

## Synthesis, characterization, and microwave-assisted catalytic activity in Heck, Suzuki, Sonogashira, and Buchwald–Hartwig cross-coupling reactions of novel benzimidazole salts bearing N-phthalimidoethyl and benzyl moieties

Hasan KÜÇÜKBAY<sup>1,\*</sup>, Ülkü YILMAZ<sup>1,2</sup>, Kemal YAVUZ<sup>1</sup>, Nesrin BUĞDAY<sup>1</sup>

<sup>1</sup>Department of Chemistry, Faculty of Science and Arts, İnönü University, Malatya, Turkey

<sup>2</sup>Battalgazi Vocational School, İnönü University, Malatya, Turkey

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**Abstract:** Five novel benzimidazole salts (**1–5**) having N-phthalimidoethyl and 4-substituted benzyl were synthesized and identified by <sup>1</sup>H NMR, <sup>13</sup>C NMR, and IR spectroscopic methods and microanalysis. A mixture of the benzimidazole salts (**1–5**), Pd(OAc)<sub>2</sub>, and K<sub>2</sub>CO<sub>3</sub> in DMF-H<sub>2</sub>O catalyzed, in high yield, the Suzuki–Miyaura and the Heck–Mizoroki cross-coupling reactions assisted by microwave irradiation in 5 min. The novel benzimidazole salts (**1–5**), Pd(OAc)<sub>2</sub>, Cs<sub>2</sub>CO<sub>3</sub>, PEG, and Cu nanoparticles catalyzed, in high yield, the Sonogashira coupling reaction promoted by microwave irradiation in 10 min. The same benzimidazole salts (**1–5**), Pd(OAc)<sub>2</sub>, Cs<sub>2</sub>CO<sub>3</sub>, and TBAB catalyzed, in moderate or low yield, the Buchwald–Hartwig reaction assisted by microwave irradiation in 60 min. The efficiency of the catalyst system in these four reactions was discussed as well as the electron-releasing and withdrawing substituent effects on the benzimidazole ligands.

**Key words:** Heck–Mizoroki coupling, Suzuki–Miyaura coupling, Sonogashira coupling, Buchwald–Hartwig coupling, benzimidazole derivatives, catalyzes, N-heterocyclic carbene, microwave

### 1. Introduction

Metal-catalyzed C–C and C–heteroatom bond formations are some of the most attractive methods in synthetic organic chemistry. Applications of these types of reactions have been continuously increasing and they have become a standard synthesis method for synthetic chemists. Several transition metal complexes including Pd, Cu, Fe, Ni, and Zn are employed for these types of bond-forming reactions.<sup>1,2</sup> Among all metals evaluated for such cross-coupling reactions, palladium has been a common metal due to its reactivity and selectivity, and tolerance of a wide range of functional groups on both coupling partners.<sup>3</sup> The catalytic activities of metal atoms also strictly depend on coordinated ligands. In general, phosphine and N-heterocyclic carbenes are used as efficient ligands. However, N-heterocyclic carbene ligands seem to be more appropriate due to their air and moisture resistances, stabilities at high temperature, and their lower toxicity than phosphine-based ligands.<sup>4,5</sup> Conventionally, organic reactions are carried out by thermal heating, which is a rather slow and inefficient method. In order to overcome this problem, microwave irradiation can be used instead of thermal heating. Furthermore, at the beginning of this century, green chemistry attracted considerable interest in the development of environmentally benign routes to numerous materials.<sup>6</sup> Among these routes, microwave irradiation has

\*Correspondence: [hasan.kucukbay@inonu.edu.tr](mailto:hasan.kucukbay@inonu.edu.tr)

Dedicated to Prof Dr Metin Balci on the occasion of his retirement.

become an effective tool in organic syntheses. Using metal catalysts in conjunction with microwaves may have significant advantages over classical heating methods since the inverted temperature gradient under microwave conditions may lead to increased lifetime of the catalyst, preventing wall effects.<sup>7,8</sup>

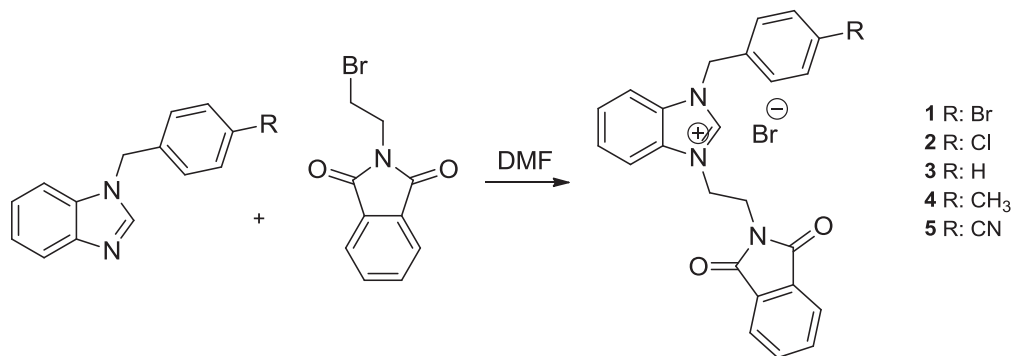
Despite the extensive literature, either on conventional heating or on microwave promoted cross-coupling reactions individually or together with the Suzuki and the Heck reactions,<sup>9–36</sup> there are limited examples that use the Mizoroki–Heck, the Suzuki–Miyaura, the Sonogashira, and the Buchwald–Hartwig reactions together in one study, except for some review reports<sup>37–41</sup> and books.<sup>42,43</sup>

Herein, we describe the synthesis of new benzimidazolium salts (**1–5**) containing 3-(2-(N-phthalimido)ethyl and 1-substituted benzyl moieties. The compounds were fully characterized by elemental analysis, and IR, <sup>13</sup>C NMR, and <sup>1</sup>H NMR spectroscopy. The microwave-assisted catalytic activity of N-heterocyclic carbene complexes of palladium was determined, generated in situ from the new benzimidazolium salts in the presence of an appropriate base. Owing to their wide applications in C–C and C–N bond formations in organic synthesis, N-heterocyclic carbenes containing imidazole or benzimidazole moieties have become an important tool in coupling reactions. In contrast to the extensive study of imidazole containing N-heterocyclic carbene complexes,<sup>44–49</sup> benzimidazole containing carbene complexes have been studied less. The present study was planned in order to explore the effectiveness of in situ formed N-heterocyclic carbene complexes containing novel benzimidazole ligands in cross coupling reactions. The catalytic efficiency of the catalyst system in these four popular reactions, namely the Mizoroki–Heck, the Suzuki–Miyaura, the Sonogashira, and the Buchwald–Hartwig reaction, as well as electron-releasing and withdrawing substituent effects on the benzimidazole ligands was discussed.

## 2. Results and discussion

New benzimidazolium bromide salts containing benzyl and N-phthalimidoethyl (**1–5**) were synthesized from the treatment of 1-benzylbenzimidazole with N-(2-bromoethyl)phthalimide in refluxing DMF with good yields of 68%–80%. The synthesis of the benzimidazolium salts **1–5** is summarized in the Scheme. The structures of the benzimidazolium salts (**1–5**) were elucidated by IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, and microanalyses. All spectral data were in accordance with the assumed structures. The IR spectra of benzimidazolium salts **1–5** have C=N and C=O stretching bands in the range of 1559–1563 cm<sup>-1</sup> and 1694–1716 cm<sup>-1</sup>, respectively. The C=N stretching frequencies of the benzimidazolium salts are slightly smaller than the normal (unconjugated) C=N stretching frequency value because of  $\pi$ -electron delocalization on the imidazolium ring.

