DOI: 10.1002/adsc.201300123

Palladium-Catalysed Regioselective Sequential C-5 and C-2 Direct Arylations of 3-Acetylpyrroles with Aryl Bromides

Yijing Xu,[a,b] Liqin Zhao,[a] Yiqun Li,[b,*] and Henri Doucet[a,*]

[a] Institut Sciences Chimiques de Rennes, UMR 6226 CNRS – Université de Rennes "Organométalliques matériaux et Catalyse", Campus de Beaulieu, 35042 Rennes, France
Fax: (+33)-(0)2-2323-6939; phone: (+33)-(0)2-2323-6384; e-mail: henri.doucet@univ-rennes1.fr
[b] Department of Chemistry, Jinan University, Guangzhou 510632, People's Republic of China
E-mail: tlyq@jnu.edu.cn

Received: February 6, 2013; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201300123.

Abstract: The $PdCl(C_3H_5)(dppb)$/KOAc system was found to be effective for the direct regioselective C-5 arylation of 3-acetylpyrroles with *ortho*-substituted aryl bromides. This procedure has been found to be tolerant to a variety of functional groups at C-2 of the aryl bromide such as methyl, formyl, nitrile, nitro, hydroxymethyl, chloro, fluoro or trifluoromethyl. The sequential direct C-5 arylation followed by C-2 arylation of such 3-substituted pyrroles allows the synthesis of 2,5-diaryl-3-acetylpyrroles in high yields.

Keywords: aryl halides; atom economy; C–H bond functionalisation; palladium; pyrroles

Among heterocycles, some 2-aryl-4-carbonylpyrrole derivatives display important biological properties. For example, Atorvastatin is used for lowering cholesterol and Isoprazone is an analgesic antipyretic agent (Figure 1). Therefore, the discovery of general and simple routes to a variety of 2-aryl-4-carbonylpyrroles has potential for medicinal chemistry.

The direct coupling of heteroarenes with aryl halides *via* a C–H bond activation/functionalisation provides a cost-effective and environmentally attractive procedure for the preparation of arylated heteroarenes.[1–4] Such couplings are very attractive compared to classical palladium-catalysed reactions such as Stille, Suzuki or Negishi couplings as they do not require the preliminary synthesis of organometallic derivatives.[5] The regioselectivity of the palladium-catalysed direct arylation of 3-substituted furans or thiophenes has been largely studied in recent years.[6,7] When using 3-formyl, 3-cyano, 3-methyl, 3-hydroxymethyl or 3-bromothiophenes, the 2-arylated thiophenes were obtained in 76–95% regioselectivity. On the other hand, the arylation of 3-acetylthiophene gave the 5-arylated thiophenes in 52–90% regioselectivities. With this thiophene derivative, the use of congested aryl bromides was found to favour the arylation at C-5 (Scheme 1).[7]

The palladium-catalysed direct arylation of 3-substituted pyrroles has attracted much less attention.[8–10] In 2006, Sames and co-workers reported a single example of the direct arylation of a 3-acetylpyrrole using iodobenzene as the coupling partner. For this coupling, 5 mol% of palladium associated to a carbene ligand were used as the catalyst, and a mixture of regioisomers was formed (Scheme 2).[10] 5-Phenyl-3-acetylpyrrole was obtained in 29% yield; whereas, 2-

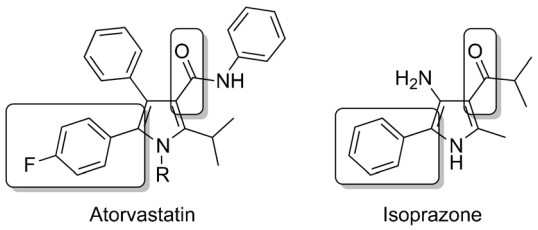
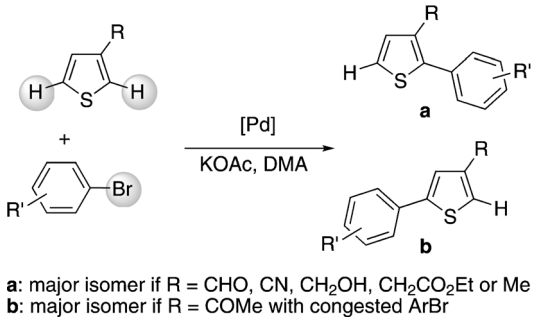
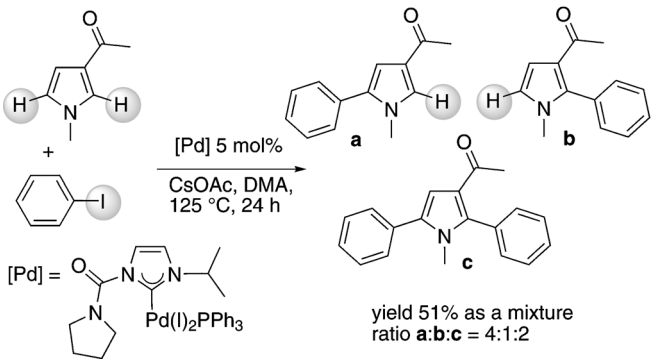


Figure 1. Examples of bioactive arylpyrroles.



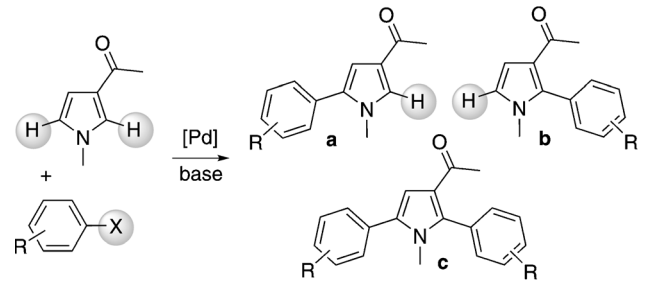
a: major isomer if R = CHO, CN, CH_2OH, CH_2CO_2Et or Me
b: major isomer if R = COMe with congested ArBr

Scheme 1. Most reactive positions for Pd-catalysed direct arylation of 3-substituted thiophenes.



Scheme 2. Reported direct arylation of 1-methyl-3-acetylpyrrole.[10]

phenyl-3-acetylpyrrole and 2,5-diphenyl-3-acetylpyrrole were produced in 7% and 14% yields, respectively. Therefore, the influence of the reaction parameters on the regioselectivity of the palladium-catalysed direct arylation of 3-substituted pyrroles needed to be investigated.



Scheme 3. Influence of the reaction conditions for the palladium-catalysed direct arylations of 1-methyl-3-acetylpyrrole with aryl halides.

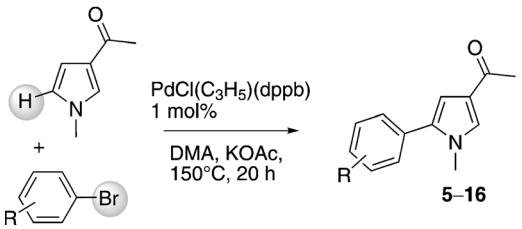
Here, we wish to report (i) on the influence of some parameters on the regioselectivity of the reaction of 3-acetylpyrrole derivatives with aryl halides; (ii) the scope of the reaction using a set of electronically and sterically diverse aryl bromides; (iii) the further reactivity of these formed 5-aryl-3-acetylpyrroles for palladium-catalysed C–H bond functionalization at C-2 of the pyrrole ring to produce 2,5-diarylpyrrole derivatives.

