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Synthesis, characterization and microwave-assisted catalytic activity of novel benzimidazole salts bearing piperidine and morpholine moieties in Heck cross-coupling reactions

Hasan Küçükbay[a]*, Nihat Şireci[b], Ülkü Yılmaz[a], Mehmet Akkurt[c], Şerife Pınar Yalçın[d], M. Nawaz Tahir[e] and Holger Ott[f]

A mixture of novel benzimidazole salts (2a–f), $Pd(OAc)_2$ and K_2CO_3 in DMF–H_2O catalyzes, in high yield, the Heck cross-coupling reaction assisted by microwave irradiation in a short time. All synthesized novel benzimidazole derivatives were characterized by elemental analysis and NMR spectroscopy. In addition, the molecular structure of 2a was determined by X-ray crystallography. Copyright © 2011 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: benzimidazole salt; carbene; palladium catalysis; coupling reaction; Heck coupling; microwave

Introduction

The Mizoroki–Heck reaction is one of the most widely used palladium-catalyzed C–C coupling reactions in organic synthesis, polymerization processes, UV screens, pharmaceuticals, preparation of hydrocarbons, and in advanced enantioselective synthesis of natural products.[1–5] The traditional Heck reaction is typically performed with 1–5 mol% of a palladium catalyst along with phosphine ligands in the presence of a suitable base. However, inert reaction conditions must be provided due to the ligands applied (especially for electron-rich phosphine ligands), which are often toxic and sensitive to air and moisture.[6,7] Because of their strong σ-donor character and low toxicity, the use of *N*-heterocyclic carbenes (NHCs) as alternative ligands to phosphine ligands in palladium-catalyzed cross-coupling reactions is recommended.[8–12] Pd(II)–NHC complexes are more attractive as pre-catalysts because of their stability to air, moisture and heating and also have an excellent long-term storage profile.[13]

The ligand-free systems consist of $Pd(OAc)_2$ or $Pd(O_2CCF_3)_2$; base and solvents have also been used as a catalyst system in Heck coupling reactions.[7,14,15] However, using the $Pd(OAc)_2$ catalytic systems containing ligands has been shown more effective catalytic activity than ligand-free palladium containing systems.

The base-free systems consist of arylboronic acid as arylpalladium precursors, $Pd(OAc)_2$, 2,9-dimethyl-1-10-phenanthroline (dmphen) as the regiocontrolling ligand, *p*-benzoquinone or atmospheric air as a reoxidant, and different solvents such as acetonitrile or deionized water have also been used as an efficient catalyst system in Heck coupling reactions.[16]

$Pd(OAc)_2$–benzimidazole or imidazole ligands could be very effective catalytic systems, particularly in Suzuki and Heck reactions.[17–18] Although there are extensive studies on the $Pd(OAc)_2$/substituted-benzimidazole or substituted-imidazole catalytic systems in Heck cross-coupling reactions, much less attention has been paid to the benzimidazole ligands containing piperidine and morpholine moieties in these systems.[19–21] The combination of the benzimidazole and piperidine or morpholine heterocycles as ligands may be a good opportunity to obtain better results in Heck cross-coupling reactions.

On the other hand, high-speed synthesis with microwaves has attracted considerable attention in recent years. The use of metal catalysts in conjunction with microwaves may have significant advantages over traditional heating methods since the inverted temperature gradient under microwave conditions may lead to an increased lifetime of catalyst through elimination

* *Correspondence to: Hasan Küçükbay, Inönü University, Faculty Science and Arts, Department of Chemistry, 44280 Malatya, Turkey. E-mail: hkucukbay@inonu.edu.tr*

a *Inönü University, Faculty Science and Arts, Department of Chemistry, 44280 Malatya, Turkey*

b *Adıyaman University, Faculty Education, 02040 Adıyaman, Turkey*

c *Erciyes University, Faculty Science and Arts, Department of Physics, 38039 Kayseri, Turkey*

d *Harran University, Faculty Science and Arts, Department of Physics, 63300 Şanlıurfa, Turkey*

e *University of Sargodha, Department of Physics, Pakistan*

f *Bruker AXS GmbH, Oestliche Rheinbrueckenstrasse 49, 76187, Karlsruhe, Germany*

of wall effects.[6,13,22]. The C–C cross-coupling in Heck reactions has also been carried out in quite short times resulting in high yields.[18,23–28]

Herein, we describe the synthesis of new benzimidazole (**1a**) and benzimidazole salts (**2a–d** and **f**) containing piperidine and morpholine moieties. The compounds were fully characterized by elemental analysis, IR, ^{13}C NMR and ^{1}H NMR spectroscopy and the molecular structure of **2a** was determined by X-ray crystallography. We also report on the microwave-assisted catalytic activity of $Pd(OAc)_2$/benzimidazole salts (**2a–f**) in Heck cross-coupling reactions.

