

Regioselective Synthesis of Chromones via Cyclocarbonylative Sonogashira Coupling Catalyzed by Highly Active Bridged-Bis(*N*-Heterocyclic Carbene)Palladium(II) Complexes

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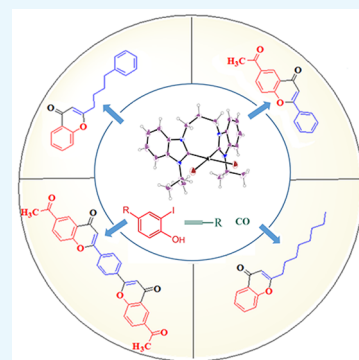


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ABSTRACT: The one-pot regioselective and catalytic synthesis of bioactive chromones and flavones was achieved via phosphine-free cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with aryl alkynes, alkyl alkynes, and dialkynes. The reactions are catalyzed by new dibromidobis(NHC)palladium(II) complexes. The new bridged *N,N'*-substituted benzimidazolium salts (L1, L2, and L3) and their palladium complexes C1, C2, and C3 were designed, prepared, and fully characterized using different physical and spectroscopic techniques. The molecular structures of complexes C1 and C3 were determined by single-crystal X-ray diffraction analysis. They showed a distorted square planar geometry, where the Pd(II) ion is bonded to the carbon atoms of two *cis* NHC carbene ligands and two *cis* bromido anions. These complexes displayed a high catalytic activity in cyclocarbonylative Sonogashira coupling reactions with low catalyst loadings. The regioselectivity of these reactions was controlled by using diethylamine as the base and DMF as the solvent.



INTRODUCTION

Chromones are valuable compounds that have attracted the attention of researchers because of their multiple uses and their utmost importance in the medical and pharmaceutical fields.^{1–3} These bioactive compounds comprise important structural moieties that showed activity in the treatment of various diseases such as anticancer,^{3–5} anti-HI,⁶ asthma,⁷ anti-inflammatory,⁸ antianalgesic,^{3,8} antimicrobial,⁹ antidiabetic,¹⁰ and antioxidant¹¹ agents (Figure 1).

Moreover, the chromones and flavones are interesting moieties in agrochemicals, insecticides, and natural products.^{1–5,12,13} They were extracted from different plant sources such as citrus lemon, sweet oranges, mandarin, grapefruit, ginger, *Casimiroa edulis*, and others.^{14–18}

The synthesis of chromones and flavones by traditional methods usually requires several step reactions.^{2,13,19,20} For example, alkyl lithium reagents were used for ortho-directed metalation of methoxymethyl aryl ethers followed by the reaction with a conjugated unsaturated aldehyde; then, the allylic alcohol intermediate was oxidized with “periodinane”. The obtained ortho-allylic ketone product was heated with acetic acid to yield the corresponding chromanone that was dehydrogenated with pyrrolidone hydrotribromide in dimethyl sulfoxide.² This method and other similar methods have drawbacks including abundant side reactions, low yields, and difficulty in separation.^{19–21} Friedel–Crafts acylation of suitably substituted benzoyl chlorides with alkynes was reported for chromone and flavone synthesis,^{22,23} but this method is associated with the use of large quantities of hazardous soluble Lewis acids (e.g., AlCl₃, FeCl₃, and TiCl₄), which made this

method as one of the most challenges for green chemistry.^{24,25} Copper(II)-catalyzed cyclization of 1-(2-hydroxyaryl)-3-aryl-1,3-propanedione under microwave irradiation was reported for the synthesis of functionalized flavones and chromones.^{26,27} Other synthetic protocols were developed in recent years such as the tandem acyl transfer-cyclization reactions catalyzed by Lewis base,²⁸ the carbonylative coupling of *p*-hydroxyacetophenones with aryl bromides²⁹ and the annulation of salicylaldehydes with benzaldehydes or alkynes.³⁰ Recently, a new improved method for the single-step synthesis of chromones and flavones was the palladium-catalyzed cyclocarbonylative Sonogashira coupling reaction of 2-halophenols with terminal alkynes.^{31–37} Different palladium complexes and protocols were evaluated in the catalytic cyclocarbonylative Sonogashira coupling reactions of different alkynes with 2-iodophenols.^{31–33} Nevertheless, these methods were associated with some shortcomings such as the high loading of palladium catalysts and the need for the phosphine ligands.^{32–35,39} Researchers have continued the investigation for the synthesis and development of efficient palladium catalysts for the cyclocarbonylative Sonogashira coupling reactions in order to overcome the problems of low catalyst activity, high loading of catalyst, long reaction time, high

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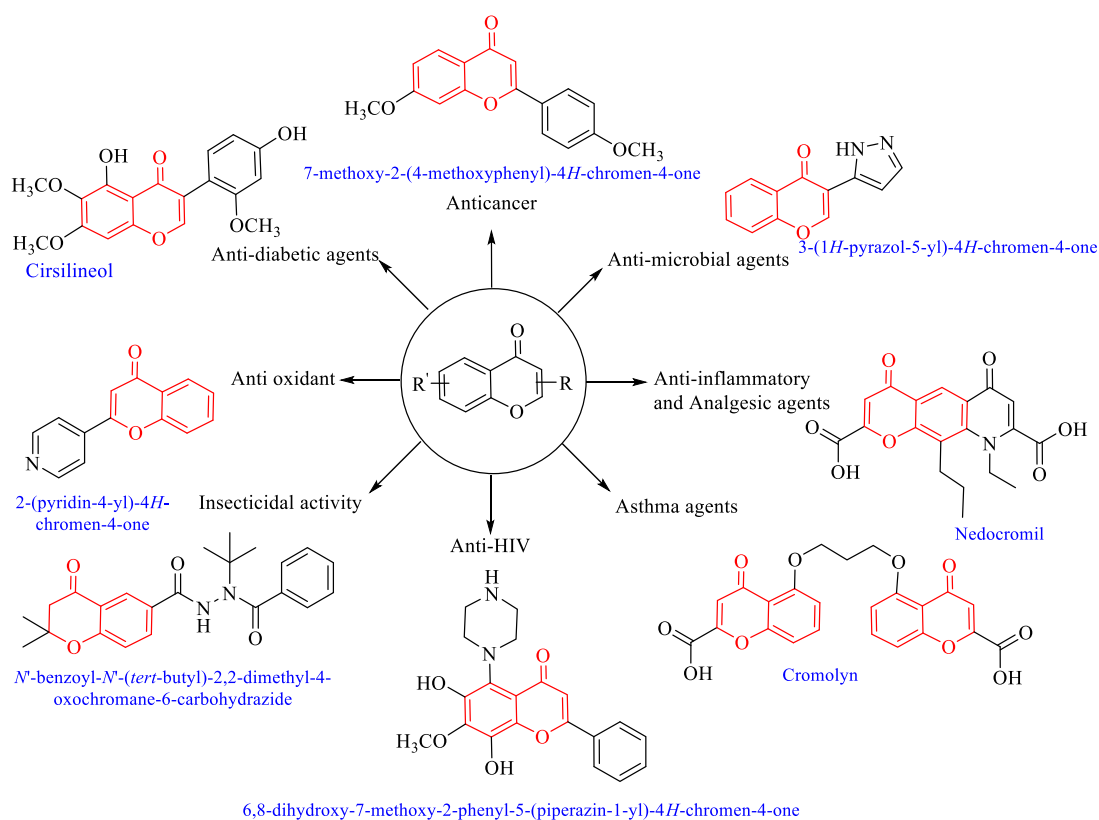


Figure 1. High scope of the pharmacological profile of chromone derivatives in the current literature.

temperature, and high CO pressure. A catalytic system including palladium complexes with mixed “phosphines” or “nitrogen”-based ligands such as pyridines, pyrroles, or imidazoles showed high activity in the synthesis of flavones and less efficacy in the production of alkyl-functionalized chromones.³⁸ The difficulty was in the control of the regioselectivity of the reaction between six-membered ring “chromones” and five-membered ring “aurones” products. There are numerous publications that report the control of the selectivity through the type of the base, catalyst, or solvent. However, most of these protocols have considered high loading of both catalysts and phosphine ligands and also led to low yields of the corresponding chromones when terminal alkyl alkynes reacted with 2-iodophenols in the presence of carbon monoxide.^{33,35,40–42}

Recently, the focus on the use of N-heterocyclic carbene (NHC)–metal complexes has increased. This field made a significant revolution in organometallic chemistry because of the catalytic applications in different organic transformations.^{43–49}

