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Synthesis of [$PdBr_2$(benzimidazole-2-ylidene)(pyridine)] complexes and their catalytic activity in the direct C—H bond activation of 2-substituted heterocycles

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ABSTRACT

A series of unsymmetrical 1,3-disubstituted benzimidazolium chlorides, **2a-f**, having two nitrogen atoms substituted by various alkyl groups were synthesized as *N*-heterocyclic carbene (NHC) precursors in high yields. The benzimidazolium salts are readily converted into the corresponding PEPPSI-type palladium–NHC complexes **3a-f** (PEPPSI = pyridine-enhanced precatalyst preparation, stabilization and initiation). The structures of all the compounds have been characterized by ^{1}H NMR, ^{13}C NMR and IR spectroscopy, as well as the X-ray diffraction technique (**3a**, **3d** and **3e**), which support the proposed structures. Next, the palladium-NHC-PEPPSI complexes were used as catalysts in the direct C(5)-arylation of 2-acetyl furan and 2-acetylthiophene with various aryl bromides. These complexes exhibited moderate to high catalytic activities and gave C—H activation selectively at the C(5)-position of 2-acetylfuran and 2-acetylthiophene.

1. Introduction

Robust synthetic routes for the synthesis of bi(hetero)aryls are still a challenging area of interest due to the lower reactivity of heterocycles in some of the recent booming arenas of synthetic chemistry. Cross-coupling reactions, such as Heck [1], Suzuki-Miyaura [2], Stille [3], Sonogashira [4] and arylation reactions [5], generally required the use of palladium catalysts to form C—C [6], and carbon-heteroatom bonds [7], are one of the most important subjects of organic chemistry and have attracted great attention [8–11]. In the literature, many practical methods have been developed for the transition metal-catalyzed arylation of heterocyclic compounds, such as pyrrole, furan and thiophene at the C(2), C(4) and C(5) positions [12]. Arylation reactions by the cleavage of C—H bonds are considered to be a more attractive strategy [13]; in this process, a variety of arylating reagents are used, including aryl halides, aryl organometallic reagents [14] and unactivated arenes. Recently, the direct arylation of (hetero) arenes by catalyzed palladium-NHC-PEPPSI complexes, in particular five-membered heterocycles such as furan and thiophene, has been widely described by a large number of researchers [15].

Organ et al. [16] are the pioneers of "Pyridine Enhanced Precatalyst Preparation Stabilization and Initiation" (PEPPSI); this method has been applied in several fields. In particular, nucleophilic *N*-heterocyclic carbenes (NHCs) have become one of the best ligands for transition metal catalysis [17]. Generally, C5-arylation is achieved with the use of PEPPSI-type palladium-NHC complexes [18]; the excellent performance of these complexes on organic transformations is due to both the strong δ-donor and weak π-acceptor ability of the NHC ligand [19]. There are many advantages to palladium-NHC-PEPPSI complexes [20]. First, it has been affirmed that the use of the pyridine group facilitates the binding of substrates to the complex in the oxidative addition step. Secondly, PEPPSI-type Pd-NHCs have high stability against oxygen and water [21]. These properties of PEPPSI-type complexes are highly important for the efficiency of the catalyst.

The direct arylation of heteroarenes with aryl halides has become a most valuable method for the formation of C(sp^2)-C(sp^2) bonds in contemporary organic synthesis, because of the numerous applications of heteroaromatic compounds, such as pharmaceuticals, cosmetics, natural products, biologically active

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compounds and functional materials [22–25]. Thiophene, furan and thiazole derivatives show valuable biological activity and present considerable interest in pharmaceutical chemistry. For example, Canagliflozin [26] is a drug for the treatment of type-2 diabetes, Nitrofurantoin [27] is a nitrofuran antibiotic used to treat uncomplicated urinary tract infections, Febuxostat [28] is prescribed to patients with gout suffering from hyperuricemia and it is used for chronic management, Vaborbactam [29] has been used in trials investigating the treatment of bacterial infections in subjects with varying degrees of renal insufficiency and Motapizone [30–35] is used against platelet aggregation (Scheme1). Because of these properties, the discovery of simple and direct routes to access heteroarene derivatives using a simple catalytic system remains an important challenge for organic chemists.

The palladium-catalyzed direct arylation of several heteroaromatics [36–48], via C—H bond activation using aryl halides has led to successes in recent years. For this reason, we synthesized some novel 1,3-disubstituted benzimidazolium salts (**2a-f**) and their palladium-NHC-PEPPSI complexes (**3a-f**). All the new compounds were characterized by different techniques, such as ^{1}H and ^{13}C NMR and IR. Also, the solid-state structures of the palladium complexes **3a**, **3d** and **3e** have been established by a single-crystal X-ray diffraction study. Next, the palladium-NHC-PEPPSI complexes were used as catalysts in the direct C(5)-arylation of 2-substituted heteroaryl derivatives (thiophene and furan) with various aryl bromides. The reactive C(2)-position of the heteroarenes was blocked to maximize the yields of the monoarylated products. The C(5)-arylated heteroaryl derivatives were selectively obtained in moderate to high yields.

Over the past few years, our research group has previously used palladium-NHC-PEPPSI complexes to catalyze organometallic reactions under different conditions [49].

2. Materials and methods

2.1. General remarks

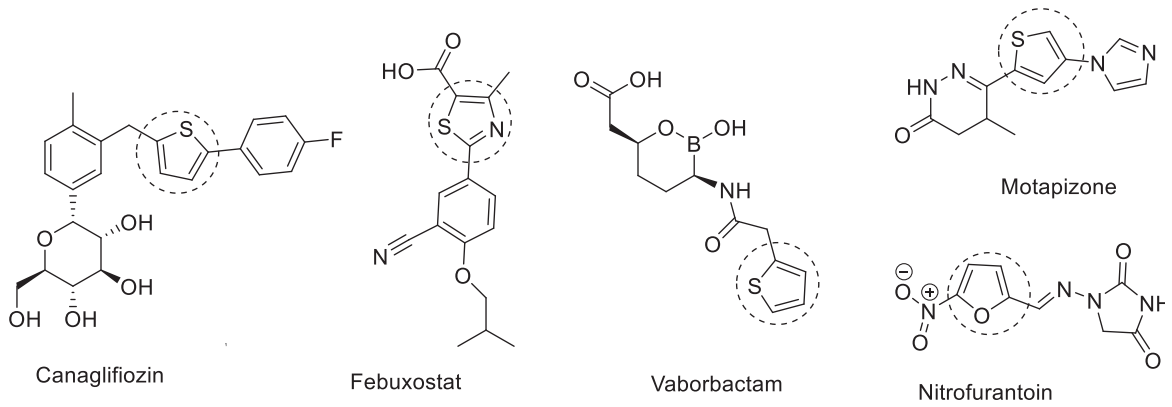
All manipulations were performed in Schlenk-type flasks under an argon atmosphere. The melting point measurements were determined in open capillary tubes with an Electrothermal-9200 melting points apparatus. The IR spectra were recorded on a Gladi ATR unit (Attenuated Total Reflection) in the range 450–4000 cm^{-1} with a Perkin Elmer Spectrum 100 Fourier-transform infrared spectrometer. Routine ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Ascend™ 400 Avance III HD NMR spectrometer with sample solutions prepared in $CDCl_3$. The chemical shifts (δ) were reported in parts per million (ppm) relative to tetramethylsilane (TMS) as an internal standard. Coupling constants (J values) are given in hertz (Hz). NMR multiplicities were abbreviated as follows: s = singlet, d = doublet, t = triplet, p = pentet, dd = doublet of doublets, tt = triplet of triplets, ddd = doublet of doublet of doublets, m = multiplet. ^{1}H NMR spectra were referenced to residual protiated solvents (δ = 7.28 ppm for $CDCl_3$) and ^{13}C NMR chemical shifts were reported relative to deuterated solvents (δ = 77.16 ppm for $CDCl_3$). The catalytic solutions were analyzed with a Shimadzu GC 2025 equipped with a GC-FID sensor and an RX-5 ms column of 30 m length, 0.25 mm diameter and 0.25 μm film thickness. The C, H and N elemental analyses were determined by an Elementar Vario MICRO CUBE.

2.2. Synthesis of 1-(1, 3-dioxolane-2-yl)methyl)benzimidazole (1)

A mixture of benzimidazole (7 g, 0.06 mol) and potassium hydroxide (8.5 g, 0.15 mol) was dissolved in DMSO (10 mL) at 50 °C for 2 h, after which 2-chloromethyl 1,3-dioxalane (7.26 g, 0.06 mol) was added and the temperature was increased to 80 °C for 72 h. The mixture was cooled to room temperature and extracted with CH_2Cl_2 (3 x15 mL) , then the solvent was removed by vacuum to give the title compound **1** (6.6 g, 94%) ,^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.92 (s, 1H, NC**H**N), 7.77 (d, J = 7.4 Hz, 1H, arom of benzimidazole), 7.46 (d, J = 7.9 Hz, 1H, arom of benzimidazole), 7.32–7.19 (m, 2H, arom of benzimidazole), 5.26–5.15 (m, 1H, C**H**CH_2), 4.31 (s, 2H, CH$C\mathbf{H_2}$), 3.77 (m, 2H, O$\mathbf{CH_2}CH_2O$), 3.68–3.58 (m, 2H, $OCH_2\mathbf{CH_2}O$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 144.28 (C), 143.49 (CH), 134.70 (C), 123.11 (CH), 122.16 (CH), 120.21 (CH), 110.27 (CH), 101.66 (CH_2), 65.59 ($2CH_2$), 47.43 (CH_2).

2.3. Synthesis of the benzimidazolium salts (2a-2f)

1-(1,3-Dioxalan-2-yl)methyl)benzimidazole (1.2 g, 1.0 mmol) was dissolved in degassed dimethylformamide (3 mL) and the alkyl halide derivative (1.0 mmol). The reaction mixture was stirred at 70 °C for 48 h under argon. After completion of the reaction, the solvent was removed by vacuum and Et_2O (15 mL) was added to the obtained solid, which was filtered off. The solid was washed with Et_2O (3 × 10 mL) and dried under a vacuum. The crude product was recrystallized from a DCM/Et_2O mixture (1:5, v/v) at room temperature, then completely dried under vacuum. All the NHC ligand precursors (**2a–2f**) were isolated as air and moisture stable in high yields.



Scheme 1. Examples of bioactive furan thiophene and thiazole derivatives.