Experimental

All preparations were carried out in inert atmosphere of argon using standard Schlenk techniques. Starting materials and reagents used were of commercial grade and purchased from Aldrich or Merck Chemical Co. Solvents were dried with standard methods and freshly distilled prior to use. All catalytic activity experiments were carried out in a microwave oven manufactured by Milestone (Milestone Start S Microwave Labstation for Synthesis) under aerobic conditions. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra were recorded using a Bruker DPX-300 high-performance digital FT NMR spectrometer. Infrared spectra were recorded from KBr pellets in the range 4000–400 cm^{-1} on a Perkin-Elmer FT-IR spectrophotometer. Elemental analyses were performed with a Leco CHNS-932 elemental analyzer. Melting points were recorded using an electrothermal-9200 melting point apparatus, and are given uncorrected.

1-Substituted benzimidazoles (**1b–d**[29–31] and **2d**[32]) that are used in this work as a starting compounds were prepared according to literature procedures. There is little information about compound **1a**,[33] so full information for compound **1a** is given in this report.

GC-MS Analysis

GC-MS spectra were recorded on an Agilient 6890 N GC and 5973 Mass Selective Detector with a HP-INNOWAX column of 60 m length, 0.25 mm diameter and 0.25 μm film thicknesses. GC-MS parameters for Heck coupling reactions were as follows: initial temperature, 60 °C; initial time, 5 min; temperature ramp 1, 30 °C/min; final temperature, 200 °C; ramp 2, 20 °C/min; final temperature 250 °C; run time 30.17 min; injector port temperature 250 °C; detector temperature 250 °C, injection volume, 1.0 μl; carrier gas helium; mass range between *m/z* 50 and 550.

Synthesis of 1-cinnamylbenzimidazole, ***1a***

Cinnamyl chloride (2.4 ml, 17.2 mmol) was added to a solution of benzimidazole (2.00 g; 16.9 mmol) and KOH (1.89 g, 33.8 mmol) in EtOH (20 ml) and the mixture was heated under reflux for 4 h. The mixture was then cooled and the resulted potassium chloride was filtered off and washed with a portion of EtOH. Volatiles were removed *in vacuo* and the residue was crystallized from EtOH. White crystals of **1a** (3.29 g, 83%) were obtained. M.p. 104–105 °C. $\upsilon_{(N=C)}$: 1563 cm^{-1}), $\upsilon_{(C=C)}$: 1670 cm^{-1}. Anal. found: C, 81.96; H, 6.02; N, 11.92%; calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. ^{1}H NMR (δ, DMSO-d_6): 8.30 (s, 1H, NC*H*N), 7.70–7.44 (m, 4H, C_6H_4), 7.34–7.19 (m, 5H, C_6H_5-cinnamyl), 6.65 (d, 1H, CH=C*H*–C_6H_5, $^{3}J_{H,H}$ = 15.9 Hz), 6.51 (dt, 1H, C*H*=CH–C_6H_5, $^{3}J_{H,CH2}$ = 6.0 Hz), 5.08 (d, CH_2–CHCHC_6H_5, ^{3}J = 6.0 Hz). ^{13}C NMR (δ, DMSO-d_6): 144.4 (NCHN), 144.0, 136.4, 134.3, 132.9, 129.1, 128.4 (C_6H_4), 126.9, 125.2, 122.8, 122.0 (C_6H_5-cinnamyl), 120.0, 111.2 (CH=*C*H–C_6H_5), 46.7 (CH_2–*C*HCHC_6H_5).

Synthesis of 1-cinnamyl-3-[2-(piperidinium-1-yl)ethyl] benzimidazolium dichloride dihydrate ***2a***

A mixture of 1-cinnamylbenzimidazole (1.17 g, 5 mmol) and 1-(2-chloroethyl)piperidine monohydrochloride (0.92g, 5 mmol) in dimethylformamide (5 ml) was refluxed for 4 h. Volatiles were removed in vacuo and the residue was crystallized from EtOH–DMF (3 : 1). Yellow crystals of **2a** (1.64 g, 78%) were obtained. M.p. 253–254 °C. $\upsilon_{(N=C)}$: 1558 cm^{-1}, $\upsilon_{(C=C)}$: 1640 cm^{-1}. Anal. found: C, 60.63; H, 7.29; N, 9.18; calcd for $C_{23}H_{33}N_3Cl_2O_2$, C, 60.79; H, 7.32; N, 9.25%. ^{1}H NMR (δ, DMSO-d_6): 11.59 (s, 1H, N*H*-piperidinium), 10.09 (s, 1H, NC*H*N), 8.28–7.72 (m, 4H, C_6H_4), 7.50, 7.37 (m, 5H, C_6H_5-cinnamyl), 7.01 (d, 1H, CH=CH–C_6H_5, $^{3}J_{H,H}$ = 15.9 Hz), 6.67 (dt, 1H, CH=CH–C_6H_5, $^{3}J_{H,CH2}$ = 6.6 Hz), 5.36 (d, CH_2–CHCHC_6H_5, ^{3}J = 6.6 Hz), 5.09 (t, 2H, CH_2CH_2-piperidine, ^{3}J = 6.0 Hz), 3.65 (m, 4H, ring methylene), 3.00 (t, 2H, CH_2CH_2-piperidine, ^{3}J = 6 Hz), 1.81 (m, 4H, ring methylene), 1.43 (m, 2H, ring methylene). ^{13}C NMR (δ, DMSO-d_6): 144.0 (NCHN), 136.1, 135.5, 131.6, 131.6, 129.2, 128.9 (C_6H_4), 127.2, 127.1, 127.0, 122.4 (C_6H_5-cinnamyl), 114.4, 114.4 (CH=*C*H–C_6H_5), 53.8 (CH_2–CHCHC_6H_5), 52.6, 49.2 (CH_2CH_2-piperidine), 41.4, 22.44, 21.7 (ring methylene).