The NHC ligands are known as strong σ -electrons donors, which enable them to form strong bonds with metals and to stabilize the metal complexes.^{50,51} Another important feature of NHCs as ligands is the flexibility to design their structures for different catalytic purposes. For instance, the electronic and steric properties can be tailored for special applications in catalysis.^{52,53} An interesting approach is the use of chelating bridged bis(N-heterocyclic carbene) ligands. The resulting complexes are expected to have more electron-rich centers and have higher thermodynamic stability by the chelate effect, as compared to the mono NHC counterparts. This would favor the oxidative addition step of the aryl halide substrate to the palladium(0) active species. Additionally, the steric properties can be controlled by varying the N-substituents. These bridged NHC–palladium complexes showed high activity in different

applications.^{54–56} There are limited publications that consider Pd–NHC complexes for the synthesis of chromones and flavones via catalytic cyclocarbonylation of ortho-functionalized aryl halides with terminal alkynes. Nevertheless, these palladium complexes were active with aryl alkynes but showed lower catalytic activity with terminal alkyl alkynes.³⁸

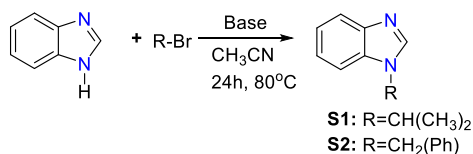
Previously, we have reported the synthesis and characterization of new mixed ligand dibromido and diiodido-palladium(II)–NHCs–pyridine ($\text{Br}_2\text{-Pd-NHC-Py}$) and ($\text{I}_2\text{-Pd-NHC-Py}$) complexes and their catalytic applications in the carbonylative Sonogashira coupling reactions and carbonylative Suzuki–Miyaura coupling reactions of aryl iodides with different alkynes or boronic acids in the presence of CO.^{57–59}

In this work, we report the results of the regioselective synthesis of chromones via the one-pot cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with aryl alkynes, alkyl alkynes, and dialkynes catalyzed by the active-bridged bis(NHC)–palladium(II) catalysts **C1**, **C2**, and **C3**. We have succeeded to crystallize the new palladium complexes **C1** and **C3** and characterize them by single-crystal X-ray diffraction analysis. Also, the study of the steric and electronic effects was conducted using various benzimidazole N-substituents. In addition, we report the catalytic synthesis of the new compound, 2,2'-(1,4-phenylene)-bis(6-acetyl-4H-chromen-4-one) (**8c**).

RESULTS AND DISCUSSION

Synthesis. N-alkylation reactions of benzimidazole with alkyl bromides (2-bromopropane, benzyl bromides) using potassium hydroxide as the base were conducted efficiently to produce 1-alkyl benzimidazoles (**S1** and **S2**) in very good yields (**Scheme 1**). Further, bridged bis-benzimidazolium bromide salts (**L1**, **L2**, and **L3**) were prepared in good to very good yields

Scheme 1. Synthesis of Alkyl-1H-benzo[d]imidazoles



by direct alkylation of the 1-alkyl benzimidazoles (**S1** and **S2**) with dibromoalkanes (1,3-dibromopropane and 1,4-dibromobutane) (**Scheme 2**). The proton NMR spectra showed downfield singlet peaks at 9.83 ppm (**L1**), 10.05 ppm (**L2**), and 10.15 ppm (**L3**), which are assigned to C-2 protons of the benzimidazole rings. These singlet peaks confirm the formation of the benzimidazolium bromides.

The bridged N-heterocyclic biscarbene palladium(II) complex-bridged-bis(NHC)PdBr₂ (**C1**, **C2**, and **C3**) were synthesized in very good yields by reacting palladium acetate with 1.0 equiv of the appropriate ligand precursor (**L1**, **L2**, or **L3**) (**Scheme 3**). The absence of the singlet peaks for the acidic C-2 protons in ¹H NMR spectra confirmed the formation of the new palladium complexes. Furthermore, ¹³C NMR spectra for the palladium–NHC complexes showed new signals assigned to C–Pd at 181.7, 181.1, and 176.3 ppm for **C1**, **C2**, and **C3**, respectively. The ESI mass spectra of the three complexes showed peaks at 546.8 (**C1**), 560.8 (**C2**), and 642.8 (**C3**) that confirm the formation of the Pd–carbene complexes.

The molecular structures of complexes **C1** and **C3** are depicted in (**Figures 2** and **3**), respectively. Selected bond distances and bond angles are given in (**Table 7**). **C1** crystallized with one molecule, located on a mirror plane, in the asymmetric unit, as a dimethylformamide solvate, while **C3** crystallized with one molecule in the asymmetric unit as mixed hydrate/dichloromethane solvate. In both complexes, the Pd(II) ion is coordinated by the chelating-bridged bis-carbene ligand and two bromide ions at cis positions, in a distorted square planar geometry. The cis bond angles are in the ranges 88.66(17)–92.97(2) and 87.4(3)–97.01(4)° in **C1** and **C3**, respectively. The Pd–C and Pd–Br bond distances are within the range reported in the literature.^{55,60} The former is 1.997(3) Å in **C1** and in the range [1.964(8)–1.985(8) Å] in **C3**, while the latter is 2.4906(4) Å in **C1** and in the range [2.4659(11)–2.4704(11) Å] in **C3**. The chelate C–Pd–C bite angle values are 88.66(17) and [87.4(3), 87.7(3)°] in **C1** and **C3**, respectively. The larger bond distances in **C1** are consistent with the larger steric hindrance of the isopropyl group opposing the formation of the chelate complex.

There are various catalytic systems used for the synthesis of chromones and flavones reported in the literature. However, they suffer from significant shortcomings such as high catalyst loading, long reaction time, the use of phosphines, and the low

selectivity.^{32–37} Recently, NHC–Pd(II) complexes were evaluated in various cross coupling reactions^{53–56} but their applications in cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with terminal alkynes are still limited, where the catalytic system is prepared in situ by mixing the palladium(II) precursors with the NHC ligands.³⁸

In this work, we have examined the application of the newly synthesized bridged-bis(NHC)PdBr₂ complexes (**C1**, **C2**, and **C3**) in the cyclocarbonylative Sonogashira coupling reactions of various 2-iodophenols with aryl and alkyl alkynes. The optimization of the reactions was conducted by using the bridged-bis(NHC)PdBr₂ complex **C1**. For this purpose, a model reaction of 2-iodophenol and phenylacetylene under pressurized CO in the presence of a catalytic amount of **C1** was adopted (**eq 1**). The results of the optimization of the reactions are summarized in **Table 1**. Only traces of 2-phenyl-4*H*-chromen-4-one (**3aa**) were obtained when a neat reaction was conducted using 1.0% mol of **C1** as the catalyst and diethylamine as the base at room temperature for 16 h (**Table 1**, entry 1). However, a conversion of 59.5% was obtained at 80 °C, and a higher conversion (85.5%) was achieved at 100 °C. These reactions produced 2-phenyl-4*H*-chromen-4-one (**3aa**) as a major compound. The isolated yield of **3aa** gradually increased by increasing the temperature (**Table 1**, entries 2–3). When diethylamine in the neat reaction was replaced by triethylamine at 80 and 100 °C using **C1**, the cyclocarbonylative of 2-iodophenols with phenylacetylene via a 6-endo cyclization mode leading to six-membered ring product “flavone” (**3aa**) and 5-exo cyclized five-membered ring product “aurone” (**4aa**) was formed. Moreover, the increase of the temperature from 80 to 100 °C increased the conversion from 85 to 100% and favors the formation of the aurone product **4aa** (57 and 66%) (**Table 1**, entries 4–5). However, when tetrahydrofuran (THF) was used as a solvent at temperatures (80 and 100 °C) with triethylamine as the solvent, the conversions dropped to 69 and 93%, respectively, with no significant change in the regioselectivity (**Table 1**, entries 6–7). Nevertheless, the use of Et₂NH as the base with THF as the solvent at 80 and 100 °C led to higher conversions (68 and 84.5%) (**Table 1**, entries 8–9). Consequently, under the same experimental conditions, triethylamine oriented the cyclocarbonylative Sonogashira reactions toward the production of aurone **4aa** as the major product. In addition, diethylamine in THF produced flavone **3aa** in high isolated yields. When potassium carbonate was used as the base in THF at 100 °C (**Table 1**, entry 10), a full conversion was observed to produce flavone **3aa** and aurone **4aa** (38%/62%). In toluene as a solvent, the cyclocarbonylative Sonogashira reaction of 2-iodophenol with phenylacetylene under the optimized conditions (Et₂NH/1.0% mol of **C1**/100 °C/16 h) was converted (97%) which led to the formation of

Scheme 2. Synthesis of Bridged NHC Salt Ligand Precursors

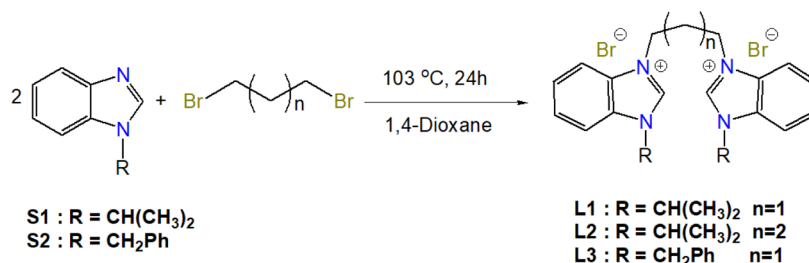


Table 1. Cyclocarbonylative Sonogashira Coupling Reactions of 2-Iodophenol (1a) with Phenylacetylene (2a) by C1^{a,b}

