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Accessing a Biologically Relevant Benzofuran Skeleton by a One-Pot Tandem Heck Alkynylation/Cyclization Reaction Using Well-Defined Palladium N-Heterocyclic Carbene Complexes

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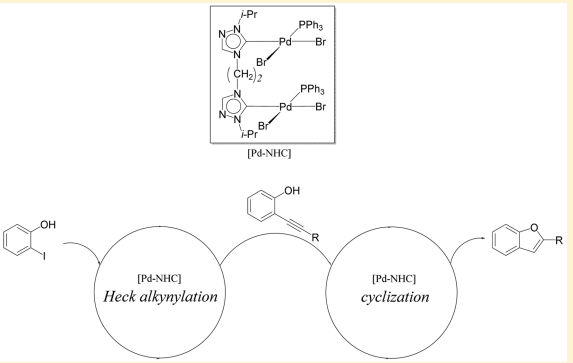
Supporting Information

ABSTRACT: Well-defined palladium N-heterocyclic carbene (NHC) complexes were employed in the one-pot tandem Heck alkynylation/cyclization sequence for preparing biologically relevant benzofuran compounds under copper-free conditions in a time-efficient step-reduced fashion. In particular, a series of binuclear palladium complexes, **1b−1e** and **2b−2e**, of the alkyl-bridged NHC ligands, namely, {1,1′-di-R_1-4,4′-R_2-di-1,2,4-triazoline-5,5′-diylid-2-ene] (R_1 = *i*-Pr; R_2 = $-(CH_2)_2-$, $-(CH_2)_3-$), and their mononuclear analogues, *trans*-(NHC)$PdBr_2$(pyridine) (**3b**) and *cis*-(NHC)-$PdBr_2(PPh_3)$ (**3c**), successfully catalyzed the one-pot tandem Heck alkynylation/cyclization reaction of 2-iodophenol with a variety of terminal alkyne substrates, yielding 2-substituted benzofuran derivatives. The mononuclear complexes **3b** and **3c** were nearly half as active as the representative dinuclear analogue **1c** under analogous reaction conditions, thereby implying that, at the same mole percent of the palladium loading, the monometallic **3b** and **3c** and the bimetallic **1c** complexes were equally effective as catalysts. The two sites of the bimetallic complex **1c** performed as two separate independent catalytic sites, displaying no cooperativity effect in the catalysis. Finally, the practical utility of the aforementioned catalysts was demonstrated for a representative catalyst **1c** through the convenient synthesis of a key intermediate, 3-[2-(benzo[*d*][1,3]dioxol-5-yl)-7-methoxybenzofuran-5-yl]propan-1-ol, in a total-synthesis protocol of the natural product Egonol.



INTRODUCTION

Benzofurans constitute an important motif ubiquitous in many bioactive compounds like BNC105,[1] amiodarone,[2] cytotoxic flavonoids,[3] and the natural products Daphnodorin A and B,[4] Egonol,[5,6] and Moracin O and P.[7,8] Hence, an efficient synthesis of benzofuran compounds is of considerable interest. In this context, the one-pot tandem reaction involving sequential Heck alkynylation reaction and intramolecular cyclization provides a step-efficient time-improved approach for construction of the benzofuran framework. Because only a handful of examples of the use of well-defined catalysts exist,[9−11] with the majority being under ligand-assisted catalysis (LAC) conditions,[12−15] we became interested in developing well-defined homogeneous catalytic systems for the one-pot tandem Heck alkynylation/cyclization reaction for accessing the benzofuran compounds.

With one of our objectives being furthering the scope of the transition-metal complexes of the N-heterocyclic carbenes (NHCs) in homogeneous catalysis[16,17] and in biomedical applications,[18] we became interested in exploring the potential of these complexes in more challenging tandem reactions. The motivation for the current work came from our earlier successes with the Sonogashira coupling under copper-free conditions (which also is popularly referred to as Heck alkynylation)[19−23] as part of a broader study on a variety of C−C[20,24−26,27−31] C−N,[31−33] and C−B[34] bond-forming reactions and founded on which we chose to undertake the next logical extension of targeting more complex transformations like that of the one-pot tandem Heck alkynylation/cyclization reaction under similar copper-free conditions for obvious reasons. In particular, we decided to explore the utility of the monometallic and bimetallic palladium NHC (Pd-NHC) complexes for the one-pot tandem Heck alkynylation/cyclization reaction. Furthermore, as a bimetallic palladium catalyst was reported to be more efficient than its monometallic counterparts,[11] and we decided to verify the same for the monometallic and bimetallic palladium complexes of our NHC ligands. Lastly, we decided to focus on the 1,2,4-triazole-derived NHC ligands primarily because of (i) a prior report of the 1,2,4-triazole-derived NHC-based palladium catalysts outperforming the imidazole-based analogues for the same one-pot tandem Heck alkynylation/cyclization reaction yielding benzofuran compounds[11] and (ii)

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the fact that the 1,2,4-triazole-derived NHCs are less explored than their imidazole-based counterparts.[35,36]

Here, in this contribution, we report a series of Pd-NHC complexes, **1b**−**1e**, **2b**−**2e**, **3b**, and **3c**, of the 1,2,4-triazole-derived NHC ligands that efficiently carried out the one-pot tandem Heck alkynylation/cyclization reaction under copper-free conditions, giving various benzofuran compounds (Figure 1). A comparison of the catalytic efficiencies of the

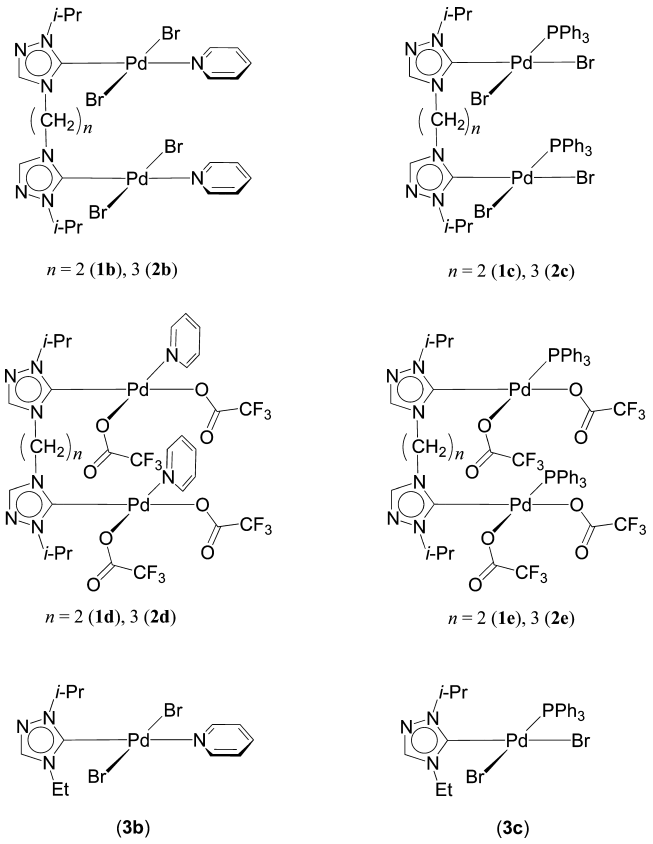

Figure 1. Palladium complexes of 1,2,4-triazole-derived NHC ligands.

monometallic and bimetallic Pd-NHC complexes was undertaken to probe the cooperativity effect, if any, present in the tandem catalysis. As a proof of concept, we further demonstrate the practical utility of these catalysts for a representative catalyst, **1c**, by synthesizing a benzofuran intermediate, namely, 3-(2-(benzo[*d*][1,3]dioxol-5-yl)-7-methoxybenzofuran-5-yl)-propan-1-ol, of a total-synthesis pathway to the bioactive natural product Egonol (Scheme 3).

RESULTS AND DISCUSSION

A series of binuclear palladium complexes, **1b**−**1e** and **2b**−**2e**, were synthesized with the view of their application in one-pot tandem Heck alkynylation/cyclization reactions for accessing the 2-substituted benzofuran-type frameworks in more convenient and fewer reaction sequences. With the intent of undertaking a comparative structure−activity-correlation study, several related variants of Pd-NHC complexes were thus synthesized (Figure 1). The binuclear PEPPSI (pyridine-enhanced precatalyst preparation, stabilization, and initiation)-themed complexes **1b** and **2b** were obtained by direct reaction of the corresponding dicationic triazolium dibromide salts **1a** and **2a** with 2 equiv of $PdBr_2$ in pyridine in the presence of K_2CO_3 as a base in 90−91% yield (Scheme 1). Upon treatment of the binuclear PEPPSI-themed complexes **1b** and **2b** with PPh_3, the corresponding mixed-NHC/phosphine complexes **1c** and **2c** were obtained in 38−84% yield. Finally, reactions of both the PEPPSI-themed **1b** and **2b** complexes and mixed-NHC/phosphine-derived **1c** and **2c** complexes with AgO$COCF_3$ yielded the trifluoroacetate derivatives **1d** and **2d** and also **1e** and **2e**, respectively, in 72−96% yield. It is worth noting that, among the **1b**−**1e** and **2b**−**2e** complexes, only the **2e** complex showed two sets of resonances in an approximate 1:4 ratio in its ^{1}H NMR spectrum at room temperature, suggesting an exchange between two conformers. The variable-temperature ^{1}H NMR experiment (Supporting Information, Figures S140−S143) indicated a faster exchange at a higher temperature, with the ratio decreasing to ca. 1:1.08 at 100 °C (Supporting Information, Figures S140−S143). The possibility of a cis−trans isomerism was ruled out based on the $^{31}P\{^1H\}$ NMR results that showed the corresponding phosphorus resonances appearing at 25.7 and 25.3 ppm in concurrence with a cis structure of the **2e** complex.[25] Subsequent structural characterization by the single-crystal X-ray diffraction study gave the molecular structure of the major conformer (Figure 2 and the Supporting Information, Figure S3).

Quite expectedly, the Pd−NCN resonance of the **1b**−**1e** and **2b**−**2e** complexes appeared at ca. 148.9−167.0 ppm in the $^{13}C\{^1H\}$ NMR spectrum in concurrence with the range observed for related complexes.[20,37] Likewise, the Pd−PPh_3 resonance for the **1c**, **2c**, **1e**, and **2e** complexes appeared at ca. 25.3−27.3 ppm in the $^{31}P\{^1H\}$ NMR spectrum, indicating cis disposition of the PPh_3 ligand with respect to the NHC ligand in these *cis*-(NHC)Pd(PPh_3)X_2-type complexes.[25,38−40]

The molecular structure of the PEPPSI-themed complexes **1b** and **2b**, the mixed-NHC/phosphine complexes **1c** and **2c**, and the trifluoroacetate analogues **1d**, **1e**, and **2e**, as determined by X-ray diffraction studies, revealed the binuclear structure of these complexes with two palladium atoms bound to two carbene centers in each of the alkyl-bridged NHC ligands (Figures 3−6 and the Supporting Information, Figures S1−S3 and Table S1). However, in no instance was chelation of two carbene centers of an alkyl-bridged NHC ligand to one palladium atom observed. This is an outcome of the longer bridging ethyl and propyl linkers present between the two carbene centers of the NHC ligands, as opposed to a shorter methylene linker, for which chelation of both carbene centers to a single palladium center was seen.[41−43]

Consistent with a d^8 configuration, the palladium center was found to be in square-planar geometry in all of the **1b**−**1e**, **2b**, **2c**, and **2e** complexes. The Pd−$C_{carbene}$ bond distances in **1b** [1.964(6) and 1.945(6) Å], **2b** [1.972(7) and 1.956(7) Å], **1c** [1.982(3) Å], **2c** [1.980(5) and 1.978(5) Å], **1d** [1.97(3) Å] **1e** [1.954(3) Å], and **2e** [1.964(5) and 1.971(5) Å] are slightly smaller than the sum of the individual covalent radii of the palladium and carbon atoms (2.12 Å).[44] The Pd−$N_{pyridine}$ bond distances in **1b** [2.083(5) and 2.084(5) Å], **2b** [2.090(6) and 2.070(6) Å], and **1d** [2.02(3) Å] are comparable to the sum of the covalent individual radii of the palladium and nitrogen atoms (2.10 Å).[44] Quite expectedly, owing to a large covalent radius of phosphorus (1.07 Å)[44] over nitrogen (0.71 Å),[44] the Pd−PPh_3 bond distances in **1c** [2.2560(8) Å], **2c** [2.2727(13) and 2.2629(14) Å], **1e** [2.2547(7) Å], and **2e** [2.2397(11) and 2.2448(11) Å] are longer than the Pd−$N_{pyridine}$ bond distances found in **1b** [2.083(5) and 2.084(5) Å], **2b** [2.090(6) and 2.070(6) Å], and **1d** [2.02(3) Å].

