Article

JOURNAL OF THE CHINESE
CHEMICAL SOCIETY

Mesoporous Silica MCM-41 Supported *N*-Heterocyclic Carbene-Pd Complex for Heck and Sonogashira Coupling Reactions

Shaheen M. Sarkar, Mashitah Mohd Yusoff and Md. Lutfor Rahman*
Faculty of Industrial Sciences & Technology, Universiti Malaysia Pahang, 26300 Gambang, Kuantan, Malaysia

(Received: Apr. 29, 2014; Accepted: Jul. 15, 2014; Published Online: ??; DOI: 10.1002/jccs.201400196)

Heterocyclic carbene-Pd complex was anchored onto the mesoporous silica MCM-41 which exhibits high catalytic activity in Heck reaction under phosphine free reaction conditions for the reaction of iodo/bromoarenes with olefinic compounds such as butyl acrylate, isopropyl acrylate and styrene. This catalytic system also showed high activity for Sonogashira coupling reaction of various aryl halides under copper, phosphine and solvent-free reaction conditions. The air and thermally stable catalyst were reused several times without significant loss of its activity. High efficiency of the catalyst along with its recycling ability and the rather low Pd-loading demonstrated in both Heck and Sonogashira coupling reactions are the merits of the presented catalyst system.

Keywords: Heck reaction; Mesoporous MCM-41; NHC-Pd catalyst; Sonogashira reaction.

INTRODUCTION

Palladium catalysts are among the most popular transition metal catalysts widely used in numerous organic syntheses and synthetic transformations.[1-4] The traditional coupling reactions are mostly catalyzed by phosphine-based palladium complexes in homogeneous solution.[5,6] One practical limit to perform homogeneous catalysis reactions is the difficulty of separation of the product from catalyst and reuse of the catalyst. In this study, heterogeneous Pd-catalyst is emerging as an alternative to the homogeneous one that suffers various limitations both commercially and environmentally. Heterogeneous catalysts have some advantages such as heat stability and ease of separation from the product when compared with homogeneous catalysts. One common strategy to prepare a heterogeneous catalyst consists of anchoring the conveniently modified transition metal complex onto an insoluble support provided the anchoring procedure and maintains the intrinsic activity and selectivity of the catalytic center.[7,8]

From these perspectives, heterogeneous catalysis seems particularly well suited since the palladium metal immobilized on a support could be easily removed by filtration leaving products virtually free of palladium residues. A number of supports such as zeolite,[9] metal oxides,[10] silica-starch,[11] polymers,[12,13] carbon nanofiber,[14] clay,[15] montmorillonite,[16] silica and magnetic mesoporous silica[17] have been used. Alternatively, molecular complexes bound to a ligand anchored on a support have also been studied as a recyclable catalyst.[18]

However, these systems do not reach the excellent activities that are observed with homogeneous catalyst and convert the interesting and broadly available aryl bromide system. In our earlier study we reported MCM-41 (Mobil Composition of Matter) supported *N*-heterocyclic carbene palladium (NHC-Pd) catalyzed Suzuki-Miyaura cross coupling reaction of aryl halide and boronic acid in aqueous *N,N'*-dimethylformamide (DMF) solution.[19] In this report, considerable effors have been made for this reaction in order to achieve a high degree of efficiency under mild reaction conditions. Herein, our recent finding is the development of highly effective heterogeneous MCM-41-supported NHC-Pd catalyst for Heck and Sonogashira coupling reactions of activated and deactivated aryl iodide and bromide under mild reaction conditions.

EXPERIMENTAL

General Information: All manipulations were performed under atmospheric conditions otherwise noted. Reagents and solvents were obtained from commercial suppliers and used without further purification. Water was deionized with a Millipore system as a Milli-Q grade. $Pd(OAc)_2$ was purchased from Aldrich chemical industries, Ltd. Proton nuclear magnetic resonance (^1H NMR, 500/400 MHz) and carbon nuclear magnetic resonance (^{13}C NMR, 125 MHz) spectra were measured with a JEOL JNM ECA-500/400 spectrometer. The ^1H NMR chemical shifts were reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C

---

* Corresponding author. Tel: +6 016 9399011; Fax: +6 09 5492766; Email: lutfor73@gmail.com

NMR chemical shifts were reported relative to deuterated chloroform ($CDCl_3$ 77.0 ppm). Elemental analyses were performed on a Yanaco CHN Corder MT-6 elemental analyzer by the chemical analysis team in Rikagaku Kenkyūjo (RIKEN), Wako, Japan. Inductively coupled plasma atomic emission spectrometry (ICP-AES) was performed on a Shimadzu ICPS-8100 equipment by the chemical analysis team in RIKEN Wako, Japan. The gas chromatography-mass spectrometry (GC-MS) was measured by an Agilent 7860A/JEOL JMS-T100GC equipped with a capillary column (DB-Wax, 0.25 mm i.d. × 30 m or HP-1, 0.32 mm i.d. × 30 m). Thin layer chromatography (TLC) analysis was performed on Merck silica gel 60 F_{254}. Column chromatography was carried out on silica gel (Wakogel C-300).

Preparation of the mesoporous MCM-41 silica: The MCM-41 was prepared according to the reported method[20] using cetyltrimethylammonium bromide as a surfactant and tetraethoxysilane as a silicate source. The MCM-41 was characterized by X-ray diffraction (XRD) and high resolution transmission electron microscopy (HRTEM) analyses.