The characteristic NCHN resonance in the <sup>1</sup>H NMR spectra and NCHN resonance in the <sup>13</sup>C NMR spectra of benzimidazolium salts (**1–5**) were observed at around 9.97–10.04 ppm and 143.2–143.4 ppm, respectively. These values are in good agreement with the previously reported results.<sup>50–53</sup>



**Scheme.** Synthetic pathways of the benzimidazolium salts (**1–5**).

## 2.1. The Heck–Mizoroki, Suzuki–Miyaura, Sonogashira, and Buchwald–Hartwig coupling reactions

Palladium-catalyzed carbon–carbon coupling reactions, such as the Mizoroki–Heck in the early 1970s, the Suzuki–Miyaura in 1990, the Sonogashira in 1975, and the Buchwald–Hartwig carbon–nitrogen coupling reaction in 1995, are now recognized as essential in the tool box of every synthetic chemist.<sup>54</sup> The resulting coupling products of these reactions are generally valuable materials like natural, biologically active, ingeniously designed organic materials with novel electronic, optical, or mechanical properties. Despite significant progress in palladium-catalyzed coupling reactions, considerable attention has been devoted to determining the mild reaction conditions and an environmentally benign, clean, economical, simple, and selective protocol for the formation of C–C and C–N bonds. In continuation of our work on C–C coupling reactions, we describe an environmentally benign highly efficient catalyst system having a benzimidazole scaffold that can be used as a precursor of N-heterocyclic carbene and make an appropriate comparison among the four famous palladium catalyzed coupling reactions.

### 2.1.1. The Heck–Mizoroki coupling reaction

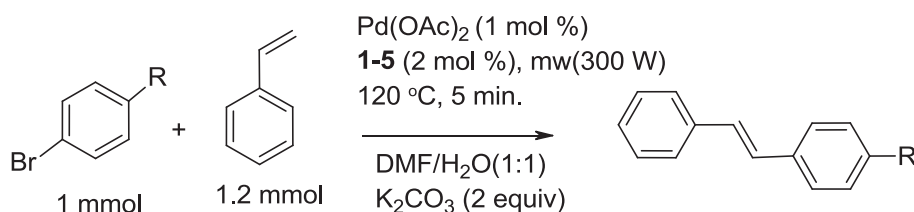
Palladium-catalyzed Heck–Mizoroki coupling has been recognized as one of the most powerful tools for the formation of C–C bonds and used in diverse areas such as the preparation of hydrocarbons, novel polymers, pharmaceuticals, organics, fine chemicals, agrochemicals, and dyes, and in new enantioselective syntheses of natural products in both academia and industry. In recent years, numerous papers have been published concerning improvements to the Heck–Mizoroki reaction, but it is still a hot topic for many research groups to explore the best catalytic system with highly selective, active, cheaper, and environmentally friendly procedures. On the basis of this perspective, we aimed to find a new and efficient catalyst system containing synthesized novel benzimidazole ligands that were precursors of N-heterocyclic carbenes with stronger  $\sigma$ -donor character and lower toxicity compared with phosphine ligands. Pd-catalyzed C–C coupling reactions are sensitive towards the nature of the base, the solvent used for the reactions, time, and temperature as well as catalyst concentration. In order to find the optimum reaction conditions for the Heck–Mizoroki coupling reaction, a series of test experiments was performed with 4-bromoanisole and styrene as model compounds. The test reactions were performed using different bases such as  $\text{Cs}_2\text{CO}_3$ ,  $\text{K}_2\text{CO}_3$ , and DBU (1,8-diazabicyclo[5.4.0]undec-7-en) and different solvents such as EtOH/ $\text{H}_2\text{O}$  and DMF/ $\text{H}_2\text{O}$  for 5 and 10 min at 80, 100, and 120 °C.

It was found that the Heck–Mizoroki coupling reaction catalyzed by benzimidazolium salt (**1**),  $\text{Pd}(\text{OAc})_2$ , and base catalyst system gave the highest yield when using DMF/ $\text{H}_2\text{O}$  mixture as a solvent and  $\text{Cs}_2\text{CO}_3$  or  $\text{K}_2\text{CO}_3$  as a base at 120 °C/300 W microwave heating for 5 min. A considerable increase could not be obtained in catalytic reaction yields by prolonging the time from 5 to 10 min. We observed a good effect on the catalytic yield by increasing the temperature from 80 °C to 120 °C/300 W for 5 min. After these results, we chose  $\text{K}_2\text{CO}_3$  as a base, since it is cheaper than  $\text{Cs}_2\text{CO}_3$  and water/DMF as a solvent. To evaluate the effect of  $\text{Pd}(\text{OAc})_2$  concentrations, the reaction was carried out in the presence of 0.5 and 1 mol %  $\text{Pd}(\text{OAc})_2$  under optimized conditions and the isolated yields of the corresponding coupling products are shown in Table 1.

Control experiments showed that the Heck–Mizoroki coupling reaction did not occur in the absence of **1**. The results obtained under optimum conditions are given in Table 1. Under the optimized reaction conditions, three different aryl halides bearing electron-donating, electron-neutral, and electron-withdrawing groups were reacted with styrene, affording the coupled products in quite good yield. Electron-deficient aromatic halides (Table 1, entries 20–24) gave higher yields than the electron-rich ones. It can also be concluded that the

electron releasing group on *p*-substituted benzyl attached to the nitrogen atom of the benzimidazolium salts slightly increased the catalytic activity (Table 1, entries 13, 18, and 23). In order to compare conventional and microwave heating systems, we also tested the catalytic yields using a conventional heating system in a preheated oil bath for 5 min at 120 °C but the desired coupling product could not be isolated (Table 1, entry 10).

**Table 1.** The Heck–Mizoroki coupling reactions of aryl halides with styrene.

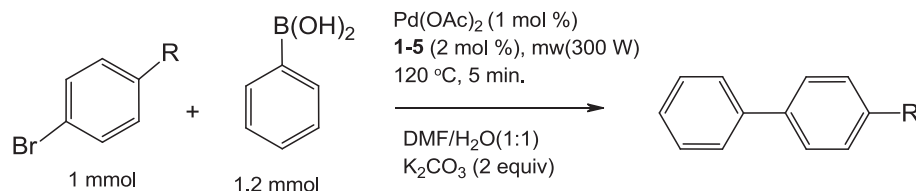


Entry	R	Salt	Yields (%) <sup>a</sup>
1	OCH <sub>3</sub>	<b>1</b>	73 <sup>b</sup>
2	OCH <sub>3</sub>	<b>1</b>	74 <sup>c</sup>
3	OCH <sub>3</sub>	<b>1</b>	84 <sup>d</sup>
4	OCH <sub>3</sub>	<b>1</b>	86 <sup>e</sup>
5	OCH <sub>3</sub>	<b>1</b>	86 <sup>f</sup>
6	OCH <sub>3</sub>	<b>1</b>	78 <sup>g</sup>
7	OCH <sub>3</sub>	<b>1</b>	76 <sup>h</sup>
8	OCH <sub>3</sub>	<b>1</b>	62 <sup>i</sup>
9	OCH <sub>3</sub>	No	n.d. <sup>j</sup>
10	OCH <sub>3</sub>	<b>1</b>	n.d. <sup>k</sup>
11	OCH <sub>3</sub>	<b>2</b>	72
12	OCH <sub>3</sub>	<b>3</b>	81
13	OCH <sub>3</sub>	<b>4</b>	86
14	OCH <sub>3</sub>	<b>5</b>	76
15	H	<b>1</b>	86
16	H	<b>2</b>	84
17	H	<b>3</b>	86
18	H	<b>4</b>	87
19	H	<b>5</b>	78
20	COOCH <sub>3</sub>	<b>1</b>	89
21	COOCH <sub>3</sub>	<b>2</b>	85
22	COOCH <sub>3</sub>	<b>3</b>	87
23	COOCH <sub>3</sub>	<b>4</b>	90
24	COOCH <sub>3</sub>	<b>5</b>	81

