

Carbon coated magnetic nanoparticles as supports in microwave-assisted palladium catalyzed Suzuki-Miyaura couplings

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Abstract

A palladium bis-*N*-heterocyclic carbene complex was immobilized on polystyrene modified, magnetic carbon coated iron nanoparticles and evaluated in Suzuki-Miyaura cross-coupling reactions under conventional and microwave heating. Under the latter conditions, both aryl bromides and aryl chlorides could be employed as substrates at low loading of catalyst (0.2 mol%), which could be readily recovered by an external magnet and reused in at least four cycles. As a possible deactivation pathway of the catalyst, the formation of palladium nanoparticles in the course of the reaction that became encapsulated in the polystyrene matrix of the support is suggested.

Keywords: magnetic nanoparticles; microwave irradiation; palladium-*N*-heterocyclic carbene catalysts; recyclable catalyst; Suzuki-Miyaura coupling.

1. Introduction

The development of efficient catalytic processes is an important quest in sustainable chemistry. Reactivity, as expressed in turnover numbers and cycles of a catalyst, selectivity as well as low energy consumption are criteria to strive towards this goal. The immobilization of catalysts on heterogeneous supports is a widely employed strategy to increase turnover numbers by allowing facile recycling and reuse of the catalyst [1]. Nevertheless, employing conventional polymers as supports is often accompanied by reduced activity of catalysts due to inaccessibility of active sites being buried in the polymer backbone and reduced mass transfer due to heterogenization. Moreover, the mechanical properties of polymer supports are not always optimal, which can lead to their degradation in the

course of handling a reaction mixture by stirring or filtration procedures. Magnetic nanoparticles have been recognized as attractive supports for catalysts owing to their good surface accessibility and facile recovery by applying an external magnetic field [2–4]. In particular, carbon coated iron and cobalt nanoparticles have been found to display especially high thermal stability as well as tolerance against basic or acidic reaction conditions [5–11]. We therefore wanted to combine such nanoparticles with a highly stable metal complex to arrive at recyclable catalysts that might be suitable for their utilization under forcing thermal conditions. Palladium-*N*-heterocyclic carbene (NHC) complexes in particular exhibit high stability against heat, moisture and air [12]. As a suitable benchmark we were intrigued by recent studies demonstrating that complexes such as **1** or **2** (Figure 1) are highly stable and show good activity in cross-coupling and Heck reactions with aryl bromides but not with aryl chlorides [13–15].

2. Experimental

2.1. General

Microwave experiments were carried out in a CEM Discover® S-Class apparatus, inductively coupled plasma optical emission spectrometry (ICP-OES) measurements were performed with Spectro Analytical Instruments ICP Modula EOP and transmission electron spectroscopy (TEM) measurements with LEO912AB electron microscope (Zeiss, Oberkochen, Germany) operating at 100 kV.

2.2. 3,3'-(5-Hydroxy-1,3-phenylene)bis(methylene)bis(1-mesityl-1H-imidazol-3-ium) bromide (**5**)

Seven hundred and eleven milligram (2.54 mmol) 3,5-bis(bromomethyl)phenol (**3**) [16] and 946 mg (5.08 mmol, 2.0 equiv.) 1-mesityl-1H-imidazole (**4**) [17] were stirred in 5 ml MeCN at 90°C in a sealed tube for 1 h. After cooling down to ambient temperature the white precipitate was washed thrice with MeCN and acetone to yield 1.42 g (2.2 mmol, 86%) **5** as a white solid. ¹H-NMR (300 MHz, DMSO): δ=10.01 (s, 1H), 9.71 (s, 2H), 8.11 (s, 2H), 8.00 (s, 2H), 7.15 (s, 4H), 7.07 (s, 1H), 6.84 (s, 2H), 5.52 (s, 4H), 2.33 (s, 6H), 2.01 (s, 12H); ¹³C-NMR (75 MHz, DMSO): δ=158.3, 140.2, 137.6, 136.7, 134.1, 131.0, 129.2, 124.1, 123.2, 118.4, 115.2, 108.4, 51.9, 20.5, 16.9; IR (neat) ν=3387, 3061, 1703, 1601, 1557, 1497, 1456, 1355, 1310, 1231, 1147, 1107, 1030, 1009, 876, 749, 714, 698, 663; MS (EI): m/z=246.0 (M²⁺); HRMS (EIMS) [M²⁺]: found 246.1450, calculated 246.1439; m.p.: 145°C (decomposition).

