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Tetrahedron Letters 47 (2006) 2399–2403
Tetrahedron Letters

Hybrid organic–inorganic silica materials containing di(2-pyridyl)methylamine–palladium dichloride complex as recyclable catalysts for Suzuki cross-coupling reactions

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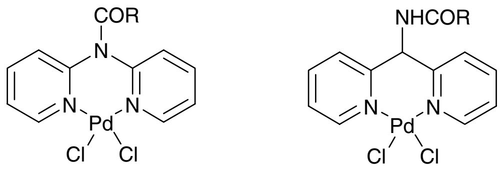
Received 23 December 2005; revised 27 January 2006; accepted 30 January 2006

Abstract—High surface hybrid silica materials containing di(2-pyridyl)methylamine–palladium dichloride complex covalently bonded to the silica matrix were prepared by sol-gel process and successfully tested as reusable catalysts for Suzuki cross-coupling reactions.

Palladium-catalyzed Suzuki cross-coupling[1] reactions have become a powerful and general methodology for C–C bond formation. On the other hand, the heterogenization of homogeneous catalysts by their immobilization on polymeric organic[2] or inorganic[3] supports is an expanding research area offering the advantage of easy product separation and catalyst recovery. Phosphines are common ligands used in palladium catalyzed reactions, but they are readily oxidized to their corresponding phosphine oxides, which can prevent the easy recovery and recycling of the catalyst. Thus, phosphine-free palladium catalysts offer the advantage of superior stability.

Some of us discovered[4] air and moisture stable phosphine-free macrocyclic triolefinic palladium(0) complexes. We have reported their immobilization onto cross-linked polystyrene,[5] and onto a silica matrix,[6] and the activity of these heterogeneous versions as recoverable catalysts in Suzuki and telomerization reactions. However, the immobilized versions of macrocyclic palladium(0) complexes were only found to be efficient with activated and deactivated aryl iodides, the ideal substrates for coupling reactions being aryl chlorides, cheaper and more widely available than their iodide counterparts.[7] Several phosphine-free palladium systems have been developed in the literature as robust and efficient catalysts (high TON and TOF) for the challenge to use aryl chlorides in coupling reactions (palladacycles, *N*-heterocyclic carbene ligands and bipyridine based systems). First, we turned our attention to bipyridine-type ligands to obtain immobilized palladium catalysts onto a silica matrix. Palladium(II) complexes of bipyridyl ligands **1** (Fig. 1) have been described by Buchmeiser[8] as efficient catalysts for C–C and C–N bond formation and they have been covalently anchored to a polymeric matrix resulting from a ROMP polymerization. Nájera[9] developed related palladium(II) complexes **2** (Fig. 1)



1

2

2a R = NH-$(CH_2)_3$-$Si(OEt)_3$

Figure 1. Palladium dichloride complexes of bipyridine ligands.

Keywords: Supported catalyst; Recoverable palladium catalyst; Sol-gel; Hybrid organic–inorganic material; Suzuki cross-coupling.

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0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.01.150

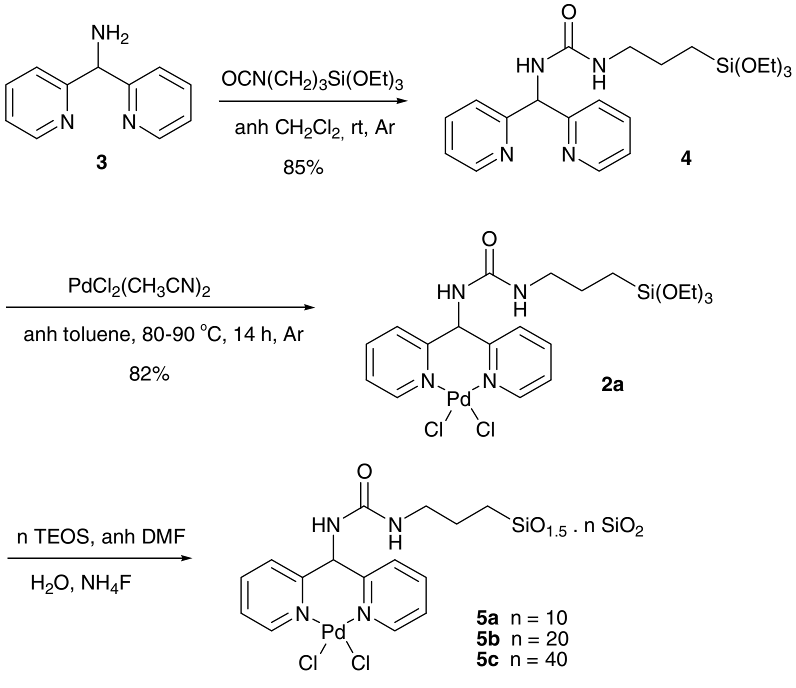
derived from di(2-pyridyl)methylamine as efficient catalysts for Heck (aryl iodides, bromides and chlorides), Suzuki (aryl bromides and chlorides) and Sonogashira (aryl iodides and bromides) reactions in organic and aqueous solvents under homogeneous conditions. Very recently, this complex has been covalently anchored to a styrene–maleic anhydride co-polymer affording a recoverable catalyst active in the above-mentioned reactions.[10]