2.3.1. 1-(1,3-Dioxalane-2-yl-methyl)-3-(4-methylbenzyl) benzimidazolium chloride (2a)

Yield 72%, white solid, m.p.: 142–143 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1557. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm:11.62 (s, 1H, NC**H**N), 7.79 (d, *J* = 8.0 Hz, 1H, $C_6\mathbf{H}_4$), 7.63–7.48 (m, 3H, C_6H_4), 7.38 (d, *J* = 8.0 Hz, 2H, $CH_2C_6\mathbf{H}_4CH_3$), 7.18 (d, *J* = 8.0 Hz, 2H, $CH_2C_6\mathbf{H}_4CH_3$), 5.85 (s, 2H, C**H**$_2$$C_6H_4CH_3$), 5.40 (t, *J* = 3.1 Hz, 1H, C**H**CH_2), 4.93 (d, *J* = 3.2 Hz, 2H, CHC**H**$_2$), 3.88–3.86 (m, 2H, OC**H**$_2$$CH_2O$), 3.85–3.83 (m, 2H, OCH_2C**H**$_2$O), 2.32 (s, 3H, $CH_2C_6H_4$C**H**$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm:144.86 (NCH), 139.24 (C), 132.30 (C), 130.80 (C), 130.01 (C), 129.74 (C), 128.21 (C), 127.01 (CH), 126.90 (CH), 113.89 (CH), 113.46 (CH), 99.98 (CH), 65.51 (CH_2), 51.39 (CH_2), 48.74 (CH_2), 21.19 (CH_3). Elemental analysis, calcd for $C_{19}H_{21}N_2O_2Cl{\cdot}H_2O$: C 62.89, H 6.39, N 7.72; found: C 61.81, H 6.29, N 7.89%.

2.3.2. 1-(1,3-Dioxalane-2-yl)methyl)-3-(4-tet-butylbenzyl) benzimidazolium bromide (2b)

Yield 94%, white solid, m.p.: 140–141 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1551. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 11.32 (s, 1H, NC**H**N), 7.81 (m, *J* = 13.7 Hz, 1H, C_6H_4), 7.66–7.53 (m, 3H, C_6H_4), 7.44–7.38 (m, *J* = 8.3 Hz, 4H, $CH_2C_6\mathbf{H}_4(C(CH_3)_3)$, 5.84 (s, 2H, C**H**$_2$$C_6H_4$(C$(CH_3)_3$)), 5.39 (t, *J* = 3.0 Hz, 1H, C**H**CH_2), 4.91 (d, *J* = 3.0 Hz, 2H, CHC**H**$_2$), 3.86 (d, *J* = 4.9 Hz, 4H, OC**H**$_2$C**H**$_2$O), 1.27 (s, 9H, $CH_2C_6H_4$(-C(C**H**$_3$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 152.60 (C), 144.25 (NCH), 132.40 (C), 130.96 (C), 129.71 (CH), 128.11 (CH), 127.19 (CH), 126.46 (CH), 113.97 (CH), 113.59 (CH), 100.00 (CH), 65.69 (CH_2), 53.57 (CH_2), 51.36 (CH_2), 48.90 (C), 34.81 (CH_3), 31.31 (CH_3). Elemental analysis, calcd for $C_{22}H_{27}N_2O_2BrxH_2Ox0.5CH_2Cl_2$: C 57.83, H 6.30, N 6.06; found: C 58.37, H 6.60, N 6.64%.

2.3.3. 1-(1,3-Dioxalane-2-yl)methyl-3-(2, 4,6-trimethylbenzyl) benzimidzolium chloride (2c)

Yield 71%, white solid, m.p.: 188–189 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1552. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 11.08 (s, 1H, NC**H**N), 7.78 (d, *J* = 8.4 Hz, 1H, C_6H_4), 7.56 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.45 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.22 (d, *J* = 8.4 Hz, 1H, C_6H_4), 6.94 (s, 2H, CH_2-$C_6\mathbf{H}_2(CH_3)_3$), 5.86 (s, 2H, C**H**$_2$$C_6H_2(CH_3)_3$), 5.35 (t, *J* = 2.9 Hz, 1H, C**H**CH_2), 4.96 (d, *J* = 2.9 Hz, 2H, CHC**H**$_2$), 3.89–3.83 (m, 2H, OC**H**$_2$-CH_2O), 3.81–3.77 (m, 2H, OCH_2C**H**$_2$O), 2.33 (s, 6H, $CH_2C_4H_2$(C**H**$_3$)$_2$ CH_3), 2.31 (s, 3H, $CH_2C_4H_2(CH_3)_2$ C**H**$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 145.53 (CNH), 140.26 (C), 138.43 (C), 132.87 (C), 131.46 (C), 130.71 (C), 127.39 (CH), 125.50 (CH), 114.35 (CH), 113.85 (CH), 100.36 (CH), 65.91 (CH_2), 49.02 (CH_2), 47.83 (CH_2), 21.57 (CH_3), 20.65 (CH_3). Elemental analysis, calcd for $C_{21}H_{25}N_2O_2ClxH_2$-O: C 64.52, H 6.96, N 7.17; found: C 65.67, H 6.68, N 7.34%.

2.3.4. 1-(1,3-Dioxolane-2- methyl)-3-(2,3,5,6-tetramethylbenzyl) benzimidazolium chloride (2d)

Yield 78%, white solid; m.p.: 167–168 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1555. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 10.68 (s, 1H, NC**H**N), 7.81 (d, *J* = 8.4 Hz, 1H, C_6H_4), 7.59 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.49 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.34 (d, *J* = 8.4 Hz, 1H, C_6H_4), 7.09 (s, 1H, C_6H_4), 5.87 (s, 2H, C**H**$_2$$C_6H$(CH3)$_4$), 5.34 (t, *J* = 2.9 Hz, 1H, C**H**CH_2), 5.00 (d, *J* = 2.9 Hz, 2H, CHC**H**$_2$), 3.86–3.83 (m, 2H, OC**H**$_2$$CH_2O$), 3.79–3.75 (m, 2H, OCH_2C**H**$_2$O), 2.27 (s, 6H, $CH_2C_6CH(CH_3)_2$C**H**$_3$)$_2$), 2.25 (s, 6H, CH_2C_6CH(C**H**$_3$)$_2$$CH_3$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 144.24 (NCH), 134.91 (C), 133.88 (C), 133.45 (C), 132.24 (C), 130.76 (C), 127.83 (CH), 126.73 (CH), 113.78 (CH), 113.07 (CH), 99.74 (CH), 65.13 (CH_2), 53.19 (CH_2), 48.41 (CH_2), 47.53 (CH_2), 20.39 (CH_3), 15.83 (CH_3). Elemental analysis, calcd for C_{21}-$H_{25}N_2O_2ClxH_2O$: C 64.52, H 6.96, N 7.17; found: C 65.67, H 6.68, N 7.34%.

2.3.5. 1-(1,3-Dioxalane-2-yl)methyl)-3-(2,3,4,5,6-pentamethylbenzyl) benzimidazolium chloride (2e)

Yield 67%, white solid, m.p. 175–176 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1558. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 10.52 (s, 1H, NC**H**N), 7.80 (d, *J* = 8.4 Hz, 1H, C_6H_4), 7.59 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.50 (t, *J* = 7.8 Hz, 1H, C_6H_4), 7.38 (d, *J* = 8.4 Hz, 1H, C_6H_4), 5.83 (s, 2H, C**H**$_2$-$C_6C(CH_3)_5$), 5.34 (t, *J* = 2.8 Hz, 1H, C**H**CH_2), 5.03 (d, *J* = 2.7 Hz, 2H, CHC**H**$_2$), 3.83 (t, *J* = 7.0 Hz, 2H, OC**H**$_2$$CH_2O$), 3.76 (t, *J* = 7.3 Hz, 2H, OCH_2C**H**$_2$O), 2.29 (s, 9H, CH_2C_6(C**H**$_3$)$_3$$(CH_3)_2$), 2.25 (s, 6H, CH_2C_6(-$CH_3)_3$(C**H**$_3$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 144.30 (CNH), 137.42 (C), 133.98 (C), 132.53 (C), 131.03 (C), 126.97 (C), 126.89 (CH), 124.78 (CH), 114.00 (CH), 113.22 (CH), 99.99 (CH), 65.39 (CH_2), 48.64 (CH_2), 48.15 (CH_2), 17.36 (CH_3), 17.05 (CH_3), 17.01 (CH_3). Elemental analysis, calcd for $C_{23}H_{29}N_2O_2Clx0.5CH_2Cl_2$: C 63.66, H 6.82, N 6.32; found: C 63.44, H 6.96, N 6.74%.

2.3.6. 1-(1,3-Dioxalane-2-yl)methyl)-3-(anthracen-9-ylmethyl) benzimidazolium chloride (2f)

Yield 58%, yellow solid, m.p. 197–198 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1564. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 11.51 (s, 1H, NC**H**N), 8.61 (s, 1H, $CH_2C_6H_4C_6\mathbf{H}C_6H_4$), 8.53 (d, *J* = 8.9 Hz, 2H, $CH_2C_6\mathbf{H}_4C_6$-$HC_6\mathbf{H}_4$), 8.09 (d, *J* = 8.5 Hz, 2H, $CH_2C_6\mathbf{H}_4C_6HC_6\mathbf{H}_4$ and C_6H_4), 7.73–7.65 (m, 3H, C_6H_4), 7.57–7.51 (m, 2H, $CH_2C_6\mathbf{H}_4C_6HC_6\mathbf{H}_4$), 7.42 (t, *J* = 7.9 Hz, 1H, $CH_2C_6\mathbf{H}_4C_6HC_6\mathbf{H}_4$), 7.18 (t, *J* = 7.9 Hz, 1H, $CH_2C_6\mathbf{H}_4C_6$-$HC_6\mathbf{H}_4$), 7.04 (d, *J* = 8.5 Hz, 1H, $CH_2C_6\mathbf{H}_4C_6HC_6\mathbf{H}_4$), 6.96 (s, 2H, C**H**$_2$-$C_6H_4C_6HC_6H_4$), 5.33 (t, *J* = 2.8 Hz, 1H, C**H**CH_2), 4.87 (d, *J* = 2.8 Hz, 2H, CHC**H**$_2$), 3.79 (t, *J* = 7.0 Hz, 2H, OC**H**$_2$$CH_2O$), 3.62 (t, *J* = 7.1 Hz, 2H, OCH_2C**H**$_2$O). ^{13}C NMR (100 MHz, DMSO) δ, ppm: 143.49 (NHC), 133.52 (C), 133.42 (C), 133.24 (C), 131.79 (C), 130.17 (C), 129.11 (CH), 128.15 (CH), 127.88 (CH), 126.94 (CH), 124.57 (CH), 123.21 (CH), 115.82 (CH), 115.25 (CH), 101.02 (CH), 65.94 (CH_2), 48.78 (CH_2), 44.78 (CH_2). Elemental analysis, calcd for $C_{26}H_{23}N_2O_2$-$ClxH_2O$: C 69.56, H 5.61, N 6.24; found: C 67.66, H 5.62, N 6.11%.