We decided to employ commercially available 1-methyl-3-acetylpyrrole as the test substrate for our study (Scheme 3, Table 1). We initially examined the influence of the nature of the halide on the selectivity of this reaction using DMA as the solvent and 1 mol% $PdCl(C_3H_5)(dppb)$ as the catalyst, as such conditions were previously found operative for some direct arylations of heteroaromatics.[3a] In the presence of iodobenzene, a complete conversion was observed, and the C-5 arylated pyrrole **1a** was obtained as the major isomer in 50% selectivity (Table 1, entries 1 and 2). However, the C-2 arylated product **1b** was also obtained in 26% selectivity, and 24% of the 2,5-diarylated pyrrole **1c** were also produced. A slightly higher selectivity in favour of the formation of **1a** was observed in the presence of bromobenzene, as **1a** was obtained in 51–55% selectivity (Table 1, entries 3 and 4). The ratio of the reactant also appears to have a minor influence on the selectivity. Then, a few other catalyst precursors were employed. However, the use of phosphine-free $Pd(OAc)_2$, or $Pd(OAc)_2$ associated to PPh_3 or dppb led to **1a–c** in similar regioselectivities (Table 1, entries 5–7). Moreover, a moderate conversion of 62% of bromobenzene was observed with phosphine-free $Pd(OAc)_2$ catalyst leading to **1a** in only 21%. Changing the base to

Table 1. Influence of the reaction conditions for the palladium-catalysed direct arylations of 1-methyl-3-acetylpyrrole with aryl halides (Scheme 3).[a]

Entry	X	R	Ratio ArBr:3-acetylpyrrole	Catalyst (mol%)	Base	Solvent	Ratio of products **a**:**b**:**c**	Yield in **a** [%]
1	I	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**1a**:**1b**:**1c:** 50:26:24	42
2	I	H	1:1.5	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**1a**:**1b**:**1c:** 50:26:24	–
3	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**1a**:**1b**:**1c:** 55:27:18	37
4	Br	H	1:1.5	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**1a**:**1b**:**1c:** 51:27:22	–
5	Br	H	1:2	$Pd(OAc)_2$ (1)	KOAc	DMA	**1a**:**1b**:**1c:** 55:26:19	21
6	Br	H	1:2	$Pd(OAc)_2$ (1) PPh_3 (2)	KOAc	DMA	**1a**:**1b**:**1c:** 51:26:23	–
7	Br	H	1:2	$Pd(OAc)_2$ (1) dppb (1)	KOAc	DMA	**1a**:**1b**:**1c** 52:27:21	–
8	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	CsOAc	DMA	**1a**:**1b**:**1c:** 52:23:25	–
9	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	NaOAc	DMA	**1a**:**1b**:**1c:** 55:27:18	–
10	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	K_2CO_3	DMA	**1a**:**1b**:**1c:** 59:31:10	–[b]
11	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMF	**1a**:**1b**:**1c:** 57:29:14	–[b]
12	Br	H	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	NMP	**1a**:**1b**:**1c:** 55:24:21	–
13	Br	4-CN	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**2a**:**2b**:**2c:** 51:25:24	41
14	Br	3-CN	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	**3a**:**3b**:**3c:** 52:23:25	40
15	Br	2-CN	1:2	$PdCl(C_3H_5)(dppb)$ (1)	KOAc	DMA	only **4a** detected	80

[a] *Reaction conditions:* base (3 equiv.), 20 h, 150 °C.
[b] Low conversion of bromobenzene.



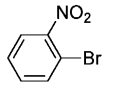
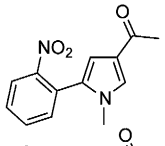
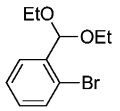
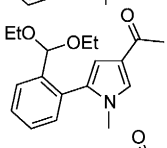
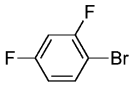
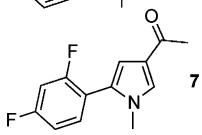
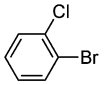
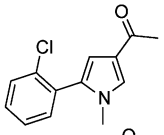
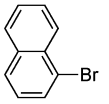
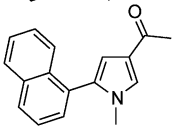
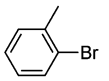
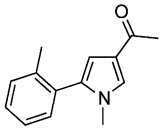
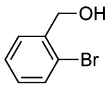
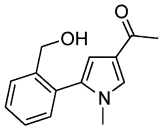
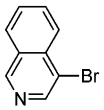
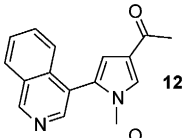
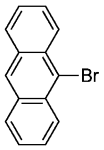
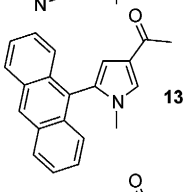
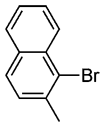
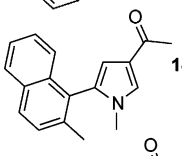
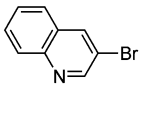
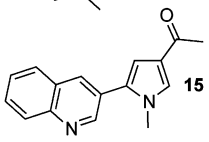
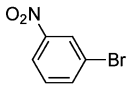
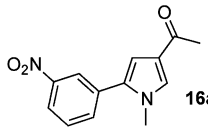
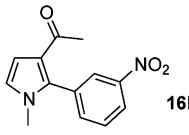
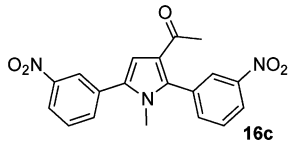
Scheme 4. Direct 5-arylations of 1-methyl-3-acetylpyrrole with various aryl bromides.

CsOAc or NaOAc also gave very similar results; whereas, K_2CO_3 gave **1a–c** in low yield due to a poor conversion of bromobenzene (Table 1, entries 8–10). DMF was found to be quite ineffective as solvent for this reaction. On the other hand, NMP gave a similar regioselectivity in **1a–c** as DMA (Table 1, entries 11 and 12).

The influence of the bromobenzene substituents on the reactivity and regioselectivity of the coupling with 1-methyl-3-acetylpyrrole was then examined. In the presence of the electron-deficient aryl bromides, 3- or 4-bromobenzonitriles, the selectivity in isomers **2a–c** and **3a–c** was very similar as with bromobenzene (Scheme 3, Table 1, entries 13 and 14).

On the other hand, a very regioselective reaction in favour of the formation of **4a** was observed in the presence of a congested aryl bromide, 2-bromobenzonitrile (Table 1, entry 15). With this reactant, no formation of 2-arylated or 2,5-diarylated pyrroles **4b** and **4c** was detected by GC/MS analysis and in the crude NMR spectrum, and **4a** was isolated in 80% yield.

