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Synthesis of *N*-Heterocyclic Carbene-Palladium-PEPPSI Complexes and Their Catalytic Activity in The Direct C-H Bond Activation

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ABSTRACT: A series of benzimidazolium salts having their two nitrogen atoms substituted by bulky groups have been synthesized. The benzimidazolium salts were readily converted into the corresponding palladium-NHC-PEPPSI complexes with general formula [$PdBr_2$(NHC)(Py)], (NHC = *N*-heterocyclic carbene; PEPPSI = pyridine-enhanced precatalyst preparation, stabilisation, and initiation). The structures of all new compounds were characterised by NMR, IR spectroscopy and microanalysis techniques, which support the proposed structures. The molecular structure of complex **2g** was determined by single-crystal X-ray diffraction study. Next, the palladium-NHC-PEPPSI complexes were used as catalysts in the direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by aryl halides. These complexes exhibited moderate to high catalytic activities and gave C-H activation selectively at the C5-position of 1-methylpyrrole-2-carboxaldehyde. Both electron-donating and electron-withdrawing substituents were well tolerated with catalytic systems based on these complexes, even non-activated aryl chlorides such as chlorobenzene or 4-chlorotoluene were coupled with pyrrole in moderate yields.

Keywords: *N*-heterocyclic carbene, benzimidazolium salts, PEPPSI-type palladium-NHC complexes, pyrroles, direct arylation.

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1. Introduction

In recent years, NHCs have become a very important class of ligands in organometallic chemistry and catalysis [1-3]. The strong σ-donating but poor π-accepting ability of these NHCs lead to the formation of many stable metal-carbene complexes. For this reason, the metal-NHC complexes have been widely used as highly reactive and rather selective catalysts for numerous chemical transformations [4-13]. Metal-NHCs have also been utilized extensively in medicinal applications [14-19]. Nowadays, many research groups around the world are currently focusing on metal-NHC complexes for various purposes.

Palladium-catalyzed bond-forming reactions are one of the most common tools synthetic chemists employ, in industry as well as in academia [20-23]. The strong palladium-NHC bonds contribute to the high stability of the active species, even at low catalyst loading and high temperatures. With a number of commercially available, stable, user-friendly, and powerful palladium-NHC catalysts, the goal of a universal cross-coupling catalyst is within reach. In particular, palladium-catalyzed cross-coupling reactions are now widely used to form C-C and C-N bond formation. Such processes include the Suzuki-Miyaura [24], Mizoroki-Heck [25], Negishi [26], Hiyama [27], Sonogashira [28], amination [29], and arylation of arenes reactions [30,31], often involving coupling of an aryl halide with a nucleophilic parthner.

Pyrrole is a very important backbone that is often present in the pharmaceuticals and biologically active compounds. As selected examples, Lipitor is the leading cholesterol lowering drug [32], Norbinaltorphimine is an opioid antagonist used in scientific research [33], Tanaproget is a progesterone-receptor agonist [34], Dopamine antagonist is a type of drug which blocks dopamine receptors by receptor antagonism [35], (Figure 1). Considering the importance of pyrroles in the pharmaceutical industry, straightforward and eco-friendly preparation of these compounds still represents a challenging task for chemists.

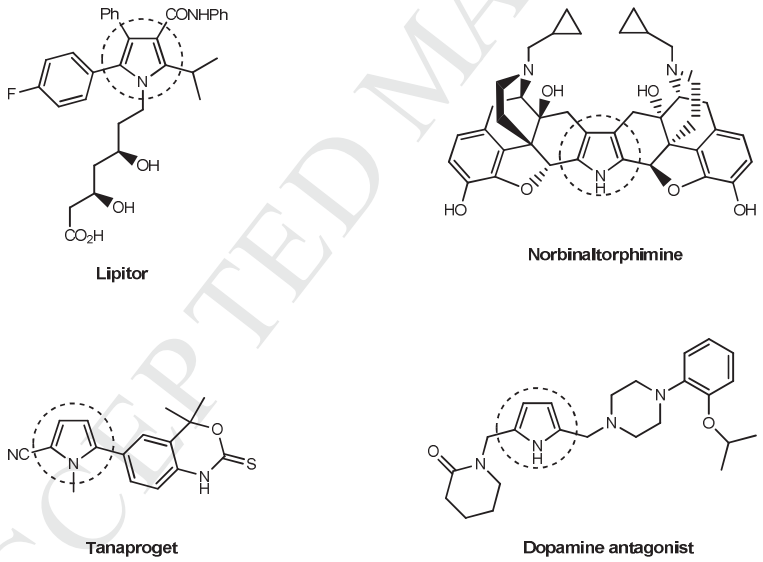
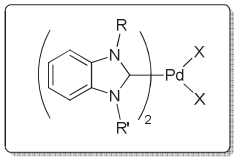


Figure 1. Examples of biologically active pyrrole derivatives.

The palladium-catalyzed direct arylation of pyrroles by a C-H bond activation using aryl halides has met great success in recent years [36]. Such arylations are known to occur preferentially at the *α*-positions to the nitrogen atom following the typical reactivity profiles of the pyrrole ring. Thus, under direct arylation conditions unsubstituted pyrroles react at C2- and(or) C5-position.

Ohta and co-workers reported that the direct C2- or C5-arylation of several heteroaromatics with aryl halides through C-H bond activation proceeds in moderate to good yields using [$Pd(PPh_3)_4$] as catalyst [37]. Since these exciting results, the palladium-catalyzed direct arylation of various heteroaromatics with aryl halides has proved to be a powerful method for the synthesis of a wide variety of arylated heterocycles [38]. In this connection, recently we have prepared novel palladium-bis(NHC) complexes and have used they as effective catalysts in the direct arylation of pyrrole

derivatives with aryl chlorides [39]. The general structure of palladyum-bis(NHC) complexes we used is shown in Scheme 1.



R =	$CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =**	$CH_2CH_2OCH_3$	**X =**	Br
R =	$CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =**	$CH_2C_6H_2(OCH_3)_3$-3,4,5	**X =**	Br
R =	$CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =**	$CH_2C_6H_3(C(CH_3)_3)$-3,5	**X =**	Br
R =	$CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =**	$CH_2C_6(CH_3)_5$-2,3,4,5,6	**X =**	Cl
R =	$CH_2C_6H_2(CH_3)_3$-2,4,6	**R' =**	$CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =**	Br
R =	$CH_2C_6H_4(CH_3)$-4	**R' =**	$CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =**	Cl
R =	$CH_2C_6H_4(OCH_3)$-3	**R' =**	$CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =**	Cl
R =	$CH_2C_6H_4(CH_3)$-4	**R' =**	$CH(C_6H_5)_2$	**X =**	Br
R =	$CH_2C_6H_5$	**R' =**	$CH_2CH_2(CHO_2CH_2CH_2)$	**X =**	Br

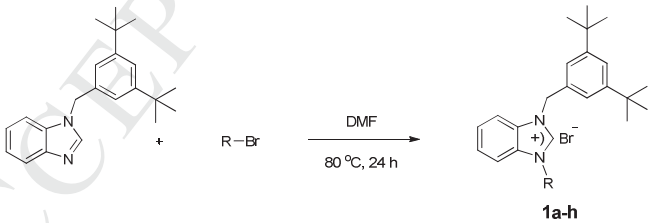
Scheme 1. General structure of recently reported palladium-bis(NHC) complexes.

Up to now, examples of palladium-catalyzed direct arylations of pyrroles by using aryl halides have been reported [36], but no reactions were found using palladium-NHC-PEPPSI catalysts in the literature. For this reason, we synthesized a series of new palladium-NHC-PEPPSI complexes with the general formula $[PdBr_2(NHC)(Py)]$, (**2a-h**). All new palladium-NHC-PEPPSI complexes were characterized by ^1H NMR, ^{13}C NMR, IR spectroscopy and elemental analysis techniques. Next, palladium-NHC-PEPPSI complexes were tested for direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde with aryl bromides and aryl chlorides. The reactive C2-position of pyrrole was blocked in order to maximize the yields of the monoarylated products.