2.4. General procedure for the synthesis of the PEPPSI-type palladium-NHC complexes (3a-3f)

The benzimidazolium salts (**2a–2f**, 1.0 mmol) with $PdCl_2$ (1.0 eq) and pyridine (2.0 eq), in the presence of K_2CO_3 (5.0 eq) and KBr (10.0 eq), were dissolved in acetonitrile at 80 °C for 10 h. Next, all volatiles were removed under vacuum and the solid residue was washed with hexane (2 × 5 mL). The crude product was purified by column chromatography using CH_2Cl_2 to afford the corresponding Pd-PEPPSI-NHC complex. The palladium complex was crystallized from a CH_2Cl_2/hexane solvent mixture (1:6, *v/v*) at room temperature, and completely dried under vacuum. The benzimidazole-2-ylidene based Pd-PEPPSI-NHC complexes were isolated as air- and moisture-stable bright yellow solids.

2.4.1. Dibromo[1-((1,3-dioxalane-2-yl)-3-(4-methylbenzyl) benzimidazol-2-ylidene](pyridine)palladium (II) (3a)

Yield 90%, yellow crystal; m.p.: 217–218 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1407. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.04 (dd, *J* = 6.5, 1.6 Hz, 2H, $NC_5\mathbf{H}_5$), 7.76 (tt, *J* = 7.6, 1.6 Hz, 1H, $NC_5\mathbf{H}_5$), 7.59 (d, *J* = 8.2 Hz, 1H, $C_6\mathbf{H}_4$), 7.46 (d, *J* = 8.0 Hz, 2H, $CH_2C_6\mathbf{H}_4CH_3$), 7.34 (ddd, *J* = 7.6, 5.0, 1.4 Hz, 1H, $NC_5\mathbf{H}_5$), 7.25–7.21 (m, 1H, $C_6\mathbf{H}_4$), 7.15 (d, *J* = 7.9 Hz, 2H, $CH_2C_6\mathbf{H}_4CH_3$), 7.12–7.07 (m, 1H, $C_6\mathbf{H}_4$), 7.03 (d, *J* = 8.1 Hz, 1H,$C_6\mathbf{H}_4$), 6.14 (s, 2H, C**H**$_2$$C_6H_4CH_3$), 5.82 (t, *J* = 4.5 Hz, 1H, C**H**CH_2), 5.10 (d, *J* = 4.5 Hz, 2H, CHC**H**$_2$), 4.12–4.08 (m, 2H, OC**H**$_2$$CH_2O$), 3.98–3.94 (m, 2H, OCH_2C**H**$_2$O), 2.33 (s, 3H, $CH_2C_6H_4$-C**H**$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 164.54 (NCH), 152.64 ($C_{pyridine}$), 137.94 (C), 137.87 (C), 135.83 (C),134.24 (C), 131.72 (C), 129.48 (CH), 128.00 (CH), 124.56 (CH), 123.16 (CH), 123.09 (CH), 111.76 (CH), 111.38 (CH), 102.49 (CH), 65.32 (CH_2), 53.58 (CH_2), 51.72 (CH_2), 21.19 (CH_3). Elemental analysis, calcd for C_{24}-

$H_{25}N_3O_2Br_2Pd$: C 44.10, H 3.85, N 6.43; found: C 43.74, H 3.81, N 6.62%.

2.4.2. Dibromo[1-((1,3-dioxalane-2-yl)-3-(4-(tert-butyl)benzyl) benzimidazol-2-ylidene)](pyridine)palladium (II) (3b)

Yield 68%, yellow crystal; m.p.: 219–220 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1404. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.03 (dd, *J* = 6.5, 1.6 Hz, 2H, $NC_5\mathbf{H_5}$), 7.75 (tt, *J* = 7.7, 1.6 Hz, 1H, $NC_5\mathbf{H_5}$), 7.59 (d, *J* = 8.2 Hz, 1H,$C_6\mathbf{H_4}$), 7.52 (d, *J* = 8.4 Hz, 2H, $NC_5\mathbf{H_5}$), 7.38–7.30 (m, 4H,CH_2C_6-$\mathbf{H_4}C(CH_3)_3$), 7.25–7.20 (m, 1H, $C_6\mathbf{H_4}$), 7.14–6.98 (m, 2H, $C_6\mathbf{H_4}$), 6.13 (s, 2H, $C\mathbf{H_2}C_6H_4C(CH_3)_3$)), 5.81 (t, *J* = 4.5 Hz, 1H, $C\mathbf{H}CH_2$), 5.09 (d, *J* = 4.5 Hz, 2H,$CHC\mathbf{H_2}$), 4.10 (t, *J* = 7.0 Hz, 2H, $OC\mathbf{H_2}CH_2O$), 3.96 (t, *J* = 6.9 Hz, 1H, OCH_2CH_2O), 1.28 (s, 9H, $CH_2C_6H_4C(C\mathbf{H_3})_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 164.51 (NCH), 152.67 (C), 151.10 ($C_{pyridine}$), 137.92 (C), 135.83 (C), 134.29 (C), 131.74 (CH), 127.82 (CH), 125.73 (CH), 124.56 (CH), 123.14 (CH), 123.07 (CH), 111.76 (CH), 111.42 (CH), 102.51 (CH), 65.32 (CH_2), 53.50 (CH_2), 51.73 (CH_2), 34.58 (CH_3), 31.31 (CH_3). Elemental analysis, calcd for $C_{27}H_{31}N_3O_2Br_2Pd$: C 46.61, H 4.49, N 6.04; found: C 46.72, H 4.56, N 6.20%.

2.4.3. Dibromo[1-((1,3-dioxalane-2-yl)-3-(2,4,6-trimethylbbenzyl) benzimidazol-2-ylidene](pyridine)palladium (II) (3c)

Yield 72%, yellow crystal; m.p.: 262–263 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1403. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.04 (dd, *J* = 6.5, 1.6 Hz, 2H, $NC_5\mathbf{H_5}$), 7.78 (tt, *J* = 7.7, 1.6 Hz, 1H, $NC_5\mathbf{H_5}$), 7.56 (d, *J* = 8.2 Hz, 1H, $C_6\mathbf{H}_4$), 7.36 (ddd, *J* = 7.6, 5.1, 1.4 Hz, 2H, $NC_5\mathbf{H_5}$), 7.18–7.14 (m, 1H, $C_6\mathbf{H}_4$), 6.95 (s, 2H, $CH_2C_6\mathbf{H_2}(CH_3)_3$), 6.94–6.89 (m, 1H, $C_6\mathbf{H}_4$), 6.28 (d, *J* = 8.4 Hz, 1H, $C_6\mathbf{H}_4$), 6.14 (s, 2H, $C\mathbf{H_2}C_6H_2(CH_3)_3$), 5.82 (t, *J* = 4.6 Hz, 1H, $C\mathbf{H}CH_2$), 5.09 (d, *J* = 4.6 Hz, 2H, $CHC\mathbf{H_2}$), 4.12–4.04 (m, 2H, $OC\mathbf{H_2}CH_2O$), 3.97–3.93 (m, 2H, $OCH_2C\mathbf{H_2}O$), 2.35 (s, 3H, $CH_2C_6H_2(C\mathbf{H}_3)_3$), 2.33 (s, 6H, $CH_2C_6H_2(C\mathbf{H}_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 164.25 (NCH), 152.64 ($C_{pyridine}$), 139.04 (C), 138.74 (C), 137.91 (C), 135.61 (C), 134.69 (C), 129.54 (CH), 127.36 (CH), 124.56 (CH), 123.17 (CH), 122.66 (CH), 111.57 (CH), 111.14 (CH), 102.59 (CH), 65.29 (CH_2), 51.73 (CH_2), 51.10 (CH_2), 22.66 (CH_3),21.14 (CH_3), 20.94 (CH_3). Elemental analysis, calcd for $C_{26}H_{29}N_3O_2Br_2Pd$: C 45.81, H 4.29, N 6.16; found: C 47.13, H 4.56, N 6.15%.

2.4.4. Dibromo-[1-((1,3-dioxalane-2-yl)methyl)-3-(2,3,5,6-tetramethylbenzyl)benzimdazol-2-ylidene](pyridine)palladium(II) (3d)

Yield 70%, yellow crystal; m.p.: 226–227 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1376. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.01 (dd, *J* = 6.4, 1.5 Hz, 2H, $NC_5\mathbf{H_5}$), 7.77 (tt, *J* = 7.7, 1.6 Hz, 1H, $NC_5\mathbf{H_5}$), 7.56 (d, *J* = 8.2 Hz, 1H, $NC_5\mathbf{H_5}$), 7.38–7.33 (m, 2H,$C_6\mathbf{H}_4$), 7.26 (s, 1H, $CH_2C_6\mathbf{H}(CH_3)_4$), 7.16 (ddd, *J* = 8.2, 3.2, 1.6 Hz, 1H,$C_6\mathbf{H_4}$), 7.10 (d, *J* = 4.4 Hz, 1H, $C_6\mathbf{H_4}$), 6.97–6.90 (m, 1H, $C_6\mathbf{H_4}$), 6.17 (s, 2H, $C\mathbf{H_2}C_6H(CH_3)_4$), 5.83 (t, *J* = 4.6 Hz, 1H, $C\mathbf{H}CH_2$), 5.09 (d, *J* = 4.6 Hz, 2H, $CH\mathbf{CH_2}$), 4.12–4.09 (m, 2H, $OC\mathbf{H_2}CH_2O$), 3.97–3.93 (m, 2H, $OCH_2C\mathbf{H_2}O$), 2.27 (s, 6H, $CH_2C_6H(C\mathbf{H}_3)_4$), 2.25 (s, 6H, $CH_2C_6H(C\mathbf{H}_3)_4$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 164.01 (NCH), 152.42 ($C_{pyridine}$), 151.51 ($C_{pyridine}$), 137.69 (C), 135.63 (C), 135.08 (C), 134.99 (C), 134.71 (C), 134.16 (CH), 132.44 (CH), 130.17 (CH), 124.37 (CH), 122.97 (CH), 122.42 (CH), 111.38 (CH), 110.95 (CH), 102.43 (CH), 65.11 (CH_2), 51.61 (CH_2), 51.36 (CH_2), 29.52 (CH_3), 20.42 (CH_3), 16.50 (CH_3),16.40 (CH_3).