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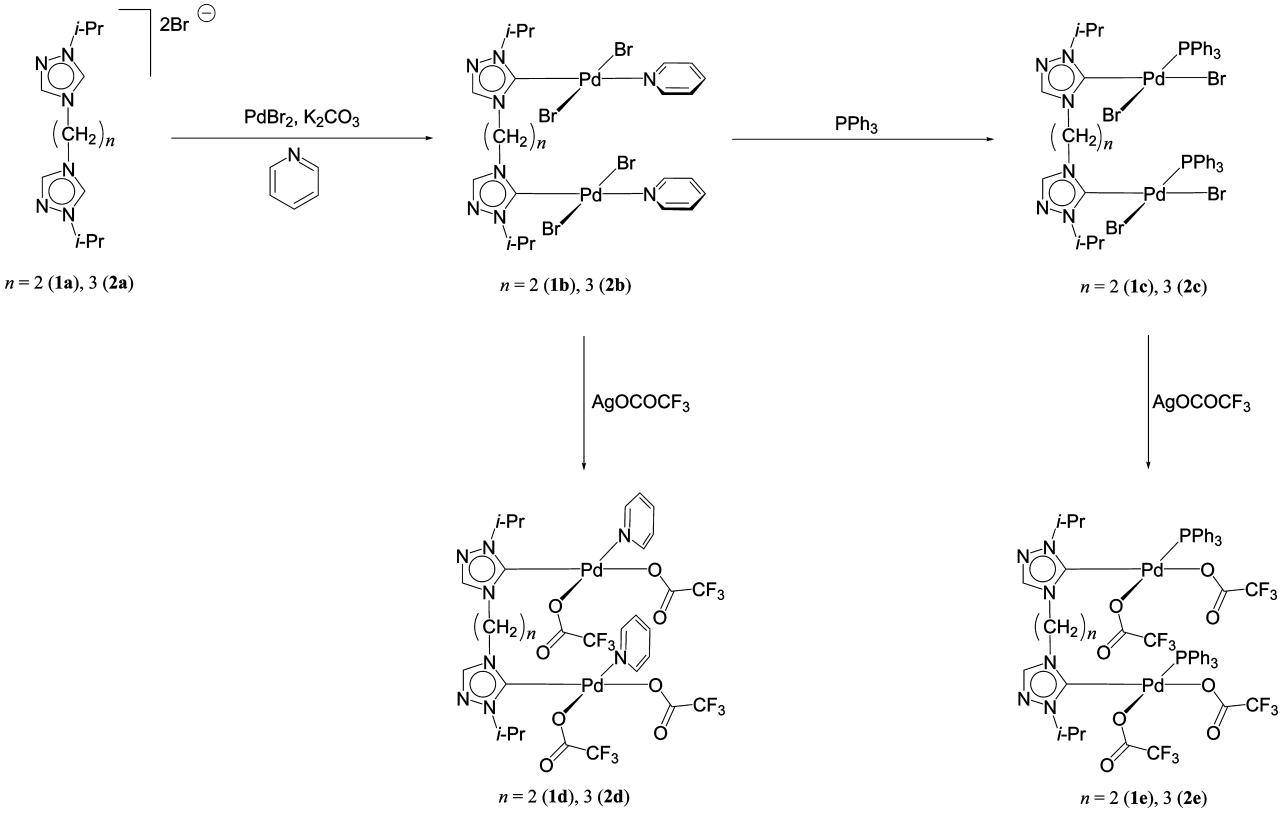
Scheme 1. Synthesis of the Palladium Complexes of Various Alkyl-Bridged Bis(1,2,4-triazole)-Derived NHC Ligands



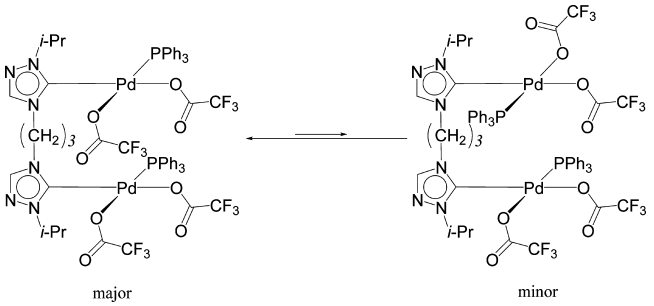


Figure 2. Conformational exchange observed in the solution ^{1}H NMR spectrum of complex **2e**.

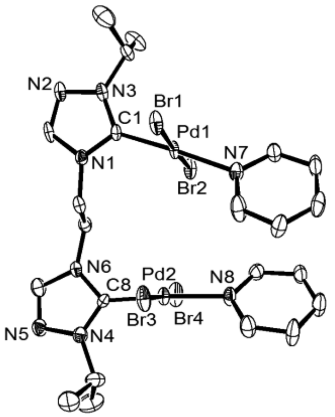
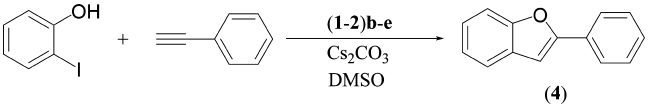


Figure 3. ORTEP diagram of **1b** with thermal ellipsoids shown at the 50% probability level. Selected bond lengths (Å) and angles (deg): Pd1−C1 1.964(6), Pd1−Br1 2.4256(11), Pd1−Br2 2.4244(10), Pd1−N7 2.083(5), Pd2−C8 1.945(6), Pd2−Br3 2.4261(11), Pd2−Br4 2.4258(11), Pd2−N8 2.084(5); C1−Pd1−Br1 89.4(2), Br1−Pd1−Br2 175.42(3), C1−Pd1−Br2 88.6(2), C1−Pd1−N7 177.3(2), N7−Pd1−Br1 90.37(17), C8−Pd2−Br3 88.3(2), Br3−Pd2−Br4 175.08(3), C8−Pd2−Br4 86.8(2), C8−Pd2−N8 175.7(3), N8−Pd2−Br4 91.89(18).

Notable is the molecular structure of **1d** showing a cis disposition of the pyridine ligand relative to the NHC ligand, which, to our knowledge, is the only structurally characterized example of a *cis*-(NHC)PdX$_2$(pyridine)-type complex (X = an anionic ligand) ever reported in the literature (Figure 5).[45] In contrast, numerous structurally characterized examples of the *trans*-(NHC)PdX$_2$(pyridine)-type complexes (X = an anionic ligand), having a pyridine ligand bound trans to the NHC ligand, are known in the literature.[45,46]

The syntheses of the monometallic analogues **3b** and **3c** were undertaken in order to probe the cooperativity effect in catalysis in these bimetallic Pd-NHC complexes, **1b**−**1e** and **2b**−**2e**, and were thus obtained by analogous synthetic procedures described earlier for the bimetallic Pd-NHC counterparts (Scheme 2). The molecular structures of the monometallic analogues **3b** and **3c** were similar to those of the their dinuclear counterparts **1b**, **2b**, **1c**, and **2c** (Supporting Information, Figures S4 and S5 and Table S2). The tandem Heck alkynylation/cyclization reaction between two representative 2-iodophenol and phenylacetylene substrates as catalyzed by the palladium complexes **1b**−**1e** and **2b**−**2e** of various alkyl-bridged bis(1,2,4-triazole)-derived NHC ligands is given in eq 1.



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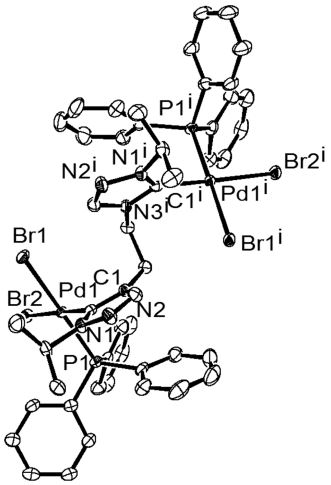

Figure 4. ORTEP diagram of **1c** with thermal ellipsoids shown at the 50% probability level. Selected bond lengths (Å) and angles (deg): Pd1−C1 1.982(3), Pd1−Br1 2.4958(8), Pd1−Br2 2.4608(4), Pd1−P1 2.2560(8); C1−Pd1−Br1 87.12(8), Br1−Pd1−Br2 93.164(14), C1−Pd1−Br2 178.48(9), C1−Pd1−P1 91.18(8), P1−Pd1−Br1 177.85(3), P1−Pd1−Br2 88.50(2).

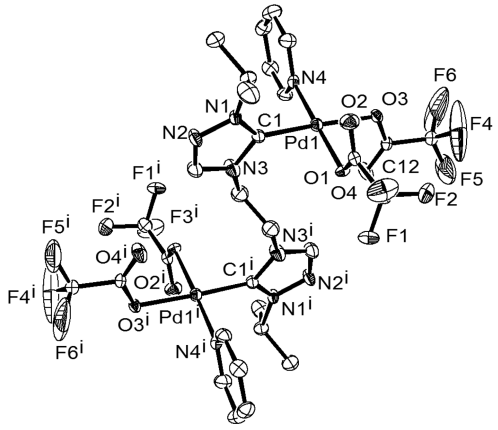

Figure 5. ORTEP diagram of **1d** with thermal ellipsoids shown at the 50% probability level. Selected bond lengths (Å) and angles (deg): Pd1−C1 1.97(3), Pd1−O3 2.07(2), Pd1−O1 2.02(2), Pd1−N4 2.02(3); C1−Pd1−O3 177.6(10), O1−Pd1−O3 87.9(9), C1−Pd1−O1 90.3(12), C1−Pd1−N4 92.0(712), N4−Pd1−O3 89.7(10), N4−Pd1−O1 177.1(9).

Significantly enough, all of the **1b−1e** and **2b−2e** complexes effectively catalyzed the one-pot tandem Heck alkynylation/cyclization reaction between *o*-iodophenol substrates with terminal alkynes, giving the desired benzofuran compounds (eq 1). In particular, the tandem reaction was performed at 1 mol % catalyst loading (**1b−1e** and **2b−2e**) for the two representative substrates, 2-iodophenol and phenylacetylene, in the presence of Cs_2CO_3 as the base at 80 °C in dimethyl sulfoxide (DMSO), yielding the desired 2-phenylbenzofuran product in 58−81% isolated yield (Table 1). The benzofuran product was purified by column chromatography in silica gel by elution with petroleum ether. More interestingly, the ethyl-bridged **1b−1e** complexes exhibited higher yields (72−81%) than the propyl analogues **2b−2e** (58−70%). Furthermore, among the ethyl-bridged **1b−1e** complexes, the *cis*-mixed-NHC/phosphine complex **1c** displayed the maximum yield of 81%. In this context, it is worth noting that we had earlier observed similar higher activity of a related *cis*-(*a*-NHC)-

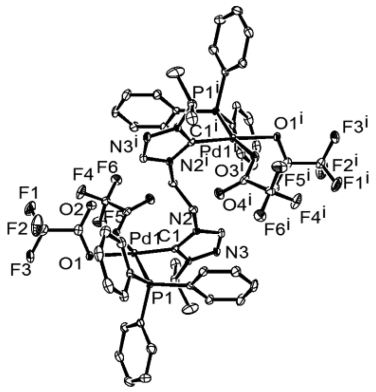

Figure 6. ORTEP diagram of **1e** with thermal ellipsoids shown at the 50% probability level. Selected bond lengths (Å) and angles (deg): Pd1−C1 1.954(2), Pd1−O3 2.0728(17), Pd1−O1 2.0790(17), Pd1−P1 2.2547(7); C1−Pd1−O3 94.50(8), O1−Pd1−O3 83.81(7), C1−Pd1−O1 177.17(8), C1−Pd1−P1 90.90(7), P1−Pd1−O3 168.95(5).