Table 2. Direct 5-arylations of 1-methyl-3-acetylpyrrole with various aryl bromides (Scheme 4).[a]

Entry	Aryl bromide	Product	Yield in **a** [%]
1		 **5**	86
2		 **6**	66
3		 **7**	78
4		 **8**	80
5		 **9**	79
6		 **10**	73
7		 **11**	69
8		 **12**	81
9		 **13**	73
10		 **14**	76
11		 **15**	58[b]
12		 **16a**	33 of **16a**
		 **16b**	
		 **16c**	
		ratio **16a**:**16b**:**16c** = 49:22:29	

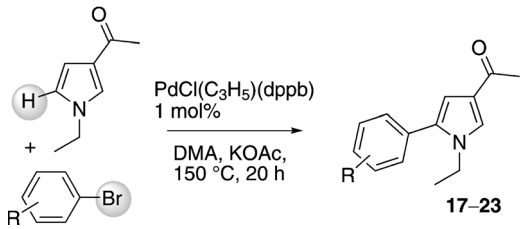
[a] *Reaction conditions:* $PdCl(C_3H_5)(dppb)$ (0.01 equiv.), aryl bromide (1 equiv.), 1-methyl-3-acetylpyrrole (2 equiv.), KOAc (3 equiv.), DMA, 20 h, 150 °C.

[b] Other arylation products observed by GC/MS analysis.

Then, we examined the scope of this procedure using other *meta*- or *ortho*-substituted aryl bromides and also heteroaryl bromides (Scheme 4, Table 2). The use of 2-bromonitrobenzene gave selectively the 5-arylated pyrrole **5** in 86% yield (Table 2, entry 1). From a protected 2-bromobenzaldehyde, **6** was isolated in 66% yield. Again, the reaction was completely regioselective, but a partial decomposition of the product was observed (Table 2, entry 2). The coupling with 2,4-difluorobromobenzene, 2-chlorobromobenzene and 1-bromonaphthalene gave **7**–**9** in 78–80% yields (Table 2, entries 3–5). It should be noted that no cleavage of the C–Cl bond of 2-chlorobromobenzene was observed in the course of this coupling allowing further transformations. Even the slightly electron-rich aryl bromide, 2-bromotoluene was reactive under these conditions to give selectively **10** in 73% yield (Table 2, entry 6). On the other hand, no reaction was observed in the presence of the more electron-rich 2-bromoanisole. The direct coupling of unprotected (2-bromophenyl)methanol with 1-methyl-3-acetylpyrrole could be very practical since it would avoid a protection/deprotection sequence, and therefore would provide a more environmentally and economically attractive access to such arylated pyrroles. We were glad to observe that coupling of this reactant proceeds nicely to give **11** in 69% yield (Table 2, entry 7). Again, the reaction was regioselective at the C-5 position. Then, a heteroarene was employed successfully. From 4-bromoisoquinoline, **12** was isolated in 81% yield (Table 1, entry 8). Two di-*ortho*-substituted aryl bromides were also reacted with 1-methyl-3-acetylpyrrole. Both 9-bromoanthracene and 1-bromo-2-methylnaphthalene led to the target products **13** and **14** in good yields (Table 2, entries 9 and 10). On the other hand, from the less congested 3-bromoquinoline, **13** was only obtained in 58% yield due to some formation of the 2-arylated pyrrole (Table 2, entry 11). We also examined the reactivity of 3-bromonitrobenzene. Again, a poor regioselectivity was observed, and **14a** was only isolated in 33% yield (Table 2, entry 12).

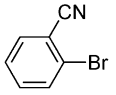
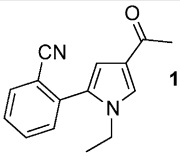
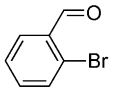
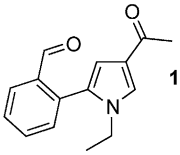
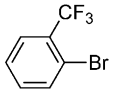
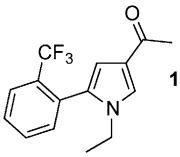
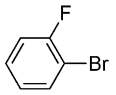
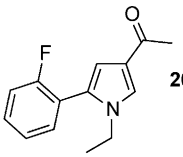
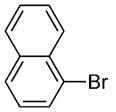
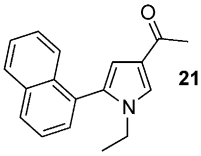
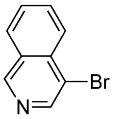
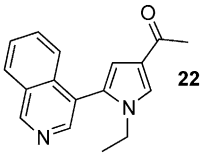
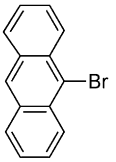
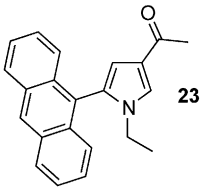
As expected, the reactivity of 1-methyl-3-acetylpyrrole and 1-ethyl-3-acetylpyrrole was found to be very similar. The reaction of 2-bromobenzonitrile, 1-bromonaphthalene or 4-bromoisoquinoline also gave regioselectively the C-5 arylated pyrroles **17**, **21** and **22** (Scheme 5, Table 3, entries 1, % and 6). With this pyrrole derivative, we also employed 2-bromobenzaldehyde, 2-bromobenzotrifluoride or 2-fluorobromobenzene as the coupling partners. In all cases, the desired C-5 arylation products **18**–**20** were obtained in high yields with complete regioselectivity (Table 3, entries 2–4).

Then, we studied the C-2 arylation with different aryl groups of two of the previously obtained 5-arylpyrroles to prepare 2,5-diarylpyrroles (Scheme 6 and

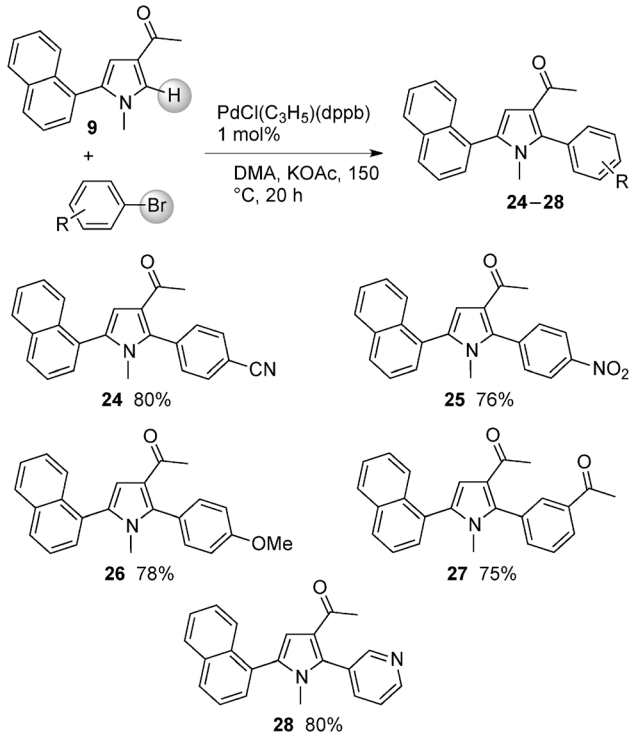


Scheme 5. Direct 5-arylations of 1-ethyl-3-acetylpyrrole with various aryl bromides.

