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

Máté Papp, Rita Skoda-Földes *

University of Pannonia, Institute of Chemistry, Department of Organic Chemistry, P.O. Box 158, H-8201 Veszprém, Hungary

ARTICLE INFO

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.

© 2013 Elsevier B.V. All rights reserved.

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

---

* Corresponding author. Tel.: +36 88 624719; fax: +36 88 624469.
E-mail address: skodane@almos.uni-pannon.hu (R. Skoda-Földes).

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)$_3$·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)$_3$·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$_2$O$_3$SiBF$_4$: 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)$_3$·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)$_3$·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
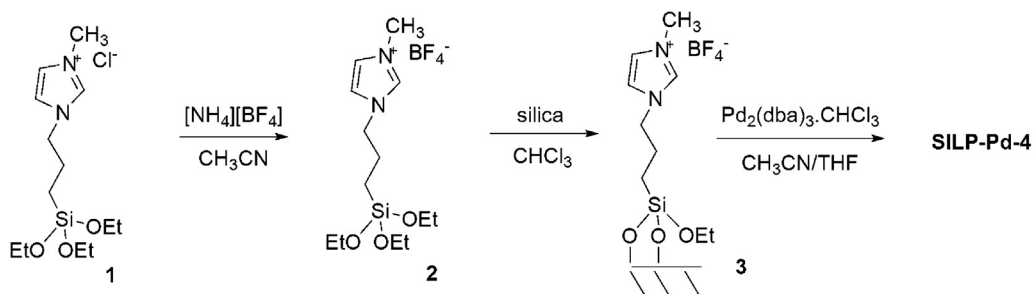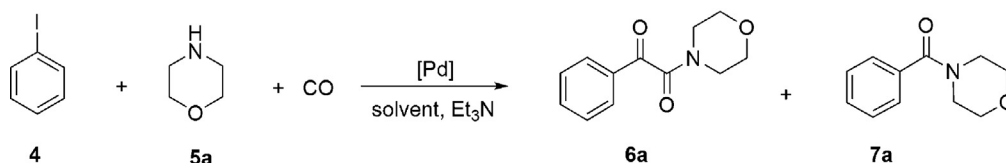**7c**: MS(m/z/rel.int.): 177(M$^+$)/13; 176/42; 148/3; 134/3; 105/100; 77/49; 51/10
7d: MS(m/z/rel.int.): 205(M$^+$)/10; 162/27; 105/100; 77/51; 51/12
7e: MS(m/z/rel.int.): 233(M$^+$)/10; 232/12; 190/14; 148/6; 134/4; 105/100; 77/28; 51/3

Table 1
Supported palladium catalysts used during the carbonylation reactions.

Catalyst	Support	Ionic liquid	Pd-precursor	Pd-content [%][a]
SILP-Pd-1	Silica	[BMIM][BF$_4$]	Pd$_2$(dba)$_3$·CHCl$_3$	0.40
SILP-Pd-2	Silica	[BMIM][BF$_4$]	Pd(OAc)$_2$	0.49
SILP-Pd-3	Silica	[BMIM][PF$_6$]	Pd$_2$(dba)$_3$·CHCl$_3$	0.33
SILP-Pd-4	**3**	–	Pd$_2$(dba)$_3$·CHCl$_3$	0.29
Pd/silica	Silica	–	Pd$_2$(dba)$_3$·CHCl$_3$	0.55

[a] (mg Pd/mg catalyst) × 100.

Scheme 1. Preparation of **SILP-Pd-4**.

Scheme 2. Aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**) as the nucleophile.