$PdI_2(PPh_3)$ complex [*a*-NHC = 1-benzyl-3-R_1-4-R_2-1,2,3-triazol-5-ylidene, where R_1 = Me and R_2 = Ph] over its PEPPSI-themed analogues *trans*-(*a*-NHC)PdI_2(pyridine) [*a*-NHC = 1-benzyl-3-R_1-4-R_2-1,2,3-triazol-5-ylidene, where R_1 = Me and R_2 = Ph] and the mixed-NHC/phosphine complexes *trans*-(*a*-NHC)$PdI_2(PPh_3)$ [*a*-NHC = 1-benzyl-3-R_1-4-R_2-1,2,3-triazol-5-ylidene, where R_1 = Me, Et and R_2 = $C_6H_{10}OH$)]-type complexes in the Hiyama coupling of aryl iodide and $PhSi(OMe)_3$ substrates.[25] The time-dependent mercury drop experiment, in which mercury additions were performed at different time intervals, showed no change within significant errors in the product yields, varying from 81% in the absence of mercury to 84% in the presence of mercury from the start of the reaction (Supporting Information, Table S3) and is indicative of the homogeneous nature of the catalysis.

A comparison of the activity of the monometallic and bimetallic complexes revealed that, at 1 mol % catalyst loading, the monometallic analogues **3b** and **3c** produced reaction yields of nearly half that of a representative bimetallic Pd-NHC complex, **1c**, and only at double the catalyst loading of 2 mol % did the monometallic analogues **3b** and **3c** match up with the reaction yield of 1 mol % of a representative bimetallic Pd-NHC complex, **1c**, under analogous reaction conditions (entry 1 of Table 2 and the Supporting Information, Table S4). This observation implied that, at the same mole percent of the palladium loading, the monometallic complexes **3b** and **3c** and the bimetallic complex **1c** were equally active, thus ruling out the possibility of the presence of a cooperativity effect in the catalysis. The two sites of the bimetallic complex, **1c**, behaved independently of each other as two separate catalytic sites.

A substrate scope study was undertaken for the most active complex **1c** with the aim of exploring the catalyst versatility. Substrates ranging from electron-donating terminal aryl alkynes, namely, 4-ethynyl-1,2-dimethoxybenzene, 1-ethynyl-4-methoxybenzene, 4-ethynyl-*N*,*N*-dimethylaniline, and 5-ethynylbenzo[*d*][1,3]dioxole (Table 2, entries 2−5), to an electron-withdrawing one, namely, 1-ethynyl-4-fluorobenzene (Table 2, entry 6), to even aliphatic analogues, namely, 1-ethynylcyclohexan-1-ol, but-3-yn-1-ol, and propargyl alcohol (Table 2, entries 7−9), were reacted with 2-iodophenol in the presence of the catalyst **1c**, giving the corresponding substituted benzofuran derivatives **5−12** in moderate-to-good isolated yield (47−84%). The electron-rich terminal aryl

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Scheme 2. Synthesis of the Monometallic Palladium Complexes of a 1,2,4-Triazole-Derived NHC Ligand

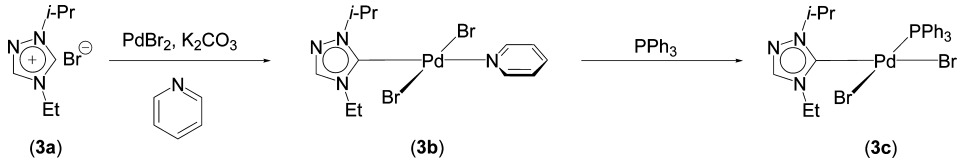
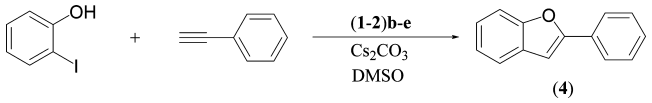
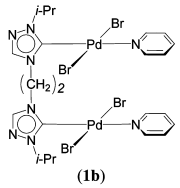
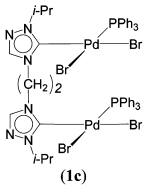
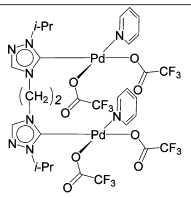
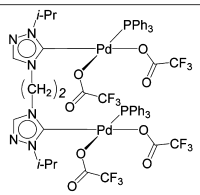
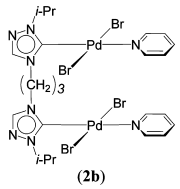
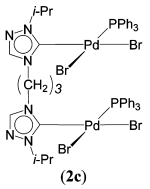
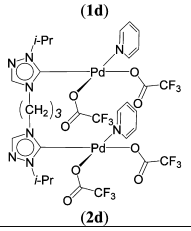
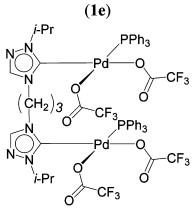


Table 1. Tandem Heck Alkynylation/Cyclization Reaction between Two Representative 2-Iodophenol and Phenylacetylene Substrates As Catalyzed by the Palladium Complexes 1b−1e and 2b−2e of Various Alkyl-Bridged Bis(1,2,4-triazole)-Derived NHC Ligands[b]



S. No.	catalyst	yield[a] (%)	catalyst	yield[a] (%)	catalyst	yield[a] (%)	catalyst	yield[a] (%)
1	 (1b)	73	 (1c)	81	 (1d)	75	 (1e)	72
2	 (2b)	66	 (2c)	61	 (2d)	70	 (2e)	58

[a]Isolated yields. [b]Reaction conditions: 2-iodophenol (0.110 g, 0.500 mmol), phenylacetylene (0.078 g, 0.760 mmol), and Cs_2CO_3 (0.489 g, 1.50 mmol) in the presence of 1 mol % catalyst and in 3 mL of DMSO. Reaction time = 4 h; temperature = 80 °C.

alkynes were more reactive, yielding the desired products **5**−**8** in 47−70% yield in 4 h of reaction time (Table 2, entries 2−5), while the electron-deficient terminal aryl alkyne 1-ethynyl-4-fluorobenzene reacted slowly over a reaction time of 24 h, producing the benzofuran product **9** in 53% yield (Table 2, entry 6). The aliphatic ones 1-ethynylcyclohexan-1-ol and but-3-yn-1-ol (Table 2, entries 7 and 8) also reacted in 24 h of reaction time, giving the corresponding products **10** and **11** in 79% and 62% yield, respectively. The propargyl alcohol was the least reactive one, producing 84% yield of the product **12** in 48 h of reaction time (Table 2, entry 9). Overall, the terminal aryl alkynes were more reactive than the aliphatic alkynes for the one-pot tandem Heck alkynylation/cyclization reaction. The catalyst **1c** proved to be ineffective for a terminal alkyne bearing ester functionality, as observed for the representative ethyl propiolate substrate. Along the same lines, the *o*-bromophenol and *o*-chlorophenol substrates yielded no product under analogous reaction conditions.

The comparison of the catalytic activities of the **1b**−**1e** and **2b**−**2e** complexes with the other reported catalysts for the one-pot tandem Heck alkynylation/cyclization reaction yielding benzofuran compounds is important. We are aware of only one prior report of the use of well-defined PEPPSI-themed (NHC)$PdCl_2$(pyridine)-type catalysts[11] analogous to that of our **1b**−**1e** and **2b**−**2e** complexes for the tandem reaction and of a few other reports of the in situ generated palladium phosphine complexes under LAC conditions.[12−15] In particular, several PEPPSI-themed (NHC)$PdCl_2$(pyridine) (NHC = 1,2,4-trimethyltriazolyldiylidene, 1,3-dimethylimidazolylidene, and 1,4-dimethyltriazolylidene) type complexes performed the one-pot tandem Heck alkynylation/cyclization reaction of 2-iodophenol with phenylacetylene, giving 2-phenylbenzofuran at 1 mol % catalyst loading in DMSO in the presence of Cs_2CO_3 as the base in 16−93% yield.[11] Furthermore, among these catalysts, the bimetallic (NHC)Pd_2Cl_4(pyridine)$_2$ (NHC = 1,2,4-trimethyltriazolyldiylidene) catalyst was the most active, exhibiting 93% of the product yield in 8 h of reaction time, while the monometallic 1,2,4-triazole-derived (NHC)-$PdCl_2$(pyridine) (NHC = 1,4-dimethyltriazolylidene) displayed 88% of the product yield after 16 h of reaction time for the reaction of 2-iodophenol with phenylacetylene. The imidazole-derived (NHC)$PdCl_2$(pyridine) (NHC = 1,3-dimethylimidazolylidene) catalyst was the least active one, exhibiting only 16% of the product yield after a longer reaction time of 20 h for the reaction of 2-iodophenol with phenylacetylene.[11] As for the non-NHC-based catalysts, a well-defined copper pincer complex, namely, dichloro{2-[(1*H*-pyrazol-1-yl-*k*N^2)methyl]-6-(1*H*-pyrazol-1-yl-*k*N^2)pyridine-*k*N}copper(II), catalyzed the reaction of various halophenol and terminal alkyne substrates at a low catalyst loading of 0.15 mol %, giving the desired benzofuran products in good-to-excellent yield but a relatively higher temperature of 130 °C.[9]

With regard to the examples from the in situ generated LAC-based systems, a tetraphosphine ligand, namely, N^2,N^2,N^6,N^6-tetrakis[(diphenylphosphanyl)methyl]pyridine-2,6-diamine (0.1 mol %), and [Pd(η^3-C_3H_5)Cl]$_2$ (0.05 mol %) catalyzed the one-pot tandem Heck alkynylation/cyclization reaction of a variety of halophenol and alkynes, giving the benzofuran

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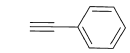
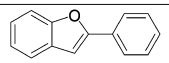
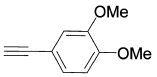
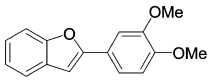
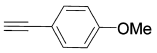
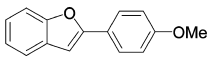
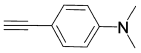
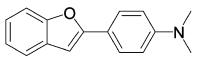
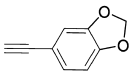
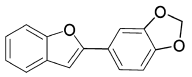
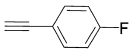
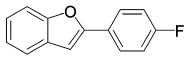
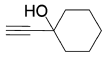
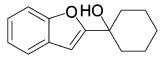
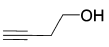
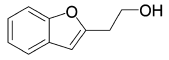
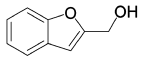
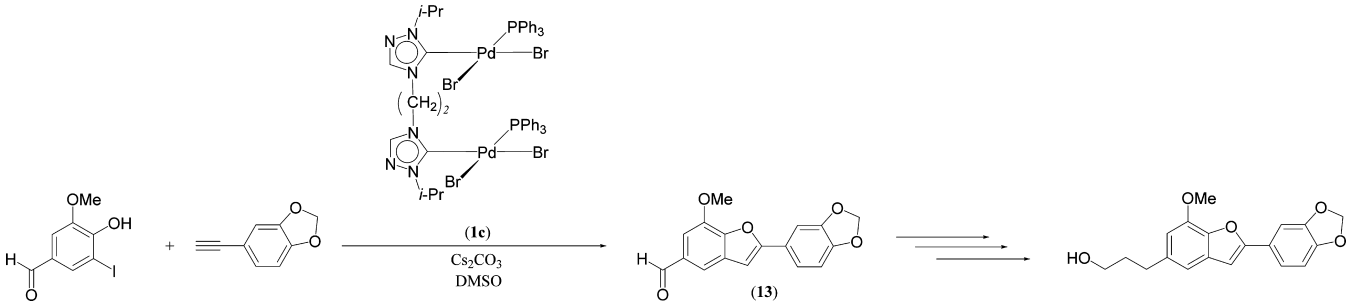
Table 2. Selected Results for the Tandem Heck Alkynylation/Cyclization Reaction of Iodophenol and Various and Terminal Alkyne Substrates As Catalyzed by 1c[b]

S.No.	iodophenol	terminal alkyne	product	time (hours)	yield[a] (%)
1			 (**4**)	4	81
2			 (**5**)	4	70
3			 (**6**)	4	67
4			 (**7**)	4	47
5			 (**8**)	4	62
6			 (**9**)	24	53
7			 (**10**)	24	79
8			 (**11**)	24	62
9			 (**12**)	48	84

[a]Isolated yields. [b]Reaction conditions: 2-iodophenol (0.500 mmol), terminal alkyne (0.750 mmol), and Cs_2CO_3 (1.50 mmol) in the presence of **1c** (1 mol %) and in 3 mL of DMSO. Temperature = 80 °C.