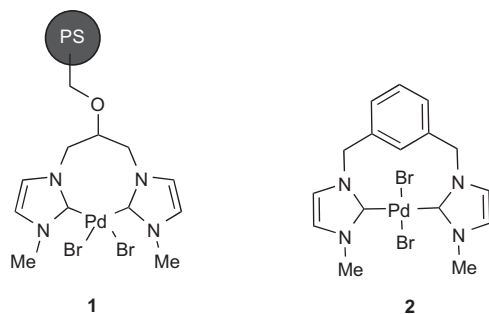


Figure 1 Successful bis-NHC-palladium complexes for Suzuki-Miyaura couplings of aryl bromides [12–14].

2.3. (3,3'-(5-Hydroxy-1,3-phenylene)bis(methylene)bis(1-mesityl-1H-imidazolium-2,2'-diylidene))palladium(II)-dichloride (7)

To 250 mg (0.38 mmol) of (5) in 10 ml dichloromethane (DCM), 98 mg (0.42 mmol, 1.1 equiv.) of Ag_2O were added. The slurry was stirred for 4 h under the exclusion of light. Subsequent filtration through a syringe filter and evaporation of the solvent furnished **6** as a white powder, which was used as such in the next step. **6** was dissolved in 10 ml of degassed dichloromethane followed by addition of 110 mg (0.38 mmol) of $\text{PdCl}_2(\text{cod})$, and the reaction mixture was stirred for 16 h. Filtration through a syringe filter and subsequent evaporation of the solvent furnished a yellow powder which was purified by precipitation from a saturated dichloromethane solution with pentane. Centrifugation of the precipitate and subsequent recrystallization from CHCl_3 gave 219 mg (0.33 mmol, 86%) of **7** as amorphous yellow platelets. $^1\text{H-NMR}$ (300 MHz, DMSO): $\delta=7.35\text{--}6.93$ (m, br, 5H), 6.93–6.41 (m, br, 7H), 5.80–5.39 (m, br, 2H), 5.24 (m, br, 2H), 2.43 (m, br, 3H), 2.30 (m, br, 1H), 2.08 (m, br, 5H), 1.97 (m, br, 3H), 1.82 (m, br, 7H); IR (neat) $\nu=2916$, 1598, 1487, 1448, 1415, 1297, 1233, 1160, 1033, 968, 934, 848, 728, 702; MS (ESMS): $[\text{M}^{2+}\text{-}2\text{Cl}^-\text{-H}^+]$ $m/z=593.3$, 594.1, 595.2, 597.1, 599.1, 600.1; CHN ($\text{C}_{32}\text{H}_{34}\text{Cl}_2\text{N}_4\text{OPd}$): calculated: C 57.54, H 5.13, N 8.39, found: C 58.12, H 5.37, N 7.26; m.p.: $>200^\circ\text{C}$ (decomposition).

2.4. Synthesis of **9** by immobilization of **7** on polystyrene modified, carbon coated iron nanoparticles **8**

To 25 mg (corresponding to 0.095 mmol benzyl chloride functionalities) of **8** in 3 ml DMF were added 70 mg (0.105 mmol, 1.1 equiv.) **7** and 30 mg (0.22 mmol, 2.0 equiv.) of K_2CO_3 . After vigorously stirring at 60°C for 18 h, the particles were recovered by the aid of an external magnet and subsequently washed with acetone, water, acetone and dichloromethane. After drying under reduced pressure 37 mg of the particles with a loading of 0.6 mmol/g (ICP-OES) was obtained. IR (neat) $\nu=3651$, 2915, 2117, 1748, 1664, 1596, 1510, 1487, 1448, 1413, 1381, 1357, 1291, 1235, 1151, 1034, 1015, 931, 847, 810, 726, 700, 654; elemental microanalysis (%): C, 70.71; H, 4.43; N, 3.92.