2. Results and discussion

2.1. Synthesis of benzimidazolium salts

The benzimidazolium salts (**1a-h**) have already been reported in the literature [40]. These salts were prepared according to general reaction pathway depicted in Scheme 2. The structures of the salts were determined by their characteristic spectroscopic data and elemental analyses. The results are consistent with the literature [40].



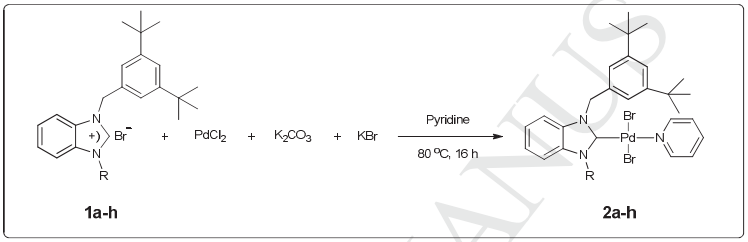
1a-h

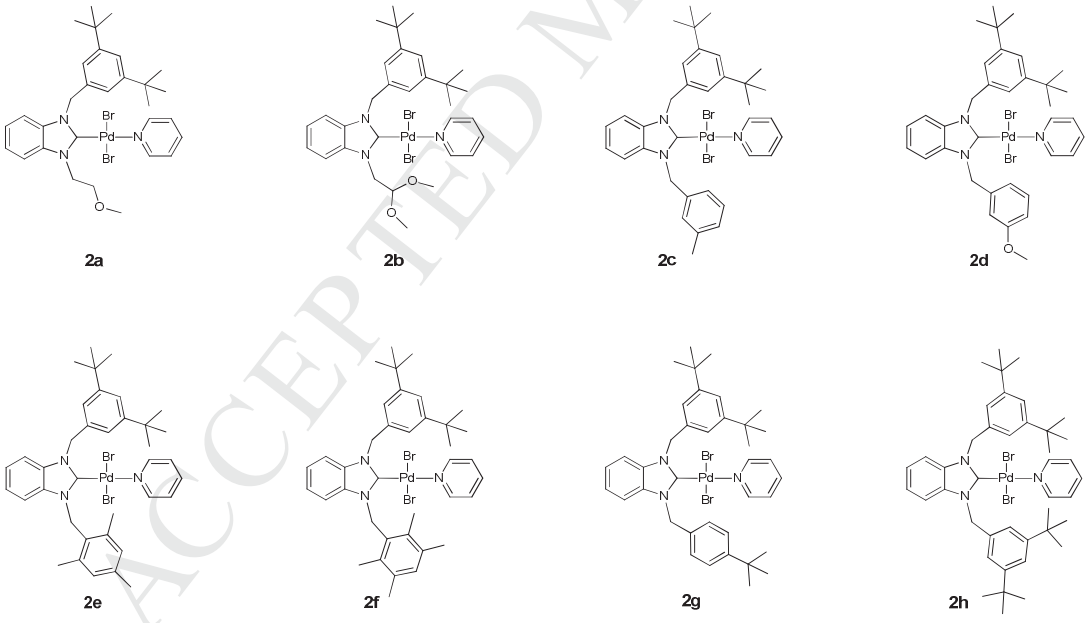
1a	**R =**	$CH_2CH_2OCH_3$
1b	**R =**	$CH_2CH(OCH_3)_2$
1c	**R =**	$CH_2C_6H_5$
1d	**R =**	$CH_2C_6H_4(OCH_3)$-3
1e	**R =**	$CH_2C_6H_2(CH_3)_3$-2,4,6
1f	**R =**	$CH_2C_6H(CH_3)_4$-2,3,5,6
1g	**R =**	$CH_2C_6H_4(C(CH_3)_3)$-4
1h	**R =**	$CH_2C_6H_3(C(CH_3)_3)$-3,5

Scheme 2. Synthesis of the benzimidazolium salts (**1a-h**).

2.2. Synthesis of palladium-NHC-PEPPSI complexes

The general procedure for the preparation of PEPPSI-type palladium-NHC complexes (**2a-h**) according to the method reported by Organ is shown in Scheme 3 [41]. Benzimidazolium salts (**1a-h**) were incorporated into the PEPPSI-type palladium-NHC complexes (**2a-h**) by reaction with $PdCl_2$ in refluxing pyridine in the presence of K_2CO_3 as a base and a large excess of KBr for 16 h. For the ^{1}H NMR spectra of the palladium-NHC-PEPPSI complexes (**2a-h**), sharp peaks in the lower field region belonging to the acidic imino proton of benzimidazolium salts (NC*H*N) were not observed between δ = 10.0-12.0 ppm. Similarly, in the ^{13}C NMR spectra, imino carbon of benzimidazolium salts (NCHN) were not observed between δ = 150-155 ppm. In the ^{1}H NMR and ^{13}C NMR spectra of the complexes **2a-h**, loss of the the characteristic peak of the acidic imino proton (NC*H*N) and imino carbon (NCHN), signal suggests the formation of the palladium-NHC-PEPPSI complexes. In addition, the characteristic carbenic carbons in compounds **2a-h** appeared in the ^{13}C NMR spectra as deshielded singlets at 163.1, 162.7, 164.2, 164.1, 163.8, 162.8, 164.1 and 163.1 ppm, respectively. The IR data also clearly indicated the presence of (CN) vibration at 1412, 1416, 1411, 1410, 1410, 1416, 1414 and 1411 cm^{-1} for **2a-h**. The formation of carbenes is correlated by a shift of the (CN) vibration from 1551-1564 cm^{-1} in the benzimidazolium salts to 1410-1416 cm^{-1} in the coordinated carbenes [40].





Scheme 3. Synthesis of the palladium-NHC-PEPPSI complexes (**2a-h**).

*2.3. Structural characterization of complex **2g***

Single crystals of complex **2g** suitable for diffraction study were obtained by slow diffusion of *n*-pentane into a dichloromethane solution of complex **2g**. The molecular structure of complex **2g** was confirmed by single-crystal X-ray diffraction analysis. This complex crystallizes in a centrosymmetric monoclinic $P2_1/n$ system and adopts a square-planar geometry. The carbene and the pyridine ligands are in the *trans*-position, with respective distances to the palladium center of 1.952(7) and 2.087(6) Å. Cell volume and density of the single crystal was calculated as 3853.1(6) $Å^3$ and 1.400 $g.cm^{-3}$. The molecular structure of complex **2g** is shown in Figure 2, and selected bond lengths and angles are summarized in Table 1.

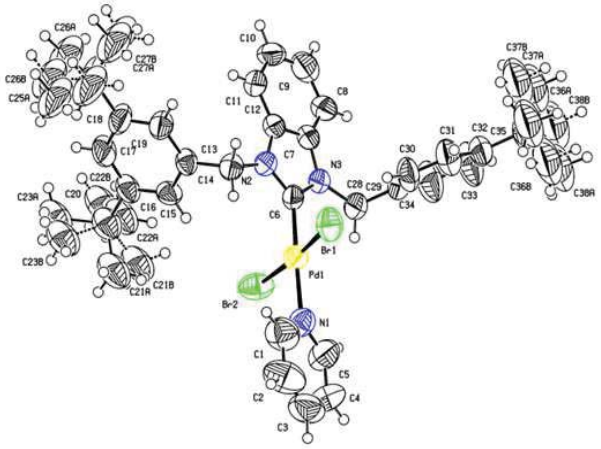


Figure 2. Perspective view of the molecular structure of **2g**.

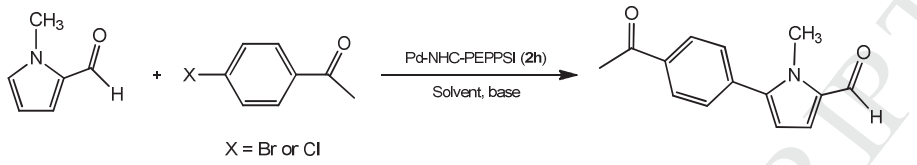
Table 1. Selected bond lengths [Å] and angles [°] for complex **2g**.