Inorganic solids such as silica, particularly known for their mechanical and thermal stability and also for their chemical inertia, represent interesting supports for heterogenizing catalysts.[11] In this context, the formation of organic–inorganic hybrids by the Sol-Gel Chemistry[12] is a convenient route to solid materials with catalytic properties.[3,13] We want to present here our work on the preparation of hybrid organic–inorganic materials from the co-gelification of the silylated monomer **2a** (Fig. 1) with different amounts of tetraethoxysilane (TEOS) and the preliminary results of the activity and recyclability of these materials in the Suzuki cross-coupling of *p*-bromoacetophenone and *m*-chlorobenzonitrile with phenylboronic acid.

Our approach is summarized in Scheme 1.

Di(2-pyridyl)methylamine **3** was prepared as recently described[14] by zinc reduction of the oxime derived from commercial di(2-pyridyl)methanone. It was immediately reacted overnight under stirring with freshly distilled 3-(triethoxysilyl)propyl isocyanate in anhydrous dichloromethane at room temperature. The resulting urea derivative **4**[15] was treated with $PdCl_2(CH_3CN)_2$ in anhydrous toluene at 80–90 °C overnight to afford the palladium(II) complex **2a**.[16] Co-gelification of the silylated monomer **2a** with different amounts of TEOS (1:10, 1:20, 1:40) was performed in dimethylformamide under standard sol-gel conditions with the stoichiometric amount of water and ammonium fluoride as catalyst, leading to palladium-containing materials **5a**–**c**.[17] These were characterized by surface area BET measurements, solid state ^{29}Si NMR and ^{13}C NMR, IR and elemental analysis, the amount of palladium being obtained by ICP (inductively coupled plasma) (Table 1). Heterogeneous catalysts are more efficient when the specific surface area is high. Great amounts of TEOS (10, 20 and 40 molar equivalents with respect to **2a**) were used in order to favour solid formation with high surface areas and indeed these vary from 337 m^2g^{-1} (for **5a**) to 504 m^2g^{-1} (for **5c**) accordingly to the BET adsorption–desorption measurements. The solid state NMR spectra (^{29}Si and ^{13}C) provide evidence for the presence of the organic ligand in the hybrid solids. The ^{29}Si spectra of **5a**–**c** show two groups of chemical shifts: T units at around −55 to −68 ppm and Q units ranging from −100 to −120 ppm. T units result from the hydrolysis-condensation of **2a** whereas Q units formed from TEOS. Only the solid state ^{13}C NMR of **5a** was performed, the organics in **5b** and **5c** being in too little amount in the corresponding hybrids to be measured in reasonable time. The spectrum of **5a** exhibits signals at 8.7 (*C*H_2–Si), 16.6 (*C*H_3 from residual ethoxy groups), 23.0 (*C*H_2–CH_2Si), 42.6 (*C*H_2–N), 58.1 (*C*H_2 from residual ethoxy groups), 74.3 (*C*H–N), 126.8, 141.7, 154.5 (3*C* from pyridine rings) and 158 (*C*=O) ppm attributable to the chemical shifts of the organic part of **5**. The signal at 8.7 ppm (CH_2–Si) confirms the covalently bonded ligand to silica.

The activity of catalysts **5a**–**c** was tested in the Suzuki cross-coupling of phenylboronic acid **7** with an aryl



Scheme 1. Preparation of hybrid silica materials **5a**–**c**.

