Catalysis Today 198 (2012) 148–153

Contents lists available at SciVerse ScienceDirect

Catalysis Today

journal homepage: www.elsevier.com/locate/cattod

Aminocarbonylation of aryl iodides with primary and secondary amines in aqueous medium using polymer supported palladium-*N*-heterocyclic carbene complex as an efficient and heterogeneous recyclable catalyst

Ziyauddin S. Qureshi, Santosh A. Revankar, Mayur V. Khedkar, Bhalchandra M. Bhanage*

Department of Chemistry, Institute of Chemical Technology, N. Parekh Marg, Matunga, Mumbai, 400 019, India

ARTICLE INFO

Article history:
Available online 12 April 2012

Keywords:
Aminocarbonylation
Aryl iodides
Heterogeneous catalysis
Palladium
Primary–secondary amine

ABSTRACT

Aminocarbonylation of aryl iodides with primary and secondary aromatic/aliphatic amines to corresponding amides using polymer supported palladium-*N*-heterocyclic carbene complex (PS-Pd-NHC) as an efficient heterogeneous, recyclable catalyst is described. The catalytic system was optimized with respect to various reaction parameters to give excellent yield of desired products. The catalyst can be easily separated by simple filtration process and recycled further up to four consecutive recycle without loss in any activity and selectivity. The protocol is advantageous due to the ease in handling of the catalyst, simple workup procedure, and environmentally benign water as solvent and effective catalyst recyclability.

1. Introduction

The synthesis of carbonyl compounds including carboxylic acids [1], amides [2], esters [3], aldehydes [4], and ketones [5] are of basic importance in organic chemistry. Palladium-catalyzed carbonylation of aryl halides for the synthesis of such compounds is one of the highly efficient protocols. In context, aminocarbonylation is one of the promising methods used for the direct one step synthesis of amides via carbonylative coupling of aryl, alkenyl, and heterocyclic halides with primary/secondary amines [6]. Various palladium-based catalytic systems such as $PdBr_2(PPh_3)_2/PdCl_2(PPh_3)_2$ [7], silica-supported bidentate arsine-palladium complex [8], silica-supported bidentate sulfur and phosphine mixed palladium complex [9], and $Pd(OAc)_2/PPh_3$ in ionic liquid [10], and so on for has been explored for this reaction. However, these catalytic systems have several limitations like requirement of air and moisture-sensitive phosphine-containing ligands, high carbon monoxide pressure, higher catalyst loading, limited substrate compatibility, and the use of organic solvents. Therefore, the efforts to develop a heterogeneous, reusable and phosphine free catalytic system which can efficiently catalyze aminocarbonylation of aryl halides are highly desirable.

Recently, *N*-heterocyclic carbene (NHC) as a ligand has found potential applications in homogeneous transition metal catalysis [11,12], because of its effective binding ability to any transition metal irrespective of their oxidation states. NHC ligand reveals very high dissociation energies compared to phosphine ligands, which have been quantified via theoretical calculation for different metals. Therefore, the binding between the NHC and transition metal is much stronger, as well as being chemically and thermally more inert toward cleavage than that of other metal complexes. Recently, polymer-supported palladium-*N*-heterocyclic carbene (PS-Pd-NHC) catalyst have been explored for Suzuki and carbonylative Suzuki coupling reactions [13], as it offers several advantages like reuse of expensive transition metals and ligands with a possibility to prevent the contamination of ligand residue in products. However, to the best of our knowledge, no such polymer-supported catalytic system has yet been explored for the simple aminocarbonylation of aryl iodides with primary and secondary amines.

In continuation of our interest on phosphine-free carbonylation reactions [14], herein we report an facile protocol for the aminocarbonylation of aryl iodides with primary and secondary amines using polymer supported palladium-NHC complex (PS-Pd-NHC) as a phosphine free, heterogeneous and recyclable catalyst (Scheme 1).