Bond lengths		Bond angles	
Pd1-C6	1.952(7)	C6-Pd1-N1	177.4(3)
Pd1-N1	2.087(6)	C6-Pd1-Br1	89.1(2)
Pd1-Br1	2.426(1)	C6-Pd1-Br2	88.8(2)
Pd1-Br2	2.420(1)	N1-Pd1-Br1	91.9(2)
N1-C1	1.320(1)	N1-Pd1-Br2	90.4(2)
N1-C5	1.330(1)	Br1-Pd1-Br2	174.37(4)
N2-C6	1.341(8)	C5-N1-Pd1	121.9(5)
N2-C13	1.451(9)	C1-N1-Pd1	121.4(6)
N3-C6	1.364(9)	N2-C6-Pd1	127.6(5)
N3-C28	1.470(8)	N3-C6-Pd1	125.7(5)

2.4. Direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde

In order to screen the experimental conditions, we selected the complex **2h** as the catalyst. We also selected the 4-bromoacetophenone and 4-chloroacetophenone as the model coupling partner. The results of the reaction parameters including solvent, base, temperature and catalyst loading are gathered in Table 2. The chemical characterizations of the products were made by GC and GC-MS. The conversions were based on the aryl halide by GC.

Table 2. Influence of the reaction conditions for palladium-NHC-PEPPSI catalyzed direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde with 4-bromoacetophenone and 4-chloroacetophenone.[a]



X = Br or Cl

Entry	Pd-NHC-PEPPSI **2h** [mol-%]	X	Solvent	Base	Time [h]	Temp. [°C]	Yield[b] [%]
1	5	Br	DMAc	Cs_2CO_3	2	150	57
2	5	Br	NMP	Cs_2CO_3	2	150	41
3	5	Br	Toluene	Cs_2CO_3	2	120	34
4	5	Br	DMAc	KOPiv.	2	150	49
5	5	Br	NMP	KOPiv.	2	150	37
6	5	Br	Toluene	KOPiv.	2	120	21
7	5	Br	DMAc	KOAc	2	150	93
8	5	Br	NMP	KOAc	2	150	70
9	5	Br	Toluene	KOAc	2	120	52
10	5	Br	DMAc	KOAc	2	120	93
11	5	Br	DMAc	KOAc	2	90	71
12	5	Br	DMAc	KOAc	1	120	92
13	5	Br	DMAc	KOAc	0.5	120	53
14	1	Br	DMAc	KOAc	1	120	90
15	0.5	Br	DMAc	KOAc	1	120	69
16	1	Cl	DMAc	KOAc	1	120	-
17	1	Cl	DMAc	KOAc	2	120	-
18	1	Cl	DMAc	KOAc	5	120	16
19	1	Cl	DMAc	KOAc	10	120	42
20	1	Cl	DMAc	KOAc	15	120	74
21	1	Cl	DMAc	KOAc	20	120	76

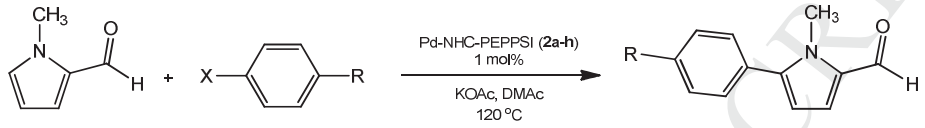
[a] Conditions: 1-methylpyrrole-2-carboxaldehyde (2.0 mmol), aryl halide (1.0 mmol), base (1.5 mmol), solvent (2 mL). [b] Yields were calculated according to aryl halide by GC and GC-MS.

When NMP or toluene were used as solvent, the reaction gave low yield of only 21-70% with Cs_2CO_3, KOPiv. or KOAc as base after 2 h at 120-150 °C (Table 2, entries 2, 3, 5, 6, 8, 9). DMAc proved to be the best tested solvent with all bases after 2 h at 150 °C (Table 2, entries 1, 4, 7). In this solvent decreasing the reaction temperature from 150 °C to 120 °C had no effect on the yield (Table 2, entry 10), but decreasing the reaction temperature from 120 °C to 90 °C had detrimental effect on the yield (Table 2, entry 11). When the reaction time was reduced from 2 h to 1 h no noticeable effect on the yield was observed (Table 2, entry 12), but when the reaction time was reduced to 0.5 h, the yield dropped to 53% (Table 2, entry 13). In the presence of 1 mol% of **2h** as the catalyst, KOAc as the base, DMAc as the solvent and 4-bromoacetophenone as the coupling partner at 120 °C for 1 h, the C5-arylated product was obtained in 90% isolated yield (Table 2, entry 14), but when the catalyst loading was reduced from 1 mol% to 0.5 mol%, the yield decreased to 69% (Table 2, entry 15). Finally, the best conditions leading to 90% yield of 4-bromoacetophenone with high selectivity in favor of the C5-arylated product were obtained when the reaction was carried out in DMAc in the presence of 1.5 equiv. of KOAc at 120 °C for 1 h (Table 2, entry 14). The DMAC / KOAc combination is commonly used for C-H arylation of 5 membered heterocycles. For this reason, the conditions are also consistent with the literature [36[b-d]].

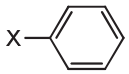
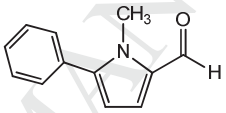
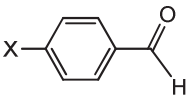
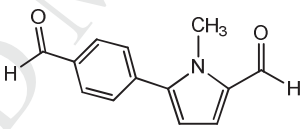
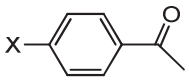
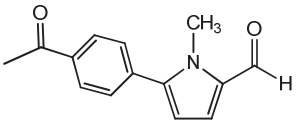
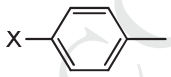
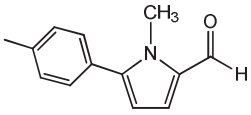
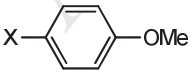
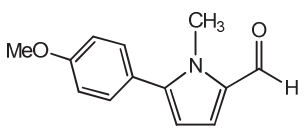
When the less reactive 4-chloroacetophenone was used as substrate in the presence of 1 mol% of catalyst **2h** and KOAc as the base at 120 °C, almost no conversion was observed after 2 h (Table 2, entry 16 and 17). When the reaction time was further increased to 20 h, the conversion was improved indicating that the catalysts were still active reaching a yield of 76% after 20 h.

Finally, the scope of the direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde was investigated with various aryl halides, including five aryl bromides and five aryl chlorides (Table 3) applying our best experimental conditions. Only a minor effect of the nature of the carbene ligand on the palladium-NHC-PEPPSI complex was observed for the coupling of aryl bromides with 1-methylpyrrole-2-carboxaldehyde. At elevated temperature, the oxidative addition of the aryl bromide to palladium is generally easy and does not require the use of very specific ligands. A more important effect of the nature of the ligand was expected for the coupling of aryl chlorides with the 1-methylpyrrole-2-carboxaldehyde. Indeed, again in all cases the coupling products were produced in good yields. Surprisingly, similar yields were obtained for the coupling of electron-deficient aryl chlorides (Table 3, entries 9-24) as with chlorobenzene (Table 3, entries 1-8). In this case, the presence of the NHC-ligands on palladium likely favors the oxidative addition step.

Table 3. Direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by using aryl halides.[a,b]



X = Br or Cl

Entry	Aryl halide	Catalyst	Product	Yield[c] [%]	
				X = Br	X = Cl
1		**2a**		62	70
2		**2b**		54	65
3		**2c**		43	51
4		**2d**		75	67
5		**2e**		70	63
6		**2f**		68	61
7		**2g**		72	70
8		**2h**		77	73
9		**2a**		47	59
10		**2b**		59	57
11		**2c**		47	43
12		**2d**		67	65
13		**2e**		56	70
14		**2f**		61	59
15		**2g**		67	63
16		**2h**		88	72
17		**2a**		38	59
18		**2b**		47	67
19		**2c**		41	61
20		**2d**		79	71
21		**2e**		59	61
22		**2f**		68	70
23		**2g**		79	72
24		**2h**		90	74
25		**2a**		50	57
26		**2b**		41	62
27		**2c**		34	42
28		**2d**		66	61
29		**2e**		56	54
30		**2f**		59	63
31		**2g**		64	60
32		**2h**		69	67
33		**2a**		40	51
34		**2b**		43	48
35		**2c**		29	32
36		**2d**		64	53
37		**2e**		50	48
38		**2f**		57	54
39		**2g**		60	62
40		**2h**		68	63

[a] Conditions: Pd-NHC-PEPPSI **2a-h** (0.01 mmol), 1-methylpyrrole-2-carboxaldehyde (2.0 mmol), aryl halide (1.0 mmol), KOAc (1.5 mmol), DMAc (2 mL), 120 °C. [b] Reaction time: 1 h for aryl bromides, 15 h for aryl chlorides. [c] Yields were calculated according to aryl halide by GC and GC-MS.