Preparation of 1-methyl-3-[(triethoxysilyl)propyl]-imidazolium chloride 1: A 50 mL round bottomed flux was charged with (3-chloropropyl)triethoxysilane (1 g, 4.166 mmol) and 1-methyl imidazole (342 mg, 4.16 mmol) in toluene and the reaction mixture was heated at 70 °C for 3 h. The solvent was evaporated and the obtained ionic liquid was washed several times by diethylether and dried under reduced pressure to give the 1-methyl-3-[(triethoxysilyl)propyl]-imidazolium chloride in 95% yield.[21,22] ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.57 (t, J = 8.0 Hz, 2 H), 1.16 (t, J = 6.9 Hz, 9 H), 1.99 (p, J = 7.6 Hz, 2 H), 3.81 (q, J = 6.9 Hz, 6 H), 4.12 (s, 3 H), 4.20 (t, J = 7.3 Hz, 2 H), 7.35 (s, 1 H), 7.62 (s, 1 H), 10.60 (s, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 6.82, 18.12, 23.92, 36.13, 51.31, 58.12, 121.92, 124.12, 138.13.

Grafting of the NHC precursor onto mesoporous MCM-41 2: MCM-41 (1 g) was suspended into a stirred solution of *N*-1-(3-triethoxysilylpropyl)-3-methylimidazolium chloride **1** (0.22 g, 0.68 mmol) in toluene. The mixture was stirred at 105 °C for 12 h and filtrated off on a glass filter and washed with methylene chloride. After drying under vacuum at 60 °C, MCM-41-supported *N*-heterocyclic carbine **2** (1.16 g) was obtained. Elemental analysis and weight gain showed that 0.75 mmol of triethoxysilylpropylimidazolium chloride **1** was grafted onto the 1.0 g of MCM-41 silica **2** (see ESI).

Preparation of the MCM-41-supported NHC-Pd/MCM-41: $Pd(OAc)_2$ (0.94 mg, 0.42 mmol) was added to a stirred solution of MCM-41-supported NHC precursor **2** (1 g, 0.75 mmol) in *N,N′*-dimethyl sulfoxide (DMSO, 10 mL).[23] The mixture was stirred for 2.5 h at 65 °C and after stirring for an additional 1 h at 110 °C, a fine brown color powder was collected by filtration. The powder was successively washed by methylene chloride and dried under vacuum at 60 °C to give MCM-41-supported NHC-Pd/MCM-41. Elemental analysis and weight gain showed that 0.22 mmol of Pd was anchored onto 1.0 g of the catalyst NHC-Pd/MCM-41 (see ESI).

General procedure for the Heck reaction: All reactions were carried out in a 4 mL glass vial equipped with a Teflon screw cap. A mixture of aryl halide (1 mmol), olefin (1.2 mol equiv), Na_2CO_3 (2 mol equiv), and the NHC-Pd/MCM-41 (2.27 mg, 0.05 mol%) in *N,N′*-dimethylacetamide: water (DMF: H_2O, 2 + 2 mL) was stirred at 130 °C for an appropriate time, monitoring periodically by GC analysis. After completion of the reaction, it was cold at room temperature and diluted with ethyl acetate (EtOAc). The immobilized NHC-Pd/MCM-41 was separated by filtration and washed by EtOAc. The organic layer was washed by H_2O, brine and dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by short column chromatography on silica gel eluted with *n*-hexane/EtOAc afforded the desired coupled products in 92-97% yields (Tables 3 and 4).

(*E*)-3-Phenylacrylic acid *n*-butyl ester 3a[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.70 (d, J = 16.0 Hz, 1 H), 7.53-7.51 (m, 2 H), 7.39-7.36 (m, 3 H), 6.46 (d, J = 16.05 Hz, 1 H), 4.21 (t, J = 6.9 Hz, 2 H), 1.72-1.67 (m, 2 H), 1.47-1.40 (sextet, J = 7.45 Hz, 2 H), 0.96 (t, J = 7.45 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.07, 144.51, 134.45, 130.16, 1128.84, 128.02, 118.28, 64.39, 30.75, 19.17, 13.72. EI-MS m/z = 204 (M^+). **(*E*)-3-(4′-tolyl)acrylic acid *n*-butyl ester 3b**[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.67 (d, J = 16.05 Hz, 1 H), 7.43 (d, J = 8.10 Hz, 2 H), 7.19 (d, J = 8.05 Hz, 2 H), 6.40 (d, J = 16.0 Hz, 1 H), 4.20 (t, J = 6.3 Hz, 2 H), 2.36 (s, 3 H), 1.71-1.65 (m, 2 H), 1.47-1.40 (m, 2 H), 0.94 (t, J = 7.45 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.28, 144.52 140.58, 131.73, 129.57, 128.02, 117.18, 64.32, 30.77, 21.42, 19.18, 13.73. EI-MS m/z = 218 (M^+). **(*E*)-3-(4′-Methoxyphenyl)acrylic acid *n*-butyl ester 3c**[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.65 (d, J = 16.0 Hz, 1 H), 7.48 (d, J = 8.6 Hz, 2 H), 6.90 (d, J = 8.5 Hz, 2 H), 6.32 (d, J = 16.0 Hz, 1 H), 4.19 (t, J = 7.0 Hz, 2 H), 3.83 (s, 3 H), 1.71-1.65 (m, 2 H), 1.45-1.41 (sextet, J = 7.5 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.42, 161.29, 144.17, 129.66, 127.20, 115.76, 114.28, 64.23, 55.33, 30.79, 19.18, 13.73. EI-MS m/z = 234 (M^+). **(*E*)-3-(4′-Nitrophenyl)-acrylic acid *n*-butyl ester 3d**[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.25 (d, J = 8.55 Hz, 2 H), 7.72-7.66 (m, 3 H), 6.58 (d, J = 16.0 Hz, 1 H), 4.24 (t, J = 6.3 Hz, 2 H), 1.73-1.67 (m, 2 H), 1.48-1.42 (m, 2 H), 0.97 (t, J = 7.7 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.10, 148.47, 141.56, 140.59, 128.60, 124.14, 122.61, 64.90, 30.68, 19.15, 13.70. EI-MS m/z = 249 (M^+). **(*E*)-3-(4-Acetyl-**