Scheme 3. Synthesis of a Benzofuran Intermediate (13) in a Total-Synthesis Sequence of the Natural Product Egonol by the One-Pot Tandem Heck Alkynylation/Cyclization Reaction As Catalyzed by 1c



products in poor-to-excellent yield (17−99%) and also at a very high temperature of 130 °C.[12] The reactions of iodoresorcinol and various alkynes were catalyzed by $Pd(PPh_3)Cl_2$ (5 mol %) in the presence of CuI (5 mol %) as a cocatalyst, giving the corresponding benzofuran product in 68−93% yield.[47] Thus, against this backdrop, the catalyst **1c** not only is efficient at 1 mol % catalyst loading and operates at a significantly lower reaction temperature of 80 °C but also is versatile with regard to exhibiting broad substrate scope in establishing its generality of usage as a catalyst for the one-pot tandem Heck alkynylation/cyclization reaction between 2-iodophenol with nine different terminal alkyne substrates for yielding the 2-substituted benzofuran compounds.

Finally, the catalyst **1c**, as demonstrated through a simple practical synthesis of a benzofuran compound (**13**), is an intermediate in the total-synthesis sequence of the bioactive natural product Egonol (Scheme 3).[5,6] In particular, one-pot tandem Heck alkynylation/cyclization reaction between 4-hydroxy-3-iodo-5-methoxybenzaldehyde (iodovanillin) and 5-ethynylbenzo[*d*][1,3]dioxole was catalyzed by **1c**, yielding the corresponding biologically relevant benzofuran intermediate **13** in DMSO in 36% yield in 4 h of reaction time at 80 °C.

A proposed mechanism based on simplified mononuclear *cis*/*trans*-$(NHC)PdX_2(L)$ (X = Br, $OCOCF_3$ and L = PPh_3, pyridine) type complexes suggests the presence of two catalytic cycles involving the Heck alkynylation cycle, followed by an intramolecular cyclization reaction, leading to the benzofuran product formation (Scheme 4). The first catalytic cycle initiates with the reduction of the palladium(II) complexes **1b−1e** and **2b−2e** to a palladium(0) species (**A**), which upon oxidative

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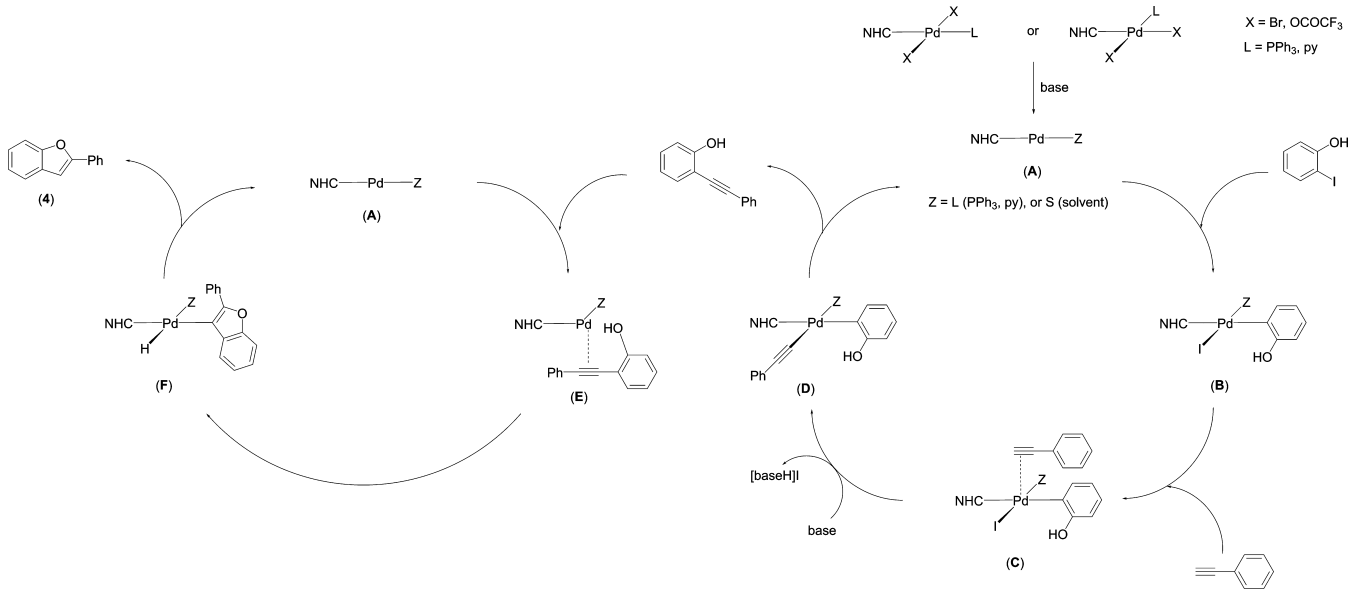
Scheme 4. Proposed Mechanism for the Tandem Heck Alkynylation/Cyclization Reaction between Two Representative 2-Iodophenol and Phenylacetylene Substrates As Catalyzed by a Simplified Mononuclear (NHC)PdX$_2$(L) (X = Br, OCOCF$_3$ and L = PPh$_3$, py) Type Complex



addition with 2-iodophenol yields an intermediate (**B**). The coordination of phenylacetylene to palladium yielded the species **C**, which yielded the intermediate **D** upon deprotonation of the palladium-coordinated terminal acetylene moiety. The completion of the Heck alkynylation cycle is accompanied by the reductive elimination of 2-(phenylethynyl)phenol from the intermediate **D**. The product of the first catalytic cycle, 2-(phenylethynyl)phenol, becomes the substrate for the next catalytic cycle. It enters the intramolecular cyclization catalytic cycle by undergoing oxidative addition to the palladium(0) species **A**, giving intermediate **E**, which upon intermolecular rearrangement produces intermediate **F**. Finally, the reductive elimination from the intermediate **F** gives the desired 2-phenylbenzofuran (**4**) along with regeneration of the palladium(0) species **A**.

CONCLUSION

In summary, a series of binuclear palladium complexes, namely, **1b−1e** and **2b−1e**, of ethyl- and propyl-bridged NHC ligands effectively catalyzed the one-pot tandem Heck alkynylation/cyclization reaction of 2-iodophenol with terminal alkynes, yielding the 2-substituted benzofuran compounds, and of these, the mixed-NHC/phosphine catalyst **1c** was the most active. The utility of the representative catalyst **1c** was demonstrated through the synthesis of a key benzofuran intermediate required in a total-synthesis sequence of the natural product Egonol, thereby projecting the potential of these catalysts in these types of one-pot tandem Heck alkynylation/cyclization reactions. Because the current study is among the first for the NHC-based catalysts, it throws open exciting new opportunities for further developments, not only for one-pot tandem Heck alkynylation/cyclization reactions for producing benzofuran-type frameworks in an efficient manner in reduced numbers of reaction steps but also for a parallel utility in other related tandem reactions. No evidence for cooperative catalysis was observed in the representative binuclear catalyst **1c** compared with their mononuclear analogues **3b** and **3c**.

EXPERIMENTAL SECTION

General Procedures. All manipulations were carried out using standard Schlenk techniques. Palladium bromide, phenylacetylene, 1-ethynyl-4-fluorobenzene, 1-ethynyl-4-methoxybenzene, 4-ethynyl-*N*,*N*-dimethylaniline, 1-ethynylcyclohexanol, but-3-yn-1-ol, and silver trifluoroacetate were purchased from Sigma-Aldrich. The ligand precursors 1,1′-diisopropyl-4,4′-ethylenedi-1,2,4-triazolium dibromide (**1a**), 1,1′-diisopropyl-4,4′-propylenedi-1,2,4-triazolium dibromide (**2a**), and 1-isopropyl-4-ethyl-1,2,4-triazolium bromide (**3a**) were synthesized according to modified literature procedures.[48] The alkynes 4-ethynyl-1,2-dimethoxybenzene and 5-ethynylbenzo[*d*][1,3]dioxole were prepared according to modified literature procedures.[49] ^{1}H, ^{13}C{^{1}H}, ^{19}F{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded on Bruker 400 MHz and Bruker 500 MHz NMR spectrometers. ^{1}H NMR peaks are labeled as singlet (s), doublet (d), triplet (t), broad (br), triplet of triplets (tt), doublet of doublets (dd), multiplet (m), and septet (sept). IR spectra were recorded on a PerkinElmer Spectrum One Fourier transform infrared spectrometer. Mass spectrometry (MS) measurements were done on a Micromass Q-Tof and Bruker Maxis Impact spectrometers. Elemental analysis was carried out on a Thermo Finnigan Flash EA 1112 series (CHNS) elemental analyzer. X-ray diffraction data for compounds **1b−1e**, **2b**, **2c**, **2e**, **3b**, and **3c** were collected on a Rigaku Hg 724+ diffractometer. Crystal data collection and refinement parameters are summarized in the Supporting Information, Tables S1 and S2. The structures were solved using direct methods and standard difference map techniques and refined by full-matrix least-squares procedures on F^2.[50,51] CCDC 927582 (**1b**), 939419 (**2b**), 954478 (**1c**), 941939 (**2c**), 1004371 (**1d**), 999451 (**1e**), 1011414 (**2e**), 1451364 (**3b**), and 1451354 (**3c**) contain the supplementary crystallographic data for this paper (Supporting Information). These data can be obtained free of charge from the Cambridge Crystallographic Data center via www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of [1,1′-Diisopropyl-4,4′-ethylenedi-1,2,4-triazoline-5,5′-diylidene]Pd$_2$Br$_4$(pyridine)$_2$ (1b). A mixture of **1a** (0.192 g, 0.470 mmol), $PdBr_2$ (0.250 g, 0.940 mmol), and K_2CO_3 (0.259 g,

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1.88 mmol) was refluxed in pyridine (5 mL, 63 mmol) for 16 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (ca. 150 mL), and then washed with an aqueous $CuSO_4$ solution (ca. 3 × 60 mL) and water (ca. 50 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum-dried to give the product **1b** as a yellow solid (0.396 g, 90%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 9.04 (d, 4H, $^3J_{HH}$ = 6 Hz, C_5H_5N), 8.28 (s, 2H, NC(3)*H*N), 7.83 (t, 2H, $^3J_{HH}$ = 6 Hz, C_5H_5N), 7.41 (t, 4H, $^3J_{HH}$ = 6 Hz, C_5H_5N), 5.74 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 5.52 (br, 4H, CH_2), 1.59 (d, 12H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 153.3 (PdNCN), 153.0 (C_5H_5N), 144.3 (NC(3)HN), 138.4 (C_5H_5N), 124.9 (C_5H_5N), 56.0 ($CH(CH_3)_2$), 47.7 (CH_2), 21.9 ($CH(CH_3)_2$). IR data (KBr pellet): 3459 (m), 3120 (w), 3049 (w), 2983 (w), 2924 (w), 2851 (w), 1740 (m), 1605 (w), 1538 (w), 1448 (s), 1369 (m), 1253 (w), 1208 (m), 1071 (w), 1048 (w), 1017 (w), 990 (w), 855 (w), 759 (m), 735 (w), 692 (m), 663 (w) cm^{-1}. HRMS (ES): *m*/*z* 858.8186 ([M − Br]$^+$). Calcd: *m*/*z* 854.8210. Anal. Calcd for $C_{22}H_{30}Pd_2N_8Br_4$: C, 28.14; H, 3.22; N, 11.93. Found: C, 28.50; H, 2.88; N, 11.66.