3. Conclusion

In conclusion, we have synthesized and characterized eight benzimidazolium salts according to literature [40], and their corresponding new Pd-NHC-PEPPSI complexes. The catalytic activity of the complexes was investigated in the direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by aryl halides. The Pd-NHC-PEPPSI complexes were all found to be suitable catalysts for the direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by aryl bromides. With Pd-NHC-PEPPSI complexes, even non-activated aryl chlorides (such as chlorobenzene or 4-chlorotoluene) were coupled with 1-methylpyrrole-2-carboxaldehyde in moderate to good yields. This good performance possibly arises from strong steric interactions between the bulky 3,5-di-*tert*-butylbenzyl substituted NHC ligand and the catalytic centre, which favours reductive elimination. We can say that there is no significant difference between these complexes on the catalytic activity of C5-arylation of 1-methylpyrrole-2-carboxaldehyde by aryl halides. The significant difference between **2d** and **2c** indicates that electronic effects are also playing some role in these processes. Finally, as the major by-products are KOAc associated to HBr instead of metallic salts, this procedure is environmentally more attractive than the classical coupling procedures.

4. Experimental

4.1. General methods

All manipulations were carried out under argon using standard Schlenk line techniques. Chemicals and solvents were purchased from Sigma-Aldrich Co. (Poole, Dorset, UK). The solvents used were purified by distillation over the drying agents indicated and were transferred under argon. Pd-NHC-PEPPSI complexes were prepared according to known methods in the literature [41]. DMAc analytical grade (99%) was not distilled before use. KOAc (99%) was employed. Elemental analyses were performed by İnönü University Scientific and Technological Research Center (Malatya, Turkey). Melting points were measures in open capillary tubes with an Electrothermal-9200 melting points apparatus. IR spectra were recorded on ATR unit in the range of 400-4000 cm^{-1} with Perkin Elmer Spectrum 100 Spectrofotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Bruker Avance AMX spectrometer operating at 400 MHz (^{1}H NMR) and at 100 MHz (^{13}C NMR) in $CDCl_3$. The NMR studies were carried out in high-quality 5 mm NMR tubes. The chemical shifts (δ) are reported in ppm relative to $CDCl_3$. Coupling constants (J values) are given in hertz. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet. ^{1}H NMR spectra are referenced to residual protiated solvents (δ = 7.26 ppm for $CDCl_3$), ^{13}C chemical shifts are reported relative to deuteriated solvents (δ = 77.16 ppm for $CDCl_3$). All catalytic reactions were monitored on an Agilent 6890N GC and Schimadzu 2010 Plus GC-MS system by GC-FID with an HP-5 column of 30 m length, 0.32 mm diameter, and 0.25 μm film thickness.

*4.2. General procedure for the preparation of benzimidazolium salts (**1a-h**)*

For the preparation of benzimidazolium salts (**1a-h**), *N*-(3,5-di-*tert*-butylbenzyl)benzimidazole, (1.0 mmol) was dissolved in anhydrous dimethylformamide (DMF), (3 mL) and alkyl bromide (1.0 mmol) was added at room temperature. The reaction mixture was stirred at 80 °C for 24 h under argon. After completion of the reaction, the DMF was removed by vacuum and diethyl ether (15 mL) was added to obtain a white crystalline solid, which was filtered off. The solid was washed with diethyl ether (3×10 mL) and dried under vacuum. The crude product was recrystallized from ethanol/diethyl ether mixture (1:2, *v/v*) and completely dried under vacuum. These known compounds were synthesized and characterized by ^{1}H NMR, ^{13}C NMR, IR and elemental analysis techniques. The results we found, are consistent with the literature [40].

*4.3. General procedure for the preparation of palladium-NHC-PEPPSI complexes (**2a-h**)*

Benzimidazolium salts (**1a-h**) (1.0 mmol) were converted, with moderated yields, into the palladium-NHC-PEPPSI complexes (**2a-h**) by reaction with $PdCl_2$ (1.0 mmol) in refluxing pyridine in the presence of K_2CO_3 (5.0 mmol) as a base and a large excess of KBr and the mixture heated with vigorous stirring at 80 °C for 16 h. The reaction mixture was diluted with CH_2Cl_2 then filtered through a pad of celite and silica gel to remove the unreacted $PdCl_2$ and benzimidazolium salt. The solvent was removed under vacuum. The pure complexes were washed with *n*-pentane (3×5 mL) and completely dried under vacuum. All complexes were isolated as air-stable yellow solids and were isolated in 58-87% yields.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(2-methoxyethyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2a**)*

Yield: 0.27 g, 77%; mp: 206-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.21 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 3.30 (s, 3H, $NCH_2CH_2OCH_3$); 4.17 (t, *J* = 6.7 Hz, 2H, $NCH_2CH_2OCH_3$); 5.01 (t, *J* = 6.7 Hz, 2H, $NCH_2CH_2OCH_3$); 6.09 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.93-7.71 and 8.98-9.00 (m, 12H, NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 31.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 35.0 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 48.8 ($NCH_2CH_2OCH_3$); 54.4 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 59.2 ($NCH_2CH_2OCH_3$); 71.4 ($NCH_2CH_2OCH_3$); 111.4, 111.5, 121.9, 122.5, 122.9, 123.0, 124.6,125.0, 133.9, 134.3, 136.0, 138.0, 138.4, 151.3, 152.7, 154.4 (NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 163.1 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1412; Anal. Calcd. for $C_{30}H_{39}Br_2N_3OPd$: C, 49.78; H, 5.43; N, 5.80. Found: C, 49.81; H, 5.50; N, 5.85.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(2,2-dimethoxyethyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2b**)*

Yield: 0.21 g, 69%; mp: 119-120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.21 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 3.44 (s, 6H, $NCH_2CH(OCH_3)_2$); 4.90 (d, *J* = 5.5 Hz, 2H, $NCH_2CH(OCH_3)_2$); 5.48 (t, *J* = 5.5 Hz, 1H, $NCH_2CH(OCH_3)_2$); 6.10 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.94-7.70 and 8.96-9.00 (m, 12H, NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 30.4 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 33.9 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 50.0 ($NCH_2CH(OCH_3)_2$); 53.4 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 55.3 ($NCH_2CH(OCH_3)_2$); 103.5 $NCH_2CH(OCH_3)_2$); 110.3, 110.9, 120.8, 121.8, 121.9, 123.6, 132.8, 133.1, 135.0, 137.0, 150.3, 151.6 (NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 162.7 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1416; Anal. Calcd. for $C_{31}H_{41}Br_2N_3O_2Pd$: C, 49.39; H, 5.48; N, 5.57. Found: C, 49.41; H, 5.50; N, 5.59.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(3-methylbenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2c**)*:

Yield: 0.19 g, 58%; mp: 208-209 °C. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.22 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 2.25 (s, 3H, $NCH_2C_6H_4(CH_3)$-3); 6.12 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.15 (s, 2H, $NCH_2C_6H_4(CH_3)$-3); 6.95-7.68 and 8.96-8.97 (m, 16H, (NC_6H_4N, $NCH_2C_6H_4(CH_3)$-3, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 21.4 ($NCH_2C_6H_4(CH_3)$-3); 31.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 35.0 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 53.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 54.4 ($NCH_2C_6H_4(CH_3)$-3); 111.4, 111.7, 122.4, 122.8, 122.9, 123.0, 124.5, 125.1, 128.6, 128.8, 134.0, 134.7, 134.8, 135.0, 137.9, 138.6, 151.4, 152.7 ($NCH_2C_6H_4(CH_3)$-3, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 164.2 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1411; Anal. Calcd. for $C_{35}H_{41}Br_2N_3Pd$: C, 54.60; H, 5.37; N, 5.46. Found: C, 54.63; H, 5.40; N, 5.49.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(3-methoxybenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2d**)*