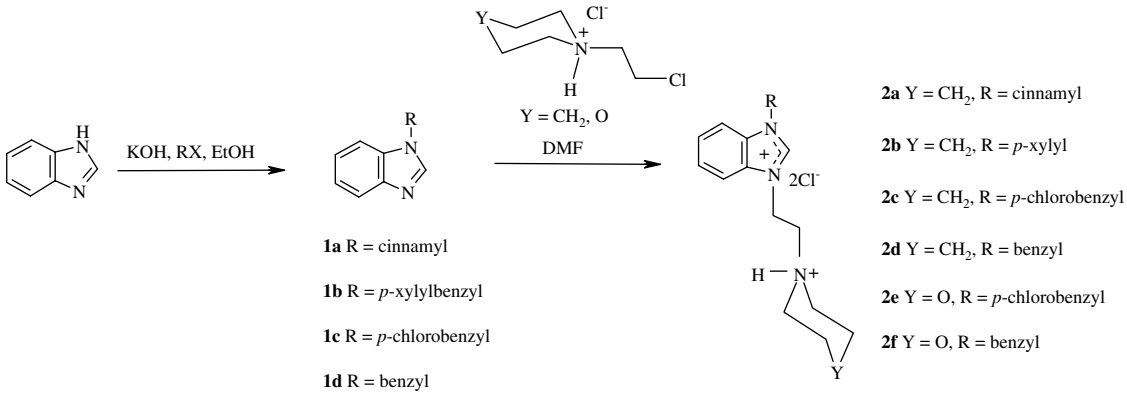
Similarly, 1-(4-methylbenzyl)-3-[2-(piperidinium-1-yl)ethyl]benzimidazolium dichloride, **2b**, 1-(4-chlorobenzyl)-3-[2-(piperidinium-1-yl)ethyl]benzimidazolium dichloride, **2c**, 1-(4-chlorobenzyl)-3-[2-(morpholinium-1-yl)ethyl]benzimidazolium dichloride, **2e** and 1-benzyl-3-[2-(morpholinium-1-yl)ethyl]benzimidazolium dichloride, **2f** were synthesized from 1-(4-methylbenzyl)benzimidazole with 1-(2-chloroethyl)piperidine monohydrochloride, 1-(4-chlorobenzyl)benzimidazole with 1-(2-chloroethyl)piperidine monohydrochloride, 1-(4-chlorobenzyl)benzimidazole with 1-(2-chloroethyl)morpholine monohydrochloride and 1-benzylbenzimidazole with 1-(2-chloroethyl)morpholine monohydrochloride, respectively.

1-(4-Methylbenzyl)-3-[2-(piperidinium-1-yl)ethyl]benzimidazolium dichloride, ***2b***

Yield 1.87 g, 83%, yellow. M.p. 210–211 °C; $\upsilon_{(N=C)}$: 1557 cm^{-1}. Anal. found: C, 58.22; H, 6.35; N, 9.16%; calcd for $C_{22}H_{29}N_3ClBr$: C, 58.61; H, 6.48; N, 9.32. ^{1}H NMR (δ, DMSO-d_6): 11.67 (s, 1H, N*H*-piperidinium), 10.38 (s, 1H, NC*H*N), 8.30–7.68 (m, 4H, C_6H_4), 7.50, 7.23 (m, 4H, xylyl), 5.78 (s, 2H, CH_2–C_6H_4), 5.16 (t, 2H, CH_2CH_2-piperidine, ^{3}J = 6 Hz), 3.67 (m, 4H, ring methylene), 3.06 (t, 2H, CH_2CH_2-piperidine, ^{3}J = 6 Hz), 2.30 (s, 3H, CH_3–C_6H_4), 1.82 (m, 4H, ring methylene), 1.43 (m, 2H, ring methylene). ^{13}C NMR (δ, DMSO-d_6): 144.05 (NCHN), 138.6, 138.6, 131.6, 131.3, 130, 129.1 (C_6H_4), 129.0, 127.1, 127.1, 114.5 (xylyl), 53.54 (CH_2–C_6H_4), 52.62, 50.32 (CH_2CH_2-piperidine), 41.52, 22.75, 21.70 (ring methylene), 21.21 (CH_3–C_6H_4).