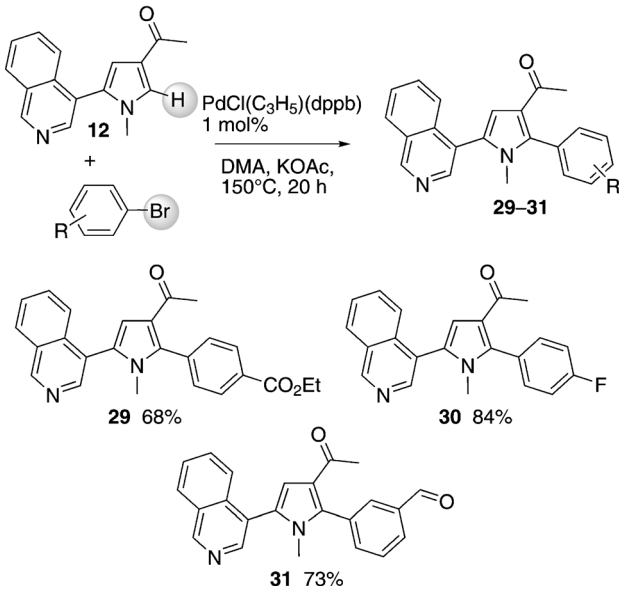
Table 3. Direct 5-arylations of 1-ethyl-3-acetylpyrrole with various aryl bromides (Scheme 5).[a]

Entry	Aryl bromide	Product	Yield [%]
1		 **17**	83
2		 **18**	80
3		 **19**	82
4		 **20**	74
5		 **21**	76
6		 **22**	79
7		 **23**	69

[a] *Reaction conditions:* $PdCl(C_3H_5)(dppb)$ (0.01 equiv.), aryl bromide (1 equiv.), 1-ethyl-3-acetylpyrrole (2 equiv.), KOAc (3 equiv.), DMA, 20 h, 150 °C.



Scheme 6. Direct 2-arylations of 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)ethanone **9** with aryl halides.



Scheme 7. Direct 2-arylations of 1-(5-isoquinolin-4-yl-1-methylpyrrol-3-yl)ethanone **12** with aryl halides.

Scheme 7). These reactions were performed using also 1 mol% $PdCl(C_3H_5)(dppb)$ as the catalyst and KOAc as the base. The electron-deficient *para*- or *meta*-substituted aryl bromides, 4-bromobenzonitrile, 4-bromonitrobenzene or 3-bromoacetophenone reacted with **9** and gave very selectively the desired products **24**, **25** and **27** in 75–80% yields. Even the electron-rich aryl bromide, 4-bromoanisole gave the expected product **26** in a high 78% yield. 3-Bromopyridine was also successfully employed to give **28** in 80% yield.

Similar results were obtained for the coupling of ethyl 4-bromobenzoate, 4-fluorobromobenzene or 3-bromobenzaldehyde with the 3-acetylpyrrole bearing an isoquinoline at C-5 **12** (Scheme 7). The desired products **29**–**31** were obtained in 68–84% yields.

In summary, we report herein the first regioselective palladium-catalysed direct C-5 arylations of C-3 substituted pyrrole derivatives with aryl halides. The influence of some reaction parameters on the regioselectivity was studied. While the influence of the electronic properties of the substituents on the aryl bromides appears to be relatively limited; on the other hand, their steric properties are important. Aryl bromides substituted at C-2 by a methyl, a cyano, a nitro, a formyl, a hydroxymethyl, a fluoro, a trifluoromethyl or a chloro gave regioselectively the 5-arylated pyrroles. We have also shown sequential transformations allowing the C-5 catalytic arylation and a C-2 different catalytic arylation leading to unsymmetrical 2,5-diarylated 3-acetylpyrroles. The major by-products of these reactions are AcOH/KBr instead of metallic salts using more classical coupling procedures. Moreover, no prior preparation of an organometallic derivative is required for these couplings, reducing the number of required steps to obtain these arylated pyrroles. As it has already been demonstrated that several useful functional groups on the pyrrole nitrogen atom, such as aryl, benzyl or SEM [2-(trimethylsilyl)-ethoxymethyl] are tolerated for such coupling,[6,11] this method should give access to several synthetically important pyrroles derivatives.

Experimental Section

General Remarks

All reactions were performed in Schlenk tubes under argon. DMA analytical grade was not distilled before use. Potassium acetate 99+ was used. Commercial aryl bromides and heteroaromatic derivatives were used without purification. ^1H (300 and 400 MHz), ^{13}C (75 and 100 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CDCl_3$ (^1H: 7.26 and ^{13}C: 77.0). Flash chromatography was performed on silica gel (230–400 mesh).

Preparation of the $PdCl(C_3H_5)(dppb)$ Catalyst[11]

An oven-dried 40-mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane were added, then the solution was stirred at room temperature for

twenty minutes. The solvent was removed under vacuum. The yellow powder was used without purification. ^{31}P NMR (81 MHz, $CDCl_3$): $\delta = 19.3$ (s).

General Procedure for the Synthesis of Compounds 1–31

As a typical experiment, the reaction of the aryl bromide (1 mmol), pyrrole derivative (1.5 or 2 mmol, see Tables) and KOAc (0.294 g, 3 mmol) at 150 °C during 20 h in DMA (4 mL) in the presence of $PdCl(C_3H_5)$(dppb) (6.08 mg, 0.01 mmol) under argon afforded the coupling product after evaporation of the solvent and purification on silica gel.

1-(1-Methyl-5-phenylpyrrol-3-yl)ethanone (1a): From bromobenzene (0.157 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **1a** was obtained as a brown oil; yield: 0.084 g (42%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.40$–7.22 (m, 6H), 6.56 (d, $J = 1.8$ Hz, 1H), 3.60 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 193.4$, 136.2, 132.0, 128.8, 128.6, 128.2, 127.7, 125.2, 109.0, 35.6, 27.0. elemental analysis: calcd. (%) for $C_{13}H_{13}NO$ (199.25): C 78.36, H 6.58; found: C 78.46, H 6.50.

The formation of 2-arylated pyrrole **1b** was also observed: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.50$–7.45 (m, 3H), 7.34 (d, $J = 7.8$ Hz, 2H), 6.68 (d, $J = 2.8$ Hz, 1H), 6.63 (d, $J = 2.8$ Hz, 1H), 3.39 (s, 3H), 2.06 (s, 3H).

The formation of 2,5-diarylated pyrrole **1c** was also observed: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.50$–7.35 (m, 10H), 6.74 (s, 1H), 3.34 (s, 3H), 2.09 (s, 3H).

4-(4-Acetyl-1-methylpyrrol-2-yl)benzonitrile (2a): From 4-bromobenzonitrile (0.182 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **2a** was obtained as a yellow solid; yield: 0.092 g (41%); mp 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.69$ (d, $J = 8.1$ Hz, 2H), 7.49 (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 1.5$ Hz, 1H), 6.72 (d, $J = 1.5$ Hz, 1H), 3.71 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.0$, 136.5, 134.1, 132.4, 129.7, 128.8, 125.6, 118.6, 111.1, 110.7, 36.0, 27.1; elemental analysis: calcd. (%) for $C_{14}H_{12}N_2O$ (224.26): C 74.98, H 5.39; found: C 75.04, H 5.49.

The formation of 2-arylated pyrrole **2b** was also observed (yellow solid; mp 148–150 °C): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.72$ (d, $J = 8.1$ Hz, 2H), 7.46 (d, $J = 8.1$ Hz, 2H), 6.68 (d, $J = 2.9$ Hz, 1H), 6.64 (d, $J = 2.9$ Hz, 1H), 3.43 (s, 3H), 2.26 (s, 3H).