Yield: 0.26 g, 78%; mp: 136-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 1.22 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 3.68 (s, 3H, $NCH_2C_6H_4(OCH_3)$-3); 6.14 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.15 (s, 2H, $NCH_2C_6H_4(OCH_3)$-3); 6.95-7.67 and 8.96-8.99 (m, 16H, NC_6H_4N, $NCH_2C_6H_4(OCH_3)$-3, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 31.4 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 35.0 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 53.7 ($NCH_2C_6H_3(C(CH_3)_3)_2$)-3,5); 54.4 ($NCH_2C_6H_4(OCH_3)$-3); 55.7 ($NCH_2C_6H_4(OCH_3)$-3); 111.4, 111.7, 112.8, 115.0, 120.3, 122.4, 123.0, 124.6, 129.7,133.9, 134.7, 134.8, 136.6, 138.0, 151.4, 152.7, 160.2 ($NCH_2C_6H_4(OCH_3)$-3, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 164.1 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1410; Anal. Calcd. for $C_{35}H_{41}Br_2N_3OPd$: C, 53.49; H, 5.26; N, 5.35. Found: C, 53.53; H, 5.32; N, 5.43.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(2,4,6-trimethylbenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2e**)*

Yield: 0.26 g, 74%; mp: 259-260 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 2.28 and 2.30 (s, 9H, $NCH_2C_6H_2(CH_3)_3$-2,4,6); 6.13 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.15 (s, 2H, $NCH_2C_6H_2(CH_3)_3$-2,4,6); 6.88-7.71 and 8.96-8.98 (m, 14H, NC_6H_4N, $NCH_2C_6H_2(CH_3)_3$-2,4,6, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0 and 21.1 ($NCH_2C_6H_2(CH_3)_3$-2,4,6); 31.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 35.0 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 50.9 ($NCH_2C_6H_2(CH_3)_3$-2,4,6); 54.4 ($NCH_2C_6H_3(C(CH_3)_3)$-3,5); 111.2, 111.3, 111.5, 121.7, 122.4, 122.5, 122.9, 124.5, 127.6, 129.6, 134.0, 134.6, 135.1, 137.9, 138.3, 138.6, 138.9, 151.2, 152.7 (NC_6H_4N, $NCH_2C_6H_2(CH_3)_3$-2,4,6, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 163.8 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1410; Anal. Calcd. for $C_{37}H_{45}Br_2N_3Pd$: C, 55.69; H, 5.68; N, 5.27. Found: C, 55.74; H, 5.74; N, 5.32.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(2,3,5,6-tetramethylbenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2f**)*

Yield: 0.29 g, 77%; mp: 267-268 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (s, 18H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 2.20 and 2.21 (s, 12H, $NCH_2C_6H(CH_3)_4$-2,3,5,6); 6.14 (s, 2H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.16 (s, 2H, $NCH_2C_6H(CH_3)_4$-2,3,5,6); 6.90-7.32, 7.63-7.69 and 8.91-8.94 (m, 13H, NC_6H_4N, $NCH_2C_6H(CH_3)_4$-2,3,5,6, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6 and 19.6 ($NCH_2C_6H(CH_3)_4$-2,3,5,6); 30.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 33.9 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 50.3 ($NCH_2C_6H(CH_3)_4$-2,3,5,6); 53.4 ($NCH_2C_6H_3(C(CH_3)_3)$-3,5); 110.1,110.5, 120.7, 121.4, 121.8, 123.4, 129.6, 131.5, 133.0, 133.3, 133.5, 134.2, 134.3, 136.8, 150.2, 151.6 (NC_6H_4N, $NCH_2C_6H(CH_3)_4$-2,3,5,6, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 162.8 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1416; Anal. Calcd. for $C_{38}H_{47}Br_2N_3Pd$: C, 56.21; H, 5.83; N, 5.17. Found: C, 56.24; H, 5.86; N, 5.20.

*Dibromo-[1-(3,5-di-tert-butylbenzyl)-3-(4-tert-butylbenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2g**)*

Yield: 0.32 g, 87%; mp: 264-265 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (s, 27H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and $NCH_2C_6H_4(C(CH_3)_3$-4); 6.14 (s, 4H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.15 (s, 4H, $NCH_2C_6H_4(C(CH_3)_3$-4); 6.95-7.66 and 8.96-8.98 (m, 16H, NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5, $NCH_2C_6H_4(C(CH_3)_3$-4) and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.4 ($NCH_2C_6H_4(C(CH_3)_3$-4); 31.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 34.6 ($NCH_2C_6H_4(C(CH_3)_3$-4); 35.0 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 53.4 ($NCH_2C_6H_4(C(CH_3)_3$-4); 54.4 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.5, 111.6, 121.9, 122.5, 122.9, 124.5, 125.8, 127.8, 132.0, 134.0, 134.8, 134.9, 137.9, 151.1, 151.4, 152.7 (NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5, $NCH_2C_6H_4(C(CH_3)_3$-4) and NC_5H_5); 164.1 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1414; Anal. Calcd. for $C_{38}H_{47}Br_2N_3Pd$: C, 56.21; H, 5.83; N, 5.17. Found: C, 56.28; H, 5.89; N, 5.25.

*Dibromo-[1,3-bis(3,5-di-tert-butylbenzyl)benzimidazole-2-ylidene](pyridine)palladium(II), (**2h**)*

Yield: 0.23 g, 67%; Yield: 0.21 g, 72%; mp: 206-207 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (s, 36H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.17 (s, 4H, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 6.92-7.64 and 8.98-9.00 (m, 15H, NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.5 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 33.9 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 53.3 ($NCH_2C_6H_3(C(CH_3)_3)_2$-3,5); 110.6, 120.7, 121.4, 121.7, 123.5, 133.0, 133.7, 136.8, 150.3, 151.7 (NC_6H_4N, $NCH_2C_6H_3(C(CH_3)_3)_2$-3,5 and NC_5H_5); 163.1 (Pd-$C_{carbene}$). IR (cm^{-1}) $\nu_{(CN)}$: 1411; Anal. Calcd. for $C_{42}H_{55}Br_2N_3Pd$: C, 58.11; H, 6.39; N, 4.84. Found: C, 58.16; H, 6.42; N, 4.86.

4.4. General procedure for the direct arylation of 1-methylpyrrole-2-carboxaldehyde

An oven dried Schlenk flask was charged with aryl halide (1.0 mmol), 1-methylpyrrole-2-carboxaldehyde (2.0 mmol), KOAc (1.5 mmol), palladium-NHC-PEPPSI complex (0.01 mmol) and DMAc (2 mL). The Schlenk tube was purged several times with argon and it was placed in a preheated oil bath at 120 ^{o}C, and the reaction mixture was stirred for different durations given in the specific tables. At the end of the reaction, the solvent was removed under vacuum, and the residue was charged directly onto a silica gel column. The products were eluted by using *n*-hexane/diethyl ether mixture (5:1, *v/v*). The yields were established by GC and GC-MS based on aryl halides.

4.5. X-ray crystallographic data

Single crystal of complex **2g** suitable for X-ray analysis were obtained by slow diffusion of *n*-pentane into a dichloromethane solution of the complex **2g**. Empirical formula = $C_{38}H_{47}Br_2N_3Pd$; *Mr* = 811.99 g.mol^{-1}; crystal system = monoclinic; space group = $P2_1/n$ system; cell lengths, *a* = 17.8083(16), *b* = 12.3036(10), *c* = 18.2077(15) Å; cell angles, $\alpha = 90^{o}$, $\beta = 111.745(2)^{\circ}$, $\gamma = 90^{o}$; cell volüme = 3853.1(6) Å^3. *Z* = 4, *d* = 1.400 g.cm^{-3}, μ = 2.583 mm^{-1}. *F*(000) = 1648; *T* = 296 K. The crystal size (0.36 × 0.28 × 0.18 mm) was studied with a Bruker Kappa ApexII CCD diffractometer using Mo-K_α radiation (λ = 0.71073 Å). The number of measured reflections are 22908 with 8267 independent reflections. The observed [$I > 2\sigma(I)$] reflections are 3325. The structure was solved by direct methods with the *SIR97* program, [42] and then refined with full-matrix least-square methods based on F^2 *SHELXL2014*/6 (Sheldrick, 2015) [43]. All non-hydrogen atoms were refined isotropically first and then with anisotropic atomic displacement parameters. The large anistropic thermal parameters and wrong C-C bond distances etc for *tert*-butyl lead to consider disorder. The terminal C-atoms of *tert*-butyl were treated as disordered over two set of sites with occupancy ratio of 0.565(6): 0.435(6) and having equal anistropic thermal parameters within the groups. The number of restraints used were 57. The H atoms were finally included in their calculated positions. A final refinement on F^2, with 8267 unique intensities and 389 parameters, converged at $\omega R(F^2) = 0.1546$, [$R(F^2 > 2\sigma(F^2)] = 0.059$ for 3325 observed reflections with $I > 2\sigma(I)$. The value of weight parameter is $w = 1/[\sigma(F_o^2) + (0.0546P)^2]$, where $P = [F_o^2 + 2(F_c)^2]/3$ and goodness of fit $S = 0.946$.

