) and 3,5-dimethylisoxazole (0.144 g, 1.5 mmol) afford **13** in 48% (0.084 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.31 (s, 3 H), 2.46 (s, 3 H), 7.19 (d, J = 4.4 Hz, 2 H), 8.67 (d, J = 4.4 Hz, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 10.9, 11.8, 114.5, 123.5, 138.7, 150.3, 158.1, 166.4. Elemental analysis calcd (%) for $C_{10}H_{10}N_2O$ (174.20): C 68.95, H 5.79. Found: C 69.11, H5.87.

4-(3-Methyl-5-phenylisoxazol-4-yl)-benzonitrile (14).[58] 4-Chlorobenzonitrile (0.138 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **14** in 73% (0.190 g) yield.

3-Methyl-4-(4-nitrophenyl)-5-phenylisoxazole (15).[58] 4-Chloronitrobenzene (0.158 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **15** in 72% (0.202 g) yield.

4-(3-Methyl-5-phenylisoxazol-4-yl)-benzaldehyde (16).[58] 4-Chlorobenzaldehyde (0.141 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **16** in 70% (0.184 g) yield.

3-Methyl-5-phenyl-4-(4-trifluoromethylphenyl)-isoxazole (17). 4-Chlorobenzotrifluoride (0.181 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **17** in 66% (0.200 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.26 (s, 3 H), 7.30−7.38 (m, 3 H), 7.43 (d, J = 8.4 Hz, 2 H), 7.50 (d, J = 8.1 Hz, 2 H), 7.70 (d, J = 8.4 Hz, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 10.5, 114.8, 124.0 (q, J = 272.3 Hz), 125.9 (q, J = 3.9 Hz), 126.9, 127.3, 128.7, 130.0, 130.1, 130.2 (q, J = 33.0 Hz), 134.5, 160.0, 164.9. Elemental analysis calcd (%) for $C_{17}H_{12}F_3NO$ (303.28): C 67.32, H 3.99. Found: C 67.41, H 4.10. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −62.6.

3-Methyl-4-(3-nitrophenyl)-5-phenylisoxazole (18).[58] 3-Chloronitrobenzene (0.158 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **18** in 38% (0.107 g) yield.

2-(3-Methyl-5-phenylisoxazol-4-yl)-benzonitrile (19).[57] 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **19** in 39% (0.101 g) yield.

2-(3-Methyl-5-phenylisoxazol-4-yl)-benzaldehyde (20). 2-Chlorobenzaldehyde (0.141 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **20** in 34% (0.089 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.06 (s, 3 H), 7.12−7.25 (m, 3 H), 7.27 (d, J = 7.0 Hz, 1 H), 7.30−7.33 (m, 2 H), 7.51 (t, J = 7.8 Hz, 1 H), 7.61 (td, J = 7.5, 1.6 Hz, 1 H), 7.97 (dd, J = 7.4, 1.5 Hz, 1 H), 9.81 (d, J = 0.9 Hz, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$), δ = 10.3, 111.8, 126.4, 126.9, 128.7, 128.8, 129.2, 130.0, 131.9, 133.5, 134.4, 134.6, 160.2, 165.1, 190.7. Elemental analysis calcd (%) for $C_{17}H_{13}NO_2$ (263.29): C 77.55, H 4.98. Found: C 77.74, H 5.09.

3-(3-Methyl-5-phenylisoxazol-4-yl)-pyridine (21).[58] 3-Chloropyridine (0.114 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **21** in 80% (0.189 g) yield.

4-(3-Methyl-5-phenylisoxazol-4-yl)-pyridine (22). 4-Chloropyridine hydrochloride (0.150 g, 1 mmol) and 3-methyl-5-phenylisoxazole (0.239 g, 1.5 mmol) afford **22** in 78% (0.184 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.28 (s, 3 H), 7.22−7.28 (m, 2 H), 7.30−7.40 (m, 3 H), 7.50 (d, J = 5.6 Hz, 2 H), 8.68 (bs, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 10.3, 113.6, 124.4, 127.0, 128.8, 130.3, 139.1, 150.4, 159.2, 165.5. Elemental analysis calcd (%) for $C_{15}H_{12}N_2O$ (236.27): C 76.25, H 5.12. Found: C 76.17, H 5.13.