Table 2
Aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**).[a]

Entry	Catalyst	Solvent	Base	Pressure [bar]	Temp. [°C]	r. time [h]	Conv. [%][b]	Selectivity for **6a** [%][b,c]
1	Pd$_2$(dba)$_3$·CHCl$_3$	DMF	Et$_3$N	1	100	3	80	50
2	Pd$_2$(dba)$_3$·CHCl$_3$	DMF	Et$_3$N	30	100	3	100	95
3	Pd(OAc)$_2$	DMF	Et$_3$N	1	100	3	53	51
4	Pd(OAc)$_2$	DMF	Et$_3$N	30	100	3	100	94
5	**SILP-Pd-1**	DMF	Et$_3$N	1	100	3	34	36
6	**SILP-Pd-1**	DMF	Et$_3$N	30	100	3	88	94
7	**SILP-Pd-1**	DMF	Et$_3$N	30	100	8	100	94
8	**SILP-Pd-1**	toluene	Et$_3$N	30	100	8	54	34
9	**SILP-Pd-1**	THF	Et$_3$N	30	100	8	42	86
10	**SILP-Pd-1**	1,4-dioxane	Et$_3$N	30	100	8	35	77
11	**SILP-Pd-1**	acetonitrile	Et$_3$N	30	100	8	95	97
12	**SILP-Pd-1**	DMF	DABCO	30	100	3	96	96
13	**SILP-Pd-1**	DMF	DABCO	30	100	8	100	96
14	**SILP-Pd-1**	DMF	Et$_3$N	30	80	3	87	98
15	**SILP-Pd-1**	DMF	Et$_3$N	30	80	8	96	99
16	**SILP-Pd-1**	DMF	Et$_3$N	30	120	3	100	76
17	**SILP-Pd-2**	DMF	Et$_3$N	1	100	3	34	29
18	**SILP-Pd-2**	DMF	Et$_3$N	30	100	3	100	92
19	**SILP-Pd-3**	DMF	Et$_3$N	30	100	3	95	97
20	**SILP-Pd-3**	DMF	Et$_3$N	30	100	8	100	96
21	**SILP-Pd-4**	DMF	Et$_3$N	30	100	3	100	89
22	**SILP-Pd-4**	toluene	Et$_3$N	30	100	3	53	8
23	**SILP-Pd-4**	1,4-dioxane	Et$_3$N	30	100	3	44	28
24	**SILP-Pd-4**	DMF	Et$_3$N	30	100	8	100	89

[a] Reaction conditions: 0.2 mmol **4**, 0.5 mmol **5a**, 0.25 mmol Et$_3$N, catalyst (with 3.6 μmol Pd-content) and 1 ml solvent.

[b] Determined by GC.

[c] mmol **6a**/(mmol **6a** + mmol **7a**) × 100.

Table 3
Recirculation experiments for aminocarbonylation of iodobenzene (4) with morpholine (5a) in the presence of SILP-Pd-1.[a]

Entry	Reaction time [h]	Run 1		Run 2		Run 3		Run 4		Run 5		Run 6	
		Conv. [%][b]	Select. [%][b,c]	Conv. [%][b]	Select. [%][b,c]	Conv. [%][b]	Select. [%][b,c]	Conv. [%][b]	Select. [%][b,c]	Conv. [%][b]	Select. [%][b,c]	Conv. [%][b]	Select. [%][b,c]
1	3	88	94	86	94	85	100	84	100	80	100	65	100
2[d]	3	96	96	95	97	88	99	87	99	88	100	77	99
3	8	100	94	100	94	100	100	93	99	92	100	90	100
4	12	100	95	100	97	100	98	100	98	100	100	100	100
5[e]	3	87	98	76	100	29	100	–	–	–	–	–	–
6[e]	8	96	99	80	100	60	100	46	100	–	–	–	–
7[f]	3	100	76	74	90	29	100	31	100	–	–	–	–

[a] Reaction conditions: 0.2 mmol 4, 0.5 mmol 5a, 0.25 mmol Et₃N, catalyst (with 3.6 μmol Pd-content) in 1 ml DMF, 30 bar CO pressure, 100 °C.
[b] Determined by GC.
[c] mmol 6a/(mmol 6a + mmol 7a) × 100.
[d] DABCO.
[e] 80 °C.
[f] 120 °C.

7f: MS(m/z/rel.int.): 217(M⁺)/38; 216/23; 202/26; 174/13; 150/11; 105/100; 77/76; 55/18.