CCDC 1567377 (for **2g**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Supporting Information (see footnote on the first page of this article): for the ^{1}H NMR, ^{13}C NMR and IR spectra of palladium-NHC-PEPPSI complexes (**2a-h**).

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References

[1] a) S. Diez-Gonzalez (Ed.) *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*, RSC, London (2017); b) C. S. J. Cazin (Ed.), *N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*, Springer, *Vol. 32*, London, (2010).

[2] F. Glorius (Ed.), *Topics in Organometallic Chemistry Vol. 21: N-Heterocyclic Carbenes in Transition Metal Catalysis*, Springer, Heidelberg, (2007).

[3] S. P. Nolan (Ed.), *N-Heterocyclic Carbenes: Effective Tools for Organometallic Synthesis*, Wiley-VCH, Weinheim, (2014).

[4] S. Díez-González, N. Marion, S. P. Nolan, Chem. Rev. 109 (2009) 3612-3676.

[5] D. Enders, O. Niemeier, A. Henseler, Chem. Rev. 107 (2007) 5606-5655.

[6] G. C. Fortman, S. P. Nolan, Chem. Soc. Rev. 40 (2011) 5151-5169.

[7] M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, Nature 510 (2014) 485-496.

[8] W. A. Herrmann, Angew. Chem. Int. Ed. 41 (2002) 1290-1309.

[9] E. Peris, R. H. Crabtree, Coord. Chem. Rev. 248 (2004) 2239-2246.

[10] N. Hadei, E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, Org. Lett. 7 (2005) 1991-1994.

[11] P. Małecki, K. Gajda, O. Ablialimov, M. Malińska, R. Gajda, K. Woźniak, A. Kajetanowicz, K. Grela, Organometallics 36 (2017) 2153-2166.

[12] R. H. Crabtree, J. Organomet. Chem. 690 (2005) 5451-5457.

[13] H. D. Velazquez, F. Verpoort, Chem. Soc. Rev. 41 (2012) 7032-7060.

[14] L. Oehninger, R. Rubbiani, I. Ot, Dalton Trans. 42 (2013) 3269-3284.

[15] W. Liua, R. Gust, Chem. Soc. Rev. 42 (2013) 755-773.

[16] W. J. Youngs, C. A. Tessier, J. C. Garrison, C. A. Quezada, A. Melaiye, S. Durmuş, M. J. Panzner, A. Kaşçatan-Nebioğlu, Med. Inorg. Chem. 23 (2005) 414-427.

[17] R. A. Haque, S. Y. Choo, S. Budagumpi, M. A. Iqbal, A. A. Abdullah, Eur. J. Med. Chem. 90 (2015) 82-92.

[18] C. V. Maftei, E. Fodor, P. G. Jones, M. Freytag, M. H. Franz, G. Kelter, H. H. Fiebig, M. Tamm, I. Neda, Eur. J. Med. Chem. 101 (2015) 431-441.

[19] M. Kaloğlu, N. Kaloğlu, İ. Özdemir, S. Günal, İ. Özdemir, Bioorg. and Med. Chem. 24 (2016) 3649-3656.

[20] S. P. Nolan (Ed.), *N-Heterocyclic Carbenes in Synthesis*, Wiley, Weinheim, (2006).

[21] D. Guest, V. H. Menezes da Silva, A. P. de Lima Batista, S. M. Roe, A. A. C. Braga, O. Navarro, Organometallics 34 (2015) 2463-2470.

[22] P. G. Gildner, T. J. Colacot, Organometallics 34 (2015) 5497-5508.

[23] O. Diebolt, P. Braunstein, S. P. Nolan, C. S. J. Cazin, Chem. Commun. 27 (2008) 3190-3192

[24] a) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett*. 20 (1979) 3437-3440; b) C. Zhang, J. Huang, M. L.Trudell, S. P. Nolan, J. Org. Chem. 64 (1999) 3804-3805; c) P. Lei, G. Meng, Y. Ling, J. An, M. Szostak, J. Org. Chem. 82 (2017) 6638-6646.

[25] S. Bräse, A. de Meijere, *Cross-coupling of organic halides with alkenes: The Heck reaction*. In: A. de Meijere, F. Diederich (Ed.) *Metal-catalyzed cross-coupling reactions*, Wiley-VCH, Weinheim, (2004).

[26] a) E. Negishi, Bull. Chem. Soc. Jpn. 80 (2007) 233-257; b) N. Hadei, E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, Org. Lett. 7 (2005) 3805-3807.

[27] H. M. Lee, S. P. Nolan, Org. Lett. 2 (2000) 2053-2055.

[28] W. A. Herrmann, C.P. Reisinger, M. Spiegler, J. Organomet. Chem. 557 (1998) 93-96.

[29] a) J. Huang, G. Grasa, S. P. Nolan, Org. Lett. 1 (1999) 1307-1309; b) G. A. Grasa, M. S. Viciu, J. Huang, S. P. Nolan, J. Org. Chem. 66 (2001) 7729-7737; c) S. R. Stauffer, S. Lee, J. P. Stambuli, S. I. Hauck, J. F. Hartwig, Org. Lett. 2 (2000) 1423-1426; d) S. Shi, M. Szostak, Chem. Commun. (2017), accepted article, DOI: 10.1039/c7cc06186b.

[30] L. Ackermann (Ed.), *Modern arylation methods*. Wiley-VCH, Weinheim, (2009).

[31] a) İ. Özdemir, S. Demir, B. Çetinkaya, C. Gourlaouen, F. Maseras, C. Bruneau, P. H. Dixneuf, J. Am. Chem. Soc. 130 (2008) 1156-1157; b) İ. Özdemir, S. Demir, N. Gürbüz, B. Çetinkaya, L. Toupet, C. Bruneau, P. H. Dixneuf, Eur. J. Inorg. Chem. 13 (2009), 1942-1949; c) H. Arslan, İ. Özdemir, D. Vanderveer, S. Demir, B. Çetinkaya, J. Coord. Chem. 62 (2009) 2591-2599; d) K. C. Nicolaou, J. S. Chen, Pure Appl. Chem. 80 (2008) 727-742.

[32] D. M. Black, R. G. Bakker-Arkema, J. W. Nawrocki, Arch. Intern. Med. 158 (1998) 577-584.

[33] P. J. Birch, A. G. Hayes, M. J. Sheehan, M. B. Tyers, Eur. J. Pharmacol. 144 (1987) 405-408.

[34] Z. Zhang, A. M. Olland, Y. Zhu, J. Biol. Chem. 280 (2005) 28468-28475.

[35] G. L. Willis, Reviews in the Neurosciences 19 (2008) 245-316.

[36] a) E. T. Nadres, A. Lazareva, O. Daugulis, J. Org. Chem. 76 (2011) 471-483; b) R. Jin, K. Yuan, E. Chatelain, J. F. Soule, H. Doucet, Adv. Synth. Catal. 356 (2014) 3831-3841; c) J. Roger, A. L. Gottumukkala, H. Doucet, ChemCatChem, 2 (2010) 20-40; d) D. Roy, S. Mom, M. Beauperin, H. Doucet, J. C. Hierso, Angew. Chem. Int. Ed. 49 (2010) 6650-6654.