4-(2-Ethylbenzofuran-3-yl)-benzonitrile (23).[59] 4-Chlorobenzonitrile (0.138 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) affords **23** in 56% (0.138 g) yield.

2-Ethyl-3-(4-nitrophenyl)-benzofuran (24).[59] 4-Chloronitrobenzene (0.158 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **24** in 75% (0.200 g) yield.

4-(2-Ethylbenzofuran-3-yl)-benzaldehyde (25).[59] 4-Chlorobenzaldehyde (0.141 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **25** in 75% (0.188 g) yield.

4-(2-Ethylbenzofuran-3-yl)-acetophenone (26).[59] 4-Chloroacetophenone (0.155 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **26** in 78% (0.206 g) yield.

2-Ethyl-3-(4-trifluoromethylphenyl)-benzofuran (27).[59] 4-Chlorobenzotrifluoride (0.181 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **27** in 44% (0.128 g) yield.

2-Ethyl-3-(3-nitrophenyl)-benzofuran (28). 3-Chloronitrobenzene (0.158 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **28** in 61% (0.163 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.39 (t, J = 7.5 Hz, 3 H), 2.90 (q, J = 7.5 Hz, 2 H), 7.28 (m, 2 H), 7.54 (m, 2H), 7.67 (m, 1 H), 7.82 (d, J = 8.0 Hz, 1 H), 8.23 (m, 1 H), 8.36 (m, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 12.8, 20.3, 111.1, 114.4, 118.8, 121.8, 123.0, 123.6, 124.1, 127.9, 129.7, 134.7, 134.9, 148.7, 154, 157.1. Elemental analysis calcd (%) for $C_{16}H_{13}NO_3$ (267.28): C 71.90, H 4.90. Found: C 72.04, H 4.85.

2-(2-Ethylbenzofuran-3-yl)-benzonitrile (29).[59] 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **29** in 53% (0.131 g) yield.

3-(2-Ethylbenzofuran-3-yl)-pyridine (30).[59] 3-Chloropyridine (0.114 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **30** in 44% (0.098 g) yield.

4-(2-Ethylbenzofuran-3-yl)-pyridine (31).[59] 4-Chloropyridine hydrochloride (0.150 g, 1 mmol) and 2-ethylbenzofuran (0.219 g, 1.5 mmol) afford **31** in 57% (0.127 g) yield.

4-(1-Ethyl-2-phenylindol-3-yl)-benzonitrile (32). 4-Chlorobenzonitrile (0.138 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) afford **32** in 88% (0.283 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.35 (t, J = 7.1 Hz, 3 H), 4.19 (q, J = 7.1 Hz, 2 H), 7.20−7.60 (m, 12 H), 7.85 (d, J = 7.9 Hz, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 15.3, 38.7, 108.3, 110.1, 113.5, 119.1, 119.4, 120.8, 122.5, 126.4, 128.6, 128.7, 129.8, 130.8, 131.4, 131.9, 136.1, 138.4, 140.5. Elemental analysis calcd (%) for $C_{23}H_{18}N_2$ (322.40): C 85.68, H 5.63. Found: C 85.79, H 5.71.

1-Ethyl-3-(4-nitrophenyl)-2-phenylindole (33). 4-Chloronitrobenzene (0.158 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) afford **33** in 84% (0.288 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.34 (t, J = 7.5 Hz, 3 H), 4.18 (q, J = 7.5 Hz, 2 H), 7.23−7.55 (m, 10 H), 7.85 (d, J = 7.9 Hz, 1 H), 8.12 (d, J = 8.9 Hz, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$), δ = 15.3, 38.7, 110.2, 113.3, 119.1, 121.0, 122.6, 123.5, 126.4, 128.8, 129.5, 130.8, 131.3, 136.1, 138.9, 142.8, 145.0. Elemental analysis calcd (%) for $C_{22}H_{18}N_2O_2$ (342.39): C 77.17, H 5.30. Found: C 77.24, H 5.47.

