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Phosphine-free double carbonylation of iodobenzene in the presence of reusable supported palladium catalysts

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ABSTRACT

Various silica supported palladium catalysts were prepared and tested in the double carbonylation of iodobenzene in the presence of secondary amines. The catalysts were proved to produce α-ketoamide products with excellent selectivity in most cases. At the same time, bulky amines hindered double carbonylation and led to the formation of amides as the main products. Under optimal conditions, the catalysts could be recycled at least six times. An increase in the reaction time led to a decrease in the amount of leached palladium.

1. Introduction

Palladium catalysed carbonylations in the presence of organic nucleophiles serve as powerful tools for the conversion of aryl/alkenyl halides or halide equivalents to carboxylic acid derivatives [1]. At the same time, only a few examples have been reported for the use of supported counterparts of the homogeneous palladium catalysts. Amino- and alkoxycarbonylation reactions of aryl halides were carried out using palladium complexes of P- [2–5], As- [6], N- [7], S- [8] and Se [9] containing ligands supported on polymers [2], silica [6–9], SBA-15 [4,5] or MCM-41 [3]. Commercially available immobilised $Pd(PPh_3)_4$ was used for aminocarbonylation in a continuous flow reactor by Csajági et al. [10] and ourselves [11].

Pd/C was found to be an efficient catalyst in alkoxycarbonylation leading to aromatic esters [12] and in carbonylation of o-dihaloarenes producing N-substituted phthalimides [13]. A microwave-assisted carbonylation in the presence of Pd/C was reported by Petricci et al. [14]. Recently, Bhanage disclosed results on a polymer supported palladium-N-heterocyclic carbene complex-catalysed aminocarbonylation of aryl iodides [15].

Most of the methods, mentioned above, led to the formation of carboxamides in the presence of amines as nucleophiles. At the same time, carbonylation reactions carried out at elevated pressures may produce α-ketoamides [16,17]. Similar compounds show interesting pharmacological properties, such as anti-HIV activity [18] or HCV protease inhibition [19]. Double carbonylation, leading to α-ketoamides, are carried out in the presence of palladium–phosphine complexes in most cases [20], and there are only a few examples for the use of phosphine-free catalysts [16,21]. However, in the latter cases the reactions were carried out under homogeneous conditions, with the exception of a single experiment with Pd/C [16]. Double carbonylation reactions catalysed by heterogeneous palladium catalysts are still rare. A silica-supported polytitazane–palladium (Ti–N–Pd) complex was used by Yan et al. [22]. The catalyst was reused ten times with almost negligible loss of activity and with a 74–77% selectivity towards α-ketoamides. A $Pd/C + PPh_3$ catalyst system afforded double carbonylated products in 64–91% yield in the presence of DABCO as the base, but the conversion dropped to 17% upon recycling of the catalyst [23]. Palladium–phosphine complexes grafted onto mesoporous silica (SBA-15) was found to be selective catalysts for double carbonylation leading to α-ketoamides with good selectivity starting from different aryl iodides and amines [5]. The catalysts were shown to retain their activity in three subsequent cycles.

In the past few years, the use of ionic liquids (ILs) as reaction media for transition metal-catalysed reactions was thoroughly investigated [24]. This method makes efficient catalyst recovery and recycling possible, but requires significant amounts of ILs, which is unattractive from an economical point of view due to the high cost of most ILs. Recently, a new approach, the so-called 'supported ionic liquid phase' (SILP) technology that combines the advantage of ILs with those of heterogeneous supports was developed [25]. Although the use of SILP-palladium catalysts is relatively well explored in Heck- and Suzuki reactions, to the best of our

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knowledge, there is no example for double carbonylation reactions carried out under such conditions.

In the present paper we report on our results concerning selective double carbonylation of aryl iodides with phosphine-free silica-palladium catalysts. The silica supports were obtained by the modification of silica gel with ILs.

2. Experimental

2.1. Preparation of supported catalysts

2.1.1. Preparation of *SILP-Pd-1*

200 mg [BMIM][BF_4] and 0.02 mmol (20.7 mg) $Pd_2(dba)_3{\cdot}CHCl_3$ was dissolved in a mixture of 2 ml acetonitrile and 2 ml THF. The mixture was stirred for 15 min at room temperature. Then 550 mg silica (Kieselgel 60 (0.040–0.063 mm), Merck, pre-treated by heating for 5 h at 250 °C) was added under stirring and the resulting mixture was stirred for 24 h. The solvents were removed in vacuo and the catalyst was dried at 35 °C in vacuo for 3 h and was stored under argon until use. Palladium content of the catalyst: 0.40% (determined by ICP).

2.1.2. Preparation of *SILP-Pd-2*

200 mg [BMIM][BF_4] and 0.04 mmol (8.7 mg) $Pd(OAc)_2$ was dissolved in a mixture of 2 ml acetonitrile and 2 ml THF. The mixture was stirred for 15 min at room temperature. Then 550 mg silica (Kieselgel 60 (0.040–0.063 mm), Merck, pre-treated by heating for 5 h at 250 °C) was added under stirring and the resulting mixture was stirred for 24 h. The solvents were removed in vacuo and the catalyst was dried at 35 °C in vacuo for 3 h and was stored under argon until use. Palladium content of the catalyst: 0.49% (determined by ICP).

2.1.3. Preparation of *SILP-Pd-3*

200 mg [BMIM][PF_6] and 0.02 mmol (20.7 mg) $Pd_2(dba)_3{\cdot}CHCl_3$ was dissolved in a mixture of 2 ml acetonitrile and 2 ml THF. The mixture was stirred for 15 min at room temperature. Then 550 mg silica (Kieselgel 60 (0.040–0.063 mm), Merck, pre-treated by heating for 5 h at 250 °C) was added under stirring and the resulting mixture was stirred for 24 h. The solvents were removed in vacuo and the catalyst was dried at 35 °C in vacuo for 3 h and was stored under argon until use. Palladium content of the catalyst: 0.33% (determined by ICP).