Synthesis of [1,1′-Diisopropyl-4,4′-ethylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2Br_4(PPh_3)_2$ (1c). A mixture of **1b** (0.300 g, 0.320 mmol) and PPh_3 (0.193 g, 0.736 mmol) was stirred in CH_2Cl_2 (ca. 20 mL) at room temperature for 6 h. The solvent was removed under vacuum to give the crude product as a yellow solid. The crude product was recrystallized from CH_3CN to give the product **1c** as a yellow solid (0.351 g, 84%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.81 (s, 2H, NC(3)*H*N), 7.76−7.39 (br, 30H, C_6H_5), 5.25 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 4.95 (d, 2H, $^2J_{HH}$ = 10 Hz, CH_2CH_2), 4.06 (d, 2H, $^2J_{HH}$ = 10 Hz, CH_2CH_2), 1.45 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 0.92 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 167.0 (PdNCN), 143.6 (NC(3)HN), 134.1 (d, $^1J_{CP}$ = 44 Hz, C_6H_5), 132.0 (C_6H_5), 129.1 (C_6H_5), 129.0 (C_6H_5), 55.9 ($CH(CH_3)_2$), 46.2 (CH_2), 22.5 ($CH(CH_3)_2$), 20.4 ($CH(CH_3)_2$). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz, 25 °C): δ 27.3 (Pd*P*Ph$_3$). IR data (KBr pellet): 3444 (m), 3104 (w), 3049 (w), 2982 (w), 2925 (w), 2851 (w), 1682 (w), 1538 (w), 1480 (m), 1435 (s), 1369 (m), 1246 (w), 1215 (w), 1163 (w), 1095 (s), 998 (w), 982 (w), 746 (m), 694 (s), 666 (w), 616 (w), 531 (s), 511 (s), 493 (m) cm^{-1}. HRMS (ES): *m*/*z* 1224.9174 ([M − Br]$^+$). Calcd: *m*/*z* 1220.9195. Anal. Calcd for $C_{48}H_{50}Pd_2N_6P_2Br_4$: C, 44.17; H, 3.86; N, 6.44. Found: C, 44.37; H, 3.60; N, 6.29.

Synthesis of [1,1′-Diisopropyl-4,4′-ethylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2(OCOCF_3)_4(pyridine)_2$ (1d). A mixture of **1b** (0.134 g, 0.143 mmol) and $AgOCOCF_3$ (0.157 g, 0.713 mmol) was stirred in CH_2Cl_2 (ca. 20 mL) at room temperature for 4 h. The reaction mixture was filtered over Celite, and the filtrate was finally dried under vacuum to give the product **1d** as a colorless solid (0.131 g, 85%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 8.56−8.54 (m, 4H, C_5H_5N), 8.07 (s, 2H, NC(3)*H*N), 7.95 (tt, 2H, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, C_5H_5N), 7.54 (t, 4H, $^3J_{HH}$ = 8 Hz, C_5H_5N), 5.73 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 5.48 (s, 4H, CH_2), 1.58 (d, 12H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 162.3 (q, $^3J_{CF}$ = 36 Hz, $OCOCF_3$), 149.8 (PdNCN), 148.7 (C_5H_5N), 144.6 (NC(3)HN), 139.7 (C_5H_5N), 125.5 (C_5H_5N), 114.2 (q, $^2J_{CF}$ = 289 Hz, $OCOCF_3$), 55.9 ($CH(CH_3)_2$), 47.6 (CH_2), 22.2 ($CH(CH_3)_2$). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 470 MHz, 25 °C): δ −74.03 (PdOCOC*F*$_3$). IR data (KBr pellet): 3434 (w), 3128 (w), 2984 (w), 1680 (s), 1609 (w), 1542 (w), 1453 (m), 1421 (w), 1407 (w), 1384 (w), 1234 (w), 1188 (s), 1137 (m), 1074 (w), 1053 (w), 990 (w), 845 (m), 789 (w), 761 (w), 728 (m), 696 (w), 522 (w) cm^{-1}. HRMS (ES): *m*/*z* 959.0262 ([M − $OCOCF_3$]$^+$). Calcd: *m*/*z* 959.0226. Anal. Calcd for $C_{30}H_{30}F_{12}N_8O_8Pd_2$: C, 33.63; H, 2.83; N, 10.46. Found: C, 33.45; H, 2.49; N, 11.06.

Synthesis of [1,1′-Diisopropyl-4,4′-ethylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2(OCOCF_3)_4(PPh_3)_2$ (1e). A mixture of **1c** (0.134 g, 0.103 mmol) and $AgOCOCF_3$ (0.135 g, 0.614 mmol) was stirred in CH_2Cl_2 (ca. 30 mL) at room temperature for 4 h. The reaction mixture was filtered over Celite, and the filtrate was dried under vacuum to give the crude product as a colorless solid. The crude product was finally purified by column chromatography using silica gel as a stationary phase and eluting with a mixed medium of CH_2Cl_2/MeOH (98:2, v/v) to give product **1e** as a colorless solid (0.105 g, 72%). ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 8.98 (s, 2H, NC(3)*H*N), 7.54−7.51 (m, 6H, C_6H_5), 7.44−7.39 (m, 24H, C_6H_5), 5.36 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 4.58−4.56 (m, 2H, CH_2), 4.39−4.35 (m, 2H, CH_2), 1.43 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 1.01 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 161.9 (br, $OCOCF_3$), 159.2 (d, $^2J_{CP}$ = 8 Hz, PdNCN), 145.2 (2C, NC(3)HN), 133.6 (d, $^3J_{CP}$ = 10 Hz, C_6H_5), 132.7 (d, $^4J_{CP}$ = 4 Hz, C_6H_5), 129.6 (d, $^2J_{CP}$ = 11 Hz, C_6H_5), 126.0 (d, $^1J_{CP}$ = 58 Hz, C_6H_5), 114.2 (d, $^2J_{CF}$ = 289 Hz, $OCOCF_3$), 56.1 ($CH(CH_3)_2$) 56.0 ($CH(CH_3)_2$) 47.4 (CH_2), 23.0 ($CH(CH_3)_2$), 20.9 ($CH(CH_3)_2$). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 202 MHz, 25 °C): δ 25.5 (Pd*P*Ph$_3$). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 470 MHz, 25 °C): δ −75.1 (PdOCOC*F*$_3$). IR data (KBr pellet): 3435 (w), 3119 (w), 3058 (w), 2993 (w), 2923 (w), 2851 (w), 1693 (s), 1584 (w), 1536 (w), 1484 (w), 1438 (w), 1407 (w), 1315 (w), 1197 (s), 1144 (m), 1099 (m), 998 (w), 908 (w), 843 (m), 791 (w), 727 (m), 713 (m), 694 (m), 537 (m), 511 (m), 497 (m) cm^{-1}. LRMS (ES): *m*/*z* 1064.2 ([M + H − $OCOCF_3$ − PPh_3]$^+$). Calcd: *m*/*z* 1062.0. Anal. Calcd for $C_{56}H_{50}F_{12}N_6O_8P_2Pd_2$: C, 46.78; H, 3.51; N, 5.85. Found: C, 45.91; H, 3.21; N, 6.34.

Synthesis of [1,1′-Diisopropyl-4,4′-propylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2Br_4(pyridine)_2$ (2b). A mixture of **2a** (0.199 g, 0.470 mmol), $PdBr_2$ (0.250 g, 0.940 mmol) and K_2CO_3 (0.259 g, 1.88 mmol) was refluxed in pyridine (5 mL, 63 mmol) for 16 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (ca. 150 mL), and then washed with an aqueous $CuSO_4$ solution (ca. 3 × 60 mL) and water (ca. 50 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum-dried to give the product **2b** as a yellow solid (0.410 g, 91%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 9.04 (d, 4H, $^3J_{HH}$ = 5 Hz, C_5H_5N), 8.39 (s, 2H, NC(3)*H*N), 7.81 (t, 2H, $^3J_{HH}$ = 7 Hz, C_5H_5N), 7.39 (t, 4H, $^3J_{HH}$ = 7 Hz, C_5H_5N), 5.74 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 4.71 (t, 4H, $^3J_{HH}$ = 7 Hz, CH_2), 3.34 (quint, 2H, $^3J_{HH}$ = 7 Hz, CH_2), 1.59 (d, 12H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 152.9 (C_5H_5N), 152.7 (Pd−NCN), 143.6 (NC(3)H−N), 138.4 (C_5H_5N), 124.9 (C_5H_5N), 55.8 ($CH(CH_3)_2$), 46.9 (CH_2), 29.1 (CH_2), 22.0 ($CH(CH_3)_2$). IR data (KBr pellet): 3445 (w), 3114 (m), 3042 (w), 2981 (m), 2933 (w), 2869 (w), 1735 (w), 1603 (m), 1531 (m), 1471 (m), 1446 (s), 1381 (m), 1350 (w), 1297 (w), 1258 (w), 1214 (w), 1194 (m), 1069 (m), 1048 (w), 1016, (w), 989, (w), 870, (w), 798 (w), 756 (s), 693 (s), 667 (m), 644 (m) cm^{-1}. HRMS (ES): *m*/*z* 872.8345 ([M − Br]$^+$). Calcd: *m*/*z* 868.8367. Anal. Calcd for $C_{23}H_{32}Pd_2N_8Br_4$: C, 28.99; H, 3.38; N, 11.76. Found: C, 28.94; H, 2.84; N, 12.37.

Synthesis of [1,1′-Diisopropyl-4,4′-propylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2Br_4(PPh_3)_2$ (2c). A mixture of **2b** (0.392 g, 0.411 mmol) and PPh_3 (0.270 g, 1.02 mmol) in CH_2Cl_2 (ca. 40 mL) was stirred at room temperature for 6 h. The solvent was removed under vacuum to give the crude product as a yellow solid. The crude product was purified by column chromatography using silica gel as a stationary phase and eluting it with a mixed medium of $CHCl_3$/MeOH (98:2, v/v) and finally crystallized overnight from CH_3CN to give product **2c** as a yellow crystalline solid (0.201 g, 38%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 8.44 (s, 2H, NC(3)*H*N), 7.48−7.30 (br, 30H, C_6H_5), 5.32 (sept, 2H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 3.79−3.74 (m, 2H, CH_2), 3.47−3.37 (m, 2H, CH_2), 2.44−2.40 (m, 2H, CH_2), 1.57 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$), 0.94 (d, 6H, $^3J_{HH}$ = 7 Hz, $CH(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 165.6 (PdNCN), 144.0 (NC(3)HN), 134.1 (d, J_{CP} = 40 Hz, C_6H_5), 131.7 (C_6H_5), 129.0 (C_6H_5), 129.0 (C_6H_5), 55.9 ($CH(CH_3)_2$), 45.0 (CH_2), 29.3 (CH_2), 22.5 ($CH(CH_3)_2$), 20.6 ($CH(CH_3)_2$). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz, 25 °C): δ 26.8 (Pd*P*Ph$_3$). IR data (KBr pellet): 3504 (w), 3051 (w), 2983 (w), 2936 (w), 1619 (w), 1535 (w), 1480 (m), 1635 (s), 1368 (w), 1331 (w), 1291 (w), 1218 (w), 1131 (w), 1095 (s), 1050 (w), 998 (w), 988 (w), 880 (w), 748 (s), 695, (s), 667, (m), 530, (s), 511 (s), 495 (m) cm^{-1}. LRMS (ES): *m*/*z* 1078.2 ([M − PPh_3 + Na]$^+$). Calcd: *m*/*z* 1074.8. Anal. Calcd for $C_{49}H_{52}Pd_2N_6P_2Br_4$: C, 44.61; H, 3.97; N, 6.37. Found: C, 44.70; H, 3.77; N, 6.36.