Table 1. Some analytical data of **5a–c**

	5a	**5b**	**5c**
% Pd	6.05	3.88	2.63
Mmol Pd/g	0.569	0.365	0.247

Table 2. Suzuki couplings with catalysts **5a–c** giving rise to **8** and **10** (Scheme 2)[a]

Cycle	**6** to **8** (%)[b]			**9** to **10** (%)[c]	
	5a	**5b**	**5c**	**5b**	
				7 h	24 h
1	100	100	100	61	82
2	100	100	99	44	59
3	96	99	98	34	38
4	97	96	98	31	34
5	96	96	97	25	26
6	95	94	98	—	—
7	97	96	96	—	—
8	98	96	97	—	—
9	97	97	95	—	—
10	94	96	95	—	—

[a] Conditions: 0.2% molar of Pd, [ArX] = 0.5 M, $PhB(OH)_2$, (1.5 equiv), K_2CO_3 (2 equiv), DMF/H_2O (95:5), 110 °C, 45 min for catalysts **5a–b** and 60 min for catalyst **5c** for the reaction of **6** to **8**, and 24 h for the reaction of **9** to **10** with catalyst **5b**.

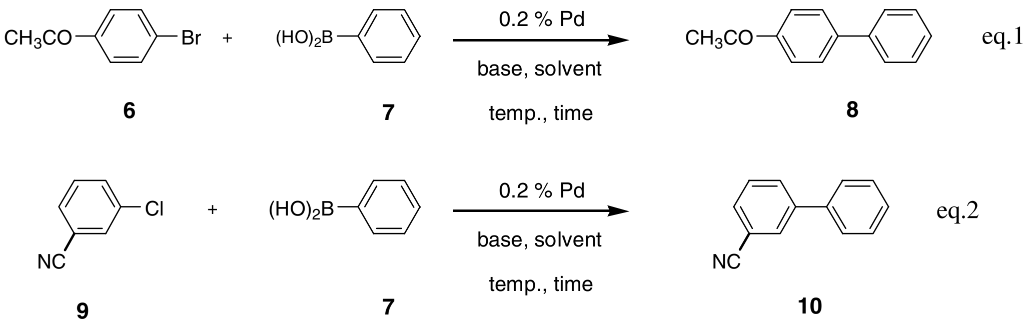
[b] Isolated yields.

[c] Conversion of **9** by GLC (undecane as internal standard).

bromide, *p*-bromoacetophenone **6,** and an aryl chloride, *m*-chlorobenzonitrile **9** (Scheme 2 and Table 2). After some experimentation ($MeOH/H_2O$ 3:1, KOH, rt, 24 h; $MeOH/H_2O$ 3:1, KOH, 60 °C, 45 min; toluene, K_2CO_3, 110 °C, 3 h) the conditions specified in Table 2 (DMF/H_2O 95:5, K_2CO_3, 110 °C, 45–60 min) were adopted for the Suzuki coupling of Eq. 1. Ten consecutive cycles with the same batch of catalyst were performed, maintaining the same reaction time in every run. The isolated yields of 4-phenylacetophenone **8** for every catalytic material are given in Table 2.[18] No significant differences were found within the materials with respect to their recyclability, but the reaction time required to achieve complete conversion of the aryl halide is longer with **5c** containing less percentage of Pd. The same reaction (Eq. 1 of Scheme 2) was also tested under the same conditions with the material **5bSi** obtained by refluxing **5b** with excess hexamethyldisilazane for capping surface silanol groups, but the reaction was slower, 4 h being required to achieve a 97% isolated yield of **8**. We noticed that the catalytic pale yellow materials **5a–c** became grey after the first cycle and darkened progressively to black. This is due to the formation of metal nanoparticles in the materials, which can be observed by high-resolution electron transmission microscopy (HRTEM) (both the inorganic matrix and the organic ligand of the hybrids can contribute to their stabilization).[19] Electron diffraction (ED) of the sample showed the pattern characteristic of face-centred cube (fcc) palladium(0). In Figure 2, we show an example of HRTEM micrographs of one of the samples (material **5c** after the fourth cycle, DMF/H_2O, K_2CO_3, 110 °C, 60 min), the size distribution of nanoparticles and the ED image (*d*-spacings = 0.239, 0.207, 0.147, 0.124 nm). The nanoparticles were not observed by TEM in the materials before being tested as catalysts, but darkening of the recovered materials after the first run was observed under any condition used (see Supplementary data). Palladium nanoparticles observed by TEM have been also recently described by Nájera.[10] The amount of Pd determined by ICP-MS in the product **8** isolated from the first cycle performed with catalyst **5a** under the conditions of Table 2 and in the solid mixture obtained in this cycle by evaporation of the filtrate were found to be 12 and 80 ppm, respectively. Nájera[10] has used water or $MeOH/H_2O$ as solvent systems in their recycling experiments with the catalyst anchored to organic polymer. In our case, the use of less amount of water and potassium carbonate as base instead of KOH improved the recyclability (the system DMF/H_2O 95:5 was better than $MeOH/H_2O$ 3:1).