No	C1 mol %	base	solvent	T (°C)	time (h)	conv. (%) ^c	selectivity (%) ^c	
							3aa (%) ^d	4aa (%) ^d
1	1.0	Et ₂ NH	Et ₂ NH	RT	16	traces	traces	traces
2	1.0	Et ₂ NH	Et ₂ NH	80	16	59.5	100 (55)	
3	1.0	Et ₂ NH	Et ₂ NH	100	16	85.5	100 (82)	
4	1.0	Et ₃ N	Et ₃ N	80	16	85	43 (34)	57 (45)
5	1.0	Et ₃ N	Et ₃ N	100	16	100	34 (30)	66 (63)
6	1.0	Et ₃ N	THF	80	16	69	40 (25)	60 (38)
7	1.0	Et ₃ N	THF	100	16	93	36 (30)	64 (56)
8	1.0	Et ₂ NH	THF	80	16	68	100 (64)	
9	1.0	Et ₂ NH	THF	100	16	84.5	100 (81)	
10	1.0	K ₂ CO ₃	THF	100	16	96	38 (33)	62 (57)
11	1.0	Et ₂ NH	Toluene	100	16	97	93 (88)	7
12	0.5	Et ₂ NH	THF	100	16	80	100 (77)	
13	0.5	Et ₂ NH	DMF	100	16	98	96 (92)	4
14	0.5	Et ₂ NH	DMF	80	16	83	100 (81)	
15	0.5	Et ₂ NH	DMF	50	16	38	100 (35)	
16	0.5	Et ₂ NH	DMF	100	12	76	100 (72)	
17	0.5	Et ₂ NH	DMF	100	6	49	100 (46)	
18	0.5	Et ₂ NH	THF	100	16	72	100 (70)	
19	0.5	Et ₂ NH	Toluene	100	16	82	95 (76)	5
20	0.5	Et ₂ NH	Et ₂ NH	100	16	79	100 (76)	
21	0.5	K ₂ CO ₃	DMF	100	16	97	70 (65)	30 (27)
22	0.5	Et ₃ N	DMF	100	16	95	60 (54)	40 (35)

^aOptimization of reaction conditions. ^bReaction conditions: C1 (mol %), 2-iodophenol (0.5 mmol), phenylacetylene (0.6 mmol), base (1.0 mmol), solvent (2.5 mL), and CO (100 psi), 100 °C. ^cDetermined by GC and GC-MS. ^dIsolated yield.

formation of the flavone “2-phenyl-4H-chromen-4-one” (3aa) as the major product; only traces of the aurone “2-benzylidenebenzofuran-3(2H)-one” (4aa) were detected. It is important to note that because of the use of an excess of Et₂NH as compared to phenylacetylene, small amounts of *N,N*-diethyl-3-phenylprop-2-ynamide were produced as a side product from the carbonylative coupling of phenylacetylene with Et₂NH.

The catalytic activity of the other synthesized bridged-bis(NHC) PdBr₂ catalysts (C2 and C3) were also evaluated under the same optimized conditions (CO/Et₂NH/DMF/100 °C/16 h). Their catalytic efficiency in the cyclocarbonylative Sonogashira coupling reactions was slightly less than C1 (Table 2). The conversions with C2 and C3 were 88 and 84%, respectively. The isolated yields of the flavone 3aa were 85 and 79%, respectively (Table 2, entries 2, 3).

In order to rationalize the relative activity of the three complexes, one can consider the relative sigma donation effects of the ligand precursors L1, L2, and L3 that can be probed by the proton NMR chemical shift of the C-2 protons of the benzimidazole rings, observed at 9.83, 10.05, and 10.15 ppm for L1, L2, and L3 respectively. The most downfield signals were consistent with the highest electron donating effect of the isopropyl group in L1 and L2 relatively to the benzyl group in L3. The results of the comparative catalytic evaluation of the corresponding palladium–NHC complexes C1, C2, and C3 are in agreement with the strong electron donating effect of the ligand in C1 and the stability of the corresponding 8-membered ring chelate.

In addition, the catalytic activity for the mono NHC palladium(II) complexes was also evaluated under the optimized reaction conditions. In fact, the two heteroleptic (NHC)–pyridine palladium(II) complexes, which were previously reported,⁵⁹ Pd–NHC–Py1 “(1,3-disopropyl-1,3-dihydro-2H-benzo[d]imidazole-2-ylidene)(pyridin-1(2H)-yl)

Table 2. Cyclocarbonylative Sonogashira Coupling Reactions of 2-Iodophenol (1a) with Phenylacetylene (2a)^{a,b}

no.	catalyst (mol %)	conv. (%) ^c	selectivity (%) ^c	
			3aa (%) ^d	4aa (%) ^d
1	C1 (0.5%)	98	96 (92)	4
2	C2 (0.5%)	88	96 (85)	4
3	C3 (0.5%)	84	95 (79)	5
4 ^e	Pd–NHC–Py1 (0.05%)	83	89 (77)	11
5 ^e	Pd–NHC–Py2(0.5%)	79	86 (72)	14
6	Pd(OAc) ₂ (0.5%) L1 (0.5%)	81	94 (75)	6
7	Pd(OAc) ₂ (5%) DPPF (10%)	100	88 (85)	12
8 ^f	Pd(OAc) ₂ (5%) DPPF (10%)	95	50 (46)	50 (45)
9	Pd(OAc) ₂ (0.5%)	38	89 (32)	11
10	PdBr ₂ (0.5%)	29	89 (24)	11
11	PdCl ₂ (PPh ₃) ₂ (0.5%)	60	86 (49)	14
12	Pd/C (10%)	90	92 (81)	8

^aEffect of the type of catalyst. ^bReaction conditions: [Pd] (mol %), 2-iodophenol (0.5 mmol), phenylacetylene (0.6 mmol), Et₂NH (1.0 mmol), DMF (2.5 mL), CO (100 psi), 100 °C, 16 h. ^cDetermined by GC and GC-MS. ^dIsolated yield. ^eHeteroleptic N-heterocyclic carbene palladium(II) complexes (Pd–NHC–Py).⁵⁹ ^fTHF was used as a solvent.

palladium(II) bromide” and Pd–NHC–Py 2 “(1-isopropyl,3-benzyl-1,3-dihydro-2H-benzo[d]imidazole-2-ylidene)(pyridin-1(2H)-yl)palladium(II) bromide” (Figure 4), were evaluated in the cyclocarbonylative Sonogashira [Pd–NHC–Py (0.5 mol %)/Et₂NH/DMF/100 psi/100 °C/16 h] (Table 2, entries 4–5). These complexes catalyzed the carbonylation reaction with very good conversions (83 and 79%, respectively) of 2-iodophenol and high selectivity (89 and 86%) toward the flavone. However, the conversion and the isolated yield of

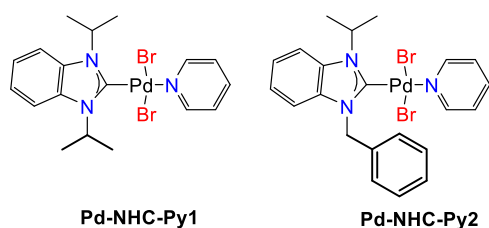


Figure 4. NHC–palladium(II)–pyridine complexes (Pd–NHC–Py1 and Pd–NHC–Py2).

flavone are lower than those obtained with the bridged-bis(NHC)PdBr₂ complexes.

Furthermore, Pd(OAc)₂ was used with an equal amount of the ligand **L1** in the cyclocarbonylative Sonogashira coupling reaction under the optimized conditions. The conversion was lower (81%) with high selectivity (94%) for the flavone **3aa** (Table 2, entry 6). This result confirms the superiority of the catalytic activity of **C1** as compared to the “in situ”-formed palladium complex.

For comparison, commercially available palladium complexes were also considered (Table 2, entries 7–12) under different protocols in the presence of other ligands, such as 1,1'-bis(diphenylphosphino)ferrocene (DPPF), and using a higher catalyst loading. The results of the catalytic evaluation confirmed again the high catalytic efficiency and selectivity of the bridged-bis(NHC)PdBr₂ catalysts **C1**, **C2**, and **C3**.