1-(4-Chlorobenzyl)-3-[2-(piperidinium-1-yl)ethyl]benzimidazolium dichloride, ***2c***

Yield 1.82 g, 85%, white. M.p. 261–262 °C; $\upsilon_{(N=C)}$: 1556 cm^{-1}. Anal. found: C, 59.02; H, 6.04; N, 9.71%; calcd for $C_{21}H_{26}N_3Cl_3$: C, 59.10; H, 6.14; N, 9.85. ^{1}H NMR (δ, DMSO-d_6): 11.62 (s, 1H, N*H*-piperidinium), 10.27 (s, 1H, NC*H*N), 8.27–7.73 (m, 4H, C_6H_4), 7.66, 7.52 (m, 4H, benzyl), 5.81 (s, 2H, CH_2–C_6H_4Cl), 5.11 (t, 2H, CH_2CH_2-piperidine, ^{3}J = 6.3 Hz), 3.60 (m, 4H, ring methylene), 3.03 (t, 2H,



Scheme 1. Synthesis pathway of benzimidazole derivatives.

CH_2CH_2-piperidine, ^3J = 6.3 Hz), 1.81 (m, 4H, ring methylene), 1.44 (m, 2H, ring methylene). ^{13}C NMR (δ, DMSO-d_6): 144.28 (NCHN), 133.94, 133.22, 131.65, 131.39, 130.91, 129.45 (C_6H_4), 129.35, 127.20, 127.15, 114.52 (benzyl), 53.57 ($CH_2-C_6H_4$), 52.66, 49.75 (CH_2CH_2-piperidine), 41.52, 22.50, 21.72 (ring methylene).

1-(4-Chlorobenzyl)-3-[2-(morpholinium-1-yl)ethyl]benzimidazolium dichloride, ***2e***

Yield 1.55 g, 72%, white. M.p. 163–164 °C. $\upsilon_{(N=C)}$: 1561 cm^{-1}. Anal. found: C, 55.57; H, 5.33; N, 9.52%; calcd for $C_{20}H_{24}N_3Cl_3O$: C, 56.02; H, 5.64; N, 9.80. ^{1}H NMR (δ, DMSO-d_6): 12.23 (s, 1H, N*H*-morpholinium), 10.40 (s, 1H, NC*H*N), 8.16–7.67 (m, 4H, C_6H_4), 7.62 and 7.50 (m, 4H, benzyl), 5.95 (s, 2H, $CH_2-C_6H_4$), 4.71 (t, 2H, CH_2CH_2-morpholine, ^3J = 5.4 Hz), 3.48 (m, 4H, ring methylene), 2.77 (t, 2H, CH_2CH_2-morpholine, ^3J = 5.4 Hz), 2.44 (m, 4H, ring methylene). ^{13}C NMR (δ, DMSO-d_6): 143.6 (NCHN), 133.9, 133.5, 131.7, 131.4, 131.0, 129.4 (C_6H_4), 129.4, 127.2, 127.1, 114.4 (benzyl), 66.6 ($CH_2-C_6H_4$), 56.1, 53.3 (CH_2CH_2-morpholine), 49.7, 44.0 (ring methylene).

1-Benzyl-3-[2-(morpholinium-1-yl)ethyl]benzimidazolium dichloride, ***2f***

Yield 1.50 g, 76%, white. M.p. 209–210 °C. $\upsilon_{(N=C)}$: 1557 cm^{-1}. Anal. found: C, 60.68; H, 6.32; N, 10.47%; calcd for $C_{20}H_{25}N_3Cl_2O$: C, 60.92; H, 6.39; N, 10.66%. ^{1}H NMR (δ, DMSO-d_6): 12.31 (s, 1H, N*H*-morpholinium), 10.40 (s, 1H, NC*H*N), 8.25–7.72 (m, 4H, C_6H_4), 7.64, 7.42 (m, 4H, benzyl), 5.81 (s, 2H, $CH_2-C_6H_4$), 5.11 (t, 2H, CH_2CH_2-morholine, ^3J = 6.9 Hz), 3.47 (m, 4H, ring methylene), 2.83 (t, 2H, CH_2CH_2-morpholine, ^3J = 6.9 Hz), 2.47 (m, 4H, ring methylene). ^{13}C NMR (δ, DMSO-d_6): 144.3 (NCHN), 134.6, 134.4, 131.6, 131.5, 129.5, 129.0, (C_6H_4), 128.8, 127.2, 127.1, 114.4 (benzyl), 63.6 ($CH_2-C_6H_4$), 53.9, 51.9 (CH_2CH_2-morpholine), 50.5, 41.4 (ring methylene).