<sup>a</sup> Isolated yields. Reactions were monitored by GC-MS. Conditions: temperature ramped to 80 °C (3 min) and held for 5<sup>b</sup> min and 10<sup>c</sup> min, temperature ramped to 100 °C (3 min) and held for 5<sup>d</sup> min, temperature ramped to 120 °C (3 min) and held for 5<sup>e</sup> min. As the base, Cs<sub>2</sub>CO<sub>3</sub><sup>f</sup> and DBU<sup>g</sup> were used. As a solvent, EtOH/H<sub>2</sub>O<sup>h</sup> (1:1) mixture was used. 0.5 mol % Pd(OAc)<sub>2</sub><sup>i</sup>. Without **1**<sup>j</sup>. On preheated oil bath, for 5<sup>k</sup> min with thermal heating at 120 °C. n.d.: not detected.

### 2.1.2. The Suzuki–Miyaura coupling reaction

Among the several methods in biaryl synthesis, the Suzuki–Miyaura cross coupling reaction is a very efficient method for the conjugation of phenylboronic acids with aryl halides under mild reaction conditions.<sup>35</sup> Although

**Table 2.** The Suzuki–Miyaura coupling reactions of aryl halides with phenylboronic acid.

Entry	R	Salt	Yields (%) <sup>a</sup>
1	OCH <sub>3</sub>	<b>1</b>	81 <sup>b</sup>
2	OCH <sub>3</sub>	<b>1</b>	83 <sup>c</sup>
3	OCH <sub>3</sub>	<b>1</b>	87 <sup>d</sup>
4	OCH <sub>3</sub>	<b>1</b>	90 <sup>e</sup>
5	OCH <sub>3</sub>	<b>1</b>	89 <sup>f</sup>
6	OCH <sub>3</sub>	<b>1</b>	82 <sup>g</sup>
7	OCH <sub>3</sub>	<b>1</b>	75 <sup>h</sup>
8	OCH <sub>3</sub>	<b>1</b>	60 <sup>i</sup>
9	OCH <sub>3</sub>	No	11 <sup>j</sup>
10	OCH <sub>3</sub>	<b>1</b>	n.d. <sup>k</sup>
11	OCH <sub>3</sub>	<b>2</b>	87
12	OCH <sub>3</sub>	<b>3</b>	89
13	OCH <sub>3</sub>	<b>4</b>	94
14	OCH <sub>3</sub>	<b>5</b>	86
15	H	<b>1</b>	92
16	H	<b>2</b>	89
17	H	<b>3</b>	94
18	H	<b>4</b>	87
19	H	<b>5</b>	86
20	COOCH <sub>3</sub>	<b>1</b>	94
21	COOCH <sub>3</sub>	<b>2</b>	90
22	COOCH <sub>3</sub>	<b>3</b>	92
23	COOCH <sub>3</sub>	<b>4</b>	96
24	COOCH <sub>3</sub>	<b>5</b>	88

<sup>a</sup> Isolated yields. Reactions were monitored by GC-MS. Conditions: temperature ramped to 80 °C (3 min) and held for 5<sup>b</sup> min and 10<sup>c</sup> min, temperature ramped to 100 °C (3 min) and held for 5<sup>d</sup> min, temperature ramped to 120 °C (3 min) and held for 5<sup>e</sup> min. As the base, Cs<sub>2</sub>CO<sub>3</sub><sup>f</sup> and DBU<sup>g</sup> were used. As a solvent, EtOH/H<sub>2</sub>O<sup>h</sup> (1:1) mixture was used. 0.5 mol % Pd(OAc)<sub>2</sub><sup>i</sup> **1**. Without **1**<sup>j</sup>. On preheated oil bath, for 5<sup>k</sup> min with thermal heating at 120 °C. n.d.: not detected.

there has been considerable research on this topic, it is still being studied to improve the catalytic system and reaction conditions. For this purpose, we also continued to improve the catalytic system containing new benzimidazolium salts for these reactions. In order to find the optimum reaction conditions for the Suzuki–Miyaura coupling reaction, a series of experiments was performed with 4-bromoanisole and phenylboronic acid as model compounds similar to the Heck–Mizoroki reaction mentioned above. It was found that the Suzuki–Miyaura coupling reaction catalyzed by benzimidazolium salt (**1**), Pd(OAc)<sub>2</sub>, and base catalyst system gave the highest yield when using DMF/H<sub>2</sub>O mixture as a solvent and K<sub>2</sub>CO<sub>3</sub> as a base at 120 °C/300 W microwave heating for 5 min. A significant increase in catalytic reaction yields could not be observed by prolonging the time from 5 to 10 min. Under the optimized conditions, reaction of 4-bromoanisole, bromobenzene, and 4-bromoacetophenone with phenylboronic acid gave quite high yield using a catalytic system consisting of 2 mol

% benzimidazole salts (**1–5**), 1 mol % Pd(OAc)<sub>2</sub>, and 2 equiv. K<sub>2</sub>CO<sub>3</sub> in DMF–H<sub>2</sub>O (1:1) at 120 °C by microwave irradiation (300 W) within only 5 min. We also tested the catalytic yields using a conventional heating system in a preheated oil bath for 5 min at 120 °C, but the desired product could not be detected. Control experiments showed that the yield of the coupling reaction was dramatically decreased to 11% in the absence of **1**. The results obtained under optimum conditions are given in Table 2. Of the three different aryl bromides used in the Suzuki–Miyaura coupling with phenylboronic acid, the ones with electron-withdrawing substituents gave the highest yields (Table 2, entries 20–24). Similar to the Heck–Mizoroki cross coupling reaction results, it can be observed that the electron releasing group on *p*-substituted benzyl attached to the nitrogen atom of the benzimidazolium salts slightly increased the catalytic activity (Table 2, entries 13, 18, and 23). The conventional heating was also inefficient in 5 min at 120 °C for the Suzuki–Miyaura reaction under optimized conditions (Table 2, entry 10).