[37] A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani, Y. Aoyagi, Heterocycles, 31 (1990) 1951-1958.

[38] a) T. Satoh, M. Miura, Chem. Lett. 36 (2007) 200-205; b) L. C. Campeau, D. R. Stuart, K. Fagnou, Aldrichimica Acta, 40 (2007) 35-41; c) I. V. Seregin, V. Gevorgyan, Chem. Soc. Rev. 36 (2007) 1173-1193; d) B. J. Li, S. D. Yang, Z. J. Shi, Synlett, 7 (2008) 949-957; e) F. Bellina, R. Rossi, Tetrahedron, 65 (2009) 10269-10310; f) C. L. Sun, B. J. Li, Z. J. Shi, Chem. Commun. 46 (2010) 677-685; g) P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu, J. You, J. Am. Chem. Soc. 132 (2010) 1822-1824; h) L. Ackermann, R. Vincente, A. R. Kapdi, Angew. Chem. Int. Ed. 48 (2009) 9792-9826; i) C. Fischmeister, H. Doucet, Green Chem. 13 (2011) 741-753.

[39] İ. Özdemir, N. Gürbüz, N. Kaloğlu, Ö. Doğan, M. Kaloğlu, C. Bruneau, H. Doucet, Beilstein J. Org. Chem. 9 (2013) 303-312.

[40] N. Kaloğlu, İ. Özdemir, S. Günal, İ. Özdemir, Appl. Organomet. Chem. (2017), accepted article, DOI: 10.1002/aoc.3803.

[41] C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson, M. G. Organ, Chem. Eur. J. 12 (2006) 4743-4748.

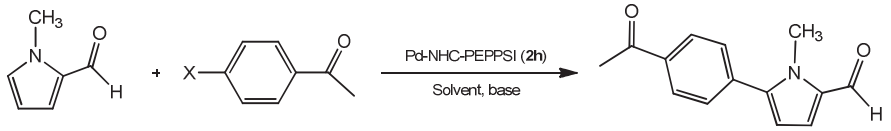
[42] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori, R. Spagna, J. Appl. Cryst. 32 (1999) 115-119.

[43] G. M. Sheldrick, Acta Cryst. C71 (2015) 3-8.

Table 1. Selected bond lengths [Å] and angles [°] for complex **2g**.

Bond lengths		Bond angles	
Pd1-C6	1.952(7)	C6-Pd1-N1	177.4(3)
Pd1-N1	2.087(6)	C6-Pd1-Br1	89.1(2)
Pd1-Br1	2.426(1)	C6-Pd1-Br2	88.8(2)
Pd1-Br2	2.420(1)	N1-Pd1-Br1	91.9(2)
N1-C1	1.320(1)	N1-Pd1-Br2	90.4(2)
N1-C5	1.330(1)	Br1-Pd1-Br2	174.37(4)
N2-C6	1.341(8)	C5-N1-Pd1	121.9(5)
N2-C13	1.451(9)	C1-N1-Pd1	121.4(6)
N3-C6	1.364(9)	N2-C6-Pd1	127.6(5)
N3-C28	1.470(8)	N3-C6-Pd1	125.7(5)

Table 2. Influence of the reaction conditions for palladium-NHC-PEPPSI catalyzed direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde with 4-bromoacetophenone and 4-chloroacetophenone.[a]

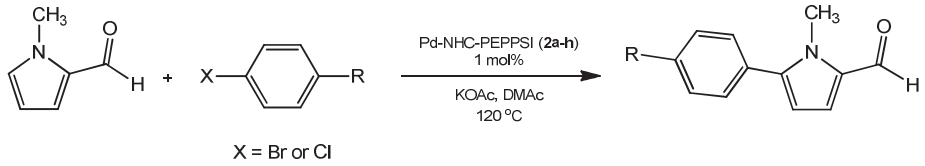


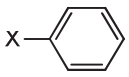
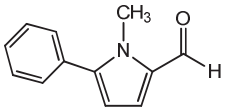
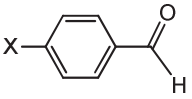
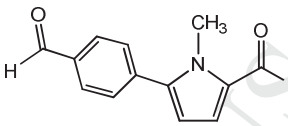
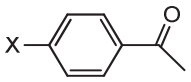
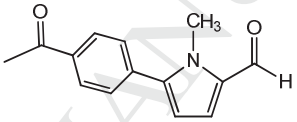
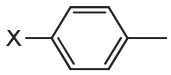
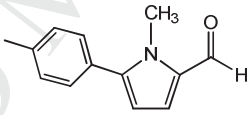
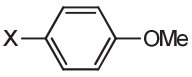
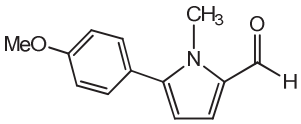
X = Br or Cl

Entry	Pd-NHC-PEPPSI **2h** [mol-%]	X	Solvent	Base	Time [h]	Temp. [°C]	Yield[b] [%]
1	5	Br	DMAc	Cs_2CO_3	2	150	57
2	5	Br	NMP	Cs_2CO_3	2	150	41
3	5	Br	Toluene	Cs_2CO_3	2	120	34
4	5	Br	DMAc	KOPiv.	2	150	49
5	5	Br	NMP	KOPiv.	2	150	37
6	5	Br	Toluene	KOPiv.	2	120	21
7	5	Br	DMAc	KOAc	2	150	93
8	5	Br	NMP	KOAc	2	150	70
9	5	Br	Toluene	KOAc	2	120	52
10	5	Br	DMAc	KOAc	2	120	93
11	5	Br	DMAc	KOAc	2	90	71
12	5	Br	DMAc	KOAc	1	120	92
13	5	Br	DMAc	KOAc	0.5	120	53
14	1	Br	DMAc	KOAc	1	120	90
15	0.5	Br	DMAc	KOAc	1	120	69
16	1	Cl	DMAc	KOAc	1	120	-
17	1	Cl	DMAc	KOAc	2	120	-
18	1	Cl	DMAc	KOAc	5	120	16
19	1	Cl	DMAc	KOAc	10	120	42
20	1	Cl	DMAc	KOAc	15	120	74
21	1	Cl	DMAc	KOAc	20	120	76

[a] Conditions: 1-methylpyrrole-2-carboxaldehyde (2.0 mmol), aryl halide (1.0 mmol), base (1.5 mmol), solvent (2 mL). [b] Yields were calculated according to aryl halide by GC and GC-MS.

Table 3. Direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by using aryl halides.[a,b]



Entry	Aryl halide	Catalyst	Product	Yield[c] [%]	
				X = Br	X = Cl
1		**2a**		62	70
2		**2b**		54	65
3		**2c**		43	51
4		**2d**		75	67
5		**2e**		70	63
6		**2f**		68	61
7		**2g**		72	70
8		**2h**		77	73
9		**2a**		47	59
10		**2b**		59	57
11		**2c**		47	43
12		**2d**		67	65
13		**2e**		56	70
14		**2f**		61	59
15		**2g**		67	63
16		**2h**		88	72
17		**2a**		38	59
18		**2b**		47	67
19		**2c**		41	61
20		**2d**		79	71
21		**2e**		59	61
22		**2f**		68	70
23		**2g**		79	72
24		**2h**		90	74
25		**2a**		50	57
26		**2b**		41	62
27		**2c**		34	42
28		**2d**		66	61
29		**2e**		56	54
30		**2f**		59	63
31		**2g**		64	60
32		**2h**		69	67
33		**2a**		40	51
34		**2b**		43	48
35		**2c**		29	32
36		**2d**		64	53
37		**2e**		50	48
38		**2f**		57	54
39		**2g**		60	62
40		**2h**		68	63

[a] Conditions: Pd-NHC-PEPPSI **2a-h** (0.01 mmol), 1-methylpyrrole-2-carboxaldehyde (2.0 mmol), aryl halide (1.0 mmol), KOAc (1.5 mmol), DMAc (2 mL), 120 °C. [b] Reaction time: 1 h for aryl bromides, 15 h for aryl chlorides. [c] Yields were calculated according to aryl halide by GC and GC-MS.