7g: MS(m/z/rel.int.): 175(M⁺)/44; 174/28; 146/28; 105/100; 77/57; 51/16

3. Results and discussion

3.1. Aminocarbonylation of iodobenzene in the presence of supported palladium catalysts

SILP catalysts were prepared either by physisorption of the ionic liquid on silica gel (**SILP-Pd-1**–**SILP-Pd-3**, Table 1) or by anchoring the ionic liquid covalently to the support (grafting, Scheme 1., **SILP-Pd-4**) [27].

Aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**) as the nucleophilic reaction partner was chosen as the model reaction (Scheme 2).

First, carbonylation was carried out at atmospheric pressure (Table 2, entry 5) and under 30 bar CO (entry 6) in DMF. As a comparison, the same reactions were executed in the presence of the $Pd_2(dba)_3$ precursor, under homogeneous conditions (entries 1, 2). At atmospheric pressure, conversion of iodobenzene was much higher with the homogeneous catalyst. Compound **6a** was obtained with only 50% and 36% selectivity (determined by GC), in the presence of $Pd_2(dba)_3 \cdot CHCl_3$ and **SILP-Pd-1**, respectively. At the same time, the α-ketoamide (**6a**) was formed with excellent selectivity in both cases under 30 bar CO pressure. By the increase of the reaction time, total conversion and similarly good selectivity were achieved with **SILP-Pd-1** (entry 7). The catalyst was less active in apolar solvents (entries 8–10). With the exception of toluene, **6a** was produced with good selectivity. In acetonitrile good conversion and excellent selectivity towards **6a** were achieved (entry 11). It should be mentioned that the use of water as the solvent led to the total conversion of iodobenzene to benzoic acid instead of amide type products. As it can be expected, when water is present in a high excess compared to morpholine, it competes successfully as a nucleophile even with the more basic amine.

The replacement of Et₃N with DABCO, a commonly used base in double carbonylation reactions [11,23,28], resulted in a slight increase in both conversion and selectivity for **6a** (entries 12, 13). As it was expected [11,29], the selectivity for the α-ketoamide (**6a**) increased with the decrease of the temperature (entries 14–16).

The SILP catalyst prepared from the Pd(OAc)₂ precursor (**SILP-Pd-2**, Table 1) showed similar performance in CO atmosphere (Table 2, entry 17), while under pressure, it was found to be a more active but less selective catalyst (entry 18) compared to **SILP-Pd-1**.

The use of **SILP-Pd-3**, obtained by the impregnation of silica gel with a solution of $Pd_2(dba)_3 \cdot CHCl_3$ in [BMIM][PF₆] (Table 1), resulted in the formation of the double carbonylated product (**6a**) in excellent yield (Table 2, entries 19, 20).

SILP-Pd-4, prepared by covalently anchoring the imidazolium moiety on silica, showed similar activity to **SILP-Pd-1** in different solvents (entries 21–24), but led to the α-ketoamide (**6a**) with lower selectivity. The selectivity difference between the two catalysts was especially marked in toluene and dioxane (compare entries 8, 22 and 10, 23). At the same time, the use of DMF resulted in only a slight decrease in the ratio of **6a** (entries 21, 24) compared to the reactions with **SILP-Pd-1** (entries 6,7).

3.2. Recirculation experiments

The efficiency of catalysts **SILP-Pd-1**–**SILP-Pd-4** was also compared upon reuse.