### 2.1.3. The Sonogashira coupling reaction

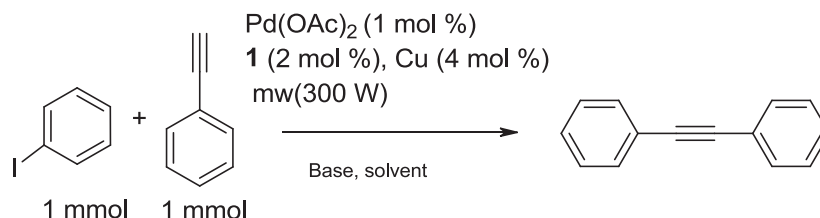
Sonogashira coupling reaction of phenylacetylene with aryl halides catalyzed with Pd complexes in the presence of copper reagent is one of the most useful techniques in organic syntheses and has been widely used in many areas such as natural product synthesis, biological active compounds, and material science.<sup>55</sup> In general, Sonogashira cross-coupling reactions proceed in the presence of palladium catalyst containing copper(I) compounds as co-catalyst and often suffer from the Glaser-type oxidative dimerization of the alkyne substrate as a side product and these reactions need prolonged reaction times. In order to prevent this side product formation and improve the Sonogashira cross coupling reactions, we used nano copper as co-catalyst instead of Cu(I) salts. After performing a series of test experiments with phenylacetylene and phenyl iodide, we obtained optimum reaction conditions for the Sonogashira cross coupling reactions (Table 3).

It was found that the Sonogashira coupling reaction catalyzed by benzimidazolium salt (**1**), Pd(OAc)<sub>2</sub>, copper nano particle, and base catalyst system gave the highest yield when using polyethylene glycol (PEG<sup>300</sup>) as a solvent and Cs<sub>2</sub>CO<sub>3</sub> as a base at 100 °C/300 W microwave heating for 10 min. Under the optimized conditions, reaction of phenyl iodide, *p*-tolyl iodide, and *p*-bromonitrobenzene with phenylacetylene gave quite high yield using a catalytic system consisting of 2 mol % benzimidazole salts (**1–5**), 1 mol % Pd(OAc)<sub>2</sub>, 4 mol % Cu nano particle, and 2 equiv. Cs<sub>2</sub>CO<sub>3</sub> in PEG<sup>300</sup> at 100 °C by microwave irradiation (300 W) within 10 min. We also tested the catalytic yields using a conventional heating system in a preheated oil bath for 10 min at 100 °C, but the desired product was not detected. Control experiments showed that the coupling reaction yields dramatically decreased to approximately half in the absence of **1**. The results obtained under optimum conditions are given in Table 4. Among the three different aryl halides used in the Sonogashira coupling with phenylacetylene, the ones with electron-withdrawing substituents were found to give results similar to those of the Heck–Mizoroki and Suzuki–Miyaura cross coupling reactions. It can be observed that the electron releasing group on *p*-substituted benzyl attached to the nitrogen atom of the benzimidazolium salts slightly increased the catalytic activity (Table 4, entries 4, 9, and 14). The conventional heating was also inefficient for 10 min at 100 °C for the Sonogashira reaction under optimized conditions (Table 3, entry 19).

Figure S1 (on the journal's website) shows XRD diffraction patterns of copper (0) nanoparticles. According to XRD diffraction, Cu nanoparticles have an Fm-3m face centered cubic structure and crystal parameters using the Jade program according to the Rietveld-refinement method are calculated as a = b = c = 3.889 Å. The strong peaks at the Bragg angles of 36.4°, 43.3°, 50.5°, and 74.1° correspond to the 002, 111, 200, and 220

facets of elemental copper.<sup>56,57</sup> The particle size of the corresponding facets 002, 111, 200, and 220 of elemental copper were determined as 15.3, 27.1, 22.2, and 21.6 nm ( $21.6 \pm 9.9$  nm) using the Debye–Scherrer equation [ $d = (0.94 \cdot \lambda_{CuK\alpha}) / (FWHM \cdot \cos\theta)$ ], respectively. These values were also found experimentally as 14.9, 27.2, 21.8, and 21.0 nm ( $21.2 \pm 10.0$  nm) from the XRD report, respectively.

**Table 3.** Test experiments for optimization of the Sonogashira coupling reactions.

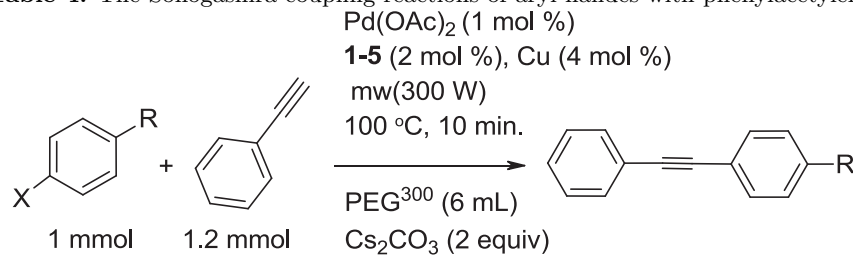


Entry	Salt	Base	Co catalyst (0.04 mol)	Solvent	Time (min)	Temperature °C	Yield, %
1	<b>1</b>	KOH	CuI	DMF	10	100	55
2	<b>1</b>	KOH	CuI	DMF	20	100	59
3	<b>1</b>	KOH	CuI	DMF	10	120	60
4	<b>1</b>	K <sub>2</sub> CO <sub>3</sub>	CuI	DMF	10	100	66
5	<b>1</b>	K <sub>2</sub> CO <sub>3</sub>	CuI	DMF	20	100	67
6	<b>1</b>	K <sub>2</sub> CO <sub>3</sub>	CuI	DMF	10	120	68
7	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuI	DMF	10	100	69
8	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuI	DMF	20	100	70
9	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuI	DMF	10	120	70
10	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	DMF	10	100	73
11	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	DMF	10	120	75
12	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	Ethylene glycol	10	100	74
13	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	Glycerol	10	100	56
14	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	EtOH	10	100	45
15	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	PEG <sup>300</sup>	10	100	94
16	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	PEG <sup>300</sup>	10	120	95
17	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	PEG <sup>300</sup>	10	100	84 <sup>a</sup>
18	no	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	PEG <sup>300</sup>	10	100	43 <sup>b</sup>
19	<b>1</b>	Cs <sub>2</sub> CO <sub>3</sub>	CuNPc	PEG <sup>300</sup>	10	100	n.d. <sup>c</sup>

Reaction conditions are same as indicated in the text. Yields are based on aryl bromide. Reactions were monitored by GC-MS. <sup>a</sup> CuNPc was used 0.02 mol. <sup>b</sup> The salt was not used. On preheated oil bath, for 10<sup>c</sup> min with thermal heating at 100 °C. n.d.: not detected.

#### 2.1.4. Buchwald–Hartwig coupling reaction

A number of biological active compounds, herbicides, conducting polymers, and components of organic light-emitting diodes contain arylamines. For many years, these types of compounds have been synthesized by classical methods, such as nitration, reduction, and reductive alkylation, and copper-mediated chemistry at high temperatures, through benzyne addition or direct nucleophilic substitution on electron-poor aromatic halides. However, following the first reports on palladium-catalyzed C–N coupling by Kosugi et al., on coupling of tin amides with aryl halides in 1994, and two reports by Buchwald and Hartwig in 1995, palladium catalyzed C–N bond forming methodology entered synthetic organic chemistry as a new method. Today, palladium-catalyzed C–N cross-coupling reactions are important tools in both academia and industry.<sup>58,59</sup> Despite considerable

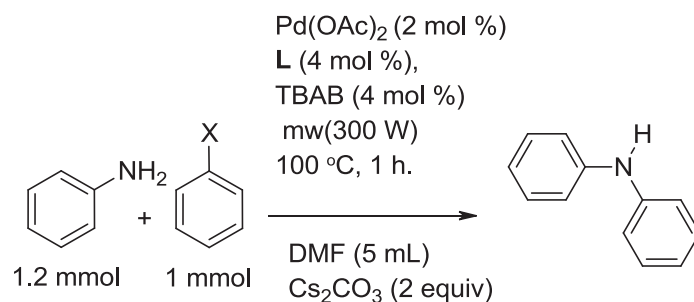
**Table 4.** The Sonogashira coupling reactions of aryl halides with phenylacetylene.