Single-crystal X-ray diffraction analysis of 1-cinnamyl-3-[2-(piperidinium-1-yl)ethyl]benzimidazolium dichloride dihydrate, ***2a***

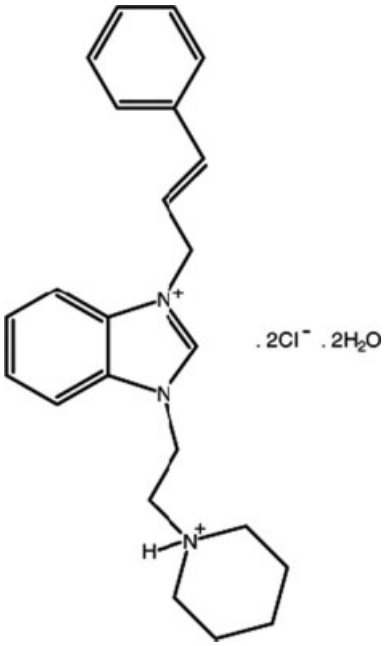
The X-ray data were collected on a Bruker X8 Prospector system equipped with a highly sensitive APEX II area detector and using an IμS X-ray microfocus source with multilayer mirrors, that give intense monochromatic CuK_α radiation (λ = 1.54178 Å). An empirical absorption correction was applied during the data processing using SADABS.[34] The structure was solved by direct methods using SHELXS[35] and refined using the SHELXL-97.[36] Initial hydrogen atom positions of the lattice solvents were located in a difference Fourier map and refined using restraints for an idealized water molecule. The remaining hydrogen atoms were placed in calculated positions (C–H=0.95–0.99 Å, N–H = 0.93 Å) and included in the refinement using the riding model, with U_{iso}(H) = 1.2 or 1.5 U_{eq} (N, C). A summary of the crystal data, experimental details and refinement results for **2a** is given in Table 1. The hydrogen bond and molecular packing geometry of compound **2a** were calculated with PLATON.[37] The graphical representations of the structure were made with ORTEP.[38]

General Procedure for the Heck Reactions

$Pd(OAc)_2$ (1 mmol%), benzimidazolium chlorides (**2a**–**f**; 2 mmol%), the aryl halide (1 mmol), styrene (1.2 mmol), K_2CO_3 (4 mmol), water (3 ml) and DMF (3 ml) were added to microwave apparatus and the mixture was heated at 80 °C (300 W) for 10 min. It was carried out over a ramp time of 3 min to reach to 80 °C temperature. At the end of reaction, the mixture was cooled, the product was extracted with ethyl acetate–*n*-hexane (1 : 5) and purified on a silica gel column. The purity of coupling products was checked by NMR and GC-MS, and the reported yields are based on aryl halide.

Results and Discussion

In this work, benzimidazolium chloride salts, which are conventional NHC precursors, containing piperidine and morpholine heterocycles, **2a**–**f**, were used. These salts were prepared from the treatment of 1-alkylbenzimidazoles (**1a**–**d**) with 1-(2-chloroethyl)piperidine monohydrochloride or 1-(2-chloroethyl)morpholine monohydrochloride in refluxing DMF with good yields of 72–85%. The synthesis of the benzimidazoles **2a**–**f** is summarized in Scheme 1. The benzimidazolium salts are air and moisture-stable in the solid state as well as in solution. The **2a**–**f** were identified by spectroscopic methods and elemental analysis. The NCHN δ[^{13}C{^{1}H}] signal of the benzimidazolium salts is usually around 142 ± 4 ppm.[39] For the benzimidazolium salts **2a**–**f** it was found to be 144.0, 144.0, 144.0, 143.6 and 144.3 ppm, respectively. These values are in good agreement with the previously reported results.[18,40,41] The NC*H*N protons of the benzimidazolium salts were observed as singlet in the ^{1}H NMR spectrum at 10.09, 10.38, 10.27, 10.46 and 10.40 ppm, respectively. These chemical shift values are typical for NC*H*N protons of benzimidazolium salts



Scheme 2. Open line structure of **2a**.

because of their increased acidity.[18,40–43] In comparison, the corresponding value of the starting material **1a** is 8.30 ppm, which is significantly smaller than in benzimidazolium salts. The cinnamyl substituents of **1a** and **2a** (Scheme 2) display a *trans* arrangement, which is also reflected in the proton NMR spectra. The coupling constant of the protons connected to the C═C double bond are both 15.9 Hz, which is a typical value for protons in a *trans* arrangement.[44]

The benzimidazole derivatives **2a–f** show IR absorption bands at 1558, 1557, 1556, 1561 and 1557 cm^{-1}, respectively, which are assigned to ν(C═N). These IR absorption values are in good agreement with previously reported values for benzimidazolium salts.[17–18] These values are slightly smaller than expected for a standard ν(C═N) because of the π-electron delocalization on the imidazolium ring.

Molecular Structure of 1-Cinnamyl-3-[2-(piperidinium-1-yl) ethyl]benzimidazolium Dichloride Dihydrate, 2a

The title compound, **2a** (Fig. 1), crystallizes in the monoclinic space group *Pc*, with two 1-cinnamyl-3-[2-(piperidinium-1-yl)ethyl] benzimidazolium cations, four chloride anions and four water molecules in the asymmetric unit.