SILP-Pd-1 could be recycled in five subsequent runs with only a small loss of activity (Table 3, entry 1). The conversion of

Table 4
Selectivity of aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**) in recirculation experiments.[a]

Entry	Catalyst	Reaction time [h]	Selectivity for **6a** [%][b,c]					
			Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
1	**SILP-Pd-2**	3	92	94	96	97	100	100
2	**SILP-Pd-2**	8	92	94	96	96	96	100
3	**SILP-Pd-3**	3	97	99	99	100	100	100
4	**SILP-Pd-3**	8	96	99	100	99	100	100
5	**SILP-Pd-4**	3	89	89	89	89	90	93
6	**SILP-Pd-4**	8	89	89	88	90	91	95
7	Pd/silica	3	90	96	98	99	98	99
8	Pd/silica	8	92	95	96	100	100	100

[a] Reaction conditions: 0.2 mmol **4**, 0.5 mmol **5a**, 0.25 mmol Et$_3$N, catalyst (with 3.6 μmol Pd-content) in 1 ml DMF, 30 bar CO pressure, 100 °C.
[b] Determined by GC.
[c] mmol **6a**/(mmol **6a** + mmol **7a**) × 100.

iodobenzene dropped to 65% only in the sixth run. Conversions were a bit higher in all of the recycling experiments when DABCO was used as the base (entry 2) instead of Et$_3$N, but similar selectivities were obtained with the two bases.

An increase in the reaction time led to better conversions (entries 3, 4) and no loss of activity was observed even in the sixth run with a reaction time of 12 h. Either a decrease (entries 5, 6) or an increase (entry 7) in the temperature resulted in a great decrease in the catalytic activity in the second run.

Interestingly, the selectivity improved upon the reuse of the catalyst. Although the increase of the temperature is unfavourable for α-ketoamide formation, **6a** was the only product that could be detected in the third run even at 120 °C (entry 7).

Under the present conditions, different catalytically active species might be produced in the reaction mixture. Pd(II) precursors were shown to be reduced to colloidal Pd(0) under carbonylation conditions by Trzeciak et al. The palladium nanoparticles (NPs) were proved to be responsible for the catalytic activity [30]. Not only Pd(II)-salts, but also Pd$_2$(dba)$_3$ may serve as a possible source for NPs [31]. At the same time, it is possible that in the first runs, not only palladium NPs but also catalytically active mononuclear palladium complexes, formed directly from the Pd(OAc)$_2$ or Pd$_2$(dba)$_3$ precursors and catalysing carbonylation with different selectivity, are also present in the reaction mixture. In the subsequent runs, they might either be leached out of the support or be reduced to NPs.

Other catalysts (**SILP-Pd-2–SILP-Pd-4**) showed similar behaviour to **SILP-Pd-1** in the recirculation experiments. The use of an increased reaction time (8 h (Fig. 2) instead of 3 h (Fig. 1)) made a more efficient recycling possible. **SILP-Pd-4** exhibited the highest activity in the sixth run in both experiments (Figs. 1 and 2). At the same time, the selectivity of double carbonylation in the
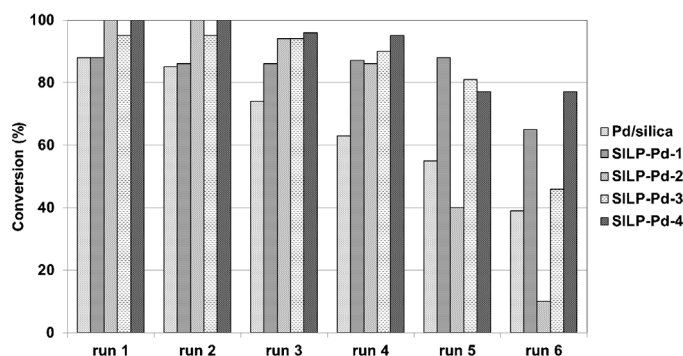

Fig. 1. Recirculation experiments for aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**) (reaction time: 3 h).
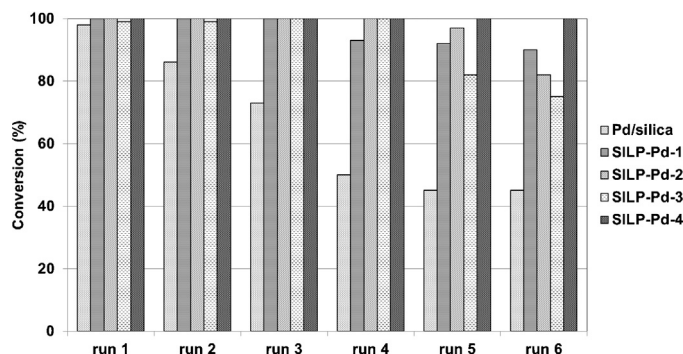