phenyl)acrylic acid *n*-butyl ester 3e[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.97 (d, J = 8.0 Hz, 2 H), 7.71 (d, J = 16.5 Hz, 1 H), 7.621 (d, J = 8.0 Hz, 2 H), 6.54 (d, J = 16.05 Hz, 1 H), 4.22 (t, J = 6.9 Hz, 2 H), 2.61 (s, 3 H), 1.72-1.67 (m, 2 H), 1.46-1.42 (m, 2 H), 0.97 (t, J = 7.45 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.28, 166.55, 142.93, 138.79, 137.94, 128.82, 128.08, 120.82, 64.65, 30.71, 26.64, 19.15, 13.70. EI-MS *m/z* = 246 (M^{+}). **(*E*)-3-(4′-Trifluoromethylphenyl)acrylic acid *n*-butyl ester 3f**[24]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.70 (d, J = 15.0 Hz, 1 H), 7.65-7.61 (m, 4 H), 6.52 (d, J = 16.0 Hz, 1 H), 4.23 (t, J = 6.7 Hz, 2 H), 1.72-1.64 (m, 2 H), 1.48-1.40 (sextet, J = 7.5 Hz, 2 H), 0.97 (t, J = 7.45 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.48, 142.63, 137.83, 131.81 (q, J = 23.2 Hz), 128.13, 125.86 (q, J = 3.57 Hz), 124.89, 122.72, 120.86, 64.69, 30.71, 19.15, 13.69. EI-MS *m/z* = 272 (M^{+}). ***n*-Butyl trans-3-(3-pyridinyl)acrylate 3g**[25]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.75 (s, 1 H), 8.61-8.60 (m, 1 H), 7.84 (d, J = 7.5 Hz, 1 H), 7.68 (d, J = 16.1 Hz, 1 H), 7.34-7.32 (m, 1 H), 6.53 (d, J = 16.1 Hz, 1 H), 4.23 (t, J = 7.0 Hz, 2 H), 1.72-1.67 (quint, J = 6.5 Hz, 2 H), 1.47-1.40 (sextet, J = 7.5 Hz, 2 H), 0.97 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) 166.37, 150.93, 149.68, 140.78, 134.16, 130.21, 123.69, 120.48, 64.68, 30.69, 19.15, 13.70. EI-MS *m/z* = 205 (M^{+}). **(*E*)-*N*-Isopropyl-cinnamamide 3h**[25]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.62 (d, J = 15.5 Hz, 1 H), 7.48-7.47 (m, 2 H), 7.36-7.33 (m, 3 H), 6.39 (d, J = 16.6 Hz, 1 H), 5.62 (brs, 1 H), 4.26-4.19 (m, 1 H), 1.22 (d, J = 6.3 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.98, 140.63, 134.91, 129.48, 128.74, 127.68, 121.06, 41.54, 22.81. EI-MS *m/z* = 189 (M^{+}). **(*E*)-*N*-isopropyl-3-(*p*-tolyl)acrylamide 3i**[26]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (d, J = 15.5 Hz, 1 H), 7.39 (d, J = 8.0 Hz, 2 H), 7.16 (d, J = 7.45 Hz, 2 H) 6.32 (d, J = 15.45 Hz, 1 H), 5.46 (brs, 1 H), 4.25-4.19 (m, 1 H), 2.35 (s, 3 H), 1.22 (d, J = 6.3 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.15, 140.63, 139.77, 132.15, 129.48, 127.66, 119.97, 41.50, 22.85, 21.36. EI-MS *m/z* = 203 (M^{+}). **(*E*)-*N*-isopropyl-3-(4-methoxyphenyl)acrylamide 3j**[27]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58 (d, J = 16.05 Hz, 1 H),7.43 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 6.26 (d, J = 16. 0 Hz, 1 H), 5.56 (brs, 1 H), 4.25-4.18 (m, 1 H), 3.81 (s, 3 H), 1.22 (d, J = 6.85 Hz, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.31, 160.72, 140.22, 129.20, 127.62, 118.69, 114.17, 55.30, 41.46, 22.84. EI-MS *m/z* = 219 (M^{+}). **(*E*)-Stilbene 3k**[28]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (d, J = 7.4 Hz, 4 H), 7.36-7.33 (m, 4 H), 7.27-7.25 (m, 2 H), 7.10 (d, J = 11.5 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.38, 128.65, 127.6, 126.49. EI-MS *m/z* = 180 (M^{+}). **(*E*)-1-Styryl-4-(trifluoromethyl)benzene 3l** [28]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60 (m, 4 H), 7.54 (d, J = 7.7 Hz, 2 H), 7.38 (t, J = 7.4 Hz, 2 H), 7.30 (t, J = 7.5 Hz, 1 H), 7.21 (d, J = 16.5 Hz, 1 H), 7.13 (d, J = 16.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 136.62, 131.19, 128.78, 128.27, 127.11, 126.76, 126.56, 125.63 (q, J = 3.57 Hz, C-F), 123.12. EI-MS *m/z* = 248 (M^{+}). **(*E*)-4-Methylstilbene 3m**[28]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (d, J = 8.0 Hz, 2 H), 7.42 (d, J = 7.5 Hz, 2 H), 7.34 (t, J = 8.0 Hz, 2 H), 7.25-7.22 (m, 1 H), 7.16 (d, J = 8.0 Hz, 2 H), 7.07 (d, J = 4.05 Hz, 2 H), 2.36 (s, 3 H).^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.51, 134.54, 129.38, 128.64, 127.69, 127.39, 126.37, 21.23. EI-MS *m/z* = 194 (M^{+}). **(*E*)-4-Methoxystilbene 3n**[28]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.49-7.44 (m, 4 H), 7.34 (t, J = 7.5 Hz, 2 H), 7.26-7.21 (m, 1 H), 7.08 (d, J=16.0 Hz, 1 H), 6.99 (d, J = 16.5 Hz, 1 H), 6.90 (d, J = 5.0 Hz, 2 H), 3.82 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.30, 137.64, 130.14, 128.63, 128.20, 127.70, 127.20, 126.61, 126.23, 114.13, 55.31. EI-MS *m/z* = 210 (M^{+}). **(*E*)-4-Styrylbenzonitrile 3o**[28]: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.63 (d, J = 8.15 Hz, 2 H), 7.57 (d, J = 6.5 Hz, 2 H), 7.53 (d, J = 7.45 Hz, 2 H), 7.38 (m, 2 H), 7.31 (t, J = 7.45 Hz, 1 H), 7.23 (t, J = 16.6 Hz, 1 H), 7.10 (d, J = 16.6 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.81, 136.26, 132.46, 132.38, 128.84, 128.62, 126.89, 126.83, 126.70, 119.00, 110.56. EI-MS *m/z* = 205 (M^{+}).