The formation of 2,5-diarylated pyrrole **2c** was also observed (yellow solid; mp 188–190 °C): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.77$ (d, $J = 8.1$ Hz, 2H), 7.74 (d, $J = 8.1$ Hz, 2H), 7.55 (d, $J = 8.1$ Hz, 2H), 7.53 (d, $J = 8.1$ Hz, 2H), 6.79 (s, 1H), 3.39 (s, 3H), 2.29 (s, 3H).

3-(4-Acetyl-1-methylpyrrol-2-yl)benzonitrile (3a): From 3-bromobenzonitrile (0.182 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **3a** was obtained as a yellow solid; yield: 0.090 g (40%); mp 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.68$ (s, 1H), 7.65–7.60 (m, 2H), 7.56 (t, $J = 7.7$ Hz, 1H), 7.38 (d, $J = 1.6$ Hz, 1H), 6.70 (d, $J = 1.6$ Hz, 1H), 3.70 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 193.1$, 133.5, 133.3, 132.9, 131.9, 131.1, 129.6, 129.1, 125.5, 118.4, 113.0, 110.2, 35.7, 27.1; elemental analysis: calcd. (%) for $C_{14}H_{12}N_2O$ (224.26): C 74.98, H 5.39; found: C 75.14, H 5.40.

The formation of 2-arylated pyrrole **3b** was also observed (yellow solid; mp 105–106 °C): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.64$ (d, $J = 7.4$ Hz, 1H), 7.57 (s, 1H), 7.52 (t, $J = 7.7$ Hz, 1H), 7.49 (t, $J = 7.7$ Hz, 1H), 6.61 (d, $J = 3.0$ Hz, 1H), 6.58 (d, $J = 3.0$ Hz, 1H), 3.37 (s, 3H), 2.20 (s, 3H).

The formation of 2,5-diarylated pyrrole **3c** was also observed (yellow solid; mp 140–142 °C): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.70$–7.50 (m, 8H), 6.68 (s, 1H), 3.31 (s, 3H), 2.23 (s, 3H).

2-(4-Acetyl-1-methylpyrrol-2-yl)benzonitrile (4a): From 2-bromobenzonitrile (0.182 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **4a** was obtained as a yellow solid; yield: 0.179 g (80%); mp 118–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.70$ (d, $J = 8.0$ Hz, 1H), 7.59 (t, $J = 7.7$ Hz, 1H), 7.43 (t, $J = 7.7$ Hz, 1H), 7.37 (d, $J = 8.0$ Hz, 1H), 6.68 (s, 1H), 3.55 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.1$, 135.6, 133.4, 132.7, 131.5, 131.3, 128.8, 128.6, 125.5, 117.8, 113.4, 111.5, 35.2, 27.0; elemental analysis: calcd. (%) for $C_{14}H_{12}N_2O$ (224.26): C 74.98, H 5.39; found: C 75.16, H 5.20.

1-[1-Methyl-5-(2-nitrophenyl)pyrrol-3-yl]ethanone (5): From 1-bromo-2-nitrobenzene (0.202 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **5** was obtained as a brown oil; yield: 0.210 g (86%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.97$ (d, $J = 8.0$ Hz, 1H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.38 (d, $J = 7.5$ Hz, 1H), 7.30 (s, 1H), 6.48 (s, 1H), 3.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.2$, 149.5, 133.7, 132.9, 130.3, 129.9, 128.0, 126.7, 125.4, 124.5, 109.7, 34.6, 27.0; elemental analysis: calcd. (%) for $C_{13}H_{12}N_2O_3$ (244.25): C 63.93, H 4.95; found: C 63.99, H 4.81.

1-[5-(2-Diethoxymethylphenyl)-1-methylpyrrol-3-yl]ethanone (6): From 1-bromo-2-diethoxymethylbenzene (0.259 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **6** was obtained as a brown oil; yield: 0.199 g (66%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.67$ (d, $J = 7.7$ Hz, 1H), 7.39 (t, $J = 7.4$ Hz, 1H), 7.30 (t, $J = 7.4$ Hz, 1H), 7.28 (s, 1H), 7.14 (d, $J = 7.5$ Hz, 1H), 6.46 (s, 1H), 3.50 (m, 2H), 3.33 (s, 3H), 3.27 (m, 2H), 2.35 (s, 3H), 1.06 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.7$, 139.6, 133.2, 131.1, 130.9, 129.0, 128.1, 127.1, 126.4, 124.9, 109.4, 100.1, 62.8, 34.9, 26.9, 14.9; elemental analysis: calcd. (%) for $C_{18}H_{23}NO_3$ (301.38): C 71.73, H 7.69; found: C 71.50, H 7.59.

1-[5-(2,4-Difluorophenyl)-1-methylpyrrol-3-yl]ethanone (7): From 1-bromo-2,4-difluorobenzene (0.193 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **7** was obtained as a yellow solid; yield: 0.183 g (78%); mp 112–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$ (s, 1H), 7.24 (dd, $J = 15.0$, 8.3 Hz, 1H), 6.92–6.80 (m, 2H), 6.54 (s, 1H), 3.49 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.2$, 163.0 (dd, $J = 251.2$, 11.9 Hz), 160.1 (dd, $J = 249.5$, 11.7 Hz), 133.1 (dd, $J = 9.5$, 4.0 Hz), 128.9, 128.1, 125.4, 116.0 (dd, $J = 15.1$, 4.0 Hz), 111.6 (dd, $J = 20.7$, 4.0 Hz), 110.5, 104.3 (t, $J = 26.2$ Hz), 35.0, 26.9; elemental analysis: calcd. (%) for $C_{13}H_{11}F_2NO$ (235.23): C 66.38, H 4.71; found: C 66.50, H 4.58.

1-[5-(2-Chlorophenyl)-1-methylpyrrol-3-yl]ethanone (8): From 1-bromo-2-chlorobenzene (0.191 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **8** was obtained as a yellow oil; yield: 0.186 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.41$ (d, $J = 7.6$ Hz, 1H), 7.32–7.23 (m, 4H), 6.51 (s, 1H), 3.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.3$, 135.0, 132.9, 132.8, 131.2, 130.1, 129.7, 127.4, 126.8, 125.2, 110.0, 34.9, 27.0; elemental analysis:

calcd. (%) for $C_{13}H_{12}ClNO$ (233.69): C 66.81, H 5.18; found: C 66.59, H 5.40.

1-(1-Methyl-5-naphthalen-1-ylpyrrol-3-yl)ethanone (9): From 1-bromonaphthalene (0.207 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **9** was obtained as a brown oil; yield: 0.197 g (79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.5 Hz, 1H), 7.60–7.40 (m, 5H), 6.71 (d, J = 1.5 Hz, 1H), 3.41 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.5, 133.8, 133.6, 133.0, 129.6, 129.1, 129.0, 128.4, 127.4, 126.7, 126.2, 125.6, 125.3, 125.2, 110.2, 34.9, 27.1; elemental analysis: calcd. (%) for $C_{17}H_{15}NO$ (249.31): C 81.90, H 6.06; found: C 81.99, H 6.14.