Fig. 2. Recirculation experiments for aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**) (reaction time: 8 h).
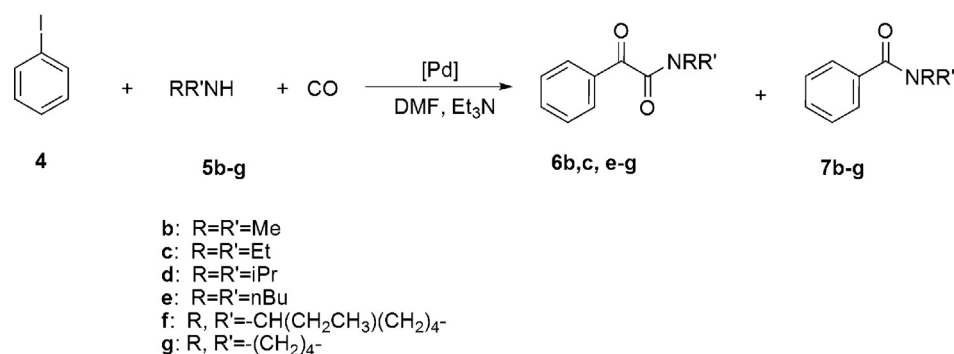
Table 5
Leaching of palladium during recirculation experiments for aminocarbonylation of iodobenzene (**4**) with morpholine (**5a**).[a]

Entry	Catalyst	r. time [h]	Pd-leaching [%][b]			Average (runs 1–6)
			Run 1	Runs 2–6		
				Total	Average	
1	**SILP-Pd-1**	3	23.7	8.1	1.6	5.3
2[c]	**SILP-Pd-1**	3	n.d.	n.d.	n.d.	6.2
3	**SILP-Pd-1**	8	18.0	5.4	1.1	3.9
4	**SILP-Pd-1**	12	17.7	5.0	1.0	3.8
5	**SILP-Pd-2**	3	n.d.	n.d.	n.d.	8.7
6	**SILP-Pd-3**	3	n.d.	n.d.	n.d.	6.4
7	**SILP-Pd-4**	3	7.6	16.0	3.2	3.9
8	**SILP-Pd-4**	8	4.5	14.0	2.8	3.1
9	Pd/silica	3	4.5	21.5	4.3	4.3

[a] Reaction conditions: 0.2 mmol **4**, 0.5 mmol **5a**, 0.25 mmol Et$_3$N, catalyst (with 3.6 μmol Pd-content) in 1 ml DMF, 30 bar CO pressure, 100 °C.
[b] Determined by ICP.
[c] Reaction temperature: 120 °C.

Scheme 3. Aminocarbonylation of iodobenzene (**4**) with secondary amines (**5b–g**).

presence of **SILP-Pd-4** (Table 4, entries 5,6) fell behind the results obtained with other supported catalysts (entries 1–4, 7–8). The increase of selectivity towards **6a** could uniformly be observed upon recycling with all of the catalysts (Table 4).

For comparison, a Pd/silica catalyst was also prepared without the use of a stabilising ionic liquid or an anchored imidazolium ligand (see Section 2.1.5). Although the selectivity of this catalyst is comparable to that of **SILP-Pd-1–SILP-Pd-4**, it showed the greatest drop of activity in both recycling experiments (with 3 h or 8 h reaction time, Figs. 1 and 2).