General procedure for Sonogashira reaction: Aryl halide (1 mmol), phenylacetylene (1.2 mol equiv), piperidine (2 mol equiv) and the NHC-Pd/MCM-41 (1 mg, 0.02 mol%) was stirred at 85 °C for an appropriate time monitoring periodically by GC analysis. The reaction mixture was cold at room temperature and diluted with EtOAc and the immobilized Pd catalyst was separated by filtration. The organic layer was washed by H_2O and dried over $MgSO_4$. Solvent was evaporated under reduced pressure and the residue was purified by short column chromatography on silica gel eluted with *n*-hexane/EtOAc to afford the corresponding coupling products in up to 95% yields (Table 5).

Diphenylacetylene 4a[29]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.52-7.47 (m, 4H), 7.35-7.28 (m, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 131.5, 128.1, 128.1, 123.2, 89.6. EI-MS *m/z* = 178 (M^{+}). **4-Methoxyphenyl-phenylacetylene 4b**[30]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.51-7.47 (m, 4 H), 7.35-7.31 (m, 3 H), 6.85 (dd, J = 8.78, 2.2 Hz, 2 H), 3.83 (s, 3 H).^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.3, 133.2, 131.2, 128.4, 127.8, 123.6, 115.4, 114.0, 89.4, 88.1, 55.2. EI-MS *m/z* = 208 (M^{+}). **Phenyl-*p*-tolyacetylene 4c**[31]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.51-7.49 (m, 2 H), 7.42 (d, J = 7.89 Hz, 2 H), 7.32-7.26 (m, 3 H), 7.12 (d, J = 7.88 Hz, 2 H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 138.2, 131.4, 129.2, 128.3, 128.3, 123.4, 120.3, 89.7, 88.6, 21.5. EI-MS *m/z* = 192 (M^{+}). **4-Acetylphenyl-phenylacetylene 4d**[32]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.92 (d, J = 8.49Hz, 2 H), 7.60 (d, J = 8.49 Hz, 2 H), 7.55-7.53 (m, 2H), 7.37-7.34 (m, 3 H), 2.59 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 197.2, 136.3, 131.9, 131.7, 128.9, 128.6, 128.1, 128.1, 122.5, 92.8, 88.4, 26.7. EI-MS *m/z* = 220 (M^{+}).

4-Nitrophenyl-phenylacetylene 4e[33]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.20 (d, *J* = 8.92 Hz, 2 H), 7.65 (d, *J* = 8.90 Hz, 2 H), 7.57-7.54 (m, 2 H), 7.41-7.37 (m, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 147.1, 132.1, 131.9, 130.3, 129.3, 128.6, 123.8, 122.1, 94.8, 87.6. EI-MS *m/z* = 223 (M^+). **4-Cyanophenyl-phenylacetylene 4f**[34]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.66-7.59 (m, 4 H), 7.57-7.54 (m, 2 H), 7.41-7.38 (m, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 132.1, 131.7, 129.2, 128.6, 128.3, 122.3, 118.6, 111.5, 93.8, 87.8. EI-MS *m/z* = 203 (M^+). **4-Trifluoromethylphenyl-phenylacetylene 4g**[35]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.64-7.61 (m, 4 H), 7.58-7.55 (m, 2 H), 7.38-7.35 (m, 3 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 131.9, 131.8, 130.0 (*J* = 54.66 Hz), 128.9, 128.5, 127.2 (*J* = 2.0 Hz), 125.4 (*J* = 6.16 Hz), 123.8, 122.6, 91.8, 87.7. EI-MS *m/z* = 246 (M^+).

RESULTS AND DISCUSSION

Preparation and characterization of the NHC-Pd/MCM-41

According to our previous work,[19] we have synthesized MCM-41-supported NHC-Pd/MCM-41 complex which processes a three methylene spacer between the nitrogen atom of NHC and MCM-41 silica backbone. The attachment of NHC-Pd complex onto MCM-41 was carried out in two step reactions (see ESI Scheme 1).

In the first step, ionic liquid **1** was heated with MCM-41 silica for 12 h in refluxing toluene. The incorporation of the NHC precursor was confirmed by both nitrogen analysis and weight gain provided MCM-41-supported NHC precursor **2** with loading ratio of 0.75 mmol/g. The MCM-41 supported NHC precursor **2** was then treated with $Pd(OAc)_2$ (84 mg, 0.375 mmol) in DMSO at 65 °C for 2.5 h and 110 °C for 1 h. The resultant brown color MCM-41-supported NHC-Pd/MCM-41 was filtrated on a glass filter and washed by methylene chloride and dried under vacuum at 60 °C to give MCM-41-supported NHC-Pd/MCM-41. Elemental analysis and weight gain showed that 0.22 mmol of Pd was anchored onto 1.0 g of the NHC-Pd/MCM-41. The amount (0.22 mmol/g) of palladium in the catalyst NHC-Pd/MCM-41 was further determined by ICP-AES analysis. D. H. Lee et al. reported that *N*-heterocyclic carbene can form a rigid and stable complex with Pd(II), and NHC-Pd catalyst contains only Pd(II) with no Pd(0). It was also confirmed that the palladium was immobilized specifically to the imidazolium ligand in the forms of Pd(NHC)OAcCl (major) and $Pd(NHC)Cl_2$(minor).[36] The HRTEM image (Fig. 1a) obtained after the modification of the parent MCM-41 and after reuse (Fig. 1b) of the NHC-Pd/MCM-41.