4-(1-Ethyl-2-phenylindol-3-yl)-benzaldehyde (34). 4-Chlorobenzaldehyde (0.141 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) affords **34** in 43% (0.139 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.35 (t, J = 7.2 Hz, 3 H), 4.19 (q, J = 7.2 Hz, 2 H), 7.20−7.55 (m, 10 H), 7.79 (d, J = 8.3 Hz, 2 H), 7.89 (d, J = 7.8 Hz, 1 H), 9.97 (s, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 15.3, 38.7, 110.1, 114.1, 119.4, 120.7, 122.4,

dx.doi.org/10.1021/cs300097v | ACS Catal. 2012, 2, 1033−1041

126.6, 128.6, 128.7, 129.6, 129.7, 130.9, 131.6, 133.3, 136.1, 138.5, 142.3, 191.8. Elemental analysis calcd (%) for $C_{23}H_{19}NO$ (325.40): C 84.89, H 5.89. Found: C 84.84, H 5.85.

4-(1-Ethyl-2-phenylindol-3-yl)-acetophenone (35). 4-Chloroacetophenone (0.155 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) affords **35** in 28% (0.095 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.19 (t, J = 7.2 Hz, 3 H), 2.45 (s, 3 H), 4.03 (q, J = 7.2 Hz, 2 H), 7.12 (t, J = 7.8 Hz, 1 H), 7.18−7.40 (m, 9 H), 7.74 (d, J = 8.5 Hz, 3 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 15.3, 26.4, 38.6, 110.0, 114.2, 119.5, 120.6, 122.3, 126.7, 128.3, 128.5, 128.6, 129.4, 130.9, 131.8, 133.9, 136.1, 138.2, 140.7, 197.7. Elemental analysis calcd (%) for $C_{24}H_{21}NO$ (339.43): C 84.92, H 6.24. Found: C 85.04, H 6.17.

1-Ethyl-3-(3-nitrophenyl)-2-phenylindole (36). 3-Chloronitrobenzene (0.158 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) affords **36** in 62% (0.212 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.34 (t, J = 7.5 Hz, 3 H), 4.18 (q, J = 7.5 Hz, 2 H), 7.23−7.50 (m, 9 H), 7.55 (d, J = 6.6 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1 H), 8.12 (d, J = 8.9 Hz, 1 H), 8.21 (t, J = 2.0 Hz, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 15.3, 38.7, 110.1, 112.9, 119.0, 120.1, 120.7, 122.5, 124.1, 126.5, 128.7, 128.8, 128.9, 130.8, 131.3, 135.4, 136.0, 137.2, 138.2, 148.3. Elemental analysis calcd (%) for $C_{22}H_{18}N_2O_2$ (342.39): C 77.17, H 5.30. Found: C 77.27, H 5.24.

2-(1-Ethyl-2-phenylindol-3-yl)-benzonitrile (37). 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) affords **37** in 57% (0.184 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.39 (t, J = 7.2 Hz, 3 H), 4.24 (q, J = 7.2 Hz, 2 H), 7.20−7.60 (m, 12 H), 7.63 (d, J = 7.7 Hz, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$) δ = 15.3, 38.9, 110.0, 112.0, 113.7, 118.7, 119.3, 120.3, 122.3, 126.5, 127.3, 128.2, 128.3, 131.0, 131.2, 132.1, 132.3, 133.2, 136.0, 138.9, 139.5. Elemental analysis calcd (%) for $C_{23}H_{18}N_2$ (322.40): C 85.68, H 5.63. Found: C 85.61, H 5.60.

3-(1-Ethyl-2-phenylindol-3-yl)-pyridine (38). 3-Chloropyridine (0.114 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) afford **38** in 61% (0.182 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.34 (t, J = 7.1 Hz, 3 H), 4.18 (q, J = 7.1 Hz, 2 H), 7.15−7.45 (m, 8 H), 7.50 (d, J = 8.2 Hz, 1 H), 7.60 (d, J = 7.9 Hz, 1 H), 7.82 (d, J = 7.9 Hz, 1 H), 8.43 (d, J = 4.1 Hz, 1 H), 8.63 (s, 1 H). ^{13}C NMR (300 MHz, $CDCl_3$), δ = 15.3, 38.7, 110.0, 111.6, 119.1, 120.5, 122.3, 123.0, 126.8, 128.5, 128.6, 130.8, 131.2, 131.4, 136.0, 136.5, 138.0, 146.5, 150.6. Elemental analysis calcd (%) for $C_{21}H_{18}N_2$ (298.38): C 84.53, H 6.08. Found: C 84.67, H 6.14.