2.4.5. Dibromo[1-((1,3-dioxalane-2-yl)-3-(2,3,4,5,6-pentamethylbenzyl)benzimidazol-2-ylidene](pyridine)palladium (II) (3e)

Yield 77%, yellow crystal; m.p.: 268–269 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1394. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.02 (dd, *J* = 6.5, 1.6 Hz, 2H, $NC_5\mathbf{H_5}$), 7.77 (tt, *J* = 7.6, 1.6 Hz, 1H, $NC_5\mathbf{H_5}$), 7.55 (d, *J* = 8.2 Hz, 1H,$C_6\mathbf{H_4}$), 7.35 (ddd, *J* = 7.6, 5.1, 1.4 Hz, 2H, $NC_5\mathbf{H_5}$), 7.17–7.12 (m, 1H, $C_6\mathbf{H_4}$), 6.93–6.84 (m, 1H, $C_6\mathbf{H_4}$), 6.24 (d, *J* = 8.4 Hz, 1H, $C_6\mathbf{H_4}$), 6.20 (s, 2H, $C\mathbf{H_2}C_6(CH_3)_5$), 5.83 (t, *J* = 4.6 Hz, 1H, $C\mathbf{H}CH_2$), 5.09 (d, *J* = 4.6 Hz, 2H, $CHC\mathbf{H_2}$), 4.14–4.08 (m, 2H, $OC\mathbf{H_2}CH_2O$), 3.98–3.90 (m, 2H, $OCH_2C\mathbf{H_2}O$), 2.33 (s, 3H, $CH_2C_6(C\mathbf{H_3})_5$), 2.29 (s, 6H, $CH_2C_6(C\mathbf{H_3})_5$), 2.25 (s, 6H, $CH_2C_6(C\mathbf{H_3})_5$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 164.79 (NCH), 153.42 ($C_{pyridine}$), 138.67 (C), 136.91 (C), 136.39 (C), 135.77 (C), 135.77 (C), 135.63 (C), 133.92 (CH), 128.42 (CH), 125.33 (CH), 123.89 (CH), 123.30 (CH), 112.26 (CH), 112.13 (CH), 103.42 (CH), 66.09 (CH_2), 53.11 (CH_2), 52.56 (CH_2), 18.45 (CH_3), 18.10 (CH_3), 17.73 (CH_3). Elemental analysis, calcd for $C_{28}H_{33}N_3O_2Br_2Pd$: C 47.38, H 4.69, N 5.92; found: C 46.53, H 4.52, N 5.81%.

2.4.6. Dibromo[1-((1,3-dioxalane-2-yl)-3-(anthracen-9-ylmethyl) benzimidazol-2-ylidene](pyridine)palladium (II) (3f)

Yield 92%, yellow crystal; m.p.: 291–292 °C. FT-IR (cm^{-1}): $\nu_{(CN)}$ 1405. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 9.00 (dd, *J* = 6.5, 1.6 Hz, 2H, $NC_5\mathbf{H_5}$), 8.65 (s, 1H, $CH_2C_6H_4C_6\mathbf{H}C_6H_4$), 8.62 (d, *J* = 4.7 Hz, 2H, $CH_2C_6\mathbf{H_4}C_6HC_6\mathbf{H_4}$ and $C_6\mathbf{H_4}$), 8.07 (d, *J* = 8.2 Hz, 2H, $CH_2C_6\mathbf{H_4}C_6HC_6$-$\mathbf{H_4}$), 7.75 (tt, *J* = 7.7, 1.6 Hz, 1H, $NC_5\mathbf{H_5}$), 7.57–7.44 (m, 5H, $CH_2C_6\mathbf{H_4}$-$C_6HC_6\mathbf{H_4}$ and$C_6\mathbf{H_4}$), 7.34 (ddd, *J* = 7.6, 5.1, 1.4 Hz, 2H, $NC_5\mathbf{H_5}$), 7.11 (s, 2H, $C\mathbf{H_2}C_6H_4C_6HC_6H_4$), 7.07–6.97 (m, 1H, $C_6\mathbf{H_4}$), 6.67–6.51 (m, 1H, $C_6\mathbf{H}_4$), 5.93 (d, *J* = 8.4 Hz, 1H, $C_6\mathbf{H}_4$), 5.87 (t, *J* = 4.5 Hz, 1H, $C\mathbf{H}CH_2$), 5.14 (d, *J* = 4.5 Hz, 2H, $CHC\mathbf{H_2}$), 4.16–4.04 (m, 2H, $OC\mathbf{H_2}$-CH_2O), 4.02–3.89 (m, 2H, $OCH_2C\mathbf{H_2}O$). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 164.52 (NCH), 152.62 ($C_{pyridine}$), 137.90 (C), 135.71 (C), 134.59 (C), 131.67 (C), 131.31 (C), 130.25 (C), 129.74 (CH), 129.20 (CH), 127.34 (CH), 125.38 (CH), 124.81 (CH), 124.56 (CH), 124.30 (CH), 123.08 (CH), 122.61 (CH), 111.59 (CH), 102.58 (CH), 65.30 CH_2), 51.79 (CH_2), 49.34 (CH_2). Elemental analysis, calcd for $C_{31}H_{27}N_3O_2Br_2Pd$: C 50.33, H 3.68, N 5.68; found: C 50.03, H 3.50, N 5.71%.

2.5. General procedure for the Pd-NHC catalyzed direct arylation of C2-substituted heteroarenes

Typically, the C(2)-substituted heteroarene (2.0 mmol), aryl bromide (1.0 mmol), KOAc (2.0 mmol) and DMA (2 mL) were added to an oven-dried Schlenk tube under an argon atmosphere. Subsequently, the Pd–carbene catalyst (**3a**–**3f**) (0.01 mmol, 1 mol %) was added to the stirred solution in the Schlenk tube, then the closed Schlenk tube was stirred at 130 °C for 1 h. (oil bath temperature). At the end of the reaction, the solution was cooled to room temperature and dichloromethane (2 mL) was added to the crude mixture. The solution was filtered through a pad of celite to remove the solid particles and then used for GC analysis. The yields were calculated according to the (hetero)aryl halide by GC analysis.

2.6. Mercury poisoning experiment

2-Acetylfuran (2.0 mmol), 4-bromobenazldeyde (1.0 mmol), KOAc (2.0 mmol) and DMA (2 mL) were added to an oven-dried Schlenk tube under an argon atmosphere. Subsequently, the Pd–carbene catalyst **3e** (0.01 mmol, 1 mol%) was added to the stirred solution in the Schlenk tube and one drop of Hg was added with a syringe to the reaction mixture. The closed Schlenk tube was stirred at 130 °C for 1 h (oil bath temperature). At the end of the reaction, the solution was cooled to room temperature and dichloromethane (2 mL) was added to the crude mixture. The solution was filtered through a pad of celite to remove the solid particles and then used for GC analysis. The yields were calculated according to the (hetero)aryl halide by GC analysis.

2.7. X-ray analysis

X-ray data of the compounds were collected with an STOE IPDS II diffractometer at room temperature using graphite-monochromated Mo Kα radiation by applying the ω-scan method. Data collection and cell refinement were carried out using X-AREA [50], while data reduction was applied using X-RED32 [50]. The structures were solved using the charge-flipping algorithm by SUPERFLIP [51] and refined using full-matrix least-squares calculations on F^2 using SHELXL-2018 [52]. All H atoms were placed geometrically and treated using a riding model, fixing the bond lengths at 0.93, 0.98, 0.97 and 0.96 Å for aromatic CH, methine CH, CH_2 and CH_3 atoms, respectively. The displacement parameters of the H atoms were fixed at $U_{iso}(H) = 1.2U_{eq}$ ($1.5U_{eq}$ CH_3) of their parent atoms. In **3d**, the dioxolane ring was disordered over two positions with occupancy factors of 0.597(9)/0.403(9) %. Crystal data, data collection and structure refinement details are collected in Table 1. The molecular graphics were generated using OLEX2 [53].

3. Results and discussion

3.1. Synthesis and spectral characterization of the benzimidazoles salts and their palladium complexes

The synthesis of the target 1,3-disubstituted benzimidazolium salts **2a–f** has been achieved via a two-step *N*-alkylation process, as depicted in Scheme 2. The step first involves the alkylation of benzimidazole with 2-chloromethyl-1,3-dioxalane in the presence of KOH in DMSO at 80 °C for 72 h to the corresponding benzimidazole, enhancing the reactivity of the other nitrogen atom. The addition of another alkylating agent to the remaining nitrogen atom gives the desired 1,3-disubstituted benzimidazolium salts **2a–f**.

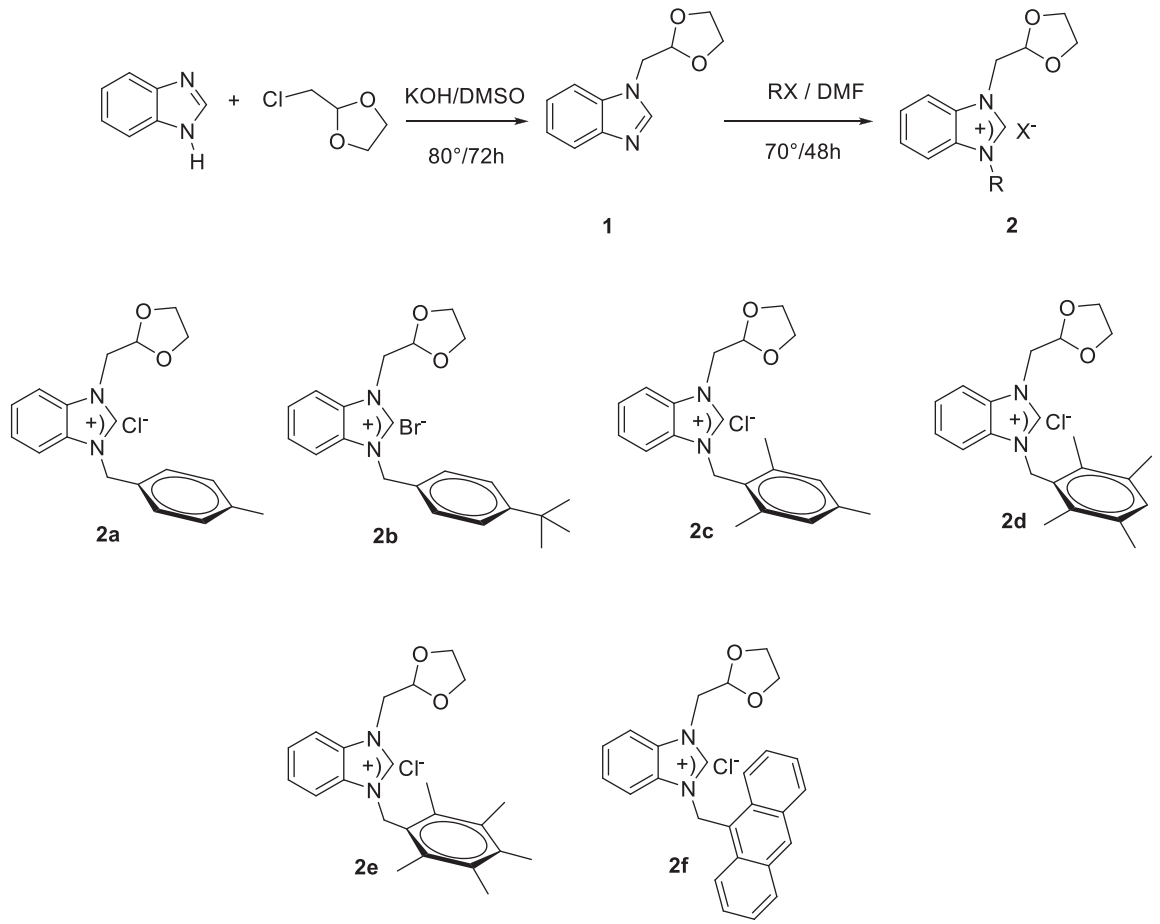
The new 1,3-disubstituted benzimidazolium salts **2a–f** were prepared by reacting 1-(1,3-dioxolane-2-yl) methyl)-benzimidazole with various alkyl chlorides in DMF at 70 °C for 48 h, Scheme 2. The salts were soluble in polar solvents like methanol, ethanol, DMSO and DMF, but insoluble in non-polar solvents like diethyl ether, dichloromethane and chloroform. The benzimidazolium salts **2a–f** are air- and moisture-stable, both in the solid-state and in solution. The benzimidazolium salts were characterized using ^{1}H NMR, ^{13}C NMR , elemental analysis and FT-IR spectroscopy, which confirmed the proposed structures. The NMR spectra of all the compounds were analyzed in d-$CDCl_3$. In the ^{1}H NMR spectra, the acidic protons (NCHN) for **2a-f** were seen at δ 11.62, 11.32, 11.08, 10.68, 10.52 and 11.51 ppm, respectively, as a characteristic sharp singlet. In the ^{13}C NMR spectra of **2a-f**, the NCHN carbon atom was detected as a typical singlet at δ 144.86, 152.60, 145.53, 144.24, 144.30 and 143.49 ppm, respectively. These NMR values are in line with those found for other benzimidazolium salts in the literature [54]. The formation of the benzimidazolium salts was also evidenced by their IR spectra, which showed an absorption at 1557, 1551, 1552, 1555, 1558 and 1564 cm^{-1} for the respective CN bond vibrations of **2a–f**.