Both images showed that the hexagonal symmetry of the pore arrays is conserved after the immobilization of NHC-Pd complex onto the MCM-41 and there is no change after the reuse of the NHC-Pd/MCM-41. This mesoporous character is also confirmed by XRD (see ESI Fig. 1c). Apparently, there is less change of the lattice parameters upon the immobilizing process. However, the surface area, pore volume and pore size decreased due to the grafting of organic moieties onto the mesoporous silica MCM-41 (Table 1).

Initial screening of catalytic performance in the Heck reaction

The heterogeneous MCM-41 supported NHC-Pd/MCM-41 was tested for its activity in the Heck coupling reaction. The coupling of iodobenzene with butyl acrylate in the presence of Na_2CO_3 with 1.5 mol% of NHC-Pd/MCM-41 was initially chosen as a model reaction (Table 2, entry 1). The catalyst showed high activity and provided corresponding coupling product in quantitative yield within 1 h reaction time. The rate of coupling is dependent on a variety of parameters such as solvent, base and catalyst loading. Thus, the reaction conditions were systematically optimized, and the results are presented in Table 2. The catalyst loading could be decreased even further, 1 to 0.01 mol%, when 1 to 5 h reaction time was required to complete the reaction (entries 2-6).

It was found that the best system for the reaction was DMA: H_2O in combination with Na_2CO_3 at 130 °C which delivered a 98% yield of the product within 2 h when 0.05 mol% of NHC-Pd/MCM-41 was used (entry 5). The catalyst loading could be decreased even further, 0.01 mol%, when longer reaction time is required to complete the reaction. The high conversion could be still maintained at 0.01 mol% of ultra-low Pd catalyst loading (entry 6). Further optimization of the reaction condition was not attempted

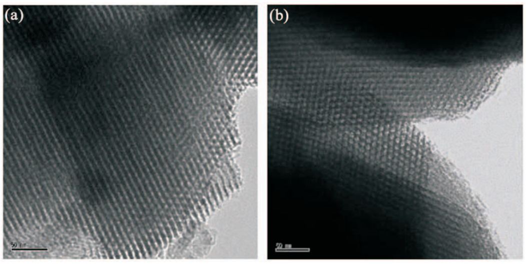
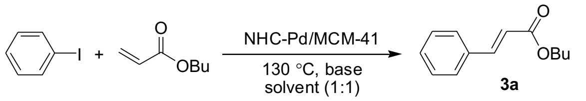


Fig. 1. (a) HRTEM image of MCM-41-supported NHC-Pd/MCM-41 before use and (b) after use of NHC-Pd/MCM-41.

Table 1. Physical property of MCM-41-supported NHC-Pd/MCM-41

Sample	Surface area	Pore diameter	Pore volume	Pd loading
MCM-41	890 m^2/g	2.2 nm	0.78 m^3/g	-
NHC-Pd/MCM-41	554 m^2/g	1.82 nm	0.45 m^3/g	0.22 mmol/g

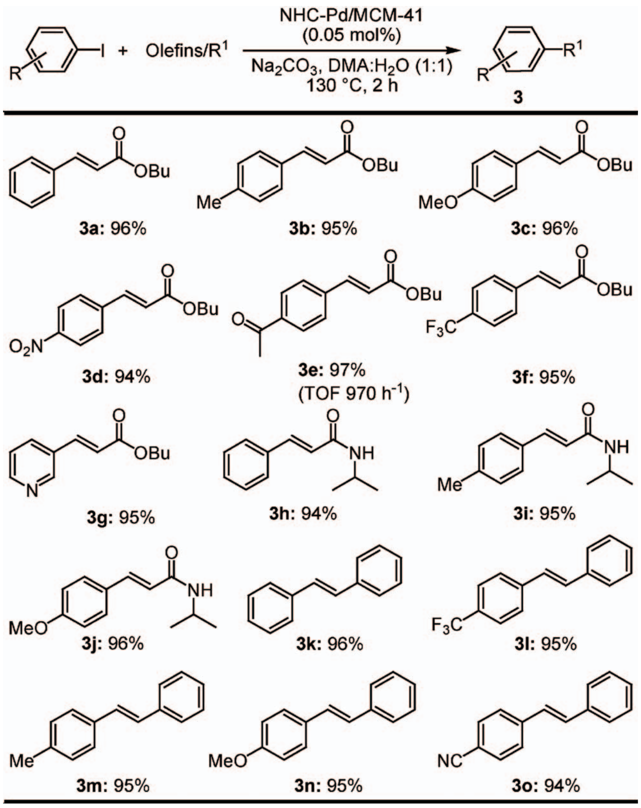
Table 2. Heck coupling of iodobenzene with butyl acrylate[a]



Entry	Solvent (1:1)	Base	Catalyst (mol%)	Time (h)	Yield (%)[b]
1	DMA:H_2O	Na_2CO_3	1.5	1	100
2	DMA:H_2O	Na_2CO_3	1.0	1	98(95)[c]
3	DMA:H_2O	Na_2CO_3	0.3	1.5	97
4	DMA:H_2O	Na_2CO_3	0.1	1.5	97
5	DMA:H_2O	Na_2CO_3	0.05	2	98(96)[c]
6	DMA:H_2O	Na_2CO_3	0.01	5	88 (85)[c]
7	DMA:H_2O	K_2CO_3	1.0	1	93
8	DMA:H_2O	NaOMe	1.0	1	94
9	DMA:H_2O	K_2PO_4	1.0	1	95
10	DMF:H_2O	Na_2CO_3	1.0	1	92
11	DMSO:H_2O	Na_2CO_3	1.0	1	94
12	NMP:H_2O	Na_2CO_3	1.0	1	95
13	Toluene:H_2O	Na_2CO_3	1.0	3.5	82

[a] Reactions were carried using 1 mmol of iodobenzene, 1.2 mol equiv of butyl acrylate, a catalytic amount of NHC-Pd/MCM-41 and 2 mol equiv of base in 4 mL of solvents. [b] GC yield determined using *n*-dodecane as an internal standard. [c] Isolated yield.