Then, we tested the material **5b** in a more challenging substrate, the *m*-chlorobenzonitrile, **9**, which was reacted with phenylboronic acid **7** to afford 3-cyanobiphenyl, **10** (Eq. 2 of Scheme 2) under the conditions of Table 2 (0.2% molar of Pd, DMF/H_2O 95:5, K_2CO_3, 110 °C). As expected, the reaction was much slower than with the aryl bromide, and even after being left for 24 h, a total conversion could not be achieved. Conversions of **9** were determined by GLC at two reaction times (7 h and 24 h) for each of the five consecutive cycles (Table 2). In this case, a significant decrease of conversion upon recycling was found, prolonged reaction times being not useful. More research is necessary to improve the results with aryl chlorides.

In summary, high surface hybrid silica materials with covalently attached di(2-pyridyl)methylamine–palladium



Scheme 2. Suzuki cross-couplings tested with catalysts **5a–c**.

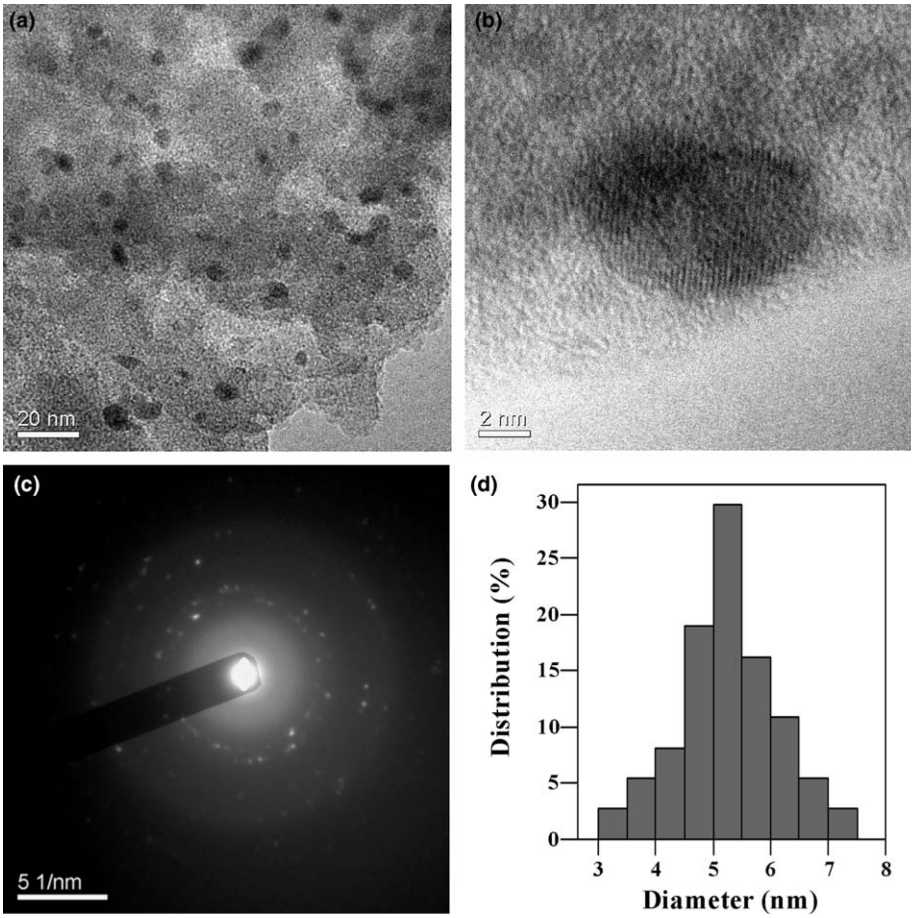


Figure 2. (a) and (b) HRTEM micrographs of Pd nanoparticles; (c) ED image; (d) Particle size distribution (104 particles; mean particle size: 5.1 ± 0.9 nm).

dichloride complex were prepared and found to be very active and recoverable catalysts for Suzuki cross-coupling of activated aryl bromides. They are also active for aryl chlorides, although further investigation is needed in order to improve the yield and the recyclability. Formation of fcc Pd(0) nanoparticles has been shown by HRTEM and ED.

Acknowledgements

Financial support from the Ministry of Science and Technology of Spain (Project BQU2002-04002-C02) *Generalitat de Catalunya* (Project SGR2001-00181), and *Universitat Autònoma de Barcelona* (Project PNL2005-10) is gratefully acknowledged. M.T. thanks *Generalitat de Catalunya* for a predoctoral scholarship. The CNRS and the French Ministry of Research and Technology are also acknowledged for fundings.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.01.150.