The general procedure for the preparation of the PEPPSI-type palladium-NHC complexes **3a–f** is shown in Scheme 3. The reactions were carried out in the presence of pyridine as an *N*-donor ligand in acetonitrile (MeCN) at 80 °C for 10 h, and the target complexes were obtained. The benzimidazolium salts **2a–f** were incorporated into the PEPPSI-type palladium–NHC complexes **3a–f** by their reaction with $PdCl_2$ in pyridine, by heating at 80 °C for 10 h in the presence of K_2CO_3 as a base. The air and moisture-stable PEPPSI-type palladium-NHC complexes are yellow in color and soluble in common organic solvents such as acetone, dichloromethane, chloroform, DMF, ethyl acetate and acetonitrile (Scheme 3).

The complexes **3a-3f** were characterized by ^{1}H NMR, ^{13}C NMR, IR and X-ray diffraction techniques. In the ^{1}H NMR spectra of the palladium-carbene complexes complexes **3a-3f**, the characteristic

Table 1
Crystal data and structure refinement parameters for **3a**, **3d** and **3e**.

Parameters	**3a**	**3d**	3e
CCDC depository	2042615	2042616	2,042,617
Color/shape	Yellow/prism	Yellow/prism	Yellow/prism
Chemical formula	$[PdBr_2(C_{19}H_{20}N_2O_2)(C_5H_5N)]$	$[PdBr_2(C_{22}H_{26}N_2O_2)(C_5H_5N)]$	$[PdBr_2(C_{23}H_{28}N_2O_2)(C_5H_5N)]$
Formula weight	653.69	695.77	709.79
Temperature (K)	296(2)	296(2)	296(2)
Wavelength (Å)	0.71073 Mo Kα	0.71073 Mo Kα	0.71073 Mo Kα
Crystal system	Orthorhombic	Monoclinic	Monoclinic
Space group	$P2_12_12_1$ (No. 19)	$C2/c$ (No. 15)	$P2_1/c$ (No. 14)
Unit cell parameters			
a, b, c (Å)	11.5282(7), 13.3631(8), 16.5657(9)	22.6751(10), 8.4460(3), 28.5415(11)	13.8789(9), 13.6413(11), 15.3642(10)
α, β, γ (°)	90, 90, 90	90, 96.922(3), 90	90, 102.057(5), 90
Volume ($Å^3$)	2552.0(3)	5426.3(4)	2844.7(4)
Z	4	8	4
$D_{calc.}$ (g/cm^3)	1.701	1.703	1.657
μ (mm^{-1})	3.883	3.658	3.491
Absorption correction	Integration	Integration	Integration
$T_{min.}$, $T_{max.}$	0.2587, 0.6374	0.4302, 0.8061	0.2679, 0.7310
F_{000}	1288	2768	1416
Crystal size (mm^3)	0.63 × 0.20 × 0.15	0.41 × 0.14 × 0.07	0.48 × 0.44 × 0.07
Diffractometer/measurement method	STOE IPDS II/ω scans	STOE IPDS II/ω scans	STOE IPDS II/ω scans
Index ranges	$-13 \le h \le 13$, $-15 \le k \le 15$, $-19 \le l \le 19$	$-29 \le h \le 29$, $-10 \le k \le 10$, $-36 \le l \le 36$	$-14 \le h \le 16$, $-16 \le k \le 16$, $-18 \le l \le 18$
θ range for data collection (°)	$1.958 \le \theta \le 25.049$	$1.437 \le \theta \le 27.443$	$2.016 \le \theta \le 25.047$
Reflections collected	23,213	23,339	26,921
Independent/observed reflections	4528/3354	6179/3230	5035/4172
$R_{int.}$	0.2157	0.0776	0.1479
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	4528/0/290	6179/223/366	5035/0/325
Goodness-of-fit on F^2	1.058	0.970	1.106
Final R indices [I greater than $2\sigma(I)$]	$R_1 = 0.0798$, $wR_2 = 0.1665$	$R_1 = 0.0695$, $wR_2 = 0.1697$	$R_1 = 0.0462$, $wR_2 = 0.1092$
R indices (all data)	$R_1 = 0.1067$, $wR_2 = 0.1810$	$R_1 = 0.1380$, $wR_2 = 0.2011$	$R_1 = 0.0585$, $wR_2 = 0.1148$
$\Delta\rho_{max}$, $\Delta\rho_{min.}$ ($e/Å^3$)	2.16, −0.70	1.30, −1.08	1.27, −0.70



Scheme 2. Synthesis and structure of the benzimidazolium salts **2a-f.**

down-field signals for the acidic C(2)-*H* protons of the benzimidazolium salts **2a-2f** disappeared. This suggests the formation of the palladium-NHC-PEPPSI complexes. Also, the formation of carbenes is correlated by a shift of the (CN) vibration from 1551 to 1564 cm^{-1} in the benzimidazolium salts to1376-1407 cm^{-1} in the coordinated carbenes [55]; the FT-IR data indicated ν(CN) at 1407, 1404, 1403, 1376, 1394 and 1405 cm^{-1} for the PEPPSI Pd-NHC complexes **3a-f**, respectively. The Pd–carbene resonances of these novel PEPPSI Pd-NHC complexes in the ^{13}C NMR spectra appeared highly downfield shifted at δ 164.54 164.51, 164.25, 164.01, 164.79 and 164.52 ppm for **3a-f**, respectively. The analytical data are in good agreement with the compositions proposed for all the newly prepared compounds.

3.2. Description of the crystal structures of the palladium-carbene complexes 3a, 3d and 3e.

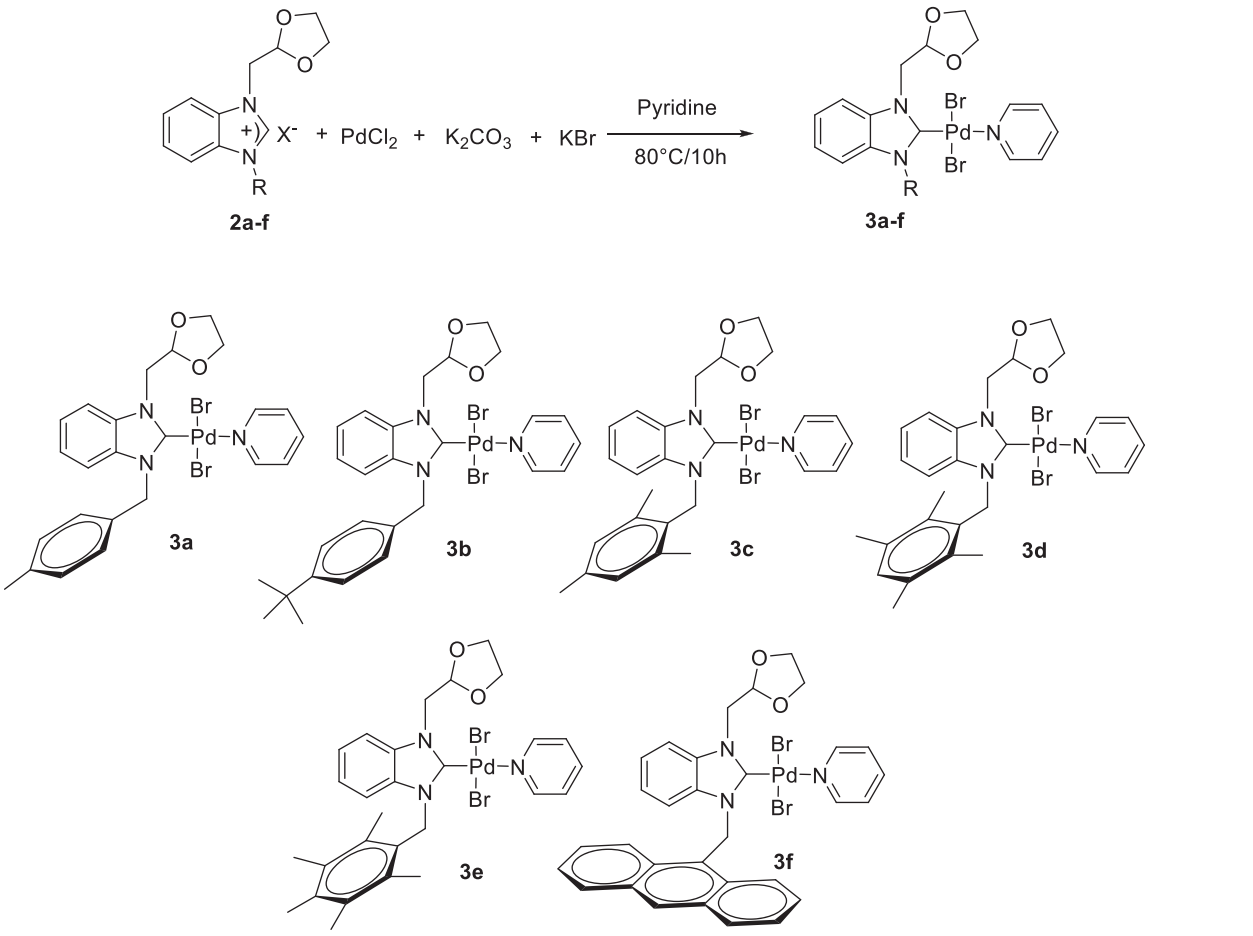
The molecular diagrams of **3a**, **3d** and **3e**, with the adopted atom-labelling scheme, are shown in Figs. 1-3, while important bond distances and angles are listed in Table 2.