The model cyclocarbonylative Sonogashira coupling reactions under optimized conditions showed high catalytic activity and selectivity with the newly synthesized bridged-bis(NHC)-PdBr₂ complexes (**C1**, **C2**, and **C3**). The catalyst **C1** was considered in the study of the scope of substrates. The reactions were conducted under the optimized experimental conditions [**C1** (0.5 mol %), 2.0 equiv of Et₂NH, 3 mL of DMF, 100 psi CO, 100 °C, 16 h]. Different 2-iodophenols were reacted with various aryl alkynes (eq 2, Table 3). Numerous chromones and flavones were produced in excellent yields via cyclocarbonylative Sonogashira coupling reactions of various aryl alkynes with different electron-withdrawing-substituted 2-iodophenols (4'-hydroxy-3'-iodoaryls). The carbonylation reaction of 2-iodophenol with alkynes that have activating electron releasing groups afforded the corresponding flavones in excellent to very good isolated yields (86–91%) (Table 3, entry 1–3). In addition, excellent yield (93%) of flavone was also obtained when the electron-withdrawing-substituted aryl alkyne (1-ethynyl-4-nitrobenzene) reacted with 2-iodophenol (Table 3, entry 4). The cyclocarbonylative Sonogashira coupling reactions of phenylacetylene and aryl alkynes having electron-donating substituents with deactivated 2-iodophenols were also very successful with excellent isolated yields (91–98%) (Table 3, entries 5–8). On the other hand, a decrease in the isolated yield of the corresponding chromone to 74% was obtained when the

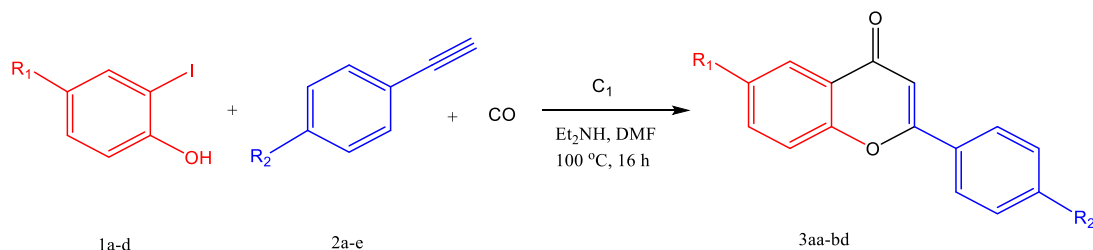
cyclocarbonylative Sonogashira coupling reaction was carried out with 2-iodophenol and 2-ethynylanisole (Table 3, entry 9), probably because of the steric hindrance of the methoxy substituent in the ortho position of an alkyne substrate.

Cyclocarbonylative Sonogashira Coupling Reactions of 2-Iodophenol (1a–b) with Alkyl Alkynes (5a–e) Catalyzed by the Bridged-Bis(NHC)PdBr₂ Complex **C1**.

The research studies of the cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with alkyl alkynes are still very limited, where low yields of chromones were produced in the presence of palladium–phosphine or palladium-mixed ligand complexes. Interestingly, various chromones were produced in good yields via the cyclocarbonylative coupling reactions of different 2-iodophenols with various alkyl alkynes catalyzed efficiently by the complex **C1** under the optimized conditions (Et₂NH/DMF/110 °C/24 h) (eq 3) (Table 4). For instance, the cyclocarbonylative coupling reaction of 2-iodophenol with 1-heptyne (Table 4, entry 1), 1-decyne (Table 4, entry 2), 6-phenyl-1-hexyne (Table 4, entry 3), and 3-cyclohexyl-1-propyne (Table 4, entry 4) was accomplished successfully to produce the corresponding chromones **6** in good to excellent yields (53–90%). These results showed a relation between the chain lengths on the alkyl alkynes and the yields of corresponding chromones. Alkynes with shorter alkyl chain, such as 1-heptyne (Table 4, entry 1), were more reactive than the alkyl alkynes having longer alkyl chains such as 1-decyne (Table 4, entry 2). The cyclocarbonylative Sonogashira coupling reactions of 2-iodophenol with either 6-phenyl-1-hexyne or 3-cyclohexyl-1-propyne led to good and very good yields (53 and 71%) of their corresponding chromones (Table 4, entries 3–4). The reactivity 2-iodophenols were improved with 4'-hydroxy-3'-iodoacetophenone (**1b**) having an electron-withdrawing substituent. The reaction of **1b** with 3-cyclohexyl-1-propyne and 1-heptyne catalyzed by **C1** gave very good to excellent isolated yields of the corresponding chromones (77–90%) (Table 4, entries 5–6). In conclusion, useful chromones were produced in high yields by the cyclocarbonylative coupling of different 2-iodophenols with various alkyl alkynes in the presence of bridged-bis(NHC)PdBr₂ as the catalyst.

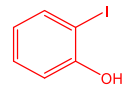
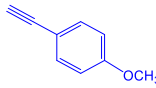
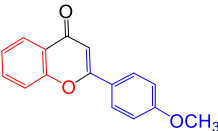
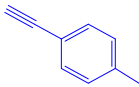
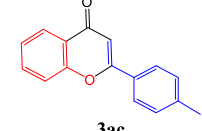
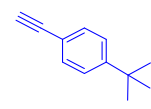
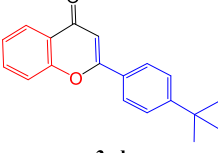
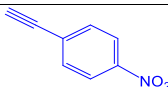
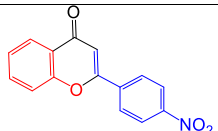
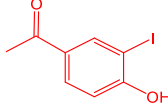
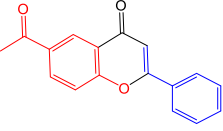
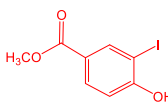
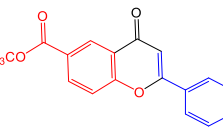
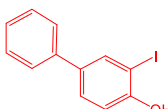
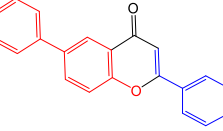
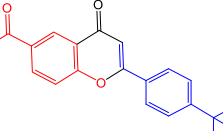
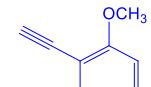
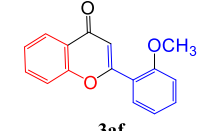
Cyclocarbonylative Sonogashira Coupling Reaction of 2-Iodophenol with Dialkynes Catalyzed by Complex **C1**.

Considering the high efficiency of the newly synthesized complexes **C1**, **C2**, and **C3**, we have investigated the cyclocarbonylative Sonogashira coupling reaction of 2-iodophenol with dialkynes. Remarkably, these reactions successfully proceeded to obtain symmetrical diflavones in very good to excellent isolated yields. For instance, the cyclocarbonylative coupling reactions of 1,4-diethynylbenzene and 1,3-diethynylbenzene with 2 equiv of 2-iodophenol or 4-hydroxy-3-iodoacetophenone proceeded smoothly to yield the corresponding *para*-diflavones (**8a**) and (**8c**) (eq 4) and (eq 4) in 86 and



Equation 2

Table 3. Cyclocarbonylative Sonogashira Coupling Reactions of 4'-Hydroxy-3'-iodoaryls (1a–d) with Aryl Alkynes (2a–e) Catalyzed by the C1^a

Entry	4'-Hydroxy-3'-iodoaryl 1	Aryl Alkyne 2	Product 3	Yield (%) ^b
1	 1a	 2b	 3ab	91
2	1a	 2c	 3ac	86
3	1a	 2d	 3ad	88
4	1a	 2e	 3ae	93
5	 1b	2a	 3ba	98
6	 1c	2a	 3ca	95
7	 1d	2a	 3da	91
8	1b	2d	 3bd	93
9	1a	 2f	 3af	74

^aReaction conditions: C1 (0.50 mol %), 4'-hydroxy, 3'-iodoaryl (0.50 mmol), aryl alkyne (0.60 mmol), Et₂NH (1.0 mmol), DMF (2.5 mL), CO (100 psi), 100 °C, 16 h. ^bIsolated yield.

92%, respectively. Furthermore, *meta*-diflavone was obtained in 74% (8b) (eq 4).

The excellent results obtained with the catalytic cyclocarbonylative coupling of 2-iodophenols with alkynes and diarylalkynes showed the high catalytic activity of the newly

synthesized bridged-N-heterocyclic carbene palladium complexes C1, C2, and C3. The complex C1 exhibited superior catalytic efficiency with much lower loading in the absence of additional phosphine ligands as compared to other reported catalytic systems in the literature (Table 5).