2. Experimental

All chemicals were procured from firms of repute. Various substrates of aryl iodides and amines were purchased from Sigma–Aldrich. All the chemicals were used as received without any further purification. Polymer-supported Palladium-*N*-heterocyclic

---

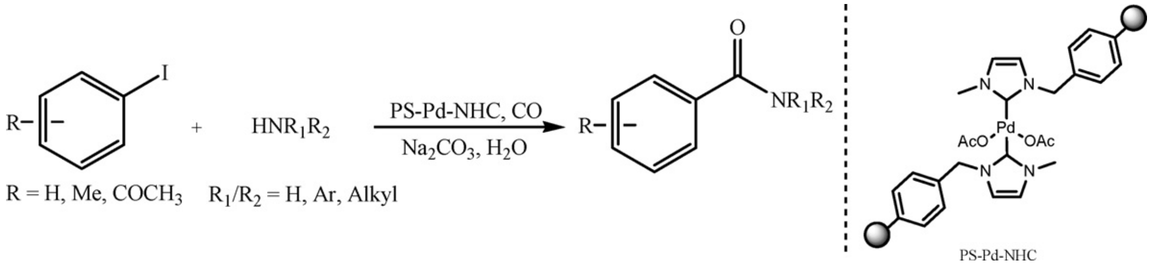
* Corresponding author. Tel.: +91 22 3361 1111; fax: +91 22 24145614.
E-mail addresses: bm.bhanage@ictmumbai.edu.in, bm.bhanage@gmail.com (B.M. Bhanage).

0920-5861/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.cattod.2012.03.039

Table 1
Optimization of the aminocarbonylation reaction using PS-Pd-NHC catalyst.[a]

Entry	Solvent	Base	Temperature (°C)	CO pressure (psi)	Time (h)	Yield (%)[b]
Effect of solvent						
1	Toluene	Na_2CO_3	100	100	8	74
2	THF	Na_2CO_3	100	100	8	90
3	None	Na_2CO_3	100	100	8	14
4[c]	Water	Na_2CO_3	100	100	8	92
5[d]	Water	Na_2CO_3	100	100	8	96
6[e]	Water	Na_2CO_3	100	100	8	88
Effect of base						
7	Water	–	100	100	8	–
8	Water	K_2CO_3	100	100	8	90
9	Water	Et_3N	100	100	8	89
Effect of temperature						
10	Water	Na_2CO_3	80	100	8	81
11	Water	Na_2CO_3	110	100	8	88
Effect of CO pressure						
12	Water	Na_2CO_3	100	150	8	94
13	Water	Na_2CO_3	100	200	8	94
Effect of time						
14	Water	Na_2CO_3	100	100	6	84
15	Water	Na_2CO_3	100	100	10	94

[a] Reaction conditions = iodobenzene (1 mmol), aniline (2 mmol), Na_2CO_3 (2 mmol), PS-Pd-NHC (50 mg, 14.2 μmol), water (10 mL), CO pressure (100 Psi), temperature (100 °C), time (8 h).
[b] GC yield.
[c] TOF = 8.2 h^{-1}.
[d] Catalyst = $Pd(OAc)_2$ and TOF = 8.5 h^{-1}.
[e] Catalyst = (5%) Pd/C.



Scheme 1. Aminocarbonylation reaction of aryl iodides with primary and secondary amines.

carbene complex (PS-Pd-NHC) used was prepared according to the reported procedure in literature [15].

2.1. Characterization of polymer-supported Pd-N-heterocyclic carbene complex (PS-Pd-NHC)

Prepared PS-Pd-NHC was characterized by solid state ^{13}C NMR (Bruker Avance^{III} 700 MHz); δ 14 (CH_3 aliphatic acetate skeleton), 38 (N—CH_3 skeleton), 41 (aliphatic polystyrene skeleton), 128 (NCH, NCH, aromatic polystyrene skeleton), 147 (NCN, aromatic polystyrene skeleton), 187 (C=O acetate skeleton). Loading of palladium catalyst on chloromethyl polystyrene resin support was evaluated by ICP-AES analysis and was found to be about 0.29 mmol g^{-1} of support.