The three complexes show slightly distorted square-planar geometries around the palladium center, which are encompassed by the carbonic carbon atom of NHC, the nitrogen atom of the pyridine ring and two bromo ligands in a *trans* configuration. The *cis* angles, varying from 87.3(6) to 93.12(11)°, and the *trans* angles, changing from 173.04(5) to 179.6(7)°, deviate from their expected values of 90 and 180°. The four-coordinate geometry index τ_4 (0 for an ideal square-planar geometry and 1 for a perfect tetrahedral geometry) [56] is 0.03 for **3a**, 0.07 for **3d** and 0.04 for **3e**. The τ_4 values show that the distortion in the coordination polyhedron of **3d** is a little more than for the other complexes.

The average Pd—C_{NHC} bond distance [1.961 Å] is smaller than the sum of the individual covalent radii of the palladium and carbon atoms (2.12 Å), while the average Pd—$N_{pyridine}$ bond distance [2.116 Å] is close to the sum of the individual covalent radii of the palladium and nitrogen atoms (2.10 Å) [57]. The Pd—Br bond lengths are in the typical range and interestingly bent toward the NHC ligand rather than toward the non-bulky pyridine ligand. These values are in good agreement with those found in other Pd-NHC-pyridine-Br_2 complexes [58–64]. In the NHC ligands, the dioxolane ring adopts an envelope conformation and the internal N—C—N ring angle at the carbene centers vary from 106.9(7) to 107.2(4)°. The carbene ring is nearly perpendicular to the $PdCNBr_2$ coordination plane, with a dihedral angle of 76.8(5)° in **3a**, 76.3(3)° in **3d** and 75.53(14)° in **3e**, which is typical for NHC complexes, reducing steric congestion. Furthermore, the dihedral angle between the pyridine ring and the coordination plane is found to be 68.9(8)° in **3a**, 53.7(6)° in **3d** and 58.3(2)° in **3e**.

3.3. Catalytic studies

Over the last two decades, the transition-metal-catalyzed direct C—H arylation of arenes with aryl halides has appeared as an efficient method for the preparation of heteroarene derivatives, such as arylated thiophenes, furans and thiazole [65]. In 1990, Ohta et al. reported the arylation of thiophenes, furans and thiazoles with aryl halides, via a C—H bond activation, in moderate to good yields using 5 mol% $Pd(PPh_3)_4$ as the catalyst [66]. Since these



Scheme 3. Synthesis of the Pd-PEPPSI complexes **3a-f.**

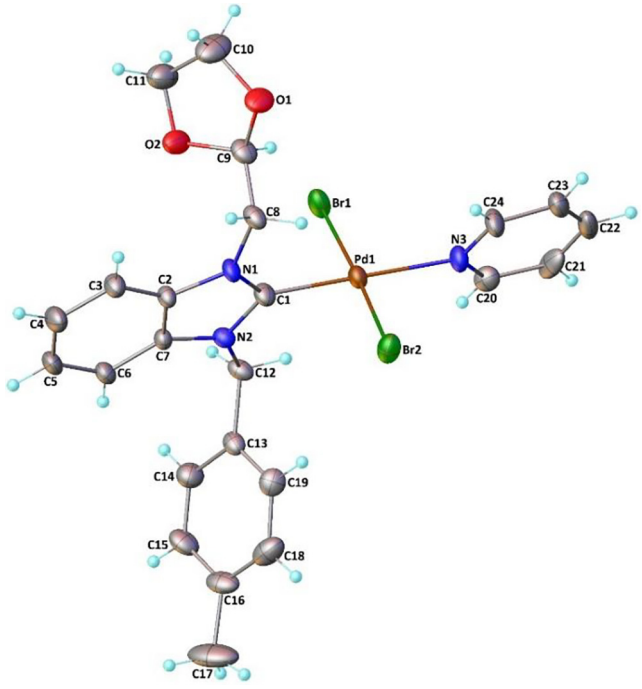


Fig. 1. Molecular structure of **3a**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

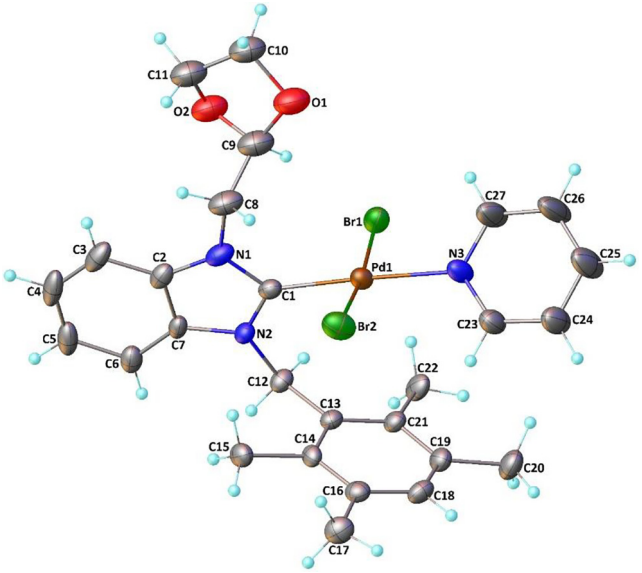


Fig. 2. Molecular structure of **3d**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii. For clarity, only the major part of the disordered dioxolane ring is shown.

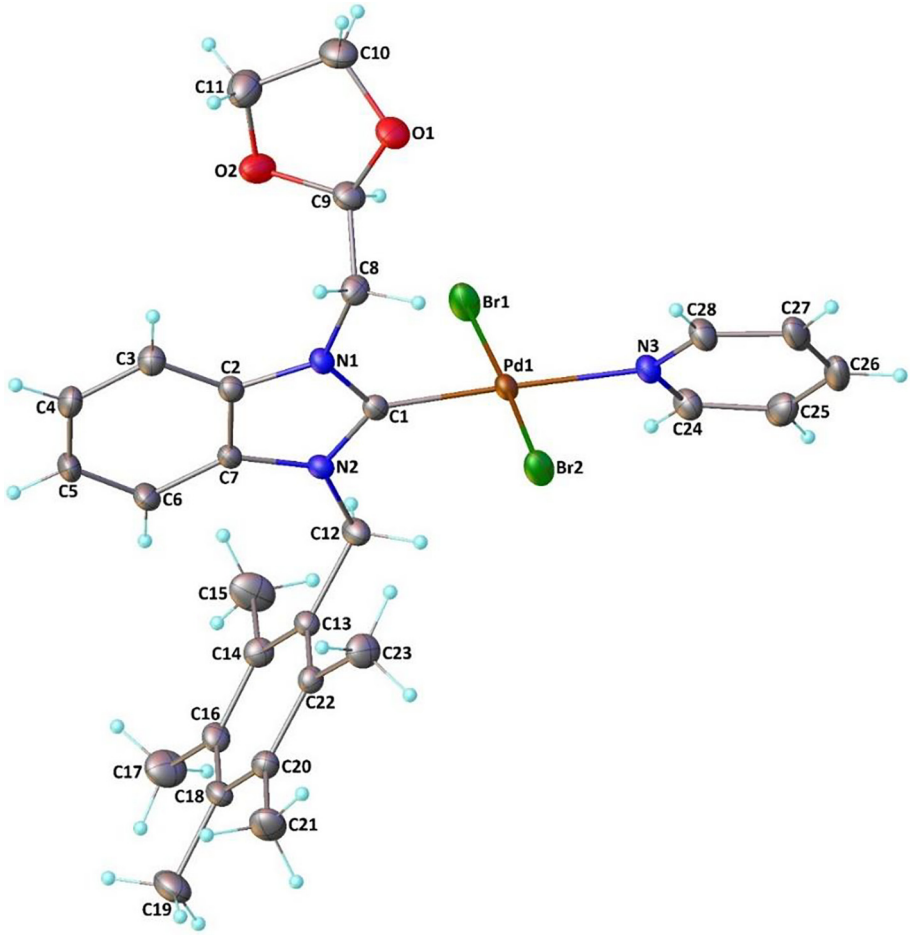


Fig. 3. Molecular structure of **3e**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

Table 2
Selected geometric parameters for **3a**, **3d** and **3e**.

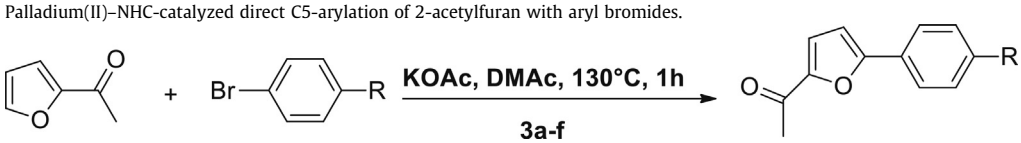
Parameters	3a	3d	3e
Bond lengths (Å)			
Pd1—Br1	2.450(2)	2.4289(11)	2.4461(6)
Pd1—Br2	2.435(2)	2.4186(12)	2.4298(6)
Pd1—N3	2.132(12)	2.097(8)	2.120(4)
Pd1—C1	1.963(16)	1.957(9)	1.964(4)
N1—C1	1.37(2)	1.363(10)	1.354(5)
N1—C2	1.416(18)	1.392(12)	1.396(6)
N2—C1	1.348(19)	1.336(10)	1.358(6)
N2—C7	1.386(19)	1.385(10)	1.404(5)
Bond angles (°)			
Br1—Pd1—Br2	175.87(9)	173.04(5)	176.32(2)
Br1—Pd1—N3	93.0(4)	92.4(2)	93.12(11)
Br2—Pd1—N3	90.6(4)	90.6(2)	90.01(11)
Br1—Pd1—C1	87.3(6)	88.8(2)	87.88(12)
Br2—Pd1—C1	89.1(6)	88.4(2)	89.03(12)
N3—Pd1—C1	179.6(7)	177.6(3)	178.47(18)
N1—C1—N2	107.1(13)	106.9(7)	107.2(4)

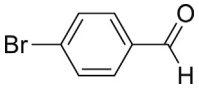
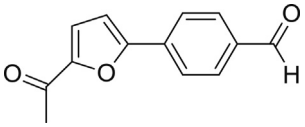
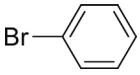
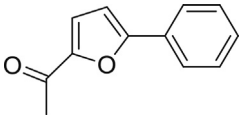
exciting results, the palladium-catalyzed direct arylation of heteroaryl derivatives with aryl halides or triflates has proved to be a powerful method for the synthesis of arylated heterocycles [67–77]. So far, to our knowledge, all the procedures reported for arylation via C—H bond activation of heteroarenes using ligand-free catalysts required 5–10 mol% catalyst, [76,77] except one which employs only 1 mol% [78]. Such couplings under a low catalyst concentration employ palladium associated with sophisticated ligands. Therefore, the discovery of more effective conditions for the direct coupling of furan derivatives with aryl halides under low catalyst loading and short-time reaction conditions (less than 2 mol% and 15 h) would be a considerable advantage for industrial applications and sustainable development. Thus, to find an effective and selective procedure allowing high yields of arylation products and using low catalyst loading and short reaction times is still subject to significant improvement.