4-(1-Ethyl-2-phenylindol-3-yl)-pyridine (39). 4-Chloropyridine hydrochloride (0.150 g, 1 mmol) and 1-ethyl-2-phenylindole (0.331 g, 1.5 mmol) affords **39** in 71% (0.212 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.28 (t, J = 7.2 Hz, 3 H), 4.13 (q, J = 7.2 Hz, 2 H), 7.18 (d, J = 6.0 Hz, 2 H), 7.20−7.50 (m, 8 H), 7.86 (d, J = 7.9 Hz, 1 H), 8.43 (d, J = 6.0 Hz, 2 H). ^{13}C NMR (300 MHz, $CDCl_3$), δ = 15.3, 38.7, 110.1, 112.4, 119.3, 120.8, 122.5, 124.0, 126.4, 128.8, 130.8, 131.5, 136.2, 138.7, 143.5, 149.5. Elemental analysis calcd (%) for $C_{21}H_{18}N_2$ (298.38): C 84.53, H 6.08. Found: C 84.41, H 6.00.

2-(4-Nitrophenyl)-benzofuran (40).[60] 4-Chloronitrobenzene (0.158 g, 1 mmol) and benzofuran (0.177 g, 1.5 mmol) afford **40** in 65% regioselectivity and 38% (0.117 g) yield.

4-(1-Methylindol-2-yl)-benzonitrile (41a) and 4-(1,2-Dimethylindol-3-yl)-benzonitrile (41b).[61] 4-Chlorobenzonitrile (0.138 g, 1 mmol) and 1-methylindole (0.196 g, 1.5 mmol) afford **41a** in 61% regioselectivity and 42% (0.098 g) yield and **41b** in 39% regioselectivity and 18% (0.042 g) yield.

1,3,5-Trimethyl-4-(4-nitrophenyl)-pyrazole (42).[62] 4-Chloronitrobenzene (0.158 g, 1 mmol) and 1,3,5-trimethylpyrazole (0.165 g, 1.5 mmol) afford **42** in 71% (0.164 g) yield.

1,3,5-Trimethyl-4-(4-formylphenyl)-pyrazole (43).[62] 4-Chlorobenzaldehyde (0.141 g, 1 mmol) and 1,3,5-trimethylpyrazole (0.165 g, 1.5 mmol) afford **43** in 66% (0.141 g) yield.

2-(1,3,5-Trimethylpyrazol-4-yl)-benzonitrile (44).[62] 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 1,3,5-trimethylpyrazole (0.165 g, 1.5 mmol) afford **44** in 78% (0.165 g) yield.

4-(2-Cyanophenyl)-1,5-dimethylpyrrole-2-carbonitrile (45).[35] 2-Chlorobenzonitrile (0.138 g, 1 mmol) and 1,5-dimethyl-2-pyrrolecarbonitrile (0.180 g, 1.5 mmol) afford **45** in 84% regioselectivity and 53% (0.117 g) yield.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jean-cyrille.hierso@u-bourgogne.fr (J.-C.H.) henri.doucet@univ-rennes1.fr (H.D.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support provided from ANR program for Sustainable Chemistry Development (ANR-09-CP2D-03 CAMELOT), Rennes Métropole, Région Bourgogne/CNRS (PARI SMT8 and 3MIM program) is acknowledged. Ms. S. Fournier is acknowledged for technical assistance.