The benzimidazole rings (N1/N2/C1–C7 and N4/N5/C24–C30) of both cations are planar with maximum deviations of 0.028(2) and 0.025(3) Å, respectively. The dihedral angle between them is 1.64(8)°. The phenyl rings (C18–C23 and C41–C46) form dihedral angles of 73.45(11) and 74.66(12)° with the respective benzimidazole ring. As expected, the two piperidinium rings of both cations exhibit a chair conformation [puckering parameters[45] are Q_T = 0.581(3) Å, θ = 180.0 (3)° and ϕ = 345 (21)° for the ring (N3/C10–C14) and Q_T = 0.569(3) Å, θ = 0.0 (3)° and ϕ = 210 (25)° for the ring (N6/C33–C37)].

The crystal structure shows N–H···Cl, N–H···O, O–H···Cl, C–H···Cl and C–H···O interactions (Table 2 and Fig. 2). A weak C–H···π-interaction may also be present.

The Heck coupling reaction

The Mizoroki–Heck reaction, the coupling of aryl halides with terminal olefins, ranges among the most important palladium-catalyzed transformations in organic synthesis.[46] The rate of

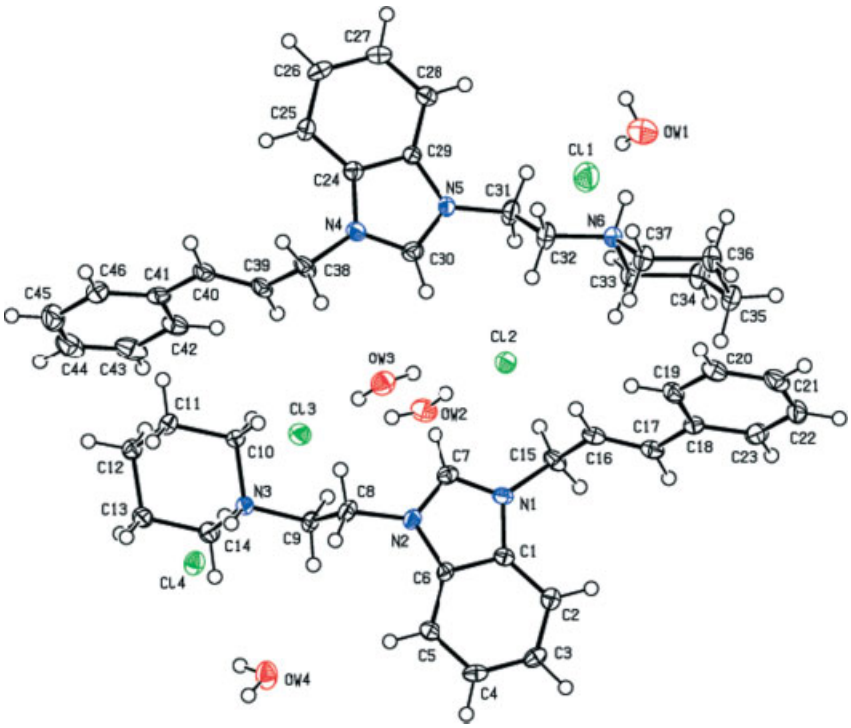


Figure 1. Molecular structure of **2a** including atom labels. The anisotropic displacement parameters are displayed at a 50% probability level.

Table 1. Crystal data and structure refinement details for **2a**

Crystal data	
$C_{23}H_{29}N_3.2(H_2O).2(Cl)$	$Z = 4$
$M_r = 454.42$	$D_x = 1.308$ Mg m^{-3}
Monoclinic, *Pc*	Cu $K\alpha$ radiation
$a = 16.1852$ (5) Å	
$b = 20.8616$ (7) Å	
$c = 6.8484$ (2) Å	$\mu = 2.72$ mm^{-1}
$\beta = 93.927$ (1)°	$T = 100$ K
$V = 2306.93$ (12) Å^3	Crystal shape block, color light yellow Crystal dimensions: 0.2 × 0.2 × 0.2 mm^3
Data collection	
X8 Prospector diffractometer	$R_{int} = 0.050$
ω and ϕ scans	$\theta_{max} = 67.6°$
Absorption correction: multi-scan (based on symmetry-related measurements)	$h = -19 \rightarrow 19$
$T_{min}/T_{max} = 0.99$	$k = -22 \rightarrow 24$
26510 measured reflections	$l = -7 \rightarrow 8$
7136 independent reflections	
7110 reflections with $I > 2\sigma(I)$	
Refinement	
Refinement on F^2	Calculated weights $w = 1/[\sigma^2(F_o^2) + (0.0895P)^2 + 0.5424P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.046$	$(\Delta/\sigma)_{max} < 0.0001$
$wR(F^2) = 0.121$	$\Delta\rho_{max} = 0.35$ e Å^{-1}
$S = 1.04$	$\Delta\rho_{min} = -0.54$ e Å^{-1}
7136 reflections	Extinction correction: none
566 parameters	Absolute structure: Flack (1983), 2952 Freidel pairs
Mixture of independent and constrained H-atom refinement	Flack parameter: 0.141 (11)