2.2. Typical procedure for aminocarbonylation of aryl iodides with primary and secondary amines in aqueous medium

To a 100 mL autoclave were added aryl iodides (1.0 mmol), amines (2 mmol), PS-Pd-NHC (50 mg, 14.5 μmol), H_2O (10 mL), and Na_2CO_3 (2.0 mmol). The reaction mixture was first stirred for 10 min and then flushed several times with CO, then filled with 100 psi of CO and the mixture was heated at 100 °C for 8 h. The progress of the reaction was monitored using GC analysis (PerkinElmer, Clarus 400) (BP-10 GC column, 30 m × 0.32 mm ID, film thickness 0.25 mm). After completion of the reaction, the mixture was cooled to room temperature. The catalyst was filtered off and products were extracted with ethyl acetate, dried

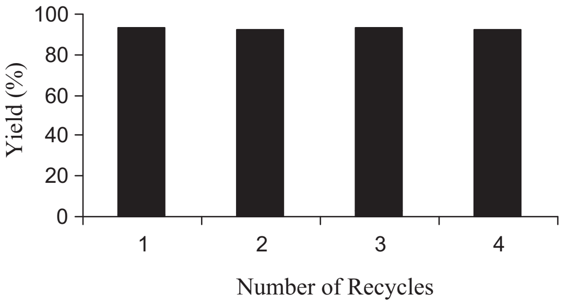


Fig. 1. Catalyst recyclability study for aminocarbonylation reaction of iodobenzene with aniline.Reaction conditions = iodobenzene (1 mmol), aniline (2 mmol), Na_2CO_3 (2 mmol), PS-Pd-NHC (50 mg, 14.2 μmol), water (10 mL), CO pressure (100 psi), temperature (100 °C), time (8 h), GC yield.

Table 2
Aminocarbonylation of aryl iodides with various aliphatic and aromatic primary amines.[a]

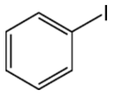
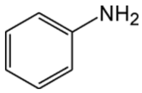
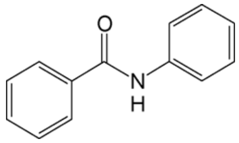
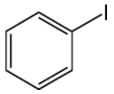
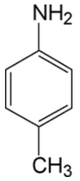
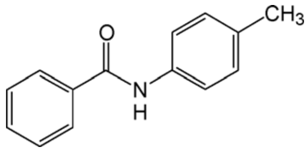
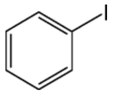
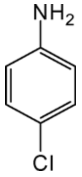
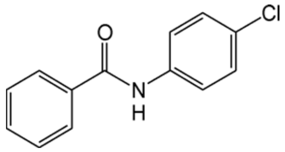
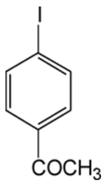
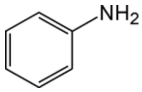
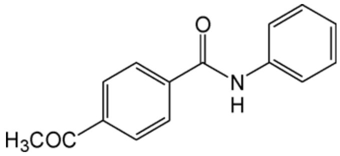
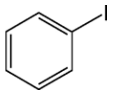
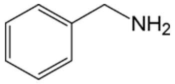
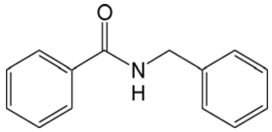
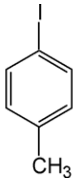
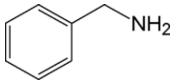
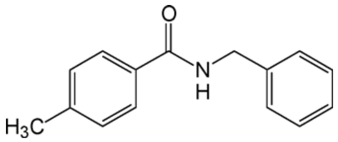
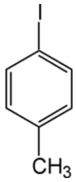
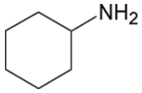
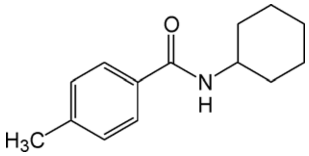
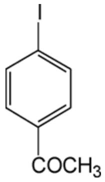
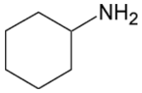
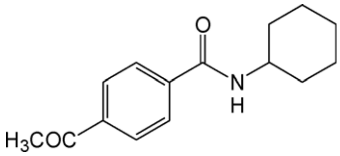
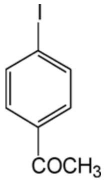
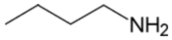
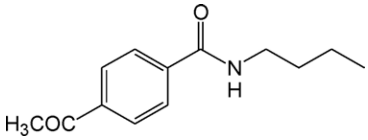
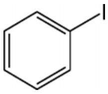
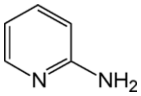
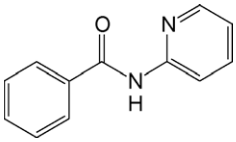
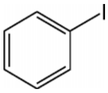
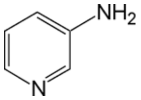