Here, we used the optimized conditions for the catalytic reaction which were determined in our previous works [15,47,58]. In a standard experiment the *C*2-substituted heteroarene (2.0 mmol), aryl bromide (1.0 mmol), KOAc (2.0 mmol), DMA (2 mL) and the Pd-NHC complex **3a-f** (0.01 mmol) were added to a Schlenk tube under an inert atmosphere. The sealed Schlenk tube was stirred at 130 °C for 1 h. The reaction mixture was cooled to room temperature at the end of the reaction, then CH_2Cl_2 (2 mL) was added and the resulting solution was filtered through a short SiO_2 pad. The filtrate was analyzed by GC. The yields were based on the corresponding (hetero)aryl halide. Initially, under the optimal conditions, the direct arylation of 2-acetylfuran with 4-bromobenzaldehyde and bromobenzene was examined and the C(5)-arylated furan derivatives were obtained. We observed good yields of the target product when 4-bromobenzaldehyde was used with 2-acetylfuran, with 78–90% GC yields (Table 3, entries 1–6). Similar results were obtained when bromobenzene was used. In this case, 2-acetyl-5-phenylfuran was obtained in 72–89% GC yield (Table 3, entries 7–12).

Using the same reaction conditions, we investigated the reactivity of 2-acetylthiophene for the Pd-catalyzed direct C(5)-arylation. As shown in Table 4, high-yield C(5)-arylated products were

Table 3
Palladium(II)–NHC-catalyzed direct C5-arylation of 2-acetylfuran with aryl bromides.



Entry	Catalyst	Aryl bromide	Product	Conv (%)	Yield (%)
1	**3a**			100	86
2	**3b**			100	90
3	**3c**			100	82
4	**3d**			88	78
5	**3e**			100	86
6	**3f**			98	85
7	**3a**			100	85
8	**3b**			100	89
9	**3c**			96	72
10	**3d**			100	88
11	**3e**			95	86
12	**3f**			98	82

[a] Conditions: [Pd] **3a-3f** (0.01 equiv., 1 mol%), 2-acetylfuran or 2-acetylthiophene (2 equiv.), (hetero)aryl halide (1 equiv.), KOAc (2 equiv.), DMA (2 mL), 130 °C. [b] Yields were calculated with respect to the (hetero)aryl halide from the results of GC spectrometry.

obtained. When 2-acetylthiophene was arylated with 4-bromobenzotrifluoride, 4-bromobenzaldehyde, bromobenzene, 4-bromoanisole and 3-bromoquinoline, products were obtained using only1 mol% of the Pd-complexes **3a–3f** as catalysts, and yields of 82–87, 68–92, 80–92, 62–70 and 77–94% were observed, respectively (Table 4, entries 1–30).

When the reaction of 2-acetylthiophene with 4-bromobenzotrifluoride was investigated, the C(5) arylated product was obtained in 87% GC yield in the presence of the catalyst **3b** (Table 2, entry 2). The reaction of 2-acetylthiophene with 4-bromobenzaldehyde gave the expected product in 92% yield in the presence of the catalyst **3a** (Table 4, entry 7). The reaction of 2-acetylthiophene with bromobenzene generated the 5-phenyl-2-acetylthiophene in 92 and 94% yields, and with 4-bromoanisole, the C(5)-arylated product was obtained in 70% yield (Table 4, entries 13, 17 and 22). We examined the reactivities of electron-deficient heterocycles, such as 3-bromoquinoline, as heteroaryl bromides. A selected reaction was observed using 3-bromoquinoline. With this substrate, the target product 5-(quinoline-3-yl)-2acetythiophene was obtained in 94% yield in presence of the **3c** and **3f** catalysts after 1 h (Table 4, entries 27, 30).

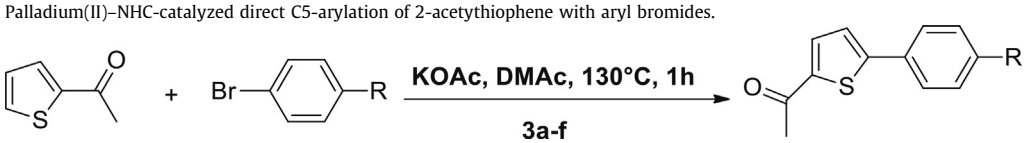
Also, we tried to evaluate the scope and limitations of the palladium-carbene catalysts **3a-3f** for the direct C(5)-arylation of 2-aldehydefuran with (hetero)aryl halides and the results are summarized in Table 5. When electron-withdrawing *para*-substituents such as aldehyde and trifluoromethyl on the aryl bromide were investigated with 2-aldehydefuran, the target products were obtained in moderate to high yields in presence of 1 mol% of the **3a-3f** catalysts after 1 h.

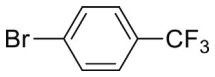
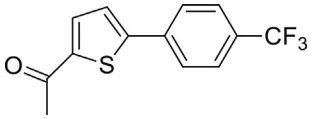
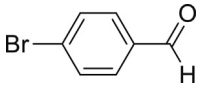
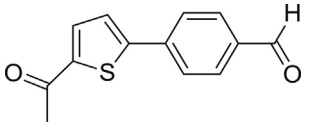
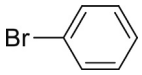
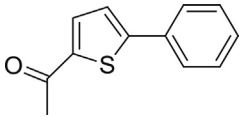
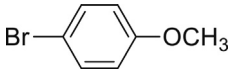
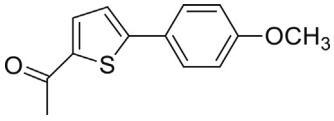
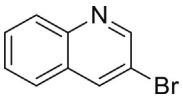
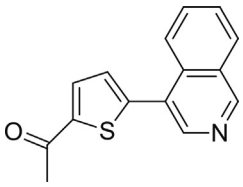
When 4-bromobenzotrifluoride and 2-aldehydefuran were reacted in the presence of the Pd-NHC catalysts (**3a-3f**), 74–88% yields were obtained (Table 5, entries 1–6). When 4-bromobenzaldehyde was used as the aryl halide, after 1 h, moderate to high yields of 72–87% were obtained in the presence of **3a**-**3f** (Table 5, entries 7–12). When 4-bromobenzaldehyde was used as the aryl halide, moderate yields (83%) were obtained in presence of the catalyst **3a** (Table 5, entry 13). Similar results were obtained when 4-bromoanisole was used. In this case, 2-aldehyde-5-(4-methoxyphenyl) was obtained in 73–79% GC yield (Table 5, entries 19–24). When the reaction of 2-aldehydefuran with 3-bromoquinoline was investigated, the C(5)-arylated product was obtained in 90% GC yield in the presence of the catalyst **3a** (Table 5, entry 25).

The Pd-catalyzed direct arylation of furan and thiophene with a variety of electrophilic reagents has been previously described [79,80]. In the previous studies, similar or close substrates have been employed with higher catalyst loading (1–20 mol%), and a higher reaction time (1–48 h) has been chosen for the direct arylation of furan and thiophene in the presence of Pd-catalysts. In the present work, 1 mol% catalyst loading was used, and the reaction time was shortened to 1 h. Moreover, thiophene and furan derivatives can be efficiently and selectively arylated at the C(5)-position. Finally, the palladium-catalyzed direct arylation of acetyl furan with aryl bromides has been as been compared to the previously published complexes. For example, 2-acetylfuran and 4-bromobenzaldeyde were chosen for comparison. Based on previous literature reports, similar substrates have been employed with higher reaction times, such as 2 h, for the direct arylation of 2-acetylfuran [81]). In the present work, the reaction time was shortened to 1 h for aryl bromides (Table 6). Moreover, in the present study satisfactory results were obtained as compared to previous results.

The ability of Hg(0) to poison metal-particle heterogeneous catalysts, by amalgamating the metal or adsorbing on the metal surface, has been known for more than 90 years and is a widely used test [82]. This experiment was performed by adding Hg(0) to the reaction solution. The suppression of the catalysis by Hg (0) is evidence for a heterogeneous catalyst; if Hg(0) does not suppress the catalysis that is evidence for a homogeneous catalyst. Hence we carried out the mercury poisoning experiment to assess whether the reaction system was homogeneous or heterogeneous. The Hg(0)-poisoning experiments were performed with the catalyst **3e** in the presence of excess Hg. The results showed no significant inhibition of conversion to products when complex **3e** was

Table 4
Palladium(II)–NHC-catalyzed direct C5-arylation of 2-acetythiophene with aryl bromides.



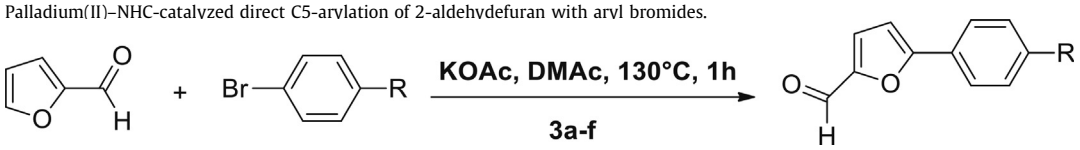
Entry	Catalyst	Arylbromide	Product	Conv (%)	Yield (%)
1	**3a**			92	86
2	**3b**			95	87
3	**3c**			90	85
4	**3d**			100	84
5	**3e**			91	86
6	**3f**			90	82
7	**3a**			99	92
8	**3b**			75	76
9	**3c**			76	68
10	**3d**			86	83
11	**3e**			78	77
12	**3f**			80	83
13	**3a**			95	92
14	**3b**			95	84
15	**3c**			96	85
16	**3d**			93	80
17	**3e**			98	94
18	**3f**			92	80
19	**3a**			94	64
20	**3b**			92	62
21	**3c**			92	62
22	**3d**			96	70
23	**3e**			91	60
24	**3f**			92	62
25	**3a**			100	77
26	**3b**			90	86
27	**3c**			98	94
28	**3d**			92	92
29	**3e**			100	92
30	**3f**			100	94

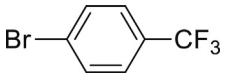
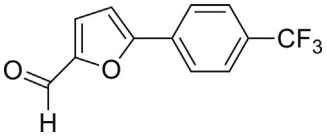
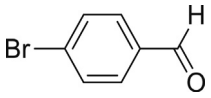
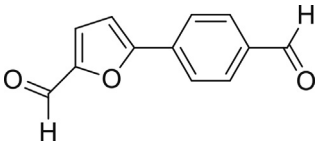
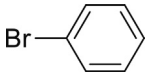
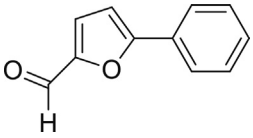
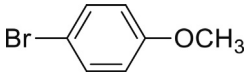
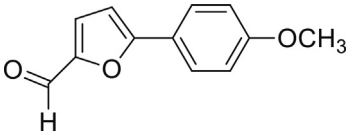
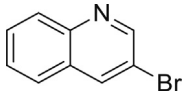
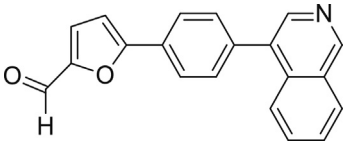
[a] Conditions: [Pd] **3a-3f** (0.01 equiv., 1 mol%), 2-acetylfuran or 2-acetylthiophene (2 equiv.), (hetero)aryl halide (1 equiv.), KOAc (2 equiv.), DMA (2 mL), 130 °C. [b] Yields were calculated with respect to the (hetero)aryl halide from the results of GC spectrometry.

used as a catalyst. Thus, the present catalysis appears to be homogeneous.