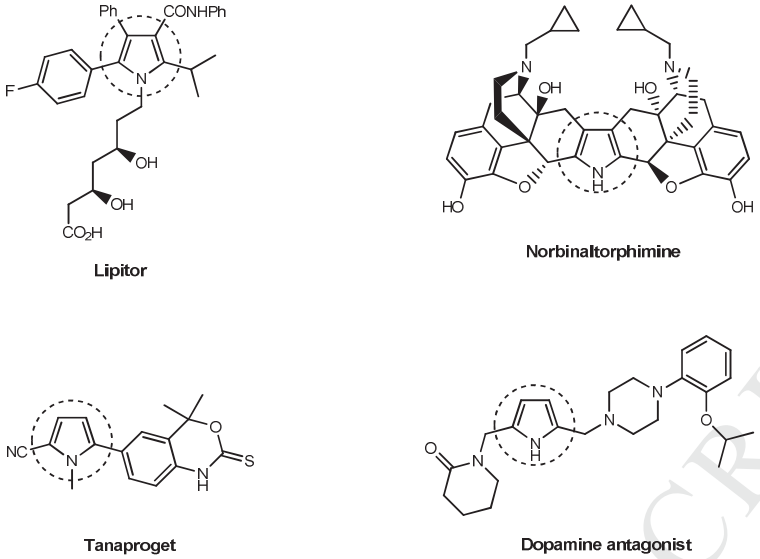


Figure 1. Examples of biologically active pyrrole derivatives.

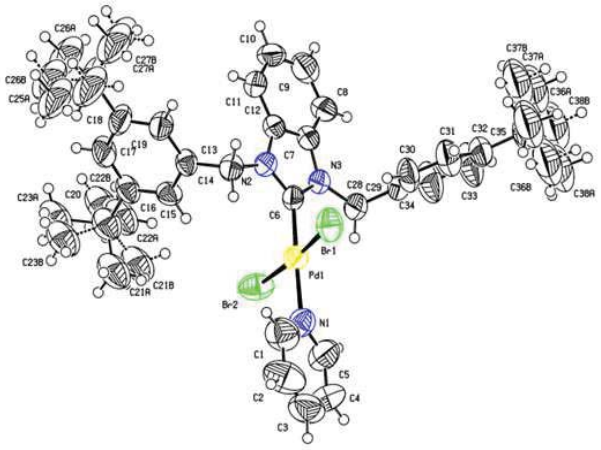
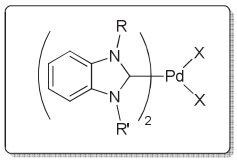
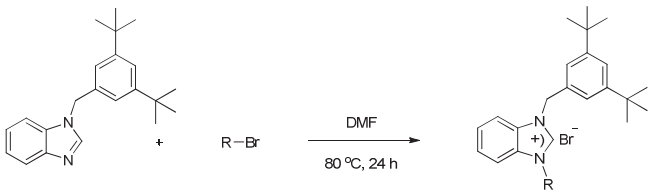


Figure 2. Perspective view of the molecular structure of **2g**.



R = $CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =** $CH_2CH_2OCH_3$	**X =** Br
R = $CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =** $CH_2C_6H_2(OCH_3)_3$-3,4,5	**X =** Br
R = $CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =** $CH_2C_6H_3(C(CH_3)_3)$-3,5	**X =** Br
R = $CH_2C_6H_3(C(CH_3)_3)$-3,5	**R' =** $CH_2C_6(CH_3)_5$-2,3,4,5,6	**X =** Cl
R = $CH_2C_6H_2(CH_3)_3$-2,4,6	**R' =** $CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =** Br
R = $CH_2C_6H_4(CH_3)$-4	**R' =** $CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =** Cl
R = $CH_2C_6H_4(OCH_3)$-3	**R' =** $CH_2CH_2OC_6H_4(OCH_2CH_3)$-2	**X =** Cl
R = $CH_2C_6H_4(CH_3)$-4	**R' =** $CH(C_6H_5)_2$	**X =** Br
R = $CH_2C_6H_5$	**R' =** $CH_2CH_2(CHO_2CH_2CH_2)$	**X =** Br

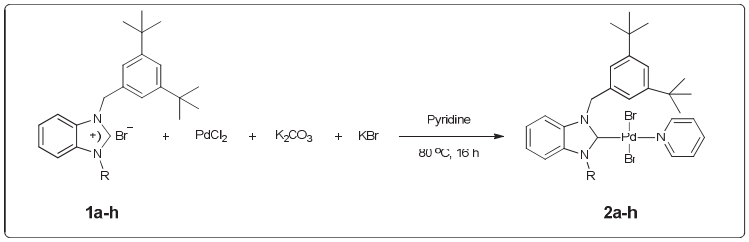
Scheme 1. General structure of recently reported palladium-bis(NHC) complexes.

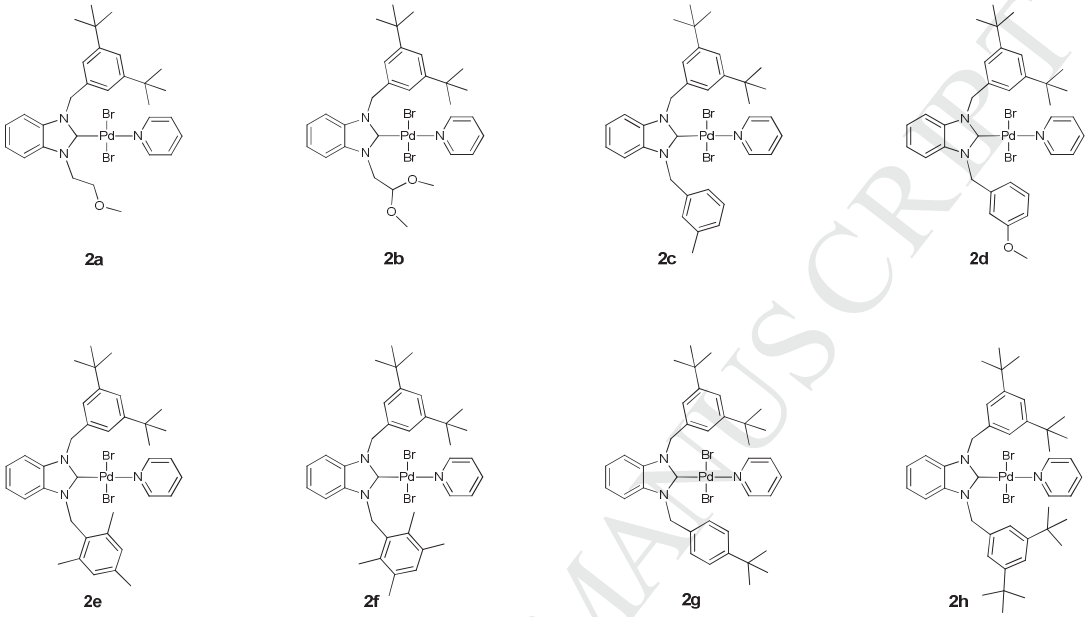


1a-h

1a **R =** $CH_2CH_2OCH_3$
1b **R =** $CH_2CH(OCH_3)_2$
1c **R =** $CH_2C_6H_5$
1d **R =** $CH_2C_6H_4(OCH_3)$-3
1e **R =** $CH_2C_6H_2(CH_3)_3$-2,4,6
1f **R =** $CH_2C_6H(CH_3)_4$-2,3,5,6
1g **R =** $CH_2C_6H_4(C(CH_3)_3)$-4
1h **R =** $CH_2C_6H_3(C(CH_3)_3)$-3,5

Scheme 2. Synthesis of the benzimidazolium salts (**1a-h**).





Scheme 3. Synthesis of the palladium-NHC-PEPPSI complexes (**2a-h**).

- A series of new palladium-NHC-PEPPSI complexes (**2a-h**) with general formula [$PdBr_2$(NHC)(Py)] were synthesized, (NHC = *N*-heterocyclic carbene; PEPPSI = pyridine-enhanced precatalyst preparation, stabilisation, and initiation).

- The obtained palladium-NHC-PEPPSI complexes were characterized by NMR (^{1}H and ^{13}C), FT-IR spectroscopy and microanalysis techniques.

- These palladium-NHC-PEPPSI complexes were used as catalysts in the direct C5-arylation of 1-methylpyrrole-2-carboxaldehyde by aryl halides.