Table 2. Hydrogen-bond parameters (Å, deg)

	D–H	H···*A*	D···A	*D*–H···*A*
N3–HN3···Cl4	0.9300	2.1500	3.082 (2)	177.00
N6–HN6···OW1	0.9300	1.9200	2.774 (3)	151.00
OW1–H101···Cl1^{i}	0.84 (2)	2.36 (2)	3.165 (3)	161 (3)
OW1–H102···Cl1	0.85 (2)	2.35 (2)	3.190 (4)	168 (3)
OW2–H103···Cl2	0.82 (2)	2.32 (2)	3.135 (2)	169 (3)
OW2–H104···Cl3	0.823 (17)	2.356 (17)	3.179 (2)	178 (4)
OW3–H105···Cl2	0.823 (19)	2.336 (18)	3.148 (2)	169 (4)
OW3–H106···Cl3	0.83 (2)	2.30 (2)	3.122 (2)	171 (2)
C5–H5···OW4^{ii}	0.9500	2.3100	3.210 (3)	158.00
C7–H7···OW2^{iii}	0.9500	2.3800	3.066 (3)	129.00
C7–H7···OW3	0.9500	2.3000	3.072 (3)	138.00
C8–H8A···Cl3^{iii}	0.9900	2.6800	3.643 (3)	166.00
C15–H15A···Cl2	0.9900	2.6000	3.557 (3)	162.00
C27–H27···Cl2^{i}	0.9500	2.8200	3.694 (3)	153.00
C28–H28···Cl1^{i}	0.9500	2.6700	3.552 (3)	154.00
C30–H30···OW2^{iii}	0.9500	2.3100	3.077 (3)	137.00
C30–H30···OW3	0.9500	2.4900	3.127 (3)	125.00
C31–H31B···Cl2	0.9900	2.8100	3.655 (3)	143.00
C33–H33A···Cl1	0.9900	2.8300	3.770 (3)	160.00
C37–H37B···Cl1^{iii}	0.9900	2.7100	3.523 (3)	140.00
C38–H38B···Cl3^{iii}	0.9900	2.8000	3.687 (3)	150.00
C12–H12A···Cg9^{iv}	0.99	2.73	3.460 (3)	130

Symmetry codes: (i) x, $1 - y$, $1/2 + z$; (ii) x, $-y$, $1/2 + z$; (iii) x, y, $1 + z$; (iv) x, y, z.

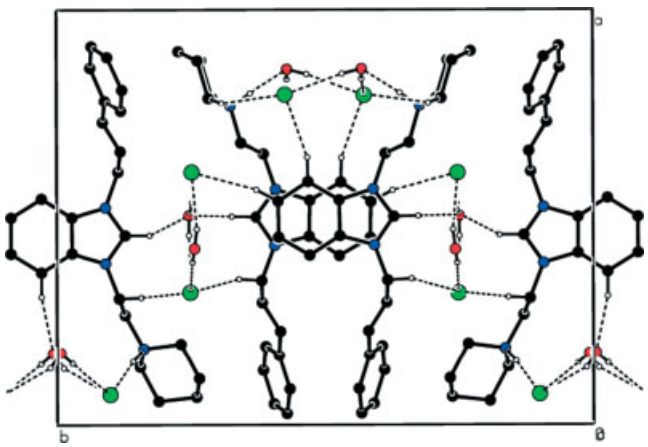
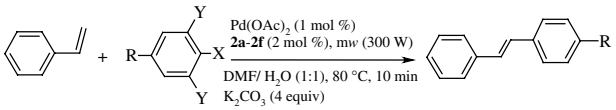


Figure 2. Packing diagram (unit cell shown) and hydrogen bonding of **2a**. Hydrogen bonds are indicated as dashed lines. Hydrogen atoms not involved in hydrogen bonding are omitted for clarity.

the coupling is dependent on a variety of parameters such as the base, the solvent, the temperature and the nature of the catalyst loading. We recently reported optimal reaction conditions for Heck coupling reactions, including bis-benzimidazolium salts and $Pd(OAc)_2$, in basic environment under microwave and conventional heating conditions.[18] In the present report, a series of aryl bromide and chloride compounds bearing electron-deficient substituents and aryl iodide were used for the coupling reaction with styrene. The recently reported optimal parameters[18] were slightly modified (80 °C/300 W) Since there are two acidic protons on benzimidazolium salts (**2a–f**) and protons on N atoms of piperidine or morpholine are more acidic than the proton of 2-position of the benzimidazole ring, which N-heterocyclic carben precursors (NC*H*N), we used 4% mol of base to remove both acidic protons of benzimidazolium dihalides. Finally, we found that 1% mol $Pd(OAc)_2$, 2% mol of **2a–f**, 4% mol of K_2CO_3 in DMF–H_2O (1 : 1) at 80 °C/300 W microwave heating led to the best conversion within 10 min. It has been observed that no increase in catalytic reactions yield is found by prolonging reaction time from 10 to 20 min (Table 3, entry 2). Furthermore, no coupling reaction occurred in the absence of **2a** within 5 min (Table 3, entry 3) and very low yield was detected within 10 min (Table 3, entry 4). We also tested the catalytic yield using a conventional heating system (i.e. preheated oil bath) after 10 and 20 min at 80 °C and the yields were detected 17 and 48%, respectively (Table 3, entries 5 and 6).