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Synthesis of [1,1′-Diisopropyl-4,4′-propylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2(OCOCF_3)_4(pyridine)_2$ (2d). A mixture of **2b** (0.153 g, 0.161 mmol) and $AgOCOCF_3$ (0.177 g, 0.803 mmol) was stirred in CH_2Cl_2 (ca. 30 mL) at room temperature for 4 h. The reaction mixture was filtered over Celite, and the filtrate was finally dried under vacuum to give the product **2d** as a light-yellow solid (0.171 g, 96%). ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 8.47−8.46 (m, 4H, C_5H_5N), 8.37 (s, 2H, NC(3)*H*N), 7.92−7.88 (m, 2H, C_5H_5N), 7.50−7.46 (m, 4H, C_5H_5N), 5.80 (sept, 2H, $^3J_{HH}$ = 7 Hz, C*H*$(CH_3)_2$), 4.77 (t, 4H, $^3J_{HH}$ = 7 Hz, C*H*$_2$), 3.17 (t, 2H, $^3J_{HH}$ = 7 Hz, C*H*$_2$), 1.57 (d, 12H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, 25 °C): δ 162.3 (q, $^3J_{CF}$ = 38 Hz, $OCOCF_3$), 149.7 (Pd−N*C*N), 148.9 (C_5H_5N), 143.5 (N*C*(3)HN), 139.6 (C_5H_5N), 125.5 (C_5H_5N), 114.2 (q, $^2J_{CF}$ = 288 Hz, $OCOCF_3$), 55.7 (CH$(CH_3)_2$) 45.9 (*C*H$_2$), 30.9 (*C*H$_2$), 22.1 (CH(*C*H$_3)_2$). ^{19}F{^{1}H} NMR ($CDCl_3$, 470 MHz, 25 °C): δ −74.2 (PdOCOC*F*$_3$). IR data (KBr pellet): 3440 (w), 3115 (w), 2983 (w), 2928 (w), 2851 (w), 1682 (s), 1537 (w), 1448 (w), 1371 (w), 1300 (w), 1210 (m), 1129 (m), 1071 (w), 838 (w), 804 (w), 759 (w), 724 (w) 694 (w), 518 (w) cm^{-1}. Anal. Calcd for $C_{31}H_{32}F_{12}Pd_2N_8O_8$: C, 34.30; H, 2.97; N, 10.32. Found: C, 34.08; H, 2.84; N, 9.79.

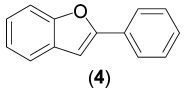
Synthesis of [1,1′-Diisopropyl-4,4′-propylenedi-1,2,4-triazoline-5,5′-diylidene]$Pd_2(OCOCF_3)_4(PPh_3)_2$ (2e). A mixture of **2c** (0.168 g, 0.127 mmol) and $AgOCOCF_3$ (0.168 g, 0.764 mmol) was stirred in CH_2Cl_2 (ca. 30 mL) at room temperature for 4 h. The reaction mixture was filtered over Celite, and the filtrate was dried under vacuum to give the product **2e** as a colorless solid (0.121 g, 65%). Both the ^{1}H and ^{13}C NMR spectra showed the presence of two isomers. The major-to-minor isomer ratio was 4:1. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): (major) δ 8.55 (s, 2H, NC(3)*H*N), 7.55−7.52 (m, 6H, C_6H_5), 7.48−7.34 (m, 24H, C_6H_5), 5.43 (sept, 2H, $^3J_{HH}$ = 7 Hz, C*H*$(CH_3)_2$), 3.95 (br, 2H, C*H*$_2$), 3.37 (br, 2H, C*H*$_2$), 2.30 (br, 2H, C*H*$_2$), 1.45 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$), 0.97 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, 25 °C): δ 161.6 (br, 4C, $OCOCF_3$), 157.6 (PdN*C*N), 157.6 (PdN*C*N), 146.0 (2C, NC(3)HN), 133.8 (C_6H_5), 133.7 (C_6H_5), 132.7 (C_6H_5), 132.6 (C_6H_5), 129.5 (C_6H_5), 129.4 (C_6H_5), 126.5 (C_6H_5), 126.0 (C_6H_5), 114.5 (q, 4C, $^2J_{CF}$ = 289 Hz, $OCOCF_3$), 56.1 (2C, *C*H$(CH_3)_2$), 45.7 (2C, *C*H$_2$), 30.3 (2C, *C*H$_2$), 23.1 (2C, CH(*C*H$_3)_2$), 20.8 (2C, CH(*C*H$_3)_2$). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, 25 °C): δ 25.7 (Pd*P*Ph$_3$). ^{19}F{^{1}H} NMR ($CDCl_3$, 470 MHz, 25 °C): δ −75.0 (PdOCOC*F*$_3$). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): (minor) δ 8.02 (s, 2H, NC(3)*H*N), 7.55−7.52 (m, 6H, C_6H_5), 7.48−7.34 (m, 24H, C_6H_5), 5.40 (sept, 2H, $^3J_{HH}$ = 7 Hz, C*H*$(CH_3)_2$), 4.34 (br, 2H, C*H*$_2$), 3.60 (br, 2H, C*H*$_2$), 2.75 (br, 2H, C*H*$_2$), 1.35 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$), 0.89 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, 25 °C): δ 161.6 (br, 4C, $OCOCF_3$), 157.6 (PdN*C*N), 157.6 (PdN*C*N), 144.1 (2C, NC(3)HN), 132.7 (C_6H_5), 132.6 (C_6H_5), 132.3 (C_6H_5), 132.2 (C_6H_5), 128.9 (C_6H_5), 128.7 (C_6H_5), 126.7 (C_6H_5), 126.0 (C_6H_5), 114.5 (q, 4C, $^2J_{CF}$ = 289 Hz, $OCOCF_3$), 56.1 (2C, *C*H$(CH_3)_2$), 46.2 (2C, *C*H$_2$), 29.9 (2C, *C*H$_2$), 22.7 (2C, CH(*C*H$_3)_2$), 20.6 (2C, CH(*C*H$_3)_2$). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, 25 °C): δ 25.3 (Pd*P*Ph$_3$). ^{19}F{^{1}H} NMR ($CDCl_3$, 470 MHz, 25 °C): δ −74.0 (PdOCOC*F*$_3$). IR data (KBr pellet): 3520 (w), 3112 (w), 3060 (w), 2991 (w), 2942 (w), 2675 (w), 2576 (w), 2329 (w), 1980 (w), 1682 (s), 1585 (w), 1538 (w), 1483 (w), 1437 (s), 1314 (w), 1195 (s), 1098 (s), 1027 (w), 998 (w), 890 (w), 842 (m), 790 (w), 747 (m), 726 (s), 694 (s), 536 (s), 512 (s), 497 (m) cm^{-1}. LRMS (ES): *m*/*z* 1339.1 ([M − $OCOCF_3$]$^+$). Calcd: *m*/*z* 1337.1. Anal. Calcd for $C_{57}H_{52}O_8F_{12}N_6P_2Pd_2$: C, 47.16; H, 3.61; N, 5.79. Found: C, 47.00; H, 3.22; N, 6.59.

Synthesis of *trans*-[1-Isopropyl-4-ethyl-1,2,4-triazol-5-ylidene]$PdBr_2$(pyridine) (3b). A mixture of **3a** (0.471 g, 2.14 mmol), $PdBr_2$ (0.569 g, 0. 2.14 mmol), and K_2CO_3 (0.443 g, 3.21 mmol) was refluxed in pyridine (5 mL, 63 mmol) for 16 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (ca. 100 mL), and then washed with an aqueous $CuSO_4$ solution (ca. 3 × 60 mL) and water (ca. 50 mL). The organic layer was separated, dried over Na_2SO_4, and finally vacuum dried to give the product **3b** as a yellow solid (0.818 g, 79%). ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 9.03 (br, 2H, C_5H_5N), 8.02 (s, 1H, NC(3)*H*N), 7.78 (t, 1H, $^3J_{HH}$ = 6 Hz, C_5H_5N), 7.37−7.34 (m, 2H, C_5H_5N), 5.74 (sept, 1H, $^3J_{HH}$ = 7 Hz, C*H*$(CH_3)_2$), 4.59 (q, 2H, $^3J_{HH}$ = 6 Hz, C*H*$_2$CH$_3$), 1.69 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C*H*$_3$), 1.60 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, 25 °C): δ 152.8 (PdNCN), 152.8 (C_5H_5N), 142.3 (NC(3)HN), 138.2 (C_5H_5N), 124.8 (C_5H_5N), 55.5 (CH$(CH_3)_2$), 44.3 (CH$_2$CH$_3$), 22.0 (CH$(CH_3)_2$), 15.6 (CH$_2$CH$_3$). IR data (KBr pellet): 3459 (m), 3119 (w), 2976 (w), 2932 (w), 2924 (w), 1634 (w), 1605 (w), 1540 (w), 1471 (w), 1448 (s), 1369 (w), 1274 (m), 1208 (m), 1125 (w), 1071 (m), 1046 (m), 1017 (m), 993 (m), 853 (w), 758 (m), 735 (w), 695 (m), 665 (w) cm^{-1}. Anal. Calcd for $C_{12}H_{18}Br_2N_4Pd$: C, 29.75; H, 3.74; N, 11.56. Found: C, 30.24; H, 4.51; N, 11.29.

Synthesis of *cis*-[1-Isopropyl-4-ethyl-1,2,4-triazol-5-ylidene]-$PdBr_2(PPh_3)$ (3c). A mixture of **3b** (0.500 g, 1.03 mmol) and PPh_3 (0.325 g, 1.24 mmol) was stirred in CH_2Cl_2 (ca. 60 mL) at room temperature for 6 h. The solvent was removed under vacuum to give the crude product as a yellow solid. The crude product was purified by column chromatography using silica gel as a stationary phase and eluting it with a mixed medium of $CHCl_3$/MeOH (98:2, v/v) to give product **3c** as a yellow solid (0.445 g, 65%). ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.73 (s, 1H, NC(3)*H*N), 7.56−7.47 (m, 9H, C_6H_5), 7.39−7.36 (m, 6H, C_6H_5), 5.29 (sept, 1H, $^3J_{HH}$ = 7 Hz, C*H*$(CH_3)_2$), 4.27 (qd, 1H, $^2J_{HH}$ = 14 Hz, $^3J_{HH}$ = 7 Hz, C*H*$_2$CH$_3$), 3.48 (qd, 1H, $^2J_{HH}$ = 14 Hz, $^3J_{HH}$ = 7 Hz, C*H*$_2$CH$_2$), 1.51 (d, 3H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$), 1.32 (t, 3H, $^3J_{HH}$ = 7 Hz, CH$_2$C*H*$_3$), 0.95 (d, 6H, $^3J_{HH}$ = 7 Hz, CH(C*H*$_3)_2$). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz, 25 °C): δ 166.6 (PdNCN), 141.8 (NC(3)HN), 134.4 (d, $^1J_{CP}$ = 11 Hz, C_6H_5), 131.5 (C_6H_5), 128.8 (C_6H_5), 128.7 (C_6H_5), 55.7 (CH$(CH_3)_2$), 44.0 (CH$_2$CH$_3$), 20.7 (CH(*C*H$_3)_2$), 20.6 (CH(*C*H$_3)_2$), 14.7 (CH$_2$CH$_3$). ^{31}P{^{1}H} NMR ($CDCl_3$, 202 MHz, 25 °C): δ 26.5 (Pd*P*Ph$_3$). IR data (KBr pellet): 2969 (w), 2925 (w), 2850 (w), 1646 (w), 1479 (w), 1435 (w), 1373 (w), 1268 (w), 1093 (s), 1027 (s), 798 (w), 746 (w), 694 (m), 531 (w) cm^{-1}. HRMS (ES): *m*/*z* 588.0227 ([M − Br]$^+$). Calcd: *m*/*z* 586.0237. Anal. Calcd for $C_{25}H_{28}Br_2N_3PPd$: C, 44.97; H, 4.23; N, 6.29. Found: C, 45.37; H, 4.19; N, 6.28.

General Procedure for the Heck Alkynylation/Cyclization Reaction of Iodophenols. In a typical catalysis run, performed in air, a 10 mL vial was charged with a mixture of the 2-iodophenol, a terminal alkyne substrate, and Cs_2CO_3 in a molar ratio of 1:1.5:3. A palladium complex (**1b**−**1e** and **2b**−**2e**; 1 mol %) was added to the mixture, followed by DMSO (ca. 3 mL) solvent, and then the reaction mixture was heated at 80 °C for a time period of *t* hours. The reaction mixture was cooled to room temperature, and water (ca. 12 mL) was added. The resulting mixture was extracted with EtOAc (ca. 50 mL). The aqueous layer was further extracted with EtOAc (ca. 3 × 20 mL). The organic layers were combined and vacuum-dried to obtain a crude product that was subsequently purified by column chromatography using silica gel as a stationary phase and eluting it with a mixed medium of petroleum ether/EtOAc to give the desired product (**4**−**12**).