1-(1-Methyl-5-*o*-tolylpyrrol-3-yl)ethanone (10): From 1-bromo-2-methylbenzene (0.171 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol ol), **10** was obtained as a brown oil; yield: 0.156 g (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.10 (m, 5H), 6.42 (s, 1H), 3.33 (s, 3H), 2.35 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.6, 138.2, 134.9, 131.6, 131.1, 130.2, 128.6, 126.9, 125.7, 125.1, 108.8, 34.6, 26.9, 19.8; elemental analysis: calcd. (%) for $C_{14}H_{15}NO$ (213.28): C 78.84, H 7.09; found: C 79.08, H 7.17.

1-[5-(2-Hydroxymethylphenyl)-1-methylpyrrol-3-yl]ethanone (11): From (2-bromophenyl)-methanol (0.187 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **11** was obtained as a yellow oil; yield: 0.158 g (69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.31–7.24 (m, 2H), 7.15 (d, J = 7.4 Hz, 1H), 6.46 (d, J = 1.7 Hz, 1H), 4.46 (s, 2H), 3.35 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 140.9, 133.4, 131.2, 130.4, 129.2, 128.3, 127.5, 127.4, 125.1, 109.4, 63.0, 34.9, 27.0; elemental analysis: calcd. (%) for $C_{14}H_{15}NO_2$ (229.27): C 73.34, H 6.59; found: C 73.45, H 6.69.

1-(5-Isoquinolin-4-yl-1-methylpyrrol-3-yl)ethanone (12): From 4-bromoisoquinoline (0.208 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **12** was obtained as a brown oil; yield: 0.202 g (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.23 (bs, 1H), 8.42 (bs, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.70–7.50 (m, 3H), 7.41 (s, 1H), 6.67 (s, 1H), 3.37 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 153.0, 144.3, 135.3, 131.1, 130.1, 128.1 (m), 127.9, 127.5, 125.4, 124.5, 123.2, 111.4, 35.1, 27.0; elemental analysis: calcd. (%) for $C_{16}H_{14}N_2O$ (250.30): C 76.78, H 5.64; found: C 76.89, H 5.51.

1-(5-Anthracen-9-yl-1-methylpyrrol-3-yl)ethanone (13): From 9-bromoanthracene (0.257 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **13** was obtained as a brown solid; yield: 0.218 g (73%); mp 140–142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.58 (s, 1H), 8.07 (d, J = 9.5 Hz, 2H), 7.69 (d, J = 9.5 Hz, 2H), 7.60 (s, 1H), 7.53 (t, J = 7.2 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 6.82 (s, 1H), 3.23 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.5, 132.1, 131.3, 131.1, 128.6, 128.4, 127.3, 126.4, 126.0, 125.9, 125.5, 125.4, 111.9, 34.7, 27.2; elemental analysis: calcd. (%) for $C_{21}H_{17}NO$ (299.37): C 84.25, H 5.72; found: C 84.35, H 5.60.

1-[1-Methyl-5-(2-methylnaphthalen-1-yl)-pyrrol-3-yl]ethanone (14): From 1-bromo-2-methylnaphthalene (0.221 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **14** was obtained as a yellow oil; yield: 0.200 g (76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J = 8.6 Hz, 2H), 7.39 (d, J = 1.7 Hz, 1H), 7.38–7.26 (m, 4H), 6.52 (d, J = 1.7 Hz, 1H), 3.17 (s, 3H), 2.39 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.6, 137.0, 134.1, 132.2, 131.9, 128.9, 128.3, 127.9, 127.6, 126.9, 126.7, 125.4, 125.3, 125.2, 110.2, 34.5, 27.1, 20.5; elemental analysis: calcd. (%) for $C_{18}H_{17}NO$ (263.33): C 82.10, H 6.51; found: C 82.19, H 6.40.

1-(1-Methyl-5-quinolin-3-ylpyrrol-3-yl)ethanone (15): From 3-bromoquinoline (0.208 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **15** was obtained as a yellow oil; yield: 0.145 g (58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 78.92 (s, 1H), 8.11–8.07 (m, 2H), 7.79 (d, J = 8.1 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.36 (d, J = 1.4 Hz, 1H), 6.74 (d, J = 1.4 Hz, 1H), 3.69 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 150.3, 147.0, 134.9, 132.5, 129.9, 129.3, 129.1, 127.9, 127.4, 125.7, 125.3, 110.5, 35.8, 27.1; elemental analysis: calcd. (%) for $C_{16}H_{14}N_2O$ (250.30): C 76.78, H 5.64; found: C 76.62, H 5.40.

1-[1-Methyl-5-(3-nitrophenyl)pyrrol-3-yl]ethanone (16a): From 1-bromo-3-nitrobenzene (0.202 g, 1 mmol) and 1-methyl-3-acetylpyrrole (0.247 g, 2 mmol), **16a** was obtained as a yellow solid; yield: 0.081 g (33%); mp 208–210 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (s, 1H), 8.14 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.32 (d, J = 1.2 Hz, 1H), 6.67 (d, J = 1.2 Hz, 1H), 3.66 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.1, 148.4, 134.4, 133.6, 133.4, 129.7, 129.3, 125.5, 123.1, 122.4, 110.4, 35.8, 27.1; elemental analysis: calcd (%) for $C_{13}H_{12}N_2O_3$ (244.25): C 63.93, H 4.95; found: C 63.68, H 4.99.

Compound **14b** was also isolated: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, J = 9.0 Hz, 1H), 8.15 (s, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.55 (t, J = 7.9 Hz, 1H), 6.63 (d, J = 2.8 Hz, 1H), 6.59 (d, J = 2.8 Hz, 1H), 3.40 (s, 3H), 2.23 (s, 3H).

Compound **14c** was also isolated: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30–8.20 (m, 4H), 7.80–7.65 (m, 2H), 7.64–7.58 (m, 2H), 6.75 (s, 1H), 3.38 (s, 3H), 2.27 (s, 3H).

2-(4-Acetyl-1-ethylpyrrol-2-yl)-benzonitrile (17): From 2-bromobenzonitrile (0.182 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **17** was obtained as a yellow oil; yield: 0.197 g (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, J = 7.6 Hz, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.50–7.30 (m, 3H), 6.64 (s, 1H), 3.82 (q, J = 7.3 Hz, 2H), 2.36 (s, 3H), 1.24 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.3, 135.9, 133.4, 132.7, 131.4, 130.8, 128.7, 126.5, 125.7, 117.8, 113.6, 111.6, 42.4, 26.9, 16.2; elemental analysis: calcd. (%) for $C_{15}H_{14}N_2O$ (238.28): C 75.61, H 5.92; found: C 75.43, H 5.99.

2-(4-Acetyl-1-ethylpyrrol-2-yl)benzaldehyde (18): From 2-bromobenzaldehyde (0.185 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **18** was obtained as a brown oil; yield: in 0.193 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.88 (s, 1H), 8.01 (d, J = 7.7 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.46 (s, 1H), 7.39 (d, J = 7.5 Hz, 1H), 6.59 (s, 1H), 3.78 (q, J = 7.3 Hz, 2H), 2.41 (s, 3H), 1.23 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.3, 191.6, 135.3, 135.1, 133.7, 131.8, 130.0, 129.1, 127.9, 126.1, 125.5, 112.2, 42.5, 27.1, 16.3; elemental analysis: calcd. (%) for $C_{15}H_{15}NO_2$ (241.29): C 74.67, H 6.27; found: C 74.49, H 6.20.