Table 3. NHC-Pd/MCM-41 catalyzed Heck reaction of aryl iodides with olefins[a]



[a] All reactions were carried using 1 mmol of aryl iodide, 1.2 mol equiv of olefin, 0.05 mol% of NHC-Pd/MCM-41, 2 mol equiv of Na_2CO_3, in 4 mL of DMA/H_2O (1:1) at 130 °C for 2 h.

due to the less amount of catalyst is required.

When the reaction was conducted in aqueous solution of DMF, DMSO, *N*-methyl-2-pyrrolidone (NMP) instead of DMA, in the presence of different bases, similar results were obtained under the same reaction conditions (entries 7-12). A longer reaction time is required when aqueous non-polar solvent (toluene: H_2O) was used (entry 13). The presence of water appears to be necessary due to the low solubility of bases in organic solvents.

With these results in hand, several Heck coupling of aryl iodides with different acrylates were then tested, and the results are summarized in Table 3. Iodobenzene react with butyl acrylate, to give the corresponding coupling product **3a** in 96% isolated yield. Excellent catalytic activity were observed in the couplings of deactivated 4-iodotoluene, 4-iodoanisole (**3b, c**) as well as activated 4-iodonitrobenzene, 4-iodoacetophenone and 4-trifluoromethyliodobenzene with butyl acrylate (**3d-f**). The deactivated aryl iodides possessing electron-donating group showed a slight drop in reactivity compared to the activated aryl iodides possessing electron-withdrawing group. The coupling of 3-iodopyridine with butyl acrylate was also excellent (**3g**). The high turnover frequency (TOF, 970 h^{-1}) value was obtained in the coupling of 4-iodoacetophenone and butyl acrylate (**3e**). The Heck coupling reaction of aryl iodides was also efficiently promoted to afford the corresponding products when isopropyl acrylamide was used as a coupling partner (**3h-j**). The bulky coupling partner styrene was also testified in this coupling reaction. All activated and deactivated aryl iodides provided the corresponding coupling products with excellent yields (**3k-o**).

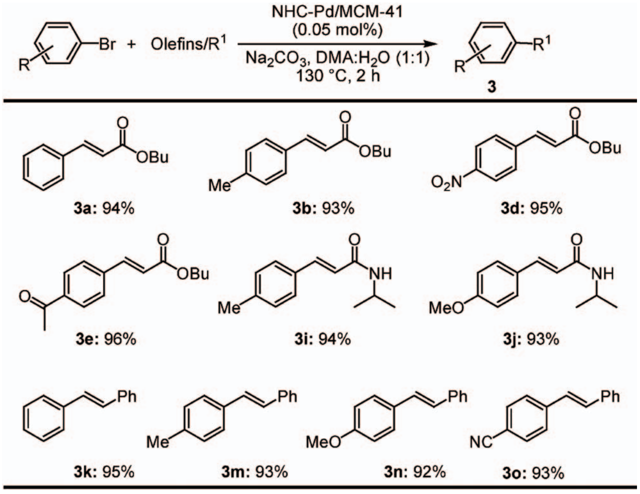
In addition, all the reactions provided approximately similar efficiency with regard to the various olefins. To give an idea of a recent similar work, Yao and co-workers obtained good yields in the Heck coupling of aryl halides and olefins using polymer-supported diphenylphosphine-

Pd complex. However, the catalytic system required longer reaction time and special equipment due to the phosphine-based ligands.[37]

The development of effective catalysts for the carbon-carbon bond formation of olefins with aryl bromides is highly important, since these are interesting substrates for industrial applications. Using diol-functionalized imidazolium ionic liquids along with $PdCl_2$, Cai et al.[38] observed moderate yields in the Heck reaction of aryl bromides with various alkenes but the reaction rates were quite slow. By observing the promising catalytic activity of NHC-Pd/MCM-41 for various aryl iodides, the catalyst was investigated for the coupling of aryl bromides and olefins. It was found that the catalyst showed outstanding activity in the coupling of bromobenzene, 4-bromotoluene, 4-nitro bromobenzene and 4-bromoacetophenone with butyl acrylate (Table 4, **3a, b, d, e**). A catalyst loading of 0.05 mol% was sufficient to achieve the high conversion within 2 h.

The Heck reaction of aryl bromides with isopropyl acrylamide and styrene were also efficiently promoted to give the corresponding coupling products in up to 95% yield (**3i-k, m-o**).

Table 4. NHC-Pd/MCM-41 catalyzed Heck reaction of aryl bromides with olefins[a]

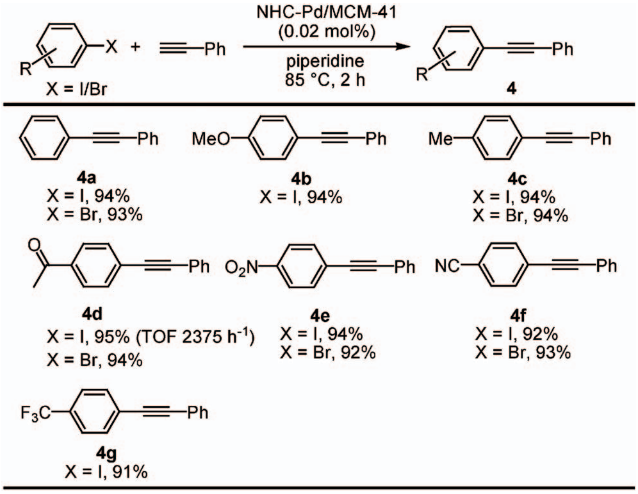


[a] All reactions were carried using 1 mmol of aryl bromide, 1.2 mol equiv of olefin, 0.05 mol% of NHC-Pd/MCM-41, 2 mol equiv of Na_2CO_3, in 4 mL of DMA/H_2O (1:1) at 130 °C for 2 h.