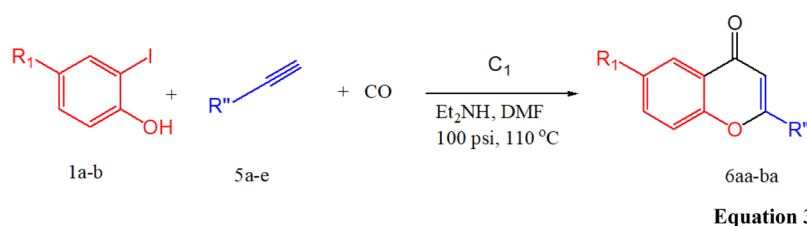


Table 4. Cyclocarbonylative Sonogashira Coupling Reactions of 4'-Hydroxy-3'-iodoaryls (1a–d) with Alkyl Alkynes (5a–e) Catalyzed by C1^a

Entry	4'-Hydroxy-3'-iodoaryl 1	Alkyl Alkyne 5	Product 6	Yield (%) ^b
1	1a	5a	6aa	81
2	1a	5b	6ab	68
3	1a	5c	6ac	53
4	1a	5d	6ad	71
5	1b	5d	6bd	77
6	1b	5a	6ba	90

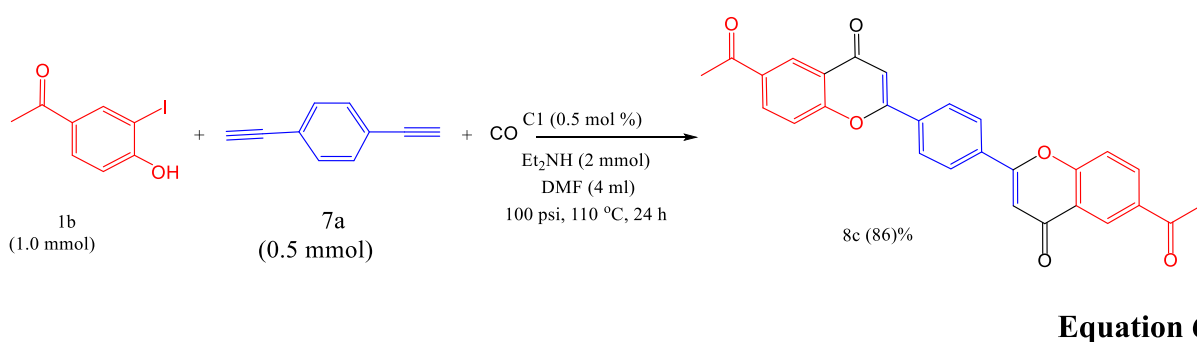
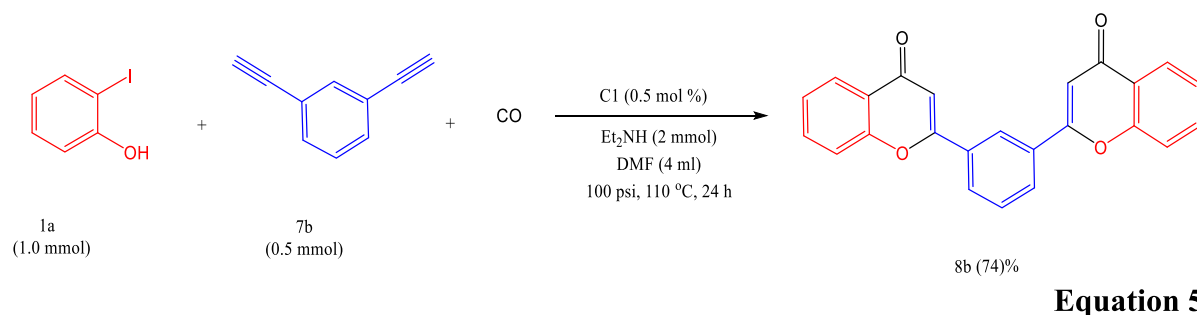
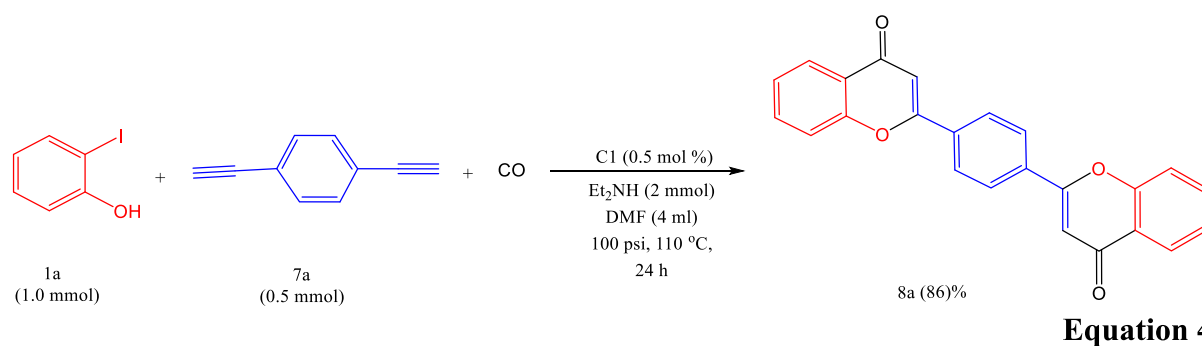
^aReaction conditions: C1 (1.0 mol %), 4'-hydroxy, 3'-iodoaryl (0.50 mmol), alkyl alkyne (0.60 mmol), Et₂NH (1.0 mmol), DMF (2.5 mL), CO (100 psi), 110 °C, 24 h. ^bIsolated yield.

Table 5. Comparison of the Activity of the New Catalytic System Including Bridged-Bis(NHC)PdBr₂ (C1) in Cyclocarbonylative Sonogashira Coupling Reactions of 2-Iodophenol and Alkynes with Literature Data

refs	catalyst	co-catalyst/ligand/additive	base	time (h)	yield (%)
33	PdCl ₂ (5 mol %)	(H ₁₃ C ₆) ₃ P ⁺ C ₁₄ H ₂₉ Br ⁻ (1.5 g)	Et ₃ N	24	64–95
31	PdCl ₂ (5 mol %)	PPh ₃ (10 mol %)	Et ₃ N	24	35–95
35	Pd(OAc) ₂ (5 mol %)	DPPF (5 mol %)	piperazine	24	30–95
32	Pd ₂ (dba) ₃ (1.5 mol %)	1,3,5,7-tetramethyl-2,4,8-trioxa-6-phenyl-6-phosphaadamantane (3 mol %)	DBU	0.5 MW	62–95
40	Pd(PPh ₃) ₄ (3 mol %)	Ac ₂ O (6 mol %)	Et ₃ N		51–82
38	Pd–NHC–Py (0.5 mol %)	imidazole (0.5 mol %) pyridine (0.5 mol %)	Et ₂ NH	24	25–98
49	Pd/C (1 mol %)		Et ₂ NH	20	74–98
this work	bridged-bis(NHC)PdBr ₂ (0.5 mol %)		Et ₂ NH	16	53–98

Plausible Mechanisms for the Cyclocarbonylative Sonogashira Coupling Reactions. Chromones and aurones were produced via carbonylative Sonogashira coupling reactions

followed by the cyclization reactions. Initially, in the presence of the base, alkynes are deprotonated and the palladium(II) precatalyst (II) undergoes a substitution of the bromides by the



acetylides to produce the palladium(II) intermediate (III), which undergoes reductive elimination of the dialkynes to generate the Pd(0) (IV) as the active catalytic species (Scheme 4, pathway A). The palladium(II) intermediate (Ar–Pd–I) (V) is then formed via the oxidative addition of 2-iodophenol to the Pd(0). The acyl palladium intermediate (VI) is formed by the insertion of carbon monoxide (CO) into the Ar–Pd bond. Then, the iodide is substituted by the acetylide to produce the palladium intermediate VII. The reductive elimination in the presence of the base yields the carbonylative Sonogashira product VIII with the subsequent regeneration of the Pd(0) catalyst.^{58,61}

The production of aurones or chromones depends on the type of base used in the reaction.

In the presence of diethylamine, the favored Michael addition to the intermediate VIII forms the Michael adduct IX (Scheme 4, pathway B), which is usually stabilized in DMF as an ideal solvent in these reactions.^{62,63} This Michael adduct (IX) was detected and identified in the reaction mixture by gas chromatography–mass spectrometry (GC–MS) [$m/z = 296.5$; $C_{19}H_{22}NO_2$ (MH^+)]. The diethylamine is then eliminated to produce the cyclic enolate X, which is converted into the corresponding chromone.