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15. Compound **4**: mp 113–114 °C; IR (ATR): 3353, 3281, 2973, 2875, 1626, 1561, 1076, 950, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.52–0.59 (m, 2H), 1.18 (t, $J = 7.0$ Hz, 9H), 1.54 (m, 2H), 3.14 (m, 2H), 3.76 (q, $J = 7.0$ Hz, 6H), 5.11 (br t, $J = 5.6$ Hz, 1H), 6.07 (d, $J = 6.6$ Hz, 1H), 6.91 (d, $J = 6.6$ Hz, 1H), 7.10 (ddd, $J = 7.5$, 4.9 and 1.1 Hz, 2H), 7.40 (d, $J = 7.9$ Hz, 2H), 7.58 (td, $J = 7.7$ and 1.8 Hz, 2H), 8.46 (d, $J = 4.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 7.9, 18.6, 23.8, 43.3, 58.6, 60.4, 122.5, 122.6, 137.1, 149.2, 157.9, 160.2. Anal. Calcd (%) for $C_{21}H_{32}N_4SiO_4$: C, 58.31; H, 7.46; N, 12.95; Si, 6.49. Found: C, 57.43; H, 8.52; N, 12.93; Si, 6.43.
16. Compound **2a**: IR (ATR): 3331, 3109, 2973, 2882, 1630, 1563, 1471, 1070, 953, 764 cm^{-1}; ^{1}H NMR (CD_3SOCD_3, 250 MHz, 329 K): δ 0.52–0.70 (m, 2H), 1.17 (t, $J = 7.0$ Hz, 9H), 1.43–1.67 (m, 2H), 3.12–3.24 (m, 2H), 3.77 (q, $J = 7.0$ Hz, 6H), 6.30–6.52 (m, 1H), 7.09–7.28 (m, 1H), 7.55 (t, $J = 6.5$ Hz, 2H), 7.66–7.96 (m, 3H), 8.03–8.24 (m, 2H), 8.83–9.00 (m, 2H). Anal. Calcd (%) for $C_{21}H_{32}N_4SiCl_2O_4Pd$: C, 41.35; H, 5.29; N, 9.19; Si, 4.60; Pd, 17.45. Found: C, 41.25; H, 5.43; N, 9.10; Si 4.46; Pd(ICP), 16.52.
17. Typical procedure: A solution of NH_4F (168 μL of a 1 M solution, 0.168 mmol of fluoride, 9.33 mmol of water), anhydrous DMF (6.8 mL) and distilled and deionized water (1035 μL, 57.5 mmol) was added to a solution of **2a** (0.252 g, 0.413 mmol) and TEOS (3.489 g, 16.4 mmol) in anhydrous DMF (10 mL). The mixture was stirred manually for a minute to get an homogeneous solution and was left at room temperature without stirring. Gelation occurred after 2 h and the gel was allowed to age for 3 days, after which it was powdered and washed successively twice with water and three times with ethanol. The solid was dried under vacuum overnight (2 mmHg, 60 °C), yielding **5c** as a yellow powder (1.274 g). IR (KBr): 3447, 1655, 1564, 1079, 959, 799, 459 cm^{-1}. Anal. (%) found: C, 8.38; H, 1.24; N, 1.86; Si, 35.00; Pd(ICP), 2.63. Materials **5a**–**b** were obtained in a similar manner except the molar ratio **2a**:TEOS. Material **5a**: Anal. (%) found: C, 11.77; H, 1.90; N, 4.43; Si, 26.82; Pd(ICP), 6.05. Material **5b**: Anal. (%) found: C, 10.32; H, 1.24; N, 2.66; Si, 29.51; Pd(ICP), 3.88.
18. Typical procedure: K_2CO_3 (1.935 g, 14 mmol) was added to a stirred mixture of **5b** (0.0384 g, 0.014 mmol of Pd), **6** (1.422 g, 7 mmol), and **7** (1.306 g, 10.5 mmol) in DMF/H_2O (95:5) (14 mL) and it was heated at 110 °C for 45 min (GLC monitoring). Product **8** precipitated by the addition of water to the crude mixture. The filtered solid was washed with water and then it was taken in ethyl acetate. Insoluble **5b** was filtered. The filtrate was dried with anhydrous sodium sulfate and the solvent was evaporated to give pure **8** (1.374 g, 100% yield). The catalyst **5b** was washed successively with water, ethanol and diethyl ether, it was dried and reused in the next run.
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