Entry	R	X	Salt	Yields (%) <sup>a</sup>
1	H	I	<b>1</b>	88
2	H	I	<b>2</b>	85
3	H	I	<b>3</b>	84
4	H	I	<b>4</b>	88
5	H	I	<b>5</b>	86
6	CH <sub>3</sub>	I	<b>1</b>	72
7	CH <sub>3</sub>	I	<b>2</b>	69
8	CH <sub>3</sub>	I	<b>3</b>	73
9	CH <sub>3</sub>	I	<b>4</b>	81
10	CH <sub>3</sub>	I	<b>5</b>	79
11	NO <sub>2</sub>	Br	<b>1</b>	94
12	NO <sub>2</sub>	Br	<b>2</b>	92
13	NO <sub>2</sub>	Br	<b>3</b>	93
14	NO <sub>2</sub>	Br	<b>4</b>	95
15	NO <sub>2</sub>	Br	<b>5</b>	91

<sup>a</sup>Isolated yields.

advances in this area, there are some notable limitations such as time, toxic ligands such as phosphines, and side products. We have published some papers concerning the C–C cross coupling reactions on the Suzuki–Miyaura and Heck–Mizoroki reactions catalyzed by Pd–NHC and reported promising results.<sup>41,44–47</sup> In this report, we also tested the efficiency of some benzimidazolium salts that were precursors of NHC ligand on the Buchwald–Hartwig coupling reactions. In order to find the optimum reaction conditions, we began our studies with the coupling of aniline and phenyl bromide. It was found that the Buchwald–Hartwig C–N coupling reaction catalyzed by benzimidazolium salt (**1**), Pd(OAc)<sub>2</sub>, and base catalyst system gave the highest yield when using DMF as a solvent and Cs<sub>2</sub>CO<sub>3</sub> as a base at 100 °C/300 W microwave heating for 60 min. A significant increase in catalytic reaction yields was not obtained by prolonging the time from 60 to 90 min. A phase transfer agent, tetrabutylammonium bromide (TBAB), was added to enhance the reactivity. As can be seen from Table 5, TBAB played a crucial role in the C–N coupling reactions (Table 5, entry 13). Under optimized conditions, the reaction of aniline with phenyl bromide gave low yield, using a catalytic system consisting of 4 mol % benzimidazole salts (**1–5**), 2 mol % Pd(OAc)<sub>2</sub>, and 2 equiv. Cs<sub>2</sub>CO<sub>3</sub> in DMF in the presence of 2 mol % TBAB at 100 °C by microwave irradiation (300 W) within 60 min. On the other hand, catalytic conversion yields were found to be moderate to high when using phenyl iodide instead of phenyl bromide. We also tested the catalytic yields using a conventional heating system in a preheated oil bath for 60 min at 100 °C, but the yield of the desired product decreased (Table 5 entry 14). The control experiment showed that the coupling reaction yield dramatically decreased to 11% in the absence of **1**. The results obtained under optimum conditions are given in Table 5.



**Table 5.** The Buchwald–Hartwig coupling reactions of phenyl halides with aniline.

Entry	X	Salt	Yields (%)
1	Br	1	n.d. <sup>a</sup>
2	Br	1	12 <sup>b</sup>
3	Br	1	49 <sup>c</sup>
4	Br	1	47 <sup>d</sup>
5	Br	1	46 <sup>e</sup>
6	Br	1	32 <sup>f</sup>
7	Br	1	23 <sup>g</sup>
8	Br	1	17 <sup>h</sup>
9	Br	1	29 <sup>i</sup>
10	Br	1	24 <sup>j</sup>
11	Br	1	45 <sup>k</sup>
12	Br	no	11 <sup>l</sup>
13	Br	1	37 <sup>m</sup>
14	Br	1	38 <sup>n</sup>
15	Br	2	43
16	Br	3	49
17	Br	4	50
18	Br	5	44
19	I	1	76
20	I	2	72
21	I	3	82
22	I	4	84
23	I	5	70

Reactions were monitored by GC-MS. Conditions: temperature ramped to 100 °C (3 min) and held for 10<sup>a</sup> min, 30<sup>b</sup> min, 60<sup>c</sup> min, and 90<sup>d</sup> min. As the base,  $\text{K}_2\text{CO}_3$ <sup>e</sup>,  $\text{KOH}$ <sup>f</sup> and  $\text{DBU}$ <sup>g</sup> were used. As a solvent,  $\text{EtOH}/\text{H}_2\text{O}$ <sup>h</sup> (1:1) mixture  $\text{DMF}/\text{H}_2\text{O}$  (1:1) and toluene<sup>j</sup> was used. 1 mol%  $\text{Pd(OAc)}_2$ <sup>k</sup>, Without salt<sup>l</sup>, Without TBAB<sup>m</sup>, On preheated oil bath for 60<sup>n</sup> min with thermal heating at 100 °C., n.d.: not detected.

### 3. Experimental

The starting materials and reagents used in the reactions were supplied commercially by Acros, Aldrich, Fluka, or Merck. The solvents were dried by standard methods and freshly distilled prior to use. All catalytic activity experiments were carried out in a microwave oven system manufactured by Milestone (Milestone Start S Microwave Labstation for Synthesis) under aerobic conditions. <sup>1</sup>H NMR (300.13 MHz) and <sup>13</sup>C NMR (75.47 MHz) spectra were recorded using a Bruker Avance 300 MHz Ultrashield high performance digital FT NMR spectrometer. Infrared spectra were recorded as KBr pellets in the range 4000–400 cm<sup>-1</sup> on a PerkinElmer FT-IR spectrophotometer. Elemental analyses were performed by LECO CHNS-932 elemental analyzer. Melting

points were recorded using an Electrothermal-9200 melting point apparatus, and were uncorrected. The structural characterization of copper nanoparticles fabricated was investigated by X-ray diffraction (XRD). An automated Rigaku RadB Dmax X-ray diffractometer with  $\text{CuK}\alpha$  radiation was used. Scan speed was selected as  $2^\circ \text{ min}^{-1}$  in the range of  $2\theta = 3\text{--}80^\circ$ .

1-(4-Bromobenzyl)benzimidazole, 1-(4-chlorobenzyl)benzimidazole, 1-benzylbenzimidazole, 1-(4-methylbenzyl)benzimidazole, and 1-(4-cyanobenzyl)benzimidazole used in this work as starting compounds were prepared according to the literature procedures.<sup>60–63</sup> Copper nanoparticles were also prepared according to the literature procedure<sup>64</sup> and were characterized by X-ray diffraction (XRD) pattern.