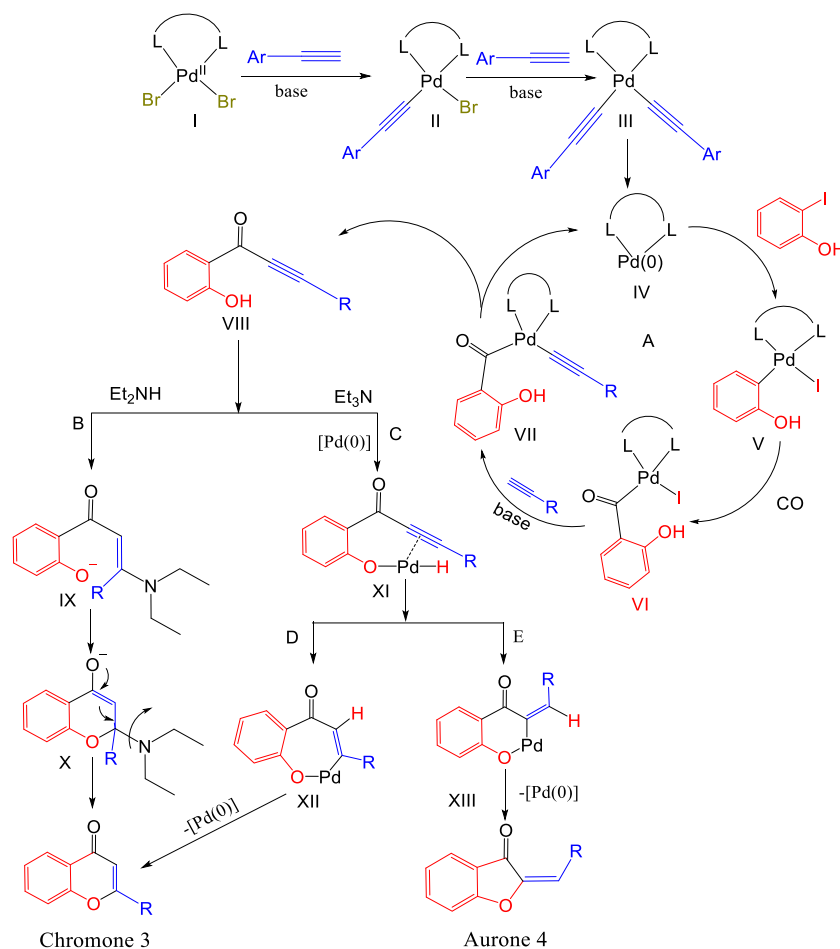
When triethylamine was used as a base, no reaction was observed in the absence of the palladium catalyst. Furthermore, the palladium catalyzed reaction in the presence of triethylamine

led to the formation of a mixture of aurones and chromones (Table 3, entries 4–7). In this case, it is suggested that the oxidative addition of O–H to the Pd(0) species generates the palladium intermediate XI (Scheme 4, pathway C). The subsequent insertion of the alkyne into Pd–H proceeds following two pathways to generate either the seven-membered metallacycle XII (pathway D) or the six-membered metallacycle XIII (pathway E) as intermediates. These undergo further reductive elimination to produce chromones and aurones, respectively.

CONCLUSIONS

High regioselectivity of phosphine-free cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with alkynes toward chromones was achieved using new bridged-bis(NHC)-PdBr₂ chelate catalysts. The preligands and the corresponding complexes C1, C2, and C3 were synthesized and fully characterized using various physical, analytical, and spectroscopic techniques including single-crystal X-ray diffraction. The catalytic efficiency was evaluated in the cyclocarbonylative Sonogashira coupling reactions of various 2-iodophenols with aryl and alkyl alkynes including the dialkynes under CO pressure and in the absence of any additional phosphine ligands. The palladium complex C1 was more active as compared to C2 and C3 complexes. In general, C1, C2, and C3 showed high catalytic activity with lower catalyst loading as compared to other known

Scheme 4. Plausible Mechanism for the Cyclocarbonylative Sonogashira Coupling Reaction Catalyzed by Bridged-Bis(NHC)PdBr₂ Complexes; Production of Chromone [Pathway B or (C,D)], and Aurone (Pathway C–E)



catalytic systems. Excellent isolated yields of the expected chromones and flavones were obtained for the cyclocarbonylative Sonogashira coupling reactions of 2-iodophenols with the aryl alkynes and good to very good yields with alkyl alkynes or aryl dialkynes. The regioselectivity of these reactions toward the chromones was favored with diethylamine as a base and in DMF as a solvent. It is worth noting the synthesis of a new compound, 2,2'-(1,4-phenylene) bis(6-acetyl-4*H*-chromen-4-one) (**8c**), by the one-pot cyclocarbonylative Sonogashira coupling reaction of 4-hydroxy-3-iodoacetophenone with 1,4-diethynylbenzene catalyzed by **C1**.

EXPERIMENTAL SECTION

Materials and Instrumentation. All precursors used for the synthesis of NHCs, palladium complexes, 2-iodophenols, and alkynes were purchased from Sigma-Aldrich and used directly as received unless specified otherwise. Flash column chromatography (packed with 60 F Silica gel from Fluka Chemie AG, Buchs, Switzerland) was used to purify the products.

¹H and ¹³C NMR spectra were recorded on a Bruker EQUIN55 (400 MHz for ¹H; 101 MHz for ¹³C) and JOEL 1500 MODEL (500 MHz for ¹H; 125 MHz for ¹³C) NMR spectrometer in different deuterated solvents like CDCl₃, CD₂Cl₂, DMSO-*d*₆, and DMF-*d*₇. Chemical shifts were reported in ppm downfield of tetramethylsilane, used as the internal standard. The collected data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet,

q = quartet and m = multiplet), and coupling constant in Hz. ¹³C NMR spectra were obtained with complete proton decoupling. The products were analyzed by GC–MS (Agilent GC–MS; GC 6890N and MS 5975B; 30 m HP-5 capillary column). A separate GC (Agilent 6890) was used to monitor the reactions and analyze the products. Mass spectra were obtained using the Fisher ESI-TOF/MS spectrometer with the ESI scan (0.104–0.499 min, 17 scans) Frag = 180.0 V. Elemental analyses for the ligand precursors, corresponding complexes, and products were performed on PerkinElmer Series 11 (CHNS/O) Analyzer 2400. Merck 60 F₂₅₄ silica gel plates (250 μm layer thickness) were used for thin-layer chromatography (TLC) analyses. Single-crystal X-ray data collection for complexes **C1** and **C3** was performed at 298 K on a Bruker D8 Quest diffractometer (Mo K α radiation λ = 0.71073 Å). Data were collected and integrated using the Bruker APEX3 software package.⁶⁴ Multiscan absorption correction was performed using SA-DABS.⁶⁵ The structures were solved by direct methods with SHELXS using the SHELXTL package and refined using full-matrix least squares procedures on *F*² via the program SHELXL-2014.⁶⁶ ORTEP3 was used for molecular graphics.⁶⁷ All hydrogen atoms were included at calculated positions using a riding model. The crystal data and refinement details for **C1** and **C3** are given in (Table 6). Selected bond lengths and bond angles are given in (Table 7).

Synthesis of 1-Alkyl Benzimidazole (S1 and S2). A dry and clean round-bottom flask was charged with benzimidazole

Table 6. Crystal and Structure Refinement Data of Compounds C1 and C3

	C1	C2
CCDC deposition #	1961539	1950067
empirical formula	C ₂₆ H ₃₅ Br ₂ N ₅ OPd	C ₃₂ H ₃₂ Br ₂ CL ₂ N ₄ OPd
formula weight	699.81	825.73
temperature (K)	298(2)	298(2)
wavelength (Å)	0.71073	0.71073
crystal system	orthorhombic	monoclinic
space group	<i>Pnma</i>	<i>P2₁/m</i>
unit cell dimensions		
<i>a</i> (Å)	16.2158(6)	10.5561(8)
<i>b</i> (Å)	18.1879(7)	23.972(2)
<i>c</i> (Å)	9.2992(4)	13.3418(11)
α (deg)	90	90
β (deg)	90	92.033(2)
γ (deg)	90	90
volume (Å ³)	2742.63(19)	3374.0(5)
<i>Z</i>	4	4
density (calculated, g/cm ³)	1.695	1.626
absorption coefficient (mm ⁻¹)	3.619	3.108
<i>F</i> (000)	1400	1640
θ range data collect. (deg)	2.512–28.371	2.564–28.367
index ranges	–21 ≤ <i>h</i> ≤ 21, –24 ≤ <i>k</i> ≤ 24, 12 ≤ <i>l</i> ≤ 12	–14 ≤ <i>h</i> ≤ 14, –31 ≤ <i>k</i> ≤ 32, –17 ≤ <i>l</i> ≤ 17
reflections collected	76,298	123,299
independent reflections	3528 [<i>R</i> (int) = 0.0387]	8604 [<i>R</i> (int) = 0.1448]
absorption correction	semiempirical from equivalents	semiempirical from equivalents
refinement method	full-matrix least-squares on <i>F</i> ²	full-matrix least-squares on <i>F</i> ²
data/restraints/parameters	3528/18/173	8604/6/399
goodness-of-fit on <i>F</i> ²	0.989	1.112
ginal <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0342, <i>wR</i> ₂ = 0.1080	<i>R</i> ₁ = 0.0716, <i>wR</i> ₂ = 0.1905
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0473, <i>wR</i> ₂ = 0.1299	<i>R</i> ₁ = 0.1308, <i>wR</i> ₂ = 0.2298
largest diff. peak and hole (e Å ³)	1.039 and –0.978	1.673 and –1.585

(10.0 mmol), excess amount of alkyl bromide (12.2 mmol), 2-bromopropane or benzyl bromide, and an appropriate base, potassium hydroxide (20.0 mmol) with 2-bromopropane or cesium carbonate (20.0 mmol) with benzyl bromide, and 1.00 mmol of tetrabutylammonium bromide. 100 mL of acetonitrile was used to dissolve the prepared mixture with continuous stirring at 80 °C for 24 h. TLC (1/1 = hexane/ethyl acetate) was used for monitoring the reaction until no free benzimidazole was observed. After the completion of the reactions, the solvents were removed under vacuum by the rotary evaporator. The oily products were collected as residues; the purification of the products was conducted by extraction two times with 30 mL ethyl acetate and 20 mL distilled water. The aqueous layers were separated and then washed with ethyl acetate. The separated organic layers were dried and washed several times by *n*-hexane.