We attributed the performance differences to the well-accordance electronic and steric properties of the NHC ligand. It is known that oxidative additions of electron-withdrawing substrates to electron-rich palladium-complexes and reductive elimination of the product from large, sterically hindered palladium-complexes proceed more readily. Therefore, the presence of an NHC ligand bearing a different second donating group, such as ether side chains, on the metal may radically increase the catalytic performance of the catalyst. The chelating nature of these ligands promotes the production of highly stable complexes. The hemilabile part of such ligands is capable of reversible dissociation to produce vacant coordination sites, allowing complexation of substrates during the catalytic cycle. In this direct C—H bond arylation, we believe that the NHC ligands bearing the 1,3-dioxalane group in complexes **3a-f** provide the synergetic steric and electronic effects to confer the metal center the appropriate properties

Table 5
Palladium(II)–NHC-catalyzed direct C5-arylation of 2-aldehydefuran with aryl bromides.



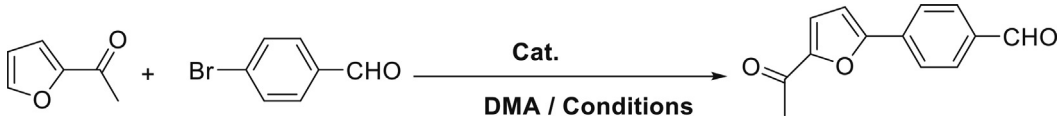
Entry	Catalyst	Arylbromide	Product	Conv (%)	Yield (%)
1	**3a**			84	74
2	**3b**			95	80
3	**3c**			88	81
4	**3d**			96	88
5	**3e**			82	75
6	**3f**			85	79
7	**3a**			99	72
8	**3b**			100	87
9	**3c**			100	83
10	**3d**			100	80
11	**3e**			100	70
12	**3f**			99	81
13	**3a**			90	83
14	**3b**			79	79
15	**3c**			73	67
16	**3d**			79	64
17	**3e**			84	78
18	**3f**			81	71
19	**3a**			83	73
20	**3b**			98	79
21	**3c**			90	75
22	**3d**			92	79
23	**3e**			91	77
24	**3f**			94	77
25	**3a**			98	95
26	**3b**			98	90
27	**3c**			96	71
28	**3d**			94	60
29	**3e**			96	78
30	**3f**			98	85

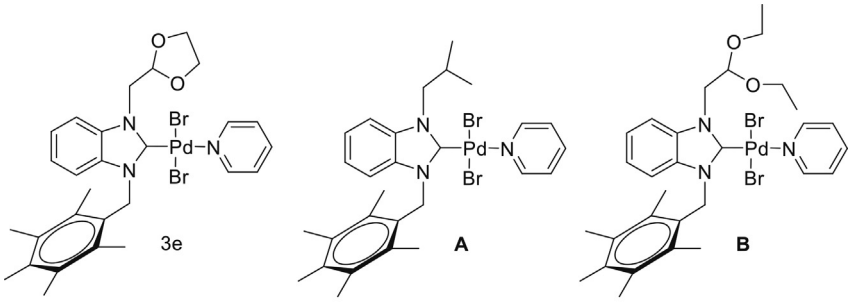
Note: [a] Conditions: [Pd] **3a-3f** (0.01 equiv., 1 mol%), 2-acetylfuran or 2-acetylthiophene (2 equiv.), (hetero)aryl halide (1 equiv.), KOAc (2 equiv.), DMA (2 mL), 130 °C. [b] Yields were calculated with respect to the (hetero)aryl halide from the results of GC spectrometry.

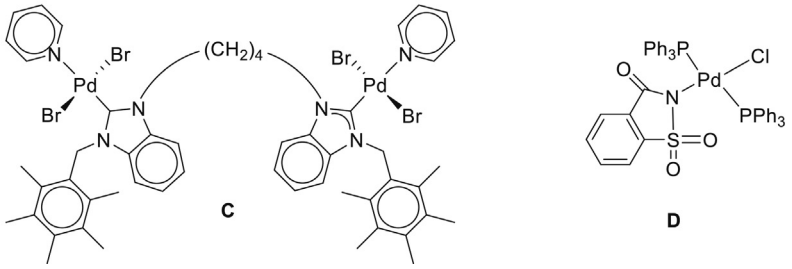
to make the key steps of the catalytic cycles optimum. The proposed catalytic pathway according to the above explanations is shown in Scheme 4.

When the proposed catalytic cycle is examined, initially, oxidative addition of the aryl halides to the pre-activated [(NHC)Py-Pd^0] species affords the [(NHC)PyX-Pd^{II}-Aryl] intermediate. In this step, the NHC ligands increase the electron density around the metal center and the oxidative addition step more readily takes place. Next, the exchange of the X ligand with KOAc gives [(NHC)Py(AcO)-Pd^{II}-Aryl]. The nature of the base used in this step is very important. Then, the intermediate [(NHC)Py(AcO)-Pd^{II}-Aryl] reacts with furan to give [(NHC)Py(furan)-Pd^{II}-Aryl] by C-H activation. In this step, the chelating nature of the 1,3-dioxalane substituent promotes the production of highly stable complexes. Finally, reductive

Table 6
Palladium-catalyzed direct C5-arylation of 2-acetylfuran.







Entry	Catalyst	Conditions	Conv. [%]	Yield [%]	Ref.
1	**3e**	130 °C, 1h	100	86	this work
2	**A**	150 °C, 2h	93	79	[81a]
3	**B**	120 °C, 2h	100	75	[81b]
4	**C**	120 °C, 2h	100	74	[81c]
5	**D**	120 °C, 2h	100	75	[81d]

elimination of the intermediate [(NHC)(Py)(furan)-Pd^{II}-Aryl] produces the desired C5-arylated furan products.

4. Conclusion

We have prepared a series of benzimidazolium salts as *N*-heterocyclic carbene precursors and their new Pd-PEPPSI-NHC complexes have been prepared in good yields. The benzimidazole ligands are easy to prepare and handle, and these ligands are most suitable to prepared PEPPSI catalysts. The catalytic activities of all the palladium complexes were investigated in the direct C(5)-arylation of 2-acetylfuran, 2-acetylthiophene and 2-aldehydefuran with (hetero)aryl halides. It was found that all the palladium complexes were effective catalysts for the C—H activation process. Also, no catalyst poisoning was observed in the presence of mercury, indicating homogeneous catalysis.

It was found that the new Pd-complexes were effective catalysts for this direct arylation. Overall, except in a few cases, satisfactory results were obtained. Since the newly prepared NHC ligands in this work are similar to each other, no significant differences were observed between the catalytic activities of the Pd-complexes. This study is of environmental and economic interest owing to the low catalyst loading and shorter reaction time. In this study, only AcOH and HBr were formed as a by-products by the use of the direct arylation method and thus by-product formation was minimized compared with the multistep traditional transition metal-catalyzed reactions. Further studies focusing on the synthesis of novel benzimidazole-2-ylidene linked palladium-PEPPSI complexes and their catalytic application for the C—H bond arylation of heteroarenes are currently underway by our research group.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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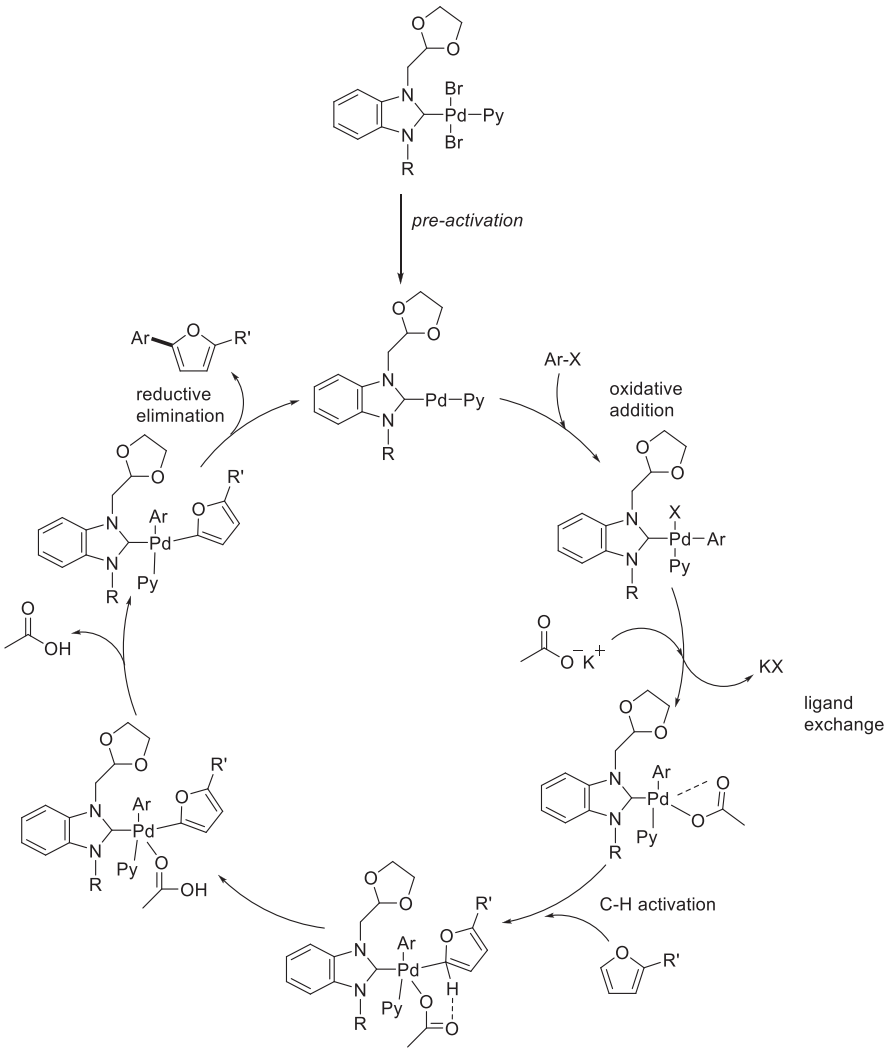

Scheme 4. Proposed catalytic pathway for the C—H bond arylation of furans.

Appendix A. Supplementary data

CCDC 2042615-2042617 contain the supplementary crystallographic data for the compounds reported in this article. These data can be obtained free of charge on application to the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk. Supplementary data to this article can be found online at https://doi.org/10.1016/j.poly.2021.115091.

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