The amount of palladium leached into the reaction mixtures was determined by ICP after the first run and in the combined mixtures of runs 2–6 (Table 5). In some cases, only total leaching of the six runs were measured (entries (2, 5, 6)). Palladium leaching was the greatest in the first run, with the exception of the Pd/silica catalyst (entry 9), and then decreased in the subsequent runs. The difference is especially marked in case of **SILP-Pd-1** (Table 5, entries 1, 3, 4) probably due to the dissolution of the adsorbed [BMIM][BF$_4$] in the solvent. According to the ^{1}H NMR spectra of the reaction mixtures, almost the total amount of [BMIM][BF$_4$], used during the preparation of **SILP-Pd-1**, leached into the liquid phase during the first run. In spite of this, a superior performance of this catalyst to Pd/silica, obtained in the absence of ionic liquid, was observed regarding either recyclability or selectivity for **6a**. The beneficial effect might be due to a stabilisation of the initially formed palladium nanoparticles at the beginning of the reaction. Among other compounds, imidazolium ionic liquids are frequently used as template, stabiliser, and immobilising agent for catalytic transition-metal NPs to prevent aggregation [32].

Although palladium loss may not be the only cause of drop of activity, palladium leaching data are in good accordance with the catalytic results in case of all of the catalysts. **SILP-Pd-2** showed the greatest decrease in activity during the six runs (Fig. 1) together with the higher amount of leached palladium (Table 5, entry 5). Also, the use of higher temperature led to an increase in palladium leaching (Table 5, entry 2) and a marked drop of catalytic activity in runs 2 and 3 (Table 3, entry 7). It should also be mentioned that in case of the Pd/silica catalyst, almost the same amount of palladium is leached in each run (Table 5, entry 9).

In the reactions carried out in the presence of **SILP-Pd-4**, palladium leaching was smaller in the first runs (compare entries 1, 7 and 3, 8 in Table 5). The presence of no imidazolium derivatives could be detected in the reaction mixtures. However, the difference between the palladium content of the reaction mixtures of the first and subsequent runs was greater than in the case of carbonylations catalysed by **SILP-Pd-1**.

An increase in the reaction time led to a decrease in the amount of leached palladium both with **SILP-Pd-1** and **SILP-Pd-4**. In case of **SILP-Pd-1**, an average loss about 1% could be observed in runs 2–6 in experiments with increased reaction time (8 or 12 h). This

is in accordance with the report of Köhler et al. [33] who, during a detailed investigation of Pd/C catalysed Heck coupling, proved that the reaction was accompanied by Pd dissolution/reprecipitation. After the total conversion of the substrate, the palladium-content of the solution was found to decrease due to the precipitation of palladium nanoparticles to the support. During double carbonylation, similarly, an increase in the reaction time leads to complete conversion of iodobenzene and together with this, decreased leaching of palladium.

3.3. Carbonylation using different secondary amines as nucleophiles

Aminocarbonylation of iodobenzene (**4**) was carried out using different nucleophiles (**5b–g**) in the presence of **SILP-Pd-1** and **SILP-Pd-4** catalysts (Scheme 3, Table 6).

Good selectivity towards double carbonylated products was achieved in most cases. As it was observed before under homogeneous conditions [34], bulky groups on the N-atom (entries 5,6) or in close vicinity of the amino group (entries 9, 10) hindered double carbonylation. Although diisopropylamine was reported to produce neither mono-, nor double carbonylated products during aminocarbonylation of iodobenzene carried out in the presence of a palladium–phosphine complexes grafted onto mesoporous silica [5], under the present reaction conditions **7d** could be obtained both with **SILP-Pd-1** and **SILP-Pd-4** with total selectivity and in acceptable yield (entries 5, 6). 2-Ethylpiperidine was converted to a mixture of **6f** and **7f** with the amide (**7f**) as the main product. With the exception of the reaction of the bulky diisopropylamine (**5d**), higher selectivity towards α-ketoamides could be observed with **SILP-Pd-1** than with **SILP-Pd-4**.