### 3.1. GC-MS analysis

GC-MS spectra were recorded on an Agilent 6890 N GC and 5973 Mass Selective Detector with an HP-INNOWAX column of 60-m length, 0.25-mm diameter and 0.25- $\mu\text{m}$  film thicknesses. GC-MS parameters for both Heck–Mizoroki and Suzuki–Miyaura coupling reactions were as follows: initial temperature  $60^\circ\text{C}$ ; initial time, 5 min; temperature ramp 1,  $30^\circ\text{C}/\text{min}$ ; final temperature,  $200^\circ\text{C}$ ; ramp 2,  $20^\circ\text{C}/\text{min}$ ; final temperature  $250^\circ\text{C}$ ; run time 30.17 min; injector port temperature  $250^\circ\text{C}$ ; detector temperature  $250^\circ\text{C}$ , injection volume, 1.0  $\mu\text{L}$ ; carrier gas, helium; mass range between  $m/z$  50 and 550.

### 3.2. Synthesis

#### 3.2.1. Synthesis of 1-(4-bromobenzyl)-3-(N-phthalimidoethyl)benzimidazolium bromide, 1

A mixture of 1-(4-bromobenzyl)benzimidazole (1.00 g, 3.48 mmol) and N-(2-bromoethyl)phthalimide (0.90 g, 3.54 mmol) in DMF (5 mL) was refluxed for 4 h. The mixture was then cooled and the volatiles were removed under vacuum. The residue was crystallized from EtOH/EtO<sub>2</sub> (1:1). Yield: 68% (1.28 g); mp  $259\text{--}260^\circ\text{C}$ .  $\nu(\text{C}=\text{N})$ :  $1559 \text{ cm}^{-1}$ ,  $\nu(\text{C}=\text{O})$ :  $1710 \text{ cm}^{-1}$ . Calcd for  $\text{C}_{24}\text{H}_{19}\text{Br}_2\text{N}_3\text{O}_2$ : C, 53.26; H, 3.54; N, 7.76%. Found: C, 53.24; H, 3.54; N, 7.74%.  $^1\text{H}$  NMR ( $\delta$ , DMSO- $d_6$ ): 4.09 (t, 2H,  $\text{CH}_2\text{-N}$ ,  $J=5.1$  Hz), 4.84 (t, 2H,  $\text{CH}_2\text{-N}$ ,  $J=5.1$  Hz), 5.57 (s, 2H,  $\text{ArCH}_2$ ), 8.21–7.38 (m, 12H,  $\text{Ar-H}$ ), 9.97 (s, 1H,  $\text{NCHN}$ ).  $^{13}\text{C}$  NMR ( $\delta$ , DMSO- $d_6$ ): 37.3 ( $\text{CH}_2$ ), 46.5 ( $\text{CH}_2$ ), 49.6 ( $\text{ArCH}_2$ ), 114.1, 114.5, 122.5, 123.7 ( $\text{BrPh-C}$ ), 127.3 ( $\text{phthalimide-C}$ ), 127.4 ( $\text{phthalimide-C}$ ), 130.9 ( $\text{benzimidazole-C}$ ), 131.3 ( $\text{benzimidazole-C}$ ), 131.7 ( $\text{phthalimide-C}$ ), 131.9 ( $\text{benzimidazole-C}$ ), 132.3 ( $\text{benzimidazole-C}$ ), 133.6 ( $\text{benzimidazole-C}$ ), 135.0 ( $\text{benzimidazole-C}$ ), 143.4 ( $\text{NCHN}$ ), 168.2 ( $\text{C}=\text{O}$ ).

Similar to the procedure above, compounds **2–5** were synthesized from appropriate 1-substituted benzimidazole and N-(2-bromoethyl)phthalimide.

#### 3.2.2. Synthesis of 1-(4-chlorobenzyl)-3-(N-phthalimidoethyl)benzimidazolium bromide, 2

Yield: 73% (1.50 g); mp  $252\text{--}253^\circ\text{C}$ . Calc. for  $\text{C}_{24}\text{H}_{19}\text{BrClN}_3\text{O}_2$ : C, 58.02; H, 3.85; N, 8.46%. Found: C, 58.01; H, 3.85; N, 8.42%. IR:  $\nu(\text{C}=\text{N})$ :  $1561$ ,  $\nu(\text{C}=\text{O})$ :  $1716 \text{ cm}^{-1}$ .  $^1\text{H}$  NMR ( $\delta$ , DMSO- $d_6$ ): 4.10 (t, 2H,  $\text{NCH}_2\text{CH}_2\text{-phthalimide}$ ,  $J=5.1$  Hz), 4.85 (t, 2H,  $\text{NCH}_2\text{CH}_2\text{-phthalimide}$ ,  $J=5.1$  Hz), 5.77 (s, 2H,  $\text{CH}_2\text{-benzyl}$ ), 7.45–8.22 (m, 12H,  $\text{Ar-H}$ ), 9.99 (s, 1H,  $\text{NCHN}$ ) ppm.  $^{13}\text{C}$  NMR ( $\delta$ , DMSO- $d_6$ ): 37.3 ( $\text{NCH}_2\text{CH}_2\text{-phthalimide}$ ), 46.5 ( $\text{NCH}_2\text{CH}_2\text{-phthalimide}$ ), 49.6 ( $\text{CH}_2\text{-benzyl}$ ), 114.1, 114.5, 123.7, 127.3 ( $\text{BrPh-C}$ ), 127.4 ( $\text{phthalimide-C}$ ), 129.4 ( $\text{phthalimide-C}$ ), 130.6 ( $\text{benzimidazole-C}$ ), 131.3 ( $\text{benzimidazole-C}$ ), 131.7 ( $\text{phthalimide}$ ), 131.9 ( $\text{benzimidazole-C}$ ), 133.3 ( $\text{benzimidazole-C}$ ), 133.9 ( $\text{benzimidazole-C}$ ), 135.0 ( $\text{benzimidazole-C}$ ),

143.4 (NCHN), 168.2 (C=O).

### 3.2.3. Synthesis of 1-benzyl-3-(N-phthalimidoethyl)benzimidazolium bromide, 3

Yield: 80% (1.78 g); mp 152–153 °C. Calc. for  $C_{24}H_{20}BrN_3O_2$ : C, 62.35; H, 4.36; N, 9.09%. Found: C, 62.00; H, 4.22; N, 8.91%. IR:  $\nu(C=N)$ : 1565,  $\nu(C=O)$ : 1711  $cm^{-1}$ .  $^1H$  NMR ( $\delta$ , DMSO- $d_6$ ): 4.12 (t, 2H,  $NCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 4.86 (t, 2H,  $NCCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 5.77 (s, 2H,  $CH_2$ -benzyl), 7.36–8.22 (m, 13H, Ar-H), 10.04 (s, 1H, NCHN) ppm.  $^{13}C$  NMR ( $\delta$ , DMSO- $d_6$ ): 37.3 ( $NCH_2CH_2$ -phthalimide), 46.5 ( $NCH_2CH_2$ -phthalimide), 50.3 ( $CH_2$ -benzyl), 114.1, 114.5, 123.7, 127.2 (BrPh- $C$ ), 127.3 (phthalimide- $C$ ), 128.4 (phthalimide- $C$ ), 129.1 (benzimidazole- $C$ ), 129.4 (benzimidazole- $C$ ), 131.4 (phthalimide- $C$ ), 131.8 (benzimidazole- $C$ ), 131.9 (benzimidazole- $C$ ), 134.2 (benzimidazole- $C$ ), 135.1 (phthalimide- $C$ ), 143.4 (NCHN), 168.2 (C=O).