2.1.4. Preparation of *SILP-Pd-4*

Ionic liquid **1** was prepared according to a known method [26].

A mixture of 10 mmol (3.23 g) of **1** and 10 mmol (1.05 g) ammonium-tetrafluoroborate and 50 ml acetonitrile was stirred at room temperature for 5 days. The precipitated solid was removed by filtration through alumina and the solvent was evaporated. The residue was dissolved in dichloromethane (50 ml) and the solution was filtered through activated charcoal and alumina. After removal of the solvent in vacuo, **2** was obtained in 65% yield. (Elemental analysis: Calc. for $C_{13}H_{27}N_2O_3SiBF_4$: C, 41.72; H, 7.27; N, 7.49; Found: C, 41.95; H, 7.35; N, 7.63.)

4.8 mmol (1.8 g) of **2** was dissolved in 50 ml chloroform and 3.0 g silica (pre-treated by heating for 5 h at 250 °C) was added. The mixture was refluxed for 24 h. Then the SILP material was filtered and washed with pentane (50 ml), acetonitrile (100 ml) and diethylether (100 ml) and was dried in vacuo to produce the supported ionic liquid **3**. The amount of ionic liquid supported on silica was determined by measuring the weight increase after heating the material to constant weight at 150 °C in vacuo (180 mg **2** on 1 g silica).

A solution of 8.95 μmol (9.3 mg) $Pd_2(dba)_3{\cdot}CHCl_3$ in 2 ml acetonitrile and 2 ml THF was stirred for 15 min. Then 500 mg of **3** was added and the resulting mixture was stirred for 24 h at room temperature. After evaporation of the solvents, the catalyst was dried at 35 °C in vacuo for 3 h. Palladium content of the catalyst: 0.29% (determined by ICP).

2.1.5. Preparation of *Pd/silica*

0.02 mmol (20.7 mg) $Pd_2(dba)_3{\cdot}CHCl_3$ was dissolved in a mixture of 2 ml acetonitrile and 2 ml THF. The mixture was stirred for 15 min at room temperature. Then 550 mg silica (Kieselgel 60 (0.040–0.063 mm), Merck, pre-treated by heating for 5 h at 250 °C) was added and the resulting mixture was stirred for 24 h. The solvents were removed in vacuo and the catalyst was dried at 35 °C in vacuo for 3 h and was stored under argon until use. Palladium content of the catalyst: 0.55% (determined by ICP).

2.2. Catalytic reactions

2.2.1. Catalytic reactions at atmospheric pressure

In a typical experiment a solution containing the palladium catalyst (with 3.6 μmol Pd-content) was placed in a Schlenk-tube. Under argon, 0.2 mmol (22.5 μl) iodobenzene (**4**), 0.5 mmol (44 μl) morpholine (**5a**), 0.25 mmol (35 μl) triethylamine and 1 ml DMF was added and the atmosphere was changed to carbon monoxide. The reaction was conducted for 3 h at 100 °C. The reaction mixture was analysed by gas chromatography.

2.2.2. Catalytic reactions at elevated pressure

In a typical experiment the catalyst (containing 3.6 μmol Pd) was placed in a stainless steel autoclave. Iodobenzene (**4**) (0.2 mmol, 22.4 μl), the amine (**5a–g**) (0.5 mmol), base (0.25 mmol) and solvent (1 ml) were transferred into it under an inert atmosphere. It was charged with carbon monoxide (30 bar) and heated with stirring in an oil bath at 100 °C for 3, 8 or 12 h. After cooling to room temperature, the liquid phase was removed with a syringe. The reaction mixture was analysed by gas chromatography and the catalyst was reused.

2.3. Analytical measurements

Reaction mixtures were analysed by gas chromatography (Hewlett Packard 5890) and GC-MS (Hewlett Packard 5971A GC-MSD, HP-1 column). Conversions and selectivities of the reactions were determined by GC.

The palladium-content of the catalysts and palladium leaching were determined by ICP.

The products **6a–c**, **6e–g** and **7a–g** were identified on the basis of their MS spectra.

6a: MS(m/z/rel.int.): 219(M^+)/6; 105/100; 77/54; 51/22
6b: MS(m/z/rel.int.): 177(M^+)/6; 105/100; 77/44; 51/17
6c: MS(m/z/rel.int.): 205(M^+)/4; 105/100; 77/75; 51/30
6e: MS(m/z/rel.int.): 261(M^+)/5; 218/5; 105/100; 77/65; 51/14
6f: MS(m/z/rel.int.): 245(M^+)/3; 216/3; 188/4; 105/100; 77/90; 51/31
6g: MS(m/z/rel.int.): 203(M^+)/1; 202/5; 175/3; 105/100; 77/73; 51/10
7a: MS(m/z/rel.int.): 191(M^+)/11; 190/34; 176/9; 160/6; 105/100; 86/12; 77/68; 51/24
7b: MS(m/z/rel.int.): 149(M^+)/20; 148/44; 105/100; 77/71; 51/22; 50/8
7c: MS(m/z/rel.int.): 177(M^+)/13; 176/42; 148/3; 134/3; 105/100; 77/49; 51/10
7d: MS(m/z/rel.int.): 205(M^+)/10; 162/27; 105/100; 77/51; 51/12
7e: MS(m/z/rel.int.): 233(M^+)/10; 232/12; 190/14; 148/6; 134/4; 105/100; 77/28; 51/3