2.5. General procedure for Suzuki-Miyaura cross-coupling reactions with the supported catalyst **9**

A mixture of **9** (3 mg, 0.2 mol%), arene R-X (1.0 mmol), boronic acid (1.1 mmol, 1.1 equiv.) and K_2CO_3 or Cs_2CO_3 (2.0 mmol, 2 equiv.) as detailed in Tables 1 or 2 in toluene (2 ml) was stirred at 70°C or heated in a closed microwave vessel at a constant power of 200 W for the indicated time. The catalyst was retained after the reaction in the vessel by applying an external magnet, the reaction mixture was decanted, and the reaction vessel containing the nanoparticles was washed with toluene, MeOH, water and MeOH (5 ml each). The combined organic fractions were extracted with water (10 ml), dried (Na_2SO_4), filtered, concentrated under reduced pressure and the residues were purified by column chromatography. The recovered catalyst was dried under reduced pressure and subsequently subjected to the next run.

3. Results and discussion

To arrive at a suitable magnetic nanoparticle supported analog to **2**, we prepared the palladium complex **7** that was attached onto polystyrene modified, carbon coated iron particles ($\text{PS}@C@Fe\text{-NP}$, **8**) [18] to give the nanocatalyst **9** with a loading of 0.6 mmol Pd/g (Scheme 1).

9 was first evaluated in Suzuki cross-couplings applying thermal heating (Table 1). At 0.2 mol% catalyst concentration, for a variety of aryl bromides quantitative conversion and high yields in the coupling with phenyl boronic acids was reached within 12 h. **9** could be readily recovered by applying an external magnet to the reaction vessel and decantation of the reaction solution and

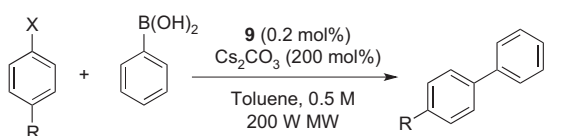
Table 1 Suzuki-Miyaura reaction catalyzed by **9** under conventional heating conditions^a.

Entry	Run	R ¹	R ²	Conversion ^b (%)
1	1	4-OMe	H	>95
2	2	4-OMe	H	>95
3	3	4-OMe	H	>95
4	4	4-OMe	H	>95
5	5	4-OMe	H	>95
6	6	4-OMe	H	>95
7	1	2,6-Me	H	61 ^c
8	2	4-NO ₂	H	95 ^c
9	3	4-C(O)Me	H	93 ^c
10	4	H	Me	91 ^c
11	5	4-OMe	H	89 ^c

^aReaction conditions: 0.5 mmol aryl halide, 0.55 mmol arylboronic acid, 1.0 mmol K_2CO_3 , 0.2 mol% starting concentration of catalyst **9** (series 1, entries 1–6; series 2, entries 7–11), 2 ml toluene, 70°C , 12 h.

^bDetermined by $^1\text{H-NMR}$.

^cIsolated yield after column chromatography.

Table 2 Suzuki-Miyaura reaction catalyzed by **9** under microwave conditions^a.


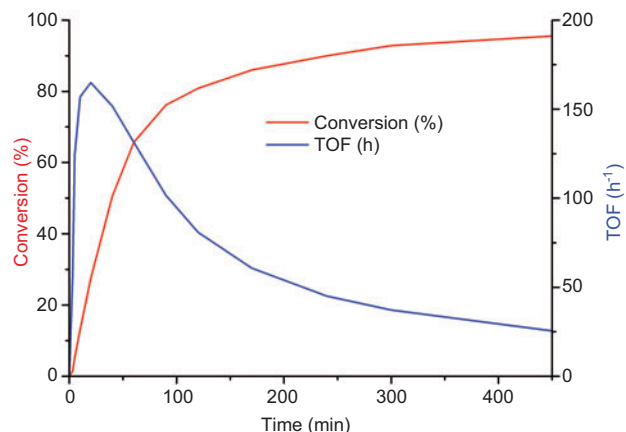
Entry	Cycle	Aryl halide		Time (min)	Yield ^b (%)
		R	X		
1	1	Me	I	5	98
2	2	MeO	Br	20	96
3	3	MeO	Br	20	94
4	4	MeO	Br	20	95
5	1	C(O)Me	Cl	60	95
6	2	C(O)Me	Cl	60	80
7	3	C(O)Me	Cl	60	68
8	4	C(O)Me	Cl	60	49

^aReaction conditions: 0.5 mmol aryl halide, 0.55 mmol phenylboronic acid, 1.0 mmol Cs₂CO₃, starting concentration of catalyst **9** (series 1, entries 1–4; series 2, entries 5–8) 0.2 mol%, 2 ml toluene, 200 W microwave heating (fixed power).