### 3.2.4. Synthesis of 1-(4-methylbenzyl)-3-(N-phthalimidoethyl)benzimidazolium bromide, 4

Yield: 79% (1.70 g); mp 154–156 °C. Calc. for  $C_{25}H_{22}BrN_3O_2$ : C, 63.03; H, 4.65; N, 8.82%. Found: C, 62.94; H, 4.62; N, 8.67%. IR:  $\nu(C=N)$ : 1565,  $\nu(C=O)$ : 1694  $cm^{-1}$ .  $^1H$  NMR ( $\delta$ , DMSO- $d_6$ ): 2.28 (s, 3H,  $CH_3$ ), 4.10 (t, 2H,  $NCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 4.84 (t, 2H,  $NCCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 5.69 (s, 2H,  $CH_2$ -benzyl), 7.15–8.20 (m, 12H, Ar-H), 9.97 (s, 1H, NCHN) ppm.  $^{13}C$ -NMR ( $\delta$ , DMSO- $d_6$ ): 21.2 ( $CH_3$ ), 37.3 ( $NCH_2CH_2$ -phthalimide), 46.4 ( $NCH_2CH_2$ -phthalimide), 50.2 ( $CH_2$ -benzyl), 114.0, 114.5, 123.7, 127.3 (BrPh- $C$ ), 127.3 (phthalimide- $C$ ), 128.5 (phthalimide- $C$ ), 129.9 (benzimidazole- $C$ ), 131.1 (benzimidazole- $C$ ), 131.4 (phthalimide- $C$ ), 131.8 (benzimidazole- $C$ ), 132.0 (benzimidazole- $C$ ), 135.0 (benzimidazole- $C$ ), 138.5 (benzimidazole- $C$ ), 143.2 (NCHN), 168.2 (C=O).

### 3.2.5. Synthesis of 1-(4-cyanobenzyl)-3-(N-phthalimidoethyl)benzimidazolium bromide, 5

Yield: 75% (1.56 g); mp 257–258 °C. Calc. for  $C_{25}H_{19}BrN_4O_2$ : C, 61.61; H, 3.93; N, 11.50%. Found: C, 61.55; H, 3.80; N, 11.39%. IR:  $\nu(C=N)$ : 1563,  $\nu(C=O)$ : 1710,  $\nu(C\equiv N)$ : 2234  $cm^{-1}$ .  $^1H$  NMR ( $\delta$ , DMSO- $d_6$ ): 4.11 (t, 2H,  $NCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 4.84 (t, 2H,  $NCCH_2CH_2$ -phthalimide,  $J = 5.1$  Hz), 5.87 (s, 2H,  $CH_2$ -benzyl), 7.54–8.21 (m, 12H, Ar-H), 9.97 (s, 1H, NCHN) ppm.  $^{13}C$  NMR ( $\delta$ , DMSO- $d_6$ ): 36.8 ( $NCH_2CH_2$ -phthalimide), 46.0 ( $NCH_2CH_2$ -phthalimide), 49.2 ( $CH_2$ -benzyl), 111.4, 113.7, 113.9, 123.2 (BrPh- $C$ ), 126.9 (phthalimide- $C$ ), 128.7 (phthalimide- $C$ ), 130.8 (benzimidazole- $C$ ), 131.3 (benzimidazole- $C$ ), 131.3 (benzimidazole- $C$ ), 131.5 (phthalimide- $C$ ), 132.8 (benzimidazole- $C$ ), 134.6 (benzimidazole- $C$ ), 139.3 (benzimidazole- $C$ ), 118.4 ( $C\equiv N$ ), 143.2 (NCHN), 167.8 (C=O).

### 3.2.6. General procedure for the Heck–Mizoroki reactions

$Pd(OAc)_2$  (1 mmol%), benzimidazolium bromides (1–5) (2 mmol%), aryl halide (1 mmol), styrene (1.2 mmol),  $K_2CO_3$  (2 mmol), water (3 mL), and DMF (3 mL) were added to the microwave apparatus and the mixture was heated at 120 °C (300 W) for 5 min. It was carried out over a ramp time of 3 min to reach 120 °C. At the end of the reaction, the mixture was cooled and the product was extracted with ethyl acetate/*n*-hexane (1:5) and filtered through a pad of silica gel with copious washing. The purity of the coupling products was checked by NMR and GC-MS and yields were determined through isolated coupling products.

### 3.2.7. General procedure for the Suzuki–Miyaura reactions

Pd(OAc)<sub>2</sub> (1 mmol%), benzimidazolium bromides (**1–5**) (2 mmol%), aryl halide (1 mmol), phenylboronic acid (1.2 mmol), K<sub>2</sub>CO<sub>3</sub> (2 mmol), water (3 mL), and DMF (3 mL) were added to the microwave apparatus and the mixture was heated at 120 °C (300 W) for 5 min. It was carried out over a ramp time of 3 min to reach 120 °C. At the end of the reaction, the mixture was cooled and the product extracted with ethyl acetate/*n*-hexane (1:5) and filtered through a pad of silica gel with copious washing. The purity of coupling products was checked by NMR and GC-MS, and yields were determined through isolated coupling products.

### 3.2.8. General procedure for the Sonogashira reactions

Pd(OAc)<sub>2</sub> (1 mmol%), benzimidazolium bromides (**1–5**) (2 mmol%), aryl halide (1 mmol), phenylacetylene (1.2 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2 mmol), copper nanoparticles, CuNPs (4 mmol), and PEG<sup>300</sup> (6 mL) were added to the microwave apparatus and the mixture was heated at 100 °C (300 W) for 10 min. It was carried out over a ramp time of 3 min to reach 100 °C. At the end of the reaction, the mixture was cooled and the product extracted with ethyl acetate/*n*-hexane (1:5) and filtered through a pad of silica gel with copious washing. The purity of coupling products was checked by NMR and GC-MS and yields were determined through isolated coupling products.

### 3.2.9. General procedure for the Buchwald–Hartwig reactions

Pd(OAc)<sub>2</sub> (2 mmol%), benzimidazolium bromides (**1–5**) (4 mmol%), phenyl bromide (1 mmol), aniline (1.2 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2 mmol), tetrabutylammonium chloride, TBAB (4 mmol%), and DMF (5 mL) were added to the microwave apparatus and the mixture was heated at 100 °C (300 W) for 60 min. It was carried out over a ramp time of 3 min to reach 100 °C. At the end of the reaction, the mixture was cooled and the product extracted with ethyl acetate/*n*-hexane (1:5) and filtered through a pad of silica gel with copious washing. The purity of coupling products was checked by GC-MS and conversions were determined by GC-MS based on phenyl bromide using the normalizing peak areas method.

## 4. Conclusions

We prepared and characterized five air- and water-stable benzimidazolium salts bearing *N*-phthalimidoethyl, substituted benzyl moieties. We also investigated their potential activities in the presence of Pd(OAc)<sub>2</sub>, base, and solvent under microwave heating for comparison purposes. These salts were active for the Heck–Mizoroki, Suzuki–Miyaura, and Sonogashira coupling reactions and gave better yields under microwave-assisted moderate conditions and very short reaction times. However, the catalyst system used in this work showed lower activity in the Buchwald–Hartwig reaction.

## Supplementary Materials

NMR spectra of the novel compounds, Suzuki–Miyaura, Mizoroki–Heck, Sonogashira products, and GC-MS chromatogram of Buchwald–Hartwig product are available free of charge on the journal's website.