1-Isopropyl-1H-benzo[d]imidazole (S1). Yield = 77%. Sticky brown oil. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.85 (s, 1H, NCHN), 7.64–7.62 (1H, m, Ar-H), 7.25–7.22 (1H, m, Ar-H), 7.11–7.08 (2H, m, Ar-H), 4.42 (1H, sep, ³J = 6.76 Hz, NCH), 1.40 (6H, d, ³J = 6.76 Hz, NC(CH₃)₂). ¹³C{¹H} NMR (500 MHz, CDCl₃): δ (ppm) 143.5 (NCN), 139.8, 132.7, 122.1, 121.5, 119.8, 109.7, (Ar-H), 47.2 (NCH), 22.02 [NC(CH₃)₂].

Anal. Calcd for C₁₀H₁₂N₂, (160): C, 74.97%; H, 7.55%; N, 17.48%. Found: C, 74.84%; H, 7.23%; N, 17.23%.

1-Benzyl-1H-benzo[d]imidazole (S2). Yield = 87%. Light yellow solid. ¹H NMR (500 MHz, CDCl₃): δ (ppm) 7.98 (1H, s, NCHN), 7.83 (1H, d, ³J = 7.63 Hz, Ar-H), 7.34–7.24 (6H, m, Ar-H), 7.18 (2H, d, ³J = 7.02 Hz, Ar-H), 5.36 (2H, m, NCH₂-Ph); ¹³C{¹H} NMR (500 MHz, CDCl₃): δ (ppm); 143.1 (NCN), 135.4, 129, 128.3, 127.06, 123.1, 122.3, 120.3, 110.04 (Ar-H), 48.8 (NCH₂); Anal. Calcd for C₁₄H₁₂N₂, (208): C, 80.74%; H, 5.81%; N, 13.45%. Found: C, 80.89%; H, 6.03%; N, 13.73%.

Synthesis of the Precursors for Alkylene-Bridged N-Heterocyclic Dicarbene Ligands (L1, L2, and L3). 1-Alkyl benzimidazole (5.0 mmol) and 2.5 mmol of dibromoalkane (1,3-dibromopropane or 1,4-dibromobutane) were introduced into a dried 100-mL round bottom flask. The mixture was refluxed in 35 mL of 1,4-dioxane under stirring at 103 °C for 12 h. The products appeared as white precipitates. They were collected by filtration and washed three times with 15 mL of 1,4-dioxane and then by 15 mL of toluene to remove any traces of the starting materials. The products were dried under vacuum and then collected as a white precipitate. Characterization of the alkylene-bridged N-heterocyclic dicarbene salts was conducted with different spectroscopic techniques including ¹H NMR, ¹³C NMR, elemental analysis, and ESI.

3,3'-(Propane-1,3-diyl)-bis(1-isopropyl-1H-benzo[d]-2imidazole-3-ium) Bromide (L1). Yield = 91%. White solid. ¹H NMR (500 MHz, DMSO-*d*₆): δ (ppm) 9.83 (2H, s, NCHN), 8.15–8.11 (4H, m, Ar-H), 7.71–7.69 (2H, m, Ar-H), 5.05 (2H, sep, ³J = 6.71 Hz, NCH), 4.67 (4H, t, ³J = 7.01 Hz, CH₂), 2.67 (2H, qui, ³J = 7.02 Hz, CH₂), 1.61 (12H, d, ³J = 6.7 Hz, NC(CH₃)₂); ¹³C{¹H} NMR (125 MHz, DMSO): δ (ppm) 140.7 (NCN), 131.3, 130.5, 126.7, 126.6, 114.1, 113.7, (Ar-H), 50.7 (NCH), 44.1 (NCH₂), 28.0 (CH₂), 21.6 (NC(CH₃)₂). Anal. Calcd for C₂₃H₃₀N₄Br₂, (522.3): C, 52.89%; H, 5.79%; N, 10.73%. Found: C: 52.37%, H: 5.8, %, N, 10.97%. ESI *m/z*: 442 [M – Br⁻]⁺, *m/z* 441 [M – Br⁻(-H⁺)].

3,3'-(Butane-1,4-diyl)-bis(1-isopropyl-1H-benzo[d]-2imidazole-3-ium) Bromide (L2). Yield = 76%. White solid. ¹H NMR (500 MHz, DMSO-*d*₆): δ (ppm) 10.05 (2H, s, NCHN), 8.13–8.11 (4H, m, Ar-H), 7.68 (4H, dd, ³J = 6.1 Hz, ³J₂ = 2.75 Hz, Ar-H), 5.05 (2H, sept, ³J = 6.71 Hz, NCH), 4.58 (4H, m, NCH₂), 2.04–1.99 (4H, m, CH₂), 1.62 [12H, d, ³J = 6.71 Hz (CH₃)₂]. ¹³C{¹H} NMR (125 MHz, DMSO): δ (ppm) 140.7 (NCN), 131.3, 130.6, 126.7, 126.6, 114.1, 113.8, (Ar-H), 50.7 (NCH), 46.3 (NCH₂), 25.6 (CH₂), 21.64 [NC(CH₃)₂]. Anal. Calcd for C₂₄H₃₂N₄Br₂, (536.3): C, 53.74%; H, 6.01%; N: 10.45%. Found: C: 52.12%, H: 5.91%, N: 10.79%. ESI *m/z*: 456 [M – Br⁻]⁺.

3,3'-(Propane-1,3-diyl)-bis(1-benzyl-1H-benzo[d]-2imidazole-3-ium) Bromide (L3). Yield = 65%. White solid. ¹H NMR (500 MHz, DMSO-*d*₆): δ (ppm) 10.15 (2H, s, NCHN), 8.14 (2H, d, ³J₁ = 7.93 Hz, Ar-H), 7.96 (2H, d, ³J₁ = 7.32 Hz, Ar-H), 7.66–7.62 (4H, m, Ar-H), 7.53 (4H, d, ³J₁ = 7.02 Hz, Ar-H), 7.39–7.36 (4H, m, Ar-H), 5.80 (4H, s, NCH₂Ph), 4.62 (4H, m, NCH₂CH₂), 2.06 (2H, m, CH₂). ¹³C{¹H} NMR (125 MHz, CDCl₃): δ (ppm); 141.31, 132.99, 131.51, 130.77, 129.27, 129.10, 128.52, 127.26, 127.14, 114.08, 113.64 (C-arom), 51.95 (NCH₂), 51.37 (NCH₂), 22.44 2(CH₂CH). Anal. Calcd for C₃₁H₃₀N₄Br₂, (618.4): C, 60.61%; H, 4.89%; N: 9.06%. Found: C: 60.83%, H: 5.11%, N: 9.79%. ESI *m/z*: 538.5 [M – Br⁻]⁺.

Synthesis of Palladium Bridged N-Heterocyclic Dicarbene Complexes (C1, C2, and C3). A round-bottom flask (50

Table 7. Selected Bond Lengths [Å] and Bond Angles [deg] for Compounds C1 and C3^a

C1		C3	
Pd(1)–C(1)#2	1.997(3)	Pd(1)–C(1)	1.964(8)
Pd(1)–C(1)	1.997(3)	Pd(1)–Br(1)	2.4659(11)
Pd(1)–Br(1)	2.4906(4)	Pd(2)–C(17)	1.985(8)
Pd(1)–Br(1)#2	2.4906(4)	Pd(2)–Br(2)	2.4704(11)
C(1)–N(2)	1.344(4)	N(1)–C(1)	1.352(10)
C(1)–N(1)	1.350(4)	N(1)–C(9)	1.395(10)
C(2)–N(1)	1.397(4)	N(2)–C(1)	1.355(9)
C(7)–N(2)	1.388(4)	N(2)–C(14)	1.372(9)
C(8)–N(1)	1.475(4)	N(2)–C(15)	1.458(9)
C(11)–N(2)	1.469(4)	N(3)–C(17)	1.339(10)
		N(3)–C(25)	1.373(9)
		N(3)–C(18)	1.463(9)
		N(4)–C(17)	1.339(8)
		N(4)–C(30)	1.401(9)
		N(4)–C(31)	1.452(9)
C(1)#2–Pd(1)–C(1)	88.66(17)	C(1)–Pd1–C(1)#1	87.4(3)
C(1)#2–Pd(1)–Br(1)	177.48(8)	C(1)–Pd(1)–Br(1)	175.0(2)
C(1)–Pd(1)–Br(1)	89.17(8)	C(1)#1–Pd(1)–Br(1)	88.5(2)
C(1)#2–Pd(1)–Br(1)#2	89.17(8)	Br1–Pd1–Br1#1	95.49(4)
C(1)–Pd(1)–Br(1)#2	177.48(8)	C(17)#2–Pd(2)–C(17)	87.7(3)
Br(1)–Pd(1)–Br(1)#2	92.97(2)	Br2#2–Pd(2)–Br(2)	97.01(4)
		C(17)–Pd(2)–Br(2)	175.2(2)
		C(17)#2–Pd(2)–Br(2)	87.6(2)