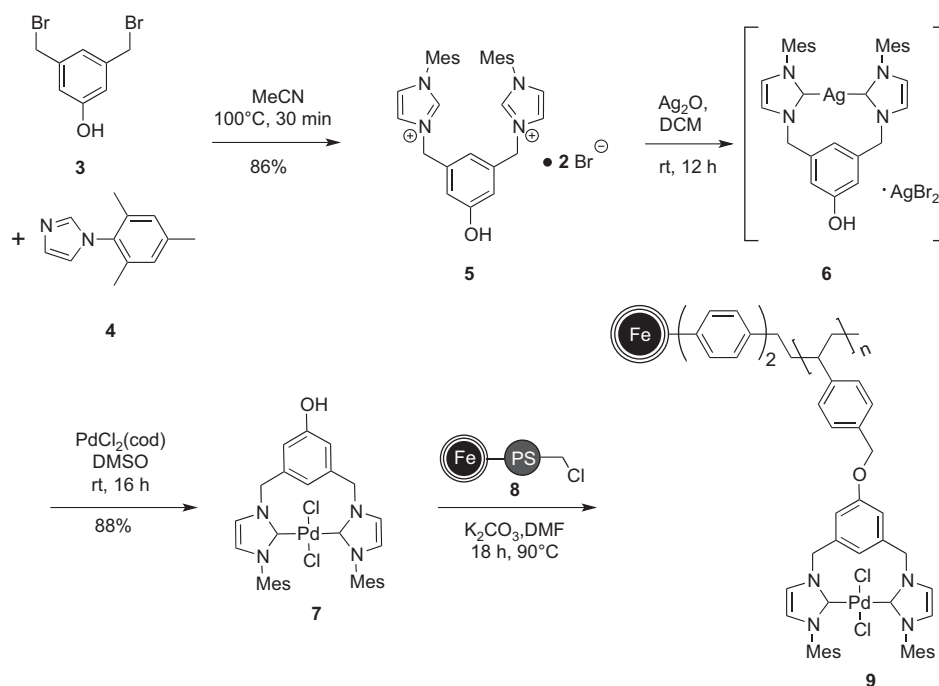
^bDetermined by GC analysis with diethylene glycol-di-*n*-butyl ether as internal standard.

was reused in subsequent runs without apparent loss of activity (Table 1, series 1: entries 1–6; series 2: entries 7–11). Monitoring the conversion versus time for the reaction of 4-bromoanisole and phenylboronic acid (Figure 2) revealed that the reaction reached 50% conversion after 1 h and 80% conversion after 2 h.

Carrying out Suzuki-Miyaura couplings under microwave irradiation (Table 2) in closed vessel conditions at 140°C not only greatly shortened the reaction times but also allowed the

**Figure 2** Time conversion and time-turn-over frequency (TOF) curves of **9** (0.2 mol%) in the Suzuki-Miyaura cross-coupling reaction between bromobenzene and phenylboronic acid.

coupling of less reactive aryl chlorides. Again, **9** was readily recycled by an external magnet and reused; nevertheless, we noted a significant drop of activity in the coupling of aryl chlorides with each cycle. TEM analysis revealed the formation of palladium nanoparticles over time and reaction cycles that apparently became trapped in the polystyrene matrix, i.e. indicating the decomposition palladium complex in **9**. This breakdown occurred under microwave conditions (140°C) but to our surprise also under thermal conditions at 70°C (Figure 3). It should be noted that ICP-OES measurements revealed, in all cases (Tables 1 and 2), that <2 ppm palladium in each cycle was released into the reaction solution. Because the number but not the size of the nanoparticles was increasing with the