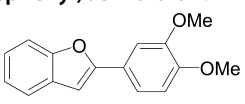
2-Phenylbenzofuran.[12]



(**4**)

Yield: 0.079 g, 81%. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 7.88 (d, 2H, $^3J_{HH}$ = 8 Hz, C_6H_5), 7.59 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.54 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.47 (t, 2H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.37 (t, 1H, $^3J_{HH}$ = 8 Hz, C_6H_5), 7.31−7.21 (m, 2H, C_6H_5), 7.04 (s, 1H, C_8H_5O). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, 25 °C): δ 156.1 (C_8H_5O), 155.1 (C_8H_5O), 130.7 (C_8H_5O), 129.4 (C_6H_5), 129.0 (C_6H_5), 128.7 (C_8H_5O), 125.1 (C_6H_5), 124.4 (C_8H_5O), 123.1 (C_8H_5O), 121.1 (C_6H_5), 111.4 (C_8H_5O), 101.5 (C_8H_5O).

2-(3,4-Dimethoxyphenyl)benzofuran.[52]

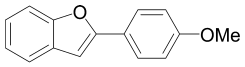


(**5**)

DOI: 10.1021/acs.inorgchem.5b02727
Inorg. Chem. XXXX, XXX, XXX−XXX

Yield: 0.089 g, 70%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.57 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.52 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.44 (dd, 1H, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, $C_8H_9O_2$), 7.38 (d, 1H, $^4J_{HH}$ = 2 Hz, $C_8H_9O_2$), 7.29−7.20 (m, 2H, C_8H_5O), 6.94 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_8H_9O_2$), 6.91 (s, 1H, C_8H_5O), 6.78 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_8H_9O_2$), 4.00 (s, 3H, CH_3 of $C_8H_9O_2$) 3.94 (s, 3H, CH_3 of $C_8H_9O_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 156.1 (C_8H_5O), 154.9 (C_8H_5O), 149.7 ($C_8H_9O_2$), 149.3 ($C_8H_9O_2$), 129.6 (C_8H_5O), 124.0 (C_8H_5O), 123.7 ($C_8H_9O_2$), 123.0 (C_8H_5O), 120.8 ($C_8H_9O_2$), 118.1 (C_8H_5O), 111.5 ($C_8H_9O_2$), 111.2 ($C_8H_9O_2$), 108.2 (C_8H_5O), 100.2 (C_8H_5O), 56.2 (CH_3 of $C_8H_9O_2$), 56.1 (CH_3 of $C_8H_9O_2$).

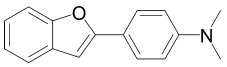
2-(4-Methoxyphenyl)benzofuran.[12]



(**6**)

Yield: 0.075 g, 67%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.80 (d, 2H, $^3J_{HH}$ = 8 Hz, C_7H_7O), 7.56 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.50 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.25−7.20 (m, 2H, C_8H_5O), 6.98 (d, 2H, $^3J_{HH}$ = 8 Hz, C_7H_7O), 6.89 (s, 1H, C_8H_5O), 3.86 (s, 3H, CH_3 of C_7H_7O). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 160.1 (C_7H_7O), 156.1 (C_8H_5O), 154.9 (C_8H_5O), 129.7 (C_8H_5O), 126.6 (C_7H_7O), 123.9 (C_8H_5O), 123.5 (C_7H_7O), 123.0 (C_8H_5O), 120.8 (C_8H_5O), 114.4 (C_7H_7O), 111.2 (C_8H_5O), 99.6 (C_8H_5O), 55.6 (CH_3 of C_7H_7O).

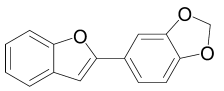
4-Benzofuran-2-yl-*N*,*N*-dimethylaniline.[53]



(**7**)

Yield:0.056 g, 47%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.74 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_8H_{10}N$), 7.50 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.48 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.26−7.18 (m, 2H, C_8H_5O), 6.81 (s, 1H, C_8H_5O), 6.78 (d, 2H, $^3J_{HH}$ = 8 Hz, $C_8H_{10}N$), 3.03 (s, 6H, CH_3 of $C_8H_{10}N$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 157.2 (C_8H_5O), 154.7(C_8H_5O), 129.4 ($C_8H_{10}N$), 130.0 (C_8H_5O), 126.3 ($C_8H_{10}N$), 123.2 (C_8H_5O), 122.8 ($C_8H_{10}N$), 120.3 (C_8H_5O), 118.8 (C_8H_5O), 112.3 ($C_8H_{10}N$), 110.9 (C_8H_5O), 98.2 (C_8H_5O), 40.5 (CH_3 of $C_8H_{10}N$).

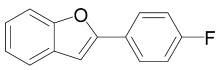
5-Benzofuran-2-ylbenzo[*d*][1,3]dioxole.[52]



(**8**)

Yield: 0.074 g, 62%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.55 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.49 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.44 (dd, 1H, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, $C_7H_5O_2$), 7.38 (d, 1H, $^4J_{HH}$ = 2 Hz, $C_7H_5O_2$), 7.27−7.20 (m, 2H, C_8H_5O), 6.88 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_7H_5O_2$), 6.86 (s, 1H, C_8H_5O), 6.01 (s, 2H, $C_7H_5O_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 156.0 (C_8H_5O), 154.8 (C_8H_5O), 148.3 ($C_7H_5O_2$), 148.2 ($C_7H_5O_2$), 129.5 (C_8H_5O), 125.0 (C_8H_5O), 124.1 ($C_7H_5O_2$), 123.1 (C_8H_5O), 120.8 ($C_7H_5O_2$), 119.3 (C_8H_5O), 111.2 ($C_7H_5O_2$), 108.9 (C_8H_5O), 105.7 ($C_7H_5O_2$), 101.5 (C_8H_5O), 100.4 ($C_7H_5O_2$).

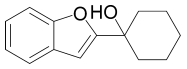
2-(4-Fluorophenyl)benzofuran.[12]



(**9**)

Yield: 0.057 g, 53%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.86−7.83 (m, 2H, C_6H_4F), 7.58 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.52 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.30−7.22 (m, 2H, C_8H_5O), 7.16−7.12 (m, 2H, C_6H_4F), 6.96 (s, 1H, C_8H_5O). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 164.1 (C_8H_5O), 162.1 (C_8H_5O), 155.1 (d, $^2J_{CF}$ = 21 Hz, C_6H_4F), 134.7 (d, $^4J_{CF}$ = 9 Hz, C_6H_4F), 129.4 (C_8H_5O), 127.1 (C_6H_4F), 127.0 (d, $^4J_{CF}$ = 9 Hz, C_6H_4F), 124.5 (C_8H_5O), 123.2 (C_8H_5O), 121.8 (C_8H_5O), 116.2 (C_6H_4F), 116.0 (C_6H_4F), 111.3 (C_8H_5O), 101.2 (C_8H_5O).

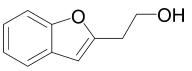
1-Benzofuran-2-ylcyclohexan-1-ol.[12]



(**10**)

Yield: 0.085 g, 79%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.52 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.44 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.26−7.18 (m, 2H, C_8H_5O), 6.59 (s, 1H, C_8H_5O), 2.09−2.04 (m, 3H, $C_6H_{11}O$), 1.93−1.90 (m, 2H, $C_6H_{11}O$), 1.80−1.73 (m, 2H, $C_6H_{11}O$), 1.62−1.54 (m, 3H, $C_6H_{11}O$), 1.43−1.36 (m, 1H, $C_6H_{11}O$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 163.0 (C_8H_5O), 154.7 (C_8H_5O), 128.5 (C_8H_5O), 124.1 (C_8H_5O), 122.8 (C_8H_5O), 122.1 (C_8H_5O), 111.4 (C_8H_5O), 101.3 (C_8H_5O), 70.8 ($C_6H_{11}O$), 36.3 ($C_6H_{11}O$), 25.6 ($C_6H_{11}O$), 22.2 ($C_6H_{11}O$).

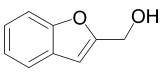
2-Benzofuran-2-ylethan-1-ol.[12]



(**11**)

Yield: 0.052 g, 62%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.49 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.42 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.25−7.17 (m, 2H, C_8H_5O), 6.50 (s, 1H, C_8H_5O), 3.98 (t, 2H, $^3J_{HH}$ = 7 Hz, CH_2), 3.04 (t, 2H, $^3J_{HH}$ = 7 Hz, CH_2), 1.84 (br, 1H, CH_2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 156.1 (C_8H_5O), 155.0 (C_8H_5O), 128.8 (C_8H_5O), 123.7 (C_8H_5O), 122.8 (C_8H_5O), 120.6 (C_8H_5O), 111.0 (C_8H_5O), 103.9 (C_8H_5O), 60.9 (CH_2), 32.2 (CH_2).

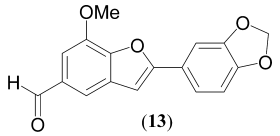
Benzofuran-2-ylmethanol.[54]



(**12**)

Yield: 0.063 g, 84%. ^{1}H NMR ($CDCl_3$, 500 MHz, 25 °C): δ 7.54 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.46 (d, 1H, $^3J_{HH}$ = 8 Hz, C_8H_5O), 7.30−7.20 (m, 2H, C_8H_5O), 6.66 (s, 1H, C_8H_5O), 4.77 (s, 2H, CH_2), 2.05 (br, 1H, CH_2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, 25 °C): δ 156.6 (C_8H_5O), 155.3 (C_8H_5O), 128.3 (C_8H_5O), 124.6 (C_8H_5O), 123.0 (C_8H_5O), 121.3 (C_8H_5O), 111.4 (C_8H_5O), 104.3 (C_8H_5O), 58.4 (CH_2).

2-Benzo[*d*][1,3]dioxol-5-yl-7-methoxybenzofuran-5-carbaldehyde.[6]



(**13**)

Yield: 0.053 g, 36%. ^{1}H NMR ($CDCl_3$, 400 MHz, 25 °C): δ 10.0 (s, 1H, CHO of $C_{10}H_7O_3$), 7.69 (s, 1H, $C_{10}H_7O_3$), 7.43 (dd, 1H, $^3J_{HH}$ = 8 Hz, $^4J_{HH}$ = 2 Hz, $C_7H_5O_2$), 7.35 (s, 1H, $C_{10}H_7O_3$), 7.34 (s, 1H, $C_7H_5O_2$), 6.96 (s, 1H, $C_{10}H_7O_3$), 6.89 (d, 1H, $^3J_{HH}$ = 8 Hz, $C_7H_5O_2$), 6.03 (s, 2H, $C_7H_5O_2$), 4.09 (s, 3H, OCH_3 of $C_{10}H_7O_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 25 °C): δ 192.0 (CHO of $C_{10}H_7O_3$), 157.9 ($C_{10}H_7O_3$), 148.3 ($C_7H_5O_2$), 148.2 ($C_7H_5O_2$), 147.6 ($C_{10}H_7O_3$), 146.1 ($C_{10}H_7O_3$), 133.6 ($C_{10}H_7O_3$), 131.2 ($C_{10}H_7O_3$), 124.0 ($C_7H_5O_2$), 119.8 ($C_7H_5O_2$), 119.2 ($C_{10}H_7O_3$), 108.9 ($C_7H_5O_2$), 105.7 ($C_7H_5O_2$), 104.7 ($C_{10}H_7O_3$), 101.7 ($C_{10}H_7O_3$), 100.4 ($C_7H_5O_2$), 56.4 (OCH_3 of $C_{10}H_7O_3$). HRMS (ES): m/z 296.0683 ($[M]^+$). Calcd: m/z 296.0679.