1-[1-Ethyl-5-(2-trifluoromethylphenyl)pyrrol-3-yl]ethanone (19): From 1-bromo-2-trifluoromethylbenzene (0.225 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **19** was obtained as a brown oil; yield: 0.230 g (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, J = 7.6 Hz, 1H), 7.53 (t, J =

7.6 Hz, 1H), 7.48 (t, J=7.6 Hz, 1H), 7.34 (s, 1H), 7.29 (d, J=7.6 Hz, 1H), 6.48 (s, 1H), 3.62 (q, J=7.3 Hz, 2H), 2.36 (s, 3H), 1.19 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.5, 133.3, 131.3, 130.8 (q, J=29.4 Hz), 130.7, 130.5, 128.9, 126.3 (q, J=5.6 Hz), 125.2, 124.9, 123.6 (q, J=273.0 Hz), 110.6, 42.3, 26.7, 15.5; elemental analysis: calcd. (%) for $C_{15}H_{14}F_3NO$ (281.27): C 64.05, H 5.02; found: C 64.18, H 5.00.

1-[1-Ethyl-5-(2-fluorophenyl)pyrrol-3-yl]ethanone (20): From 1-bromo-2-fluorobenzene (0.175 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **20** was obtained as a brown oil; yield: 0.171 g (74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38 (d, J=1.1 Hz, 1H), 7.32 (dd, J=12.9, 5.8 Hz, 1H), 7.26 (t, J=7.4 Hz, 1H), 7.14 (t, J=7.5 Hz, 1H), 7.08 (t, J=7.5 Hz, 1H), 6.53 (s, 1H), 3.79 (q, J=7.3 Hz, 2H), 2.36 (s, 3H), 1.25 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.7, 160.4 (d, J=247.2 Hz), 132.7 (d, J=3.0 Hz), 130.6 (d, J=8.1 Hz), 129.5, 126.1, 125.9, 124.6 (d, J=3.7 Hz), 120.4 (d, J=5.4 Hz), 116.1 (d, J=22.0 Hz), 110.8, 42.9, 27.3, 16.4; elemental analysis: calcd (%) for $C_{14}H_{14}FNO$ (231.27): C 72.71, H 6.10; found: C 72.47, H 6.24.

1-(1-Ethyl-5-naphthalen-1-ylpyrrol-3-yl)ethanone (21): From 1-bromonaphthalene (0.207 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **21** was obtained as a brown oil; yield: 0.200 g (76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.85–7.75 (m, 2H), 7.54 (d, J=8.5 Hz, 1H), 7.50–7.30 (m, 5H), 6.57 (d, J=1.5 Hz, 1H), 3.58 (bs, 2H), 3.41 (s, 3H), 1.08 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 133.6, 133.2, 133.1, 129.8, 129.1, 129.0, 128.3, 126.7, 126.2, 125.7, 125.5, 125.3, 125.2, 110.5, 42.6, 27.1, 16.5; elemental analysis: calcd. (%) for $C_{18}H_{17}NO$ (263.33): C 82.10, H 6.51; found: C 82.07, H 6.68.

1-(1-Ethyl-5-isoquinolin-4-ylpyrrol-3-yl)ethanone (22): From 4-bromoisoquinoline (0.208 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **22** was obtained as a brown oil; yield: 0.209 g (79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ= 9.27 (bs, 1H), 8.46 (bs, 1H), 8.02 (d, J=8.0 Hz, 1H), 7.70–7.55 (m, 3H), 7.52 (s, 1H), 6.68 (s, 1H), 3.69 (q, J=7.3 Hz, 2H), 2.43 (s, 3H), 1.17 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.6, 153.4, 144.8, 135.9, 131.4, 129.6, 128.5, 128.2, 127.9, 126.3, 126.0, 124.8, 123.7, 111.8, 42.9, 27.3, 16.7; elemental analysis: calcd. (%) for $C_{17}H_{16}N_2O$ (264.32): C 77.25, H 6.10; found: C 77.29, H 6.34.

1-(5-Anthracen-9-yl-1-ethylpyrrol-3-yl)ethanone (23): From 9-bromoanthracene (0.257 g, 1 mmol) and 1-ethyl-3-acetylpyrrole (0.275 g, 2 mmol), **23** was obtained as a white solid; yield: 0.216 g (69%); mp 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.48 (s, 1H), 7.98 (d, J=8.5 Hz, 2H), 7.64 (d, J=8.5 Hz, 2H), 7.60 (s, 1H), 7.41 (t, J=7.2 Hz, 2H), 7.35 (t, J=7.2 Hz, 2H), 6.68 (s, 1H), 3.41 (q, J= 7.3 Hz, 2H), 2.44 (s, 3H), 0.97 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.6, 132.2, 131.3, 130.5, 128.5, 128.4, 126.4, 126.1, 126.0, 125.7, 125.4, 125.3, 111.9, 42.1, 26.7, 16.4; elemental analysis: calcd. (%) for $C_{22}H_{19}NO$ (313.39): C 84.31, H 6.11; found: C 84.50, H 6.28.

4-(3-Acetyl-1-methyl-5-naphthalen-1-ylpyrrol-2-yl)benzonitrile (24): From 4-bromobenzonitrile (0.182 g, 1 mmol) and 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)-ethanone **9** (0.373 g, 1.5 mmol), **24** was obtained as a yellow solid; yield: 0.280 g (80%); mp 206–208 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.88–7.78 (m, 2H), 7.69 (d, J=8.2 Hz, 2H), 7.65–7.60 (m, 1H), 7.50 (d, J=8.2 Hz, 2H), 7.48–7.40 (m, 4H), 6.68 (s, 1H), 3.04 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.5, 137.3, 135.6, 133.8, 133.7, 133.0, 132.0, 131.7, 129.6, 129.4, 129.2, 128.6, 127.0, 126.3, 125.4, 125.3, 123.0, 118.6, 112.3, 112.0, 32.8, 28.7; elemental analysis: calcd. (%) for $C_{24}H_{18}N_2O$ (350.41): C 82.26, H 5.18; found: C 82.06, H 5.47.

1-[1-Methyl-5-naphthalen-1-yl-2-(4-nitrophenyl)pyrrol-3-yl]ethanone (25): From 1-bromo-4-nitrobenzene (0.202 g, 1 mmol) and 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)-ethanone **9** (0.373 g, 1.5 mmol), **25** was obtained as a yellow solid; yield: 0.281 g (76%); mp 182–184 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.23 (d, J=8.8 Hz, 2H), 7.90–7.80 (m, 2H), 7.65–7.60 (m, 1H), 7.57 (d, J=8.8 Hz, 2H), 7.50–7.40 (m, 4H), 6.67 (s, 1H), 3.01 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.6, 147.7, 139.2, 135.2, 135.1, 134.0, 133.7, 133.0, 131.9, 129.4, 129.3, 128.6, 127.0, 126.3, 125.4, 125.3, 123.4, 123.1, 112.1, 32.7, 28.7; elemental analysis: calcd. (%) for $C_{23}H_{18}N_2O_3$ (370.40): C 74.58, H 4.90; found: C 74.38, H 4.99.