■ REFERENCES

(1) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174.
(2) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200.
(3) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269.
(4) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, 949.
(5) Ackermann, L.; Vincente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792.
(6) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20.
(7) Fischmeister, C.; Doucet, H. *Green. Chem.* **2011**, *13*, 741.
(8) Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951.
(9) Hodgetts, K. J.; Kershaw, M. T. *Org. Lett.* **2003**, *5*, 2911.
(10) Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754.
(11) Cameron, M.; Foster, B. S.; Lynch, J. E.; Shi, Y.-J.; Dolling, U.-H. *Org. Proc. Res. Devel.* **2006**, *10*, 398.
(12) Gottumukkala, A. L.; Doucet, H. *Eur. J. Inorg. Chem.* **2007**, 3629.
(13) Iwasaki, M.; Yorimitsu, H.; Oshima, K. *Chem. Asian J.* **2007**, *2*, 1430.
(14) Verrier, C.; Martin, T.; Hoarau, C.; Marsais, F. *J. Org. Chem.* **2008**, *73*, 7383.
(15) Liégault, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K. *J. Org. Chem.* **2009**, *74*, 1826.
(16) Tamba, S.; Okubo, Y.; Tanaka, S.; Monguchi, D.; Mori, A. *J. Org. Chem.* **2010**, *75*, 6998.
(17) Joo, J. M.; Toure, B. B.; Sames, D. *J. Org. Chem.* **2010**, *75*, 4911.
(18) Strotman, N. A.; Chobanian, H. R.; Guo, Y.; He, J.; Wilson, J. E. *Org. Lett.* **2010**, *12*, 3578.