Table 6
Aminocarbonylation of iodobenzene (**4**) with secondary amines (**5b–g**).[a]

Entry	Nucleophile	Catalyst	Conversion [%][b]	6:7 ratio[b]
1	**5b**	**SILP-Pd-1**	100	77:23
2	**5b**	**SILP-Pd-4**	100	69:31
3	**5c**	**SILP-Pd-1**	100	89:11
4	**5c**	**SILP-Pd-4**	90	85:15
5	**5d**	**SILP-Pd-1**	73	0:100
6	**5d**	**SILP-Pd-4**	60	0:100
7	**5e**	**SILP-Pd-1**	100	88:12
8	**5e**	**SILP-Pd-4**	97	73:27
9	**5f**	**SILP-Pd-1**	85	44:56
10	**5f**	**SILP-Pd-4**	85	29:71
11	**5g**	**SILP-Pd-1**	100	93:7
12	**5g**	**SILP-Pd-4**	95	88:12

[a] Reaction conditions: 0.2 mmol **4**, 0.5 mmol **5**, 0.25 mmol Et$_3$N, catalyst (with 3.6 μmol Pd-content) in 1 ml DMF at 30 bar CO pressure and 100 °C, reaction time: 3 h.
[b] Determined by GC.

4. Conclusions

Various phosphine-free silica supported palladium catalysts were prepared and tested in the double carbonylation of iodobenzene in the presence of secondary amines. Catalysts obtained via simple impregnation of silica with a mixture of a palladium precursor and an ionic liquid (**SILP-Pd-1–SILP-Pd-3**) were proved to convert iodobenzene (**4**) and morpholine (**5a**) to the α-ketoamide **6a** with excellent selectivity. A palladium catalyst supported on silica, grafted with imidazolium ions (**SILP-Pd-4**), showed similarly good activity but slightly lower selectivity for the double carbonylation product. 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. Carbonylations carried out with different secondary amines led to α-ketoamides with good selectivity in most cases. At the same time, similarly to the homogeneous reactions, bulky amines hinder double carbonylation and lead to the formation of amides as the main products.