Heterogeneous Sonogashira cross-coupling reaction

Sonogashira cross-coupling of an aryl halides and a terminal alkynes are useful tool for the synthesis of aryl-substituted acetylene compounds.[39] This method has been widely used for the synthesis of natural products,[40] biologically active molecules[41] nonlinear optical materials and molecular electronics[42] dendrimeric and polymeric materials[43] macrocycles with acetylene links[44] and polyalkynylated molecules.[45] With the heterogeneous Pd catalyst in hand, we investigated its catalytic activity towards Sonogashira coupling reaction of various aryl iodides with phenylacetylene in the presence of piperidine. The results are summarized in Table 5. The supported Pd catalyst promoted the Sonogashira coupling reaction using only 0.02 mol% of NHC-Pd/MCM-41 under solvent-free conditions (Table 5). The high TOF (**4d**, 2375 h^{-1}) was obtained when 4-iodoacetophenone was as an aryl halide. It is worth to note that the catalytic activities in the coupling of bromobenzene and substituted bromobenzenes were also excellent. The results came as a bit of a surprise since most of the reactions were complete within a very short time with nearly 100% conversion and 100% selectivity.

Table 5. NHC-Pd/MCM-41 catalyzed Sonogashira reaction of aryl halides[a]

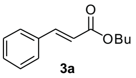
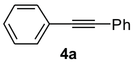


[a] All reactions were carried using 1 mmol of aryl halide, 1.2 mol equiv of phenyl acetylene, 0.02 mol% of NHC-Pd/MCM-41, 2 mol equiv of piperidine under solvent free condition at 85 °C for 2 h.

Recycling of the catalyst

The recycling of the catalyst is an important issue in heterogeneous catalysis. Again, we turn our attention to reusability of our Pd catalyst. Catalyst was reused five times in the reactions of iodobenzene with acrylate and phenylacetylene. The NHC-Pd/MCM-41 was recovered and reused by the following steps: the reaction mixture was cooled to room temperature and diluted with EtOAc and filtered. The solid catalyst was washed with dichloromethane and dried at 80 °C under vacuum, and then used in

Table 6. Heck and Sonogashira reaction with recycle catalyst NHC-Pd/MCM-41[a]

Reaction	Run	Yield (%)
Heck  **3a**	1	96
	2	96
	3	94
	4	92
	5	91 (<0.2 ppm Pd was leached out)
Sonogashira  **4a**	1	94
	2	93
	3	93
	4	90
	5	88

[a] Reactions were carried out according to Table 3 and 5.

the next run without changing the reaction conditions. After carrying out the reaction, the catalyst had consistent catalytic activity as shown in Table 6. Only slight loss of catalytic activity was observed under the same reaction conditions as for initial run. The slight loss of catalyst activity after cycles case may be due to the loss of palladium from the support during the reaction. Thus, it is reasonable to believe that the immobilized catalyst can be repeatedly used for large-scale production without significant loss of its catalytic activity.

Heterogeneity test

In order to check the heterogeneity (Table 3, **3a**) of the catalyst, we considered two experiments: (a) to determine the Pd content in the solution, a part of the filtrate was placed in a 50 mL crucible after removing the solvent it was calcined at 600 °C for 3 h. The residue was dissolved in 20 mL aqua-regia and diluted to 50 mL. The Pd leaching in solution was determined by inductively coupled plasma mass spectrometry (ICP-MS) analysis. It revealed that the leaching of Pd from the complex into the solution was lower than 0.20 ppm, which suggests the heterogeneous nature of the prepared NHC-Pd/MCM-41 catalyst. (b) The reaction was carried out in a similar manner as the general procedure for Heck reaction (Table 3, **3a**). After 50% conversion of the starting material the reaction mixture was filtered off and the aqueous solution was heated under identical reaction conditions for an additional 1 h and analyzed for further conversion. No starting material was converted to the corresponding product after removal of the catalyst (Fig. 2). This experiment also indicated that the Heck reactions we investigated followed a heterogeneous pathway.

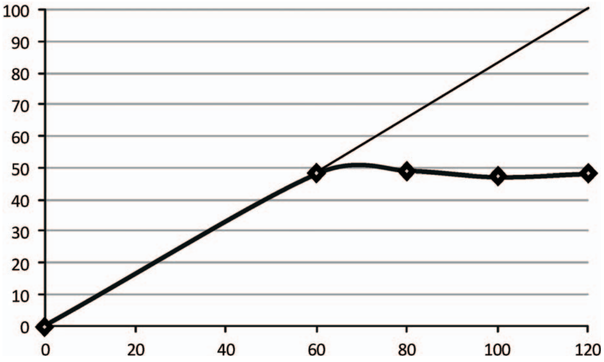


Fig. 2. Hot filtration test of iodobenzene with butyl acrylate (Table 3, **3a**).

CONCLUSIONS

In conclusion, we have synthesized MCM-41-supported NHC-Pd catalyst and it has been applied to the Heck and Sonogashira coupling reactions of activated and deactivated aryl iodides and bromides. The NHC-Pd catalyst promoted both of these reactions with high catalytic activity. The heterogeneity studies disclosed that the reaction occurs at the heterogeneous pathway. The catalyst was recovered from the reaction by simple filtration and used for five times without significant loss of activity. This catalyst can be regarded as an important step toward a simple system with the potential for commercial exploitation of heterogeneous catalysts in the coupling reactions.

ACKNOWLEDGEMENT

This work is supported by University Malaysia Pahang, fund no. RDU 140343. The authors are grateful to Professor Myung-Jong Jin, Inha University, South Korea and Professor Yasuhiro Uozumi, RIKEN, Wako, Japan for giving us valuable guidelines in this work.