**Scheme 1** Synthesis of polystyrene modified, carbon coated iron nanoparticle supported palladium complex **9**.

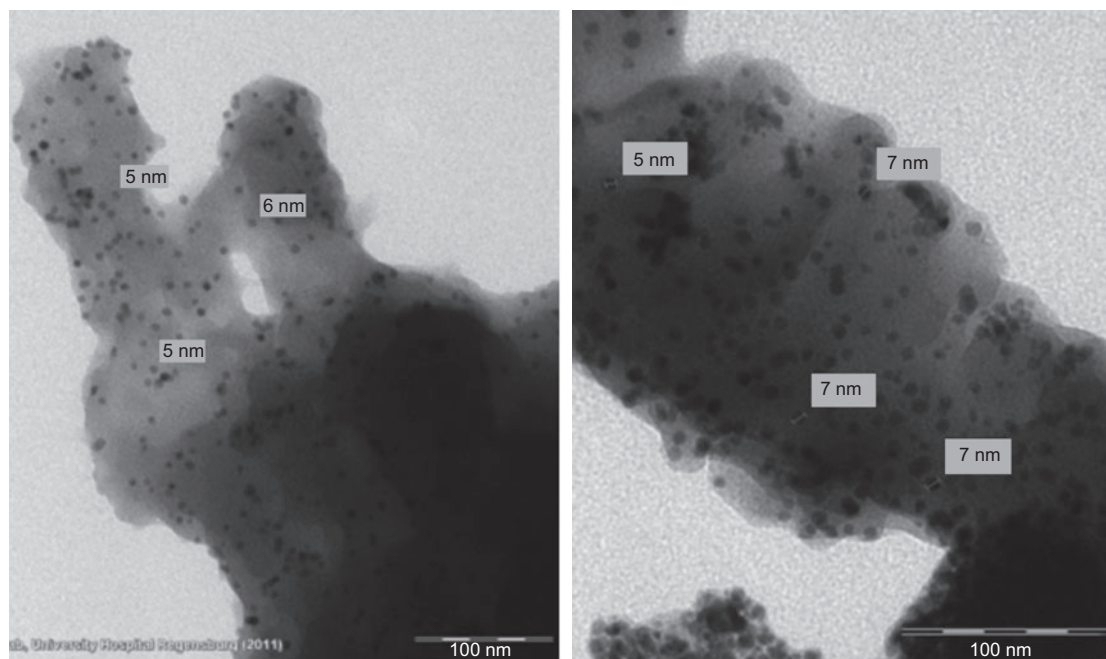


Figure 3 Representative TEM micrographs of **9** after heating under conventional heating taken after one (left) and four (right) reaction cycles (for conditions see Table 1, entries 1–4). Palladium nanoparticles (5–7 nm) are formed that are encapsulated in the polystyrene matrix (upper left part in each image) that is attached to the carbon coated iron particle (20–50 nm, lower right part in each image).

reaction cycles performed, it is assumed that these palladium nanoparticles do not leach to a significant extent from the polystyrene matrix as opposed to being trapped in there upon cooling the reaction mixture. Although this finding might open up an interesting strategy for nanoparticle synthesis in a polymer matrix that is, in return, attached to magnetic nanoparticles, we must conclude for our current study that the palladium nanoparticles formed do not exhibit the same, if any, catalytic activity for the Suzuki-Miyaura cross-coupling.

In conclusion, the immobilization of palladium NHC complex **7** to iron nanoparticles **8** resulted in a magnetically recyclable catalyst **9** that was successfully employed in Suzuki-Miyaura coupling reactions of aryl halides. In particular, it was shown that under microwave irradiation, even aryl chlorides can be employed as substrates. As a possible pathway for catalyst deactivation, the formation of palladium nanoparticles was identified that are encapsulated into the polystyrene matrix of the support.

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Robert Grass is a Senior Scientist at ETH Zurich, Switzerland. He studied Chemical Engineering at ETH Zurich where he also completed his PhD in the Prof. Stark's group in 2007. Robert is a co-founder and CEO of TurboBeads Llc, a spin-off company commercializing magnetic nanobeads.