1-[2-(4-Methoxyphenyl)-1-methyl-5-naphthalen-1-ylpyrrol-3-yl]ethanone (26): From 4-bromoanisole (0.187 g, 1 mmol) and 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)-ethanone **9** (0.373 g, 1.5 mmol), **26** was obtained as a brown oil; yield: 0.277 g (78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.98–7.78 (m, 2H), 7.85–7.75 (m, 1H), 7.60–7.50 (m, 4H), 7.44 (d, J=8.2 Hz, 2H), 7.06 (d, J=8.2 Hz, 2H), 6.84 (s, 1H), 3.90 (s, 3H), 3.13 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=194.1, 160.2, 138.6, 133.7, 133.1, 132.6, 132.0, 130.3, 129.1, 129.0, 128.4, 126.7, 126.1, 125.8, 125.3, 124.7, 123.4, 114.0, 111.0, 55.2, 32.5, 28.8; elemental analysis: calcd. (%) for $C_{24}H_{21}NO_2$ (355.43): C 81.10, H 5.96; found: C 81.19, H 6.08.

1-[2-(3-Acetylphenyl)-1-methyl-5-naphthalen-1-ylpyrrol-3-yl]ethanone (27): From 3-bromoacetophenone (0.199 g, 1 mmol) and 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)ethanone **9** (0.373 g, 1.5 mmol), **27** was obtained as a yellow oil; yield: 0.275 g (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.08 (s, 1H), 8.03 (d, J=8.0 Hz, 1H), 7.95–7.90 (m, 2H), 7.76–7.67 (m, 2H), 7.65–7.50 (m, 5H), 6.78 (s, 1H), 3.11 (s, 3H), 2.65 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 197.5, 193.7, 137.3, 136.9, 135.5, 133.7, 133.2, 133.1, 133.0, 130.5, 129.9, 129.2, 129.1, 128.7, 128.6, 128.5, 126.9, 126.2, 125.6, 125.3, 123.0, 111.5, 32.7, 28.8, 26.6; elemental analysis: calcd. (%) for $C_{25}H_{21}NO_2$ (367.44): C 81.72, H 5.76; found: C 81.89, H 5.89.

1-(1-Methyl-5-naphthalen-1-yl-2-pyridin-3-ylpyrrol-3-yl)ethanone (28): From 3-bromopyridine (0.158 g, 1 mmol) and 1-(1-methyl-5-naphthalen-1-ylpyrrol-3-yl)-ethanone **9** (0.373 g, 1.5 mmol), **28** was obtained as a yellow oil; yield: 0.261 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.80–8.60 (m, 2H), 7.93 (d, J=8.0 Hz, 1H), 7.91 (d, J=8.0 Hz, 1H), 7.85 (d, J=8.0 Hz, 1H), 7.74–7.68 (m, 1H), 7.58–7.50 (m, 4H), 7.45–7.40 (m, 1H), 6.78 (s, 1H), 3.13 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.6, 170.5, 150.9, 149.5, 138.4, 134.1, 133.5, 133.4, 132.9, 129.5, 129.1, 128.5, 128.4, 126.8, 126.1, 125.4, 125.2, 123.3, 123.0, 111.7, 32.8, 28.7; elemental analysis: calcd. (%) for $C_{22}H_{18}N_2O$ (326.39): C 80.96, H 5.56; found: C 81.09, H 5.41.

Ethyl 4-(3-acetyl-5-isoquinolin-4-yl-1-methylpyrrol-2-yl)-benzoate (29): From ethyl 4-bromobenzoate (0.229 g, 1 mmol) and 1-(5-isoquinolin-4-yl-1-methylpyrrol-3-yl)etha-

none **12** (0.357 g, 1.5 mmol), **29** was obtained as a yellow solid; yield: 0.270 g (68%); mp 90–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.24$ (bs, 1H), 8.50 (bs, 1H), 8.10 (d, $J = 8.2$ Hz, 2H), 7.99 (d, $J = 8.0$ Hz, 1H), 7.75–7.55 (m, 3H), 7.49 (d, $J = 8.2$ Hz, 2H), 6.77 (s, 1H), 4.33 (q, $J = 7.1$ Hz, 2H), 3.08 (s, 3H), 2.15 (s, 3H), 1.33 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.6$, 166.0, 153.2, 144.6, 137.8, 136.8, 135.4, 131.4, 130.8, 129.6, 128.3, 128.1, 127.7, 124.6, 123.6, 123.5, 112.6, 61.2, 33.1, 28.9, 14.3; elemental analysis: calcd. (%) for $C_{25}H_{22}N_2O_3$ (398.45): C 75.36, H 5.57; found: C 75.09, H 5.41.

1-[2-(4-Fluorophenyl)-5-isoquinolin-4-yl-1-methylpyrrol-3-yl]ethanone (30): From 1-bromo-4-fluorobenzene (0.175 g, 1 mmol) and 1-(5-isoquinolin-4-yl-1-methylpyrrol-3-yl)-ethanone **12** (0.357 g, 1.5 mmol), **30** was obtained as a yellow solid; yield: 0.289 g (84%); mp 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.23$ (bs, 1H), 8.48 (bs, 1H), 7.98 (d, $J = 8.0$ Hz, 1H), 7.75–7.50 (m, 3H), 7.45–7.35 (m, 2H), 7.25–7.10 (m, 2H), 6.76 (s, 1H), 3.06 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 193.6$, 162.9 (d, $J = 248.8$ Hz), 153.0, 144.5, 137.9, 135.4, 132.5 (d, $J = 8.0$ Hz), 131.2, 129.1, 128.2, 128.1 (d, $J = 3.2$ Hz), 128.0, 127.6, 124.5, 123.7, 123.4, 115.6 (d, $J = 22.3$ Hz), 112.2, 32.8, 28.8; elemental analysis: calcd. (%) for $C_{22}H_{17}FN_2O$ (344.38): C 76.73, H 4.98; found: C 76.60, H 4.76.

3-(3-Acetyl-5-isoquinolin-4-yl-1-methylpyrrol-2-yl)benzaldehyde (31): From 3-bromobenzaldehyde (0.185 g, 1 mmol) and 1-(5-isoquinolin-4-yl-1-methylpyrrol-3-yl)ethanone **12** (0.357 g, 1.5 mmol), **31** was obtained as a brown oil; yield: 0.258 g (73%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 10.09$ (s, 1H), 9.37 (bs, 1H), 8.62 (bs, 1H), 8.10 (d, $J = 8.2$ Hz, 1H), 8.00–7.95 (m, 2H), 7.85–7.65 (m, 5H), 6.84 (s, 1H), 3.16 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 196$, 191.8, 153.3, 144.7, 137.2, 136.8, 136.5, 135.6, 131.6, 131.4, 130.1, 129.6, 129.2, 128.4, 128.2, 127.8, 124.6, 123.7, 123.3, 112.7, 33.0, 28.8; elemental analysis: calcd. (%) for $C_{23}H_{18}N_2O_2$ (354.40): C 77.95, H 5.12; found: C 77.78, H 5.31.

Acknowledgements

We are grateful to the "Chinese Scholarship Council" for a grant to Z. L. and to the "Jinan University short-term overseas research program" for a grant to X. Y. We thank CNRS and "Rennes Metropole" for providing financial support.

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Palladium-Catalysed Regioselective Sequential C-5 and C-2 Direct Arylations of 3-Acetylpyrroles with Aryl Bromides

Adv. Synth. Catal. **2013**, *355*, 1 – 11

Yijing Xu, Liqin Zhao, Yiqun Li,* Henri Doucet*