^aSymmetry codes: #1 = *x*, *−y* + 3/2, *z*; #2 = *x*, *−y* + 1/2, *z*.

mL) was charged with bridged N-heterocyclic dicarbene ligand precursors (L1, L2, or L3) (0.50 mmol), palladium(II) acetate (0.50 mmol), and 15 mL of dimethyl sulfoxide as a solvent. The orange solutions were heated at 70 °C for 24 h under stirring. The products were obtained as white precipitates. They were collected by filtration and washed twice with 15 mL of distilled water and then 15 mL of hexane. The residues were purified by extraction three times with dichloromethane/H₂O (5 mL/5 mL). Finally, the dichloromethane extracts were evaporated in vacuum and the products were obtained as white crystals. Single crystals for complex C1 were obtained by the slow crystallization procedure using a saturated solution of dichloromethane/acetonitrile (10:1) (v/v). Full characterization of the three complexes was accomplished by different physical and spectroscopic techniques such as ¹H and ¹³C NMR, ESI-MS, elemental analysis, and single-crystal X-ray diffraction analysis.

Dibromido (1,1'-Diisopropyl-3,3'-propylenedibenzimidazole-2,2-diylidene)palladium(II) (C1). Yield = 92%. White solid. ¹H NMR (500 MHz, DMF-*d*₇): δ (ppm) 8.08 (2H, d, ³J = 8.24 Hz, Ar-H), (the signals of aromatic protons overlap with the solvent signal), 7.97 (2H, d, ³J = 8.24 Hz, Ar-H), 7.45–7.37 (4H, m, Ar-H), 5.99 (2H, m, NCH), 5.43 (2H, m, CH₂), 5.11 (2H, m, CH₂), 2.19 (2H, m, CH₂CH₂CH₂), 1.94 [6H, d, ³J = 6.71 Hz, NC(CH₃)₂], 1.78 [6H, d, ³J = 5.80 Hz, NC(CH₃)₂]. ¹³C{¹H} NMR (125 MHz, CD₂CL₂): δ (ppm); 181 (Pd–C) [carbene signal (NC_{binim}N)], 135.2, 133.3, 132.3, 123.8, 123.7, 123.4, 123.1, 122.9, 113.2, 113, 110.7, 110.5 (Ar-H), 55.4 (NCH), 53.4 (NCH), 49.5 (NCH₂), 47.8 (NCH₂), 30.0 (CH₂), 28.5 (CH₂), 22.1, 21.7, 21.3 [NC(CH₃)₂]; Anal. Calcd for C₂₃H₂₈N₄Br₂Pd, (626.74): C, 44.08%; H, 4.50%; N, 8.94%; Found: C, 43.86%; H, 4.25%; N, 8.63%. ESI *m/z*: 546.82 [M – Br]⁺.

Dibromido (1,1'-Diisopropyl-3,3'-butylenedibenzimidazole-2,2-diylidene)palladium(II) (C2). Yield = 68%. Orange solid. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.49 (2H, d, ³J = 7.28 Hz, Ar-H), 7.30 (2H, d, ³J = 7.44 Hz Ar-H), 7.17–7.14

(4H, m, Ar-H), (the signals of aromatic protons overlap with the solvent signal), 6.00–5.96 (2H, m, NCH), 5.75–5.71 (2H, m, NCH₂), 4.45–4.41 (2H, m, NCH₂), 1.80–1.45 (4H, m, NCH₂CH₂). The signals of methylene protons were not assigned clearly because of the overlap with the isopropyl methyl signals, 1.74 [6H, d, ³J = 6.56 Hz (CH₃)₂], 1.69 [6H, d, ³J = 7.16 Hz (CH₃)₂]. ¹³C{¹H} NMR (125 MHz, CD₂CL₂): δ (ppm); 181.1 (Pd–C) [carbene signal (NC_{binim}N)], 135.9, 132.9, 122.9, 122.8, 112.9, 111.0, (Ar-H), 48.2 (NCH), 30.1 (NCH₂), 27.7 (CH₂), 21.2 [NC(CH₃)₂]. Anal. Calcd for C₂₄H₃₀N₄Br₂Pd, (640.7): C, 44.99%; H, 4.72%; N, 8.74%; Found, C, 44.78%; H, 4.89%; N, 8.53%. ESI *m/z*: 560.00 [M – Br]⁺.

Dibromido (1,1'-Dibenzyl-3,3'-propylenedibenzimidazole-2,2-diylidene)palladium(II) (C3). Yield = 73%. White crystals. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.71–7.69 (m, 2H, C–H-pyr), 7.48 (m, 4H, C–H-arom), 7.45–7.41 (m, 6H, C–H arom), 7.35–7.29 [m, 6H, C–H-(phenyl)], 5.87 (s, 4H, CH₂-Ph), 5.25 (m, 4H, NCH₂), 1.67 (m, 2H, NC(CH₂)). ¹³C NMR (125 MHz, CD₂CL₂): δ (ppm) 176.39 (Pd–C), 135.14, 134.96, 133.86, 129.08, 128.38, 127.58, 127.42, 127.29, 124.11, 123.86, 112.37, 110.27 (C-arom), 52.39 NCH₂, 49.50 NCH₂, 31.93 NCH₂, 29.90 NCH₂, 23.00 CH₂. Anal. Calcd for C₃₁H₂₈Br₂N₄Pd, (722.8): C, 51.51%; H, 3.90%; N, 7.75%. Found: C, 50.82; H, 4.03; N, 7.93. ESI *m/z*: 642.90 [M – Br]⁺.

Procedure for the Cyclocarbonylative Sonogashira Coupling Reactions. Chromones and flavones were synthesized via cyclocarbonylative Sonogashira coupling reactions that were carried out in a 45 mL stainless steel autoclave equipped with a glass liner, gas inlet valve, and pressure gauge. Palladium–bis(NHC) complex (0.50 mol %), functionalized 2-iodophenol (0.50 mmol), alkyne (0.55 mmol), base (1.00 mmol) and an anhydrous solvent (2 mL) were charged into the glass liner of the autoclave. Then, the autoclave was vented carefully three times with carbon monoxide and then pressurized to 100 psi of

carbon monoxide. The mixture was stirred and heated to the required temperature for a specific period of time. At the end of the reaction period, the autoclave was cooled down to room temperature and the excess of CO was discharged carefully under the fume hood. The reaction was extracted three times with 5 mL of distilled water and 10 mL of ethyl acetate. The ethyl acetate extracts were combined and concentrated in a rotary evaporator under reduced pressure. Flash chromatography was used to purify the reaction mixture using silica gel and an eluent (pentane/ethyl acetate = 7:1) to afford the corresponding chromones or flavones. Various physical and spectroscopic techniques such as ^1H and ^{13}C NMR, GC, and GC–MS were used to fully characterize the products. The spectral data of the chromones and flavones prepared in this study were in full agreement with those reported in the literature.^{33,35–37,40,41,49,68}

Analytical and Spectroscopic Data of the New Compound [2,2'-(1,4-Phenylene) bis(6-acetyl-4H-chromen-4-one)] (8c). Yield = 92%. Yellowish green solid. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.81 (2H, s, C–H-*arom*), 8.38 (2H, d, $^3J = 9.2$ Hz, C–H-*arom*), 8.15 (4H, s, C–H-*arom*), 7.68 (2H, d, $^3J = 8.38$ Hz, C–H-*arom*), 6.96 (2H, s, C–H-*arom*), 3.89 (6H, s, O=C– CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) 196.58 (C=O), 177.91 (C=O), 163.84, 158.85, 133.99, 132.91, 127.26, 126.39, 123.45, 118.95, 107.89 (C-*arom*), 26.73 (O=C– CH_3). IR (ν cm^{-1}), para aromatic overtone at 1900 (2000–1700), 1766, 1689, 1626, 1591, 1505, 1459, 1253, 1157. GC–MS *m/z*: 449.44(M^+). Anal. Calcd for $\text{C}_{28}\text{H}_{18}\text{O}_6$ (450.45): C, 74.66%; H, 4.04%; Found: C, 75.12; H, 4.11.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.0c04706>.

Crystallographic data for the compound C1 (CIF)

Crystallographic data for the compound C3 (CIF)

^1H NMR and ^{13}C NMR spectra and ESI spectra (PDF)

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Notes

The authors declare no competing financial interest.

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