(19) Ozdemir, I.; Goek, Y.; Oezeroglu, O.; Kaloglu, M.; Doucet, H.; Bruneau, C. *Eur. J. Inorg. Chem.* **2010**, 1798.
(20) Kumar, P. V.; Lin, W.-S.; Shen, J.-S.; Nandi, D.; Lee, H. M. *Organometallics* **2011**, *30*, 5160.
(21) Wang, L.; Yi, W.-b.; Cai, C. *Chem. Commun.* **2011**, *47*, 806.
(22) Pierre, C.; Baudoin, O. *Org. Lett.* **2011**, *13*, 1816.
(23) Song, G.; Su, Y.; Gong, X.; Han, K.; Li, X. *Org. Lett.* **2011**, *13*, 1968.
(24) Chiong, H. A.; Daugulis, O. *Org. Lett.* **2007**, *9*, 1449.
(25) Nadres, E. T.; Lazareva, A.; Daugulis, O. *J. Org. Chem.* **2011**, *76*, 471.
(26) Iwasaki, M.; Yorimitsu, H.; Oshima, K. *Chem. Asian J.* **2007**, *2*, 1430.
(27) Ackermann, L.; Vicente, R.; Born, R. *Adv. Synth. Catal.* **2008**, *350*, 741.
(28) Mohebbi, A. R.; Wudl, F. *Chem.—Eur. J.* **2011**, *17*, 2642.
(29) Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581.
(30) Roger, J.; Mom, S.; Beaupérin, M.; Royer, S.; Meunier, P.; Ivanov, V. V.; Doucet, H.; Hierso, J.-C. *ChemCatChem* **2010**, *2*, 296.
(31) Smaliy, R. V.; Beaupérin, M.; Cattey, H.; Meunier, P.; Hierso, J.-C.; Roger, J.; Doucet, H.; Coppel, Y. *Organometallics* **2009**, *28*, 3152.
(32) Roy, D.; Mom, S.; Beaupérin, M.; Doucet, H.; Hierso, J.-C. *Angew. Chem., Int. Ed.* **2010**, *49*, 6650.
(33) Roy, D.; Mom, S.; Lucas, D.; Cattey, H.; Hierso, J.-C.; Doucet, H. *Chem.—Eur. J.* **2011**, *17*, 6453.
(34) Roger, J.; Doucet, H. *Adv. Synth. Catal.* **2009**, *351*, 1977.
(35) Fall, Y.; Doucet, H.; Santelli, M. *ChemSusChem* **2009**, *2*, 153.
(36) Derridj, F.; Roger, J.; Djebbar, S.; Doucet, H. *Org. Lett.* **2010**, *12*, 4320.
(37) Roger, J.; Požgan, F.; Doucet, H. *Adv. Synth. Catal.* **2010**, *352*, 696.
(38) Triphosphane **1** possesses three equivalent PPh_2 groups with an unrestricted rotation of the cyclopentadienyl rings. Phosphane **2** is of the same family but with a restricted rotation ability because of the mutual hindrance of two *t-Bu* groups; therefore, the conformation of ferrocene is controlled. Phosphane **3** and **4** bear a third phosphorus with either a more electron-donating phosphanyl group [$P(\text{-}i\text{-}Pr_2)$] or a more electron-withdrawing phosphanyl group $-P[(\text{methyl})\text{furyl}]_2$. Phosphane **5** is a diphosphane and does not undergo tridentate coordination effect. For details see references 30−33 and 39−41.
(39) Platon, M.; Luchao, C.; Mom, S.; Richard, P.; Saeys, M.; Hierso, J.-C. *Adv. Synth. Catal.* **2011**, *353*, 3403.
(40) Beaupérin, M.; Fayad, E.; Amardeil, R.; Cattey, H.; Richard, P.; Brandès, S.; Meunier, P.; Hierso, J.-C. *Organometallics* **2008**, *27*, 1506.
(41) Mom, S.; Beaupérin, M.; Roy, D.; Royer, S.; Amardeil, R.; Cattey, H.; Doucet, H.; Hierso, J.-C. *Inorg. Chem.* **2011**, *50*, 11592.
(42) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754.
(43) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118.
(44) For an example of intramolecular reaction see: Choi, Y. L.; Lee, H.; Kim, B. T.; Choi, K.; Heo, J.-N. *Adv. Synth. Catal.* **2010**, *352*, 2041.
(45) Ivanov, V. V.; Hierso, J.-C.; Fihri, A.; Amardeil, R.; Meunier, P. *Organometallics* **2006**, *25*, 989.
(46) Hierso, J.-C.; Smaliy, R.; Amardeil, R.; Meunier, P. *Chem. Soc. Rev.* **2007**, *36*, 1754.
(47) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.
(48) Allen, D. W.; Taylor, B. F. *J. Chem. Soc., Dalton Trans.* **1982**, 51.
(49) Chevykalova, M. N.; Manzhukova, L. F.; Artemova, N. V.; Luzikov, Y. N.; Nifant'ev, I. E.; Nifant'ev, E. E. *Russ. Chem. Bull., Int. Ed.* **2003**, *52*, 78.
(50) NMR chemical shifts are not in general reliable data to assess the σ,π-donating properties of nucleus.
(51) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*, 2nd ed.; John Wiley & Sons: New York, 2001.
(52) Noel, M.; Vasu, K. I. *Cyclic Voltammetry and the Frontiers of Electrochemistry*; Aspect Publication Ltd, 1990.
(53) Evrard, D.; Lucas, D.; Mugnier, Y.; Meunier, P.; Hierso, J.-C. *Organometallics* **2008**, *27*, 2643.
(54) Nataro, C.; Campbell, A. N.; Ferguson, M. A.; Incarvito, C. D.; Rheingold, A. L. *J. Organomet. Chem.* **2003**, *673*, 47.
(55) Pilloni, G.; Longato, B.; Corain, B *J. Organomet. Chem.* **1991**, *420*, 57.
(56) Lu, S.; Strelets, V. V.; Ryan, M. F.; Pietro, W. J.; Lever, A. B. P. *Inorg. Chem.* **1996**, *35*, 1013.
(57) Hansch, C. *Chem. Rev.* **1991**, *91*, 165.
(58) Fall, Y.; Reynaud, C.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2009**, 4041.
(59) Ionita, M.; Roger, J.; Doucet, H. *ChemSusChem* **2010**, *3*, 367.
(60) Kitamura, Y.; Sako, S.; Tsutsui, A.; Monguchi, Y.; Maegawa, T.; Kitade, Y.; Sajiki, H. *Adv. Synth. Catal.* **2010**, *352*, 718.
(61) Denmark, S. E.; Baird, J. D.; Regens, C. S. *J. Org. Chem.* **2008**, *73*, 1440.
(62) Fall, Y.; Doucet, H.; Santelli, M. *Synthesis* **2010**, 127.