REFERENCES

1. Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.
2. Lamblin, M.; Hardy, L. N.; Hierso, J. C.; Fouquet, E.; Felpin, F. X. *Adv. Synth. Catal.* **2010**, *352*, 33.
3. Dahan, A.; Portnoy, M. *J. Am. Chem. Soc.* **2007**, *129*, 5860.
4. Sarkar, S. M.; Alam, Md. N.; Miah, Md. R. *React. Kinet. Catal. Lett.* **2009**, *96*, 175.
5. Nadri, S.; Joshaghani, M.; Rafiee, E. *Appl. Catal. A: Gen.* **2009**, *362*, 163.
6. Anastas, P. T.; Kirchhoff, M. M. *Acc. Chem. Res.* **2002**, *35*, 686.
7. Vassylyev, O.; Chen, J.; Panarello, A. P.; Khinast, J. G. *Tetrahedron Lett.* **2005**, *46*, 6865.
8. Alam, Md. N.; Sarkar, S. M.; Miah, Md. R. *React. Kinet.*

Catal. Lett. **2009**, *98*, 383.

9. Choi, M.; Lee, D. H.; Ryoo, R. *Angew. Chem. Int. Ed.* **2009**, *48*, 3673.
10. Su, F. Z.; Liu, Y. M.; Cao, Y.; Fan, K. N. *Angew. Chem. Int. Ed.* **2008**, *47*, 334.
11. Nezhad, A. K.; Panahi, F. *Green. Chem.* **2011**, *13*, 2408.
12. Karimi, B.; Behzadnia, H.; Farhangi, E.; Jafari, E.; Zamani, A. *Curr. Org. Synth.* **2010**, *7*, 643.
13. Firouzabadi, H.; Iranpoor, N.; Kazemi, F.; Gholinejad, M. *J. Mol. Catal. A: Gen.* **2012**, *357*, 154.
14. Zhu, J.; Zhou, J.; Zhao, T.; Zhou, X.; Chen, D.; Yuan, W. *Appl. Catal. A: Gen.* **2009**, *352*, 243.
15. Datta, K. K. R.; Eswaramoorthy, M.; Rao, C. N. R. *J. Mater. Chem.* **2007**, *17*, 613.
16. Sidhpuria, K. B.; Patel, H. A.; Parikh, P. A.; Bahadur, P.; Bajaj, H. C.; Jasra, R. V. *Appl. Clay Sci.* **2009**, *42*, 386.
17. Li, J.; Zhang, Y.; Han, D.; Gao, Q.; Li, C. *J. Mol. Catal. A: Chem.* **2009**, *298*, 31.
18. Jin, L.; Liebscher, J. *Chem. Rev.* **2007**, *107*, 133.
19. Alam, Md. N.; Sarkar, S. M. *Reac. Kinet. Mech. Cat.* **2011**, *103*, 493.
20. Gallis, K. W.; Landry, C. C. *Chem. Mater.* **1997**, *9*, 2035.
21. Gadenne, B.; Hesemann, P.; Moreau, J. J. E. *Chem. Commun.* **2004**, *15*, 1768.
22. Brenna, S.; Posse, T.; Furrer, J.; Blumel, J. *Chem. Eur. J.* **2006**, *12*, 2880.
23. Herrmann, W. A.; Schwarz, J.; Gardiner, M. G. *Organometallics* **1999**, *18*, 4082.
24. Mino, T.; Shirae, Y.; Sasai, Y.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 6834.
25. Iranpoor, N.; Firouzabadi, H.; Motevalli, S.; Talebi, M. J. *Organomet. Chem.* **2012**, *708-709*, 118.
26. Sarkar, S. D.; Studer, A. *Org. Lett.* **2010**, *9*, 1992.
27. Huang, Z. Z.; Wen, L. W.; Huang, X. *Synth. Commun.* **1990**, *17*, 2579.
28. Xu, H. J.; Zhao, Y. Q.; Zhou, X. F. *J. Org. Chem.* **2011**, *76*, 8036.
29. Carpino, L. A.; Chen, H. W. *J. Am. Chem. Soc.* **1979**, *101*, 390.
30. Huggins, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 3002.
31. Paquett, L. A.; Wittenbrook, L. S. *J. Am. Chem. Soc.* **1967**, *89*, 4483.
32. Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **1999**, *12*, 3305.
33. Hunter, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5765.
34. Yoshida, K.; Fueno, T. *J. Org. Chem.* **1973**, *38*, 1045.
35. Kiplinger, J. L.; King, M. A.; Fechtenkötter, A.; Arif, A. M.; Richmond, T. G. *Organometallics* **1996**, *15*, 5292.
36. Lee, D. H.; Kim, J. H.; Jun, B. H.; Kang, H.; Park, J.; Lee, Y. S. *Org. Lett.* **2008**, *10*, 1609.
37. Yao, C.; Li, H.; Wu, H.; Liu, Y.; Wu, P. *Catal. Commun.* **2009**, *10*, 1099.
38. Cai, Y.; Liu, Y. *Catal. Commun.* **2009**, *10*, 1390.
39. Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.
40. Paterson, I.; Davies, R. D. M.; Marquez, R. *Angew. Chem. Int. Ed.* **2001**, *40*, 603.
41. Cosford, N. D. P.; Tehrani, L. Roppe, J.; Schweiger, E.; Smith, N. D.; Anderson, J.; Bristow, L.; Brodkin, J.; Jiang, X.; McDonald, I.; Rao, S.; Washburn, M.; Varney, M. A. *J. Med. Chem.* **2003**, *46*, 204.
42. Brunsveld, L.; Meijer, E. W.; Prince, R. B.; Moore, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 7978.
43. Li, J.; Ambroise, A.; Yang, S. I.; Diers, J. R.; Seth, J.; Wack, C. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 8927.
44. Höger, S.; Rosselli, S.; Ramminger, A. D.; Enkelmann, V. *Org. Lett.* **2002**, *4*, 4269.
45. Onitsuka, K.; Fujimoto, M.; Ohshiro, N.; Takahashi, S. *Angew. Chem. Int. Ed.* **1999**, *38*, 689.