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## References

1. Mehta, V. P.; Van der Eycken, E. *Chem. Soc. Rev.* **2011**, *40*, 4925–4936.
2. Beller, M.; Bolm, C. *Transition Metals for Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2004.
3. Yin, L.; Liebscher, J. *Chem. Rev.* **2007**, *107*, 133–173.
4. Linninger, C. S.; Herdtweck, E.; Hoffmann, S. D.; Herrmann, W. A.; Kühn, F. E. *J. Mol. Struct.* **2008**, *890*, 192–197.
5. Marion, N.; Nolan, S. P. *Accout. Res.* **2008**, *41*, 1440–1449.
6. Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press, New York, NY, USA, 1998.
7. Kappe, C. O. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250–6284.
8. Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717–727.
9. Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147–168.
10. Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151.
11. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
12. Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2–7.
13. Suzuki, A. *ChemComm.* **2005**, 4759–4763.
14. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009–3066.
15. Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11–59.
16. Heck, R. F. *Synlett* **2006**, 2855–2860.
17. Akba, O.; Durap, F.; Aydemir, M.; Baysal, A.; Gümgüm, B.; Özkar, S. *J. Organomet. Chem.* **2009**, *694*, 731–736.
18. Leadbeater, N. E.; Marco, M. *Org. Lett.* **2002**, *4*, 2973–2976.
19. Dawood, K. M. *Tetrahedron* **2007**, *63*, 9642–9651.
20. Astruc, D. *Inorg. Chem.* **2007**, *46*, 1884–1894.
21. Prokopcová, H.; Ramirez, J.; Fernández, E.; Kappe, C. O. *Tetrahedron Lett.* **2008**, *49*, 4831–4835.
22. Martinez, A. V.; Invernizzi, F.; Leal-Duaso, A.; Mayoral, J. A.; Garcia, J. I. *RSC Adv.* **2015**, *5*, 10102–10109.
23. Yin, L.; Liebscher, J. *Chem. Rev.* **2007**, *107*, 133–173.
24. Tudose, A.; Delaude, L.; Andre, B.; Demonceau, A. *Tetrahedron Lett.* **2006**, *47*, 8529–8533.
25. Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Angew. Chem. Int. Ed.* **2007**, *46*, 2768–2813.
26. Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467–4470.
27. Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46–49.
28. Thomas, A. M.; Sujatha, A.; Anilkumar, G. *RSC Adv.* **2014**, *4*, 21688–21698.
29. Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem. Int. E.* **1995**, *34*, 1348–1350.
30. Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609–3612.
31. Hartwig, J. F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2046–2067.
32. Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131–209.
33. Larhed, M.; Hallberg, A. *J. Org. Chem.* **1996**, *61*, 9582–9584.
34. Mercan, D.; Çetinkaya, E.; Çetinkaya, B. *J. Organomet. Chem.* **2011**, *696*, 1359–1366.
35. Mohanty, S.; Suresh, D.; Balakrishna, M. S.; Mague, J. T. *Tetrahedron* **2008**, *64*, 240–247.
36. Alonso, F.; Beletskaya, I. P.; Yus, M. *Tetrahedron* **2008**, *64*, 3047–3101.
37. Mehta, V. P.; Appukkuttan, P.; Van der Eycken, E. *Curr. Org. Chem.* **2011**, *15*, 265–283.

38. Beletskaya, I.; Tyurin, V. *Molecules* **2010**, *15*, 4792–4814.
39. Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.
40. Appukkuttan, P.; Van der Eycken, E. *Eur. J. Org. Chem.* **2008**, 1133–1155.
41. Küçükbay, H.; Şireci, N.; Yılmaz, Ü.; Deniz, S.; Akkurt, M.; Baktır, Z.; Büyükgüngör, O. *Turk. J. Chem.* **2012**, *36*, 201–217.
42. Nolan, S. P. *N-Heterocyclic Carbenes in Synthesis*; Wiley-VCH: Weinheim, Germany, 2006.
43. Colacot, T. *New Trends in Cross-Couplings: Theory and Applications*; RSC: London, UK, 2014.
44. Gstottmayr, C. W. K.; Böhm, V. P. W.; Herdtweck, E.; Grosche, M.; Herrmann W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1363–1365.
45. Selvrakumar, K.; Zagf, Spontanberg, M.; Beller, M. *Chem. Eur. J.* **2002**, *8*, 3901–3906.
46. Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398–3416.
47. Lebel, H.; Jonas, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046–5047.
48. Paczol, A.; Benyer, A. C.; Kotschy, A. *J. Org. Chem.* **2006**, *71*, 5969–5979.
49. Özdemir, İ.; Demir, S.; Gürbüz, N.; Çetinkaya, B.; Toupet, L.; Bruneau, C.; Dixneuf, P. H. *Eur. J. Inorg. Chem.* **2009**, 1942–1949.
50. Yılmaz, Ü.; Şireci, N.; Deniz, S.; Küçükbay, H. *Appl. Organomet. Chem.* **2010**, *24*, 414–420.
51. Küçükbay, H.; Şireci, N.; Yılmaz, Ü.; Akkurt, M.; Yalçın, Ş. P.; Tahir, M. N.; Ott, H. *Appl. Organomet. Chem.* **2011**, *25*, 255–261.
52. Yılmaz, Ü.; Küçükbay, H.; Şireci, N.; Akkurt, M.; Günal, S.; Durmaz, R.; Tahir, M. N. *Appl. Organomet. Chem.* **2011**, *25*, 366–373.
53. Yılmaz, Ü.; Küçükbay, H.; Türktekin, Ç. S.; Akkurt, M.; Büyükgüngör, O. *Turk. J. Chem.* **2013**, *37*, 721–733.
54. Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644–4680.
55. Sabounvhei, S. J.; Ahmadi, M. *Catal. Commun.* **2013**, *37*, 114–121.
56. Cao, X.; Yu, F.; Li, L.; Yao, Z.; Xie, Y. *J. Cryst. Growth.* **2003**, *254*, 164–168.
57. Wang, Y.; Biradar, A. V.; Wang, G.; Sharma, K. K.; Duncan, C. T.; Rangan, S.; Asefa, T. *Chem. Eur. J.* **2010**, *16*, 10735–10743.
58. Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534–1544.
59. Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 15914–15917.
60. Wan, Y.; Wallinder, C.; Plouffe, B.; Beaudry, H.; Mahalingam, A. K.; Wu, X.; Johansson, B.; Holm, M.; Botoros, M.; Karlen, A.; et al. *J. Med. Chem.* **2004**, *47*, 5995–6008.
61. Xia, Q. Q.; Chen, W. Z.; Qiu, H. Y.; Direct, C. N. *J. Org. Chem.* **2011**, *76*, 7577–7582.
62. Nikitenko, A. A.; Khafizova, G.; Gross, J. L. *PCT Int. Appl.* **2010**, *WO 20100009029*, A2 2010121.
63. Filipiskikh, T. P.; Pozharskii, A. F.; Koroleva, V. N.; Simonov, A. M.; Zvezdina, E. A. *Khim. Geterotsikl. Soedin.* **1972**, *6*, 809–811.
64. Yang, Q.; Wang, Y.; Lin, D.; Zhang, M. *Tetrahedron Lett.* **2013**, *54*, 1994–1997.