Acknowledgments

References

[1] (a) L. Kollár (Ed.), Modern Carbonylation Methods, Wiley-VCH, 2008;
(b) R. Grigg, S.P. Mutton, Tetrahedron 66 (2010) 5515–5548.
[2] A. Mansour, M. Portnoy, J. Mol. Catal. A 250 (2006) 40–43.
[3] W. Hao, J. Sha, S. Sheng, M. Cai, Catal. Commun. 10 (2008) 257–260.
[4] M. Genelot, V. Dufaud, L. Djakovitch, Tetrahedron 67 (2011) 976–981.
[5] M. Genelot, N. Villandier, A. Bendjeriou, P. Jaithong, L. Djakovitch, V. Dufaudz, Catal. Sci. Technol. 2 (2012) 1886–1893.
[6] (a) M. Cai, Y. Huang, R. Hu, C. Song, J. Mol. Catal. A 208 (2004) 17–20;
(b) M. Cai, Y. Huang, R. Hu, C. Song, J. Mol. Catal. A 212 (2004) 151–154.
[7] M. Lagasi, P. Moggi, J. Mol. Catal. A 182–183 (2002) 61–72.
[8] M. Cai, H. Zhao, Y. Huang, J. Mol. Catal. A 238 (2005) 41–45.
[9] M. Cai, J. Zhou, H. Zhao, C. Song, React. Funct. Polym. 50 (2002) 191–195.
[10] C. Csájági, B. Borcsek, K. Niesz, I. Kovács, Z. Székelyhidi, Z. Bajkó, L. Ürge, F. Darvas, Org. Lett. 10 (2008) 1589–1592.
[11] J. Balogh, A. Kuik, L. Ürge, F. Darvas, J. Bakos, R. Skoda-Földes, J. Mol. Catal. A 302 (2009) 76–79.
[12] C. Ramesh, R. Nakamura, Y. Kubota, M. Miwa, Y. Sugi, Synthesis (2003) 501–504.
[13] M.V. Khedkar, S.R. Khan, D.N. Sawant, D.B. Bagal, B.M. Bhanage, Adv. Synth. Catal. 353 (2011) 3415–3422.
[14] J. Salvadori, E. Balducci, S. Zaza, E. Petricci, M. Taddei, J. Org. Chem. 75 (2010) 1841–1847.
[15] Z.S. Qureshi, S.A. Revankar, M.V. Khedkar, B.M. Bhanage, Catal. Today 198 (2012) 148–153.
[16] T. Kobayashi, M. Tanaka, J. Organomet. Chem. 233 (1982) C64–C66.
[17] (a) F. Ozawa, H. Soyama, T. Yamamoto, A. Yamamoto, Tetrahedron Lett. 23 (1982) 3383–3386.
[18] T. Wang, Z. Zhang, O.B. Wallace, M. Deshpande, H. Fang, Z. Yang, L.M. Zadjura, D.L. Tweedie, S. Huang, F. Zhao, S. Ranadive, B.S. Robinson, Y.F. Gong, K. Ricarrdi, T.P. Spicer, C. Deminie, R. Rose, H.H. Wang, W.S. Blair, P.Y. Shi, P.F. Lin, R.J. Colonno, N.A. Meanwell, J. Med. Chem. 46 (2003) 4236–4239.
[19] L. Chatel-Chaix, M. Baril, D. Lamarre, Viruses 2 (2010) 1752–1765.
[20] C.F.J. Barnard, Organometallics 27 (2008) 5402–5422.
[21] V. de la Fuente, J. Godard, E. Zangrando, C. Claver, S. Castillón, Chem. Commun. 48 (2012) 1695–1697.
[22] Y.Y. Yan, H.P. Zuo, Z.L. Jin, React. Funct. Polym. 32 (1997) 21–24.
[23] J. Liu, S. Zheng, W. Su, C. Xia, Chin. J. Chem. 27 (2009) 623–627.
[24] (a) S. Liu, J. Xiao, J. Mol. Catal. A 270 (2007) 1–43;
(b) V.I. Pârvulescu, C. Hardacre, Chem. Rev. 107 (2007) 2615–2665;
(c) Y. Liu, S.S. Wang, W. Liu, Q.X. Wan, H.H. Wu, G.H. Gao, Curr. Org. Chem. 13 (2009) 1322–1346;
(d) H. Olivier-Bourbigou, L. Magna, D. Morvan, Appl. Catal., A 373 (2010) 1–56.
[25] (a) A. Riisager, R. Fehrmann, M. Haumann, P. Wasserscheid, Top. Catal. 40 (2006) 91–102;
(b) Y. Gu, G. Li, Adv. Synth. Catal. 351 (2009) 817–847;
(c) Q.H. Zhang, S.G. Zhang, Y.Q. Deng, Green Chem. 13 (2011) 2619–2637.
[26] L. Han, M.S. Park, S.J. Choi, Y.J. Kim, S.M. Lee, A.W. Park, Catal. Lett. 142 (2012) 259–266.
[27] C. Van Doorslaer, J. Wahlen, P. Mertens, K. Binnemans, D. De Vos, Dalton Trans. 39 (2010) 8377–8390.
[28] Y. Uozumi, T. Arii, T. Watanabe, J. Org. Chem. 66 (2001) 5272–5274.
[29] E. Takács, C. Varga, R. Skoda-Földes, L. Kollár, Tetrahedron Lett. 48 (2007) 2453–2456.
[30] A.M. Trzeciak, W. Wojtków, J. Ziółkowski, J. Wrzyszcz, M. Zawadzki, New J. Chem. 28 (2004) 859–863.
[31] F. Gayet, J.-D. Marty, N. Lauth-de Viguerie, Arkivoc (xvii) (2008) 61–76.
[32] D. Astruc, Inorg. Chem. 46 (2007) 1884–1894.
[33] R.G. Heidenreich, J.G.E. Krauter, J. Pietsch, K. Köhler, J. Mol. Catal. A 182–183 (2002) 499–509.
[34] Z. Szarka, R. Skoda-Földes, A. Kuik, Z. Berente, L. Kollár, Synthesis (2003) 545–550.