A complete list of the results obtained with optimal conditions is given in Table 3. Altogether five different aryl halides bearing electron-donating and electron-withdrawing groups reacted with styrene and gave the coupled products in high yield. As expected, the yields of the Heck coupling reactions with styrene and aryl chlorides with electron-deficient substituents were found to be very high. It is noteworthy that aryl chlorides are the most useful substrates because their costs are low and they are commercially available.[47]

Table 3. Heck coupling reactions of aryl halides with styrene



Entry	Y	R	X	Salt	Yield (%)
1	H	H	I	**2a**	76[a]
2	H	H	I	**2a**	99[b]
3	H	H	I	**no**	n.d[c]
4	H	H	I	**no**	09[d]
5	H	H	I	**2a**	17[e]
6	H	H	I	**2a**	48[f]
7	H	H	I	**2a**	99
8	H	H	I	**2b**	99
9	H	H	I	**2c**	97
10	H	H	I	**2d**	98
11	H	H	I	**2e**	95
12	H	H	I	**2f**	96
13	H	OCH_3	I	**2a**	97
14	H	OCH_3	I	**2b**	97
15	H	OCH_3	I	**2c**	95
16	H	OCH_3	I	**2d**	96
17	H	OCH_3	I	**2e**	93
18	H	OCH_3	I	**2f**	95
19	CH_3	CH_3	I	**2a**	97
20	CH_3	CH_3	I	**2b**	96
21	CH_3	CH_3	I	**2c**	95
22	CH_3	CH_3	I	**2d**	96
23	CH_3	CH_3	I	**2e**	93
24	CH_3	CH_3	I	**2f**	95
25	H	$COCH_3$	Br	**2a**	99
26	H	$COCH_3$	Br	**2b**	99
27	H	$COCH_3$	Br	**2c**	97
28	H	$COCH_3$	Br	**2d**	99
29	H	$COCH_3$	Br	**2e**	94
30	H	$COCH_3$	Br	**2f**	96
31	H	NO_2	Cl	**2a**	93
32	H	NO_2	Cl	**2b**	93
33	H	NO_2	Cl	**2c**	89
34	H	NO_2	Cl	**2d**	91
35	H	NO_2	Cl	**2e**	85

Yields are based on the aryl halide. Reactions were monitored by GC-MS. Conditions: temperature ramped to 80 °C (3 min) and held 5[a] min and 20[b] min. Temperature ramped to 80 °C (3 min) and held 10[c] min and 20[d] min without salt (**2a**). On preheated oil bath, 10[e] min and 20[f] min with thermal heating. n.d., Not detected.

The benzimidazolium salt bearing an electron-releasing cinnamyl and *p*-xylyl substituent (**2a** and **2b**) are the most effective of the salts examined. The piperidine and morpholine substituents on the nitrogen atoms of the benzimidazolium salts also affect the catalytic activity. The less electronegative character of nitrogen compared with oxygen may be responsible for the better catalytic activities of benzimidazolium salts in Heck coupling reactions. *Ortho*-substituents on the aryl iodide also slightly affect the reaction rates due to their steric or coordination properties (Table 3, entries 19–24). It is important to note that the ends of the all these reactions were clearly observed by black particles in the reaction mixture, which are probably palladium nanoparticles. The reactivity of the aryl halide component on Heck coupling reactions decreases in the order I > Br > Cl, which is in good agreement with previous reports.[19] However, the Heck coupling reaction with aryl chlorides with electron withdrawing substituents did not give a detectable amount of Heck coupling products in conventional heating systems.[19,48] On the contrary good yields were obtained for all aryl halides with styrene using the microwave heating system (Table 3).

Conclusions

We prepared five benzimidazolium salts bearing piperidine and morpholine substituents (**2a–f**) from 1-substituted benzimidazoles (**1a–d**) and corresponding piperidine or morpholine chlorides. The use of palladium catalyst systems including benzimidazole salts in the Heck reactions gives better yields under microwave-assisted moderate conditions and very short reaction times compared with those given in literature.[19] The Heck reactions were carried out using 300 W power microwave irradiation at 80 °C in only 10 min. It can be concluded that Heck coupling reactions may be accelerated by microwave irradiation even if aryl chlorides bearing electron-withdrawing nitro substituents, contrary to some literature information.[19,49–51]

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Supporting Information

Supporting information can be found in the online version of this article. CCDC holds the supplementary crystallographic data 782253. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax (+44) 1223-336-033; or email deposit@ccdc.cam.ac.uk.

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