Mercury Drop Experiment Performed at Varying Time Intervals. *1. Mercury Addition at the Start of the Reaction.* A 10 mL vial was charged with a mixture of 2-iodophenol, phenylacetylene, and Cs_2CO_3 in a molar ratio of 1:1.5:3, and mercury (0.121 g, 0.603 mmol) was added subsequently. The palladium complex **1c** (1 mol %) was added to the mixture, followed by DMSO (ca. 3 mL) solvent, and then the reaction mixture was heated at 80 °C for 4 h. The reaction mixture was cooled to room temperature, and water (ca. 12 mL) was added. The resulting mixture was extracted with EtOAc (ca. 50 mL). The water layer was further extracted with EtOAc (ca. 3 × 20 mL). The organic layers were combined and vacuum-dried to give crude product as a brown solid, which was purified by column chromatography using silica gel as a stationary phase and eluting it

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with neat petroleum ether to give product **4** as a white solid (0.082 g, 84%).

2. Mercury Addition after 1 h of Reaction Time. A 10 mL vial was charged with a mixture of 2-iodophenol, phenylacetylene, and Cs_2CO_3 in a molar ratio of 1:1.25:3. The palladium complex **1c** (1 mol %) was added to the mixture, followed by DMSO (ca. 3 mL) solvent, and then the reaction mixture was heated at 80 °C for 1 h. Mercury (0.126 g, 0.628 mmol) was added, and the reaction mixture was further heated at 80 °C for 3 h. The reaction mixture was cooled to room temperature, and water (ca. 12 mL) was added. The resulting mixture was extracted with EtOAc (ca. 50 mL). The water layer was further extracted with EtOAc (ca. 3 × 20 mL). The organic layers were combined and vacuum-dried to give crude product as a brown solid, which was purified by column chromatography using silica gel as a stationary phase and eluting it with neat petroleum ether to give product **4** as a white solid (0.070 g, 72%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.5b02727.

NMR, IR, mass, and elemental analysis data of the palladium complexes **1b**−**1e**, **2b**−**2e**, **3b**, and **3c**, an X-ray metrical data comparison table, ORTEP plots of **2b**, **2c**, **2e**, **3b**, and **3c**, and mercury(0) drop test results (PDF)

X-ray crystallographic data in CIF format (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Flynn, B. L.; Gill, G. S.; Grobelny, D. W.; Chaplin, J. H.; Paul, D.; Leske, A. F.; Lavranos, T. C.; Chalmers, D. K.; Charman, S. A.; Kostewicz, E.; Shackleford, D. M.; Morizzi, J.; Hamel, E.; Jung, M. K.; Kremmidiotis, G. *J. Med. Chem.* **2011**, *54*, 6014−6027.

(2) Singh, S. N.; Fletcher, R. D.; Fisher, S. G.; Singh, B. N.; Lewis, H. D.; Deedwania, P. C.; Massie, B. M.; Colling, C.; Lazzeri, D. *N. Engl. J. Med.* **1995**, *333*, 77−82.

(3) Shi, Y.-Q.; Fukai, T.; Sakagami, H.; Chang, W.-J.; Yang, P.-Q.; Wang, F.-P.; Nomura, T. *J. Nat. Prod.* **2001**, *64*, 181−188.

(4) Yuan, H.; Bi, K. J.; Li, B.; Yue, R. C.; Ye, J.; Shen, Y. H.; Shan, L.; Jin, H. Z.; Sun, Q. Y.; Zhang, W. D. *Org. Lett.* **2013**, *15*, 4742−4745.

(5) Naveen, M.; Reddy, C. U.; Hussain, M. M.; Chaitanya, M.; Narayanaswamy, G. *J. Heterocycl. Chem.* **2013**, *50*, 1064−1066.

(6) Choi, D. H.; Hwang, J. W.; Lee, H. S.; Yang, D. M.; Jun, J.-G. *Bull. Korean Chem. Soc.* **2008**, *29*, 1594−1596.

(7) Xia, Y.; Jin, Y.; Kaur, N.; Choi, Y.; Lee, K. *Eur. J. Med. Chem.* **2011**, *46*, 2386−2396.

(8) Kaur, N.; Xia, Y.; Jin, Y.; Dat, N. T.; Gajulapati, K.; Choi, Y.; Hong, Y.-S.; Lee, J. J.; Lee, K. *Chem. Commun. (Cambridge, U. K.)* **2009**, 1879−1881.

(9) Moure, M. J.; SanMartin, R.; Dominguez, E. *Adv. Synth. Catal.* **2014**, *356*, 2070−2080.

(10) Anga, S.; Kottalanka, R. K.; Pal, T.; Panda, T. K. *J. Mol. Struct.* **2013**, *1040*, 129−138.

(11) Zanardi, A.; Mata, J. A.; Peris, E. *Organometallics* **2009**, *28*, 4335−4339.

(12) Zhou, R.; Wang, W.; Jiang, Z.-J.; Wang, K.; Zheng, X.-l.; Fu, H.-Y.; Chen, H.; Li, R.-X. *Chem. Commun. (Cambridge, U. K.)* **2014**, *50*, 6023−6026.

(13) Konno, T.; Chae, J.; Ishihara, T.; Yamanaka, H. *Tetrahedron* **2004**, *60*, 11695−11700.

(14) Arcadi, A.; Blesi, F.; Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Marinelli, F. *Tetrahedron* **2013**, *69*, 1857−1871.

(15) Sarkar, S.; Pal, R.; Chatterjee, N.; Dutta, S.; Naskar, S.; Sen, A. K. *Tetrahedron Lett.* **2013**, *54*, 3805−3809.

(16) Kumar, A.; Ghosh, P. *Eur. J. Inorg. Chem.* **2012**, *2012*, 3955−3969.

(17) Prakasham, A. P.; Ghosh, P. *Inorg. Chim. Acta* **2015**, *431*, 61−100.

(18) John, A.; Ghosh, P. *Dalton Trans.* **2010**, *39*, 7183−7206.

(19) John, A.; Modak, S.; Madasu, M.; Katari, M.; Ghosh, P. *Polyhedron* **2013**, *64*, 20−29.

(20) Dash, C.; Shaikh, M. M.; Ghosh, P. *Eur. J. Inorg. Chem.* **2009**, *2009*, 1608−1618.

(21) John, A.; Shaikh, M. M.; Ghosh, P. *Dalton Trans.* **2009**, 10581−10591.

(22) Ray, L.; Barman, S.; Shaikh, M. M.; Ghosh, P. *Chem. - Eur. J.* **2008**, *14*, 6646−6655.

(23) Samantaray, M. K.; Shaikh, M. M.; Ghosh, P. *J. Organomet. Chem.* **2009**, *694*, 3477−3486.

(24) Samantaray, M. K.; Dash, C.; Shaikh, M. M.; Pang, K.; Butcher, R. J.; Ghosh, P. *Inorg. Chem.* **2011**, *50*, 1840−1848.

(25) Modak, S.; Gangwar, M. K.; Nageswar Rao, M.; Madasu, M.; Kalita, A. C.; Dorcet, V.; Shejale, M. A.; Butcher, R. J.; Ghosh, P. *Dalton Trans.* **2015**, *44*, 17617−17628.

(26) Rao, M. N.; Haridas, M.; Gangwar, M. K.; Rajakannu, P.; Kalita, A. C.; Ghosh, P. *Eur. J. Inorg. Chem.* **2015**, *2015*, 1604−1615.

(27) Katari, M.; Rajaraman, G.; Ghosh, P. *J. Organomet. Chem.* **2015**, *775*, 109−116.

(28) Samantaray, M. K.; Shaikh, M. M.; Ghosh, P. *Organometallics* **2009**, *28*, 2267−2275.

(29) Ray, S.; Shaikh, M. M.; Ghosh, P. *Eur. J. Inorg. Chem.* **2009**, *2009*, 1932−1941.

(30) Ray, L.; Shaikh, M. M.; Ghosh, P. *Dalton Trans.* **2007**, 4546−4555.

(31) Ray, L.; Shaikh, M. M.; Ghosh, P. *Organometallics* **2007**, *26*, 958−964.

(32) Dash, C.; Shaikh, M. M.; Butcher, R. J.; Ghosh, P. *Inorg. Chem.* **2010**, *49*, 4972−4983.

(33) Dash, C.; Shaikh, M. M.; Butcher, R. J.; Ghosh, P. *Dalton Trans.* **2010**, *39*, 2515−2524.

(34) Kumar, A.; Bheeter, L. P.; Gangwar, M. K.; Sortais, J.-B.; Darcel, C.; Ghosh, P. *J. Organomet. Chem.* **2015**, *786*, 63−70.

(35) Ros, A.; Alcarazo, M.; Iglesias-Siguenza, J.; Diez, E.; Alvarez, E.; Fernandez, R.; Lassaletta, J. M. *Organometallics* **2008**, *27*, 4555−4564.

(36) Gnanamgari, D.; Moores, A.; Rajaseelan, E.; Crabtree, R. H. *Organometallics* **2007**, *26*, 1226−1230.

(37) Chan, K.-T.; Tsai, Y.-H.; Lin, W.-S.; Wu, J.-R.; Chen, S.-J.; Liao, F.-X.; Hu, C.-H.; Lee, H. M. *Organometallics* **2010**, *29*, 463−472.

(38) Gierz, V.; Seyboldt, A.; Maichle-Moessmer, C.; Froehlich, R.; Rominger, F.; Kunz, D. *Eur. J. Inorg. Chem.* **2012**, *2012*, 1423−1429.

(39) Schneider, S. K.; Herrmann, W. A.; Herdtweck, E. *J. Mol. Catal. A: Chem.* **2006**, *245*, 248−254.

(40) Guo, S.; Huynh, H. V. *Organometallics* **2014**, *33*, 2004−2011.

DOI: 10.1021/acs.inorgchem.5b02727
Inorg. Chem. XXXX, XXX, XXX−XXX

(41) Albrecht, M.; Crabtree, R. H.; Mata, J.; Peris, E. *Chem. Commun. (Cambridge, U. K.)* **2002**, 32−33.
(42) Unger, Y.; Meyer, D.; Strassner, T. *Dalton Trans.* **2010**, *39*, 4295−4301.
(43) Mercs, L.; Labat, G.; Neels, A.; Ehlers, A.; Albrecht, M. *Organometallics* **2006**, *25*, 5648−5656.
(44) Cordero, B.; Gomez, V.; Platero-Prats, A. E.; Reves, M.; Echeverria, J.; Cremades, E.; Barragan, F.; Alvarez, S. *Dalton Trans.* **2008**, 2832−2838.
(45) *Cambridge Structural Database*, version 5.36; Cambridge Crystallographic Data Centre: Cambridge, U.K., 2014.
(46) Valente, C.; Calimsiz, S.; Hoi, K. H.; Mallik, D.; Sayah, M.; Organ, M. G. *Angew. Chem., Int. Ed.* **2012**, *51*, 3314−3332.
(47) Berliner, M. A.; Cordi, E. M.; Dunetz, J. R.; Price, K. E. *Org. Process Res. Dev.* **2010**, *14*, 180−187.
(48) Riederer, S. U.; Gigler, P.; Hoegerl, M.; Herdtweck, E.; Bechlars, B.; Herrmann, W. A.; Kuehn, F. E. *Organometallics* **2010**, *29*, 5681−5692.
(49) Ueda, H.; Yamaguchi, M.; Kameya, H.; Sugimoto, K.; Tokuyama, H. *Org. Lett.* **2014**, *16*, 4948−4951.
(50) Sheldrick, G. M. *SHELXL-97, Program for refinement of crystal structures*; University of Gottingen: Gottingen, Germany, 1997.
(51) Sheldrick, G. M. *SHELXS-97, Program for solution of crystal structures*; University of Gottingen: Gottingen, Germany, 1997.
(52) Liao, L.-Y.; Shen, G.; Zhang, X.; Duan, X.-F. *Green Chem.* **2012**, *14*, 695−701.
(53) Cano, R.; Yus, M.; Ramon, D. J. *Tetrahedron* **2012**, *68*, 1393−1400.
(54) Gabriele, B.; Mancuso, R.; Salerno, G. *J. Org. Chem.* **2008**, *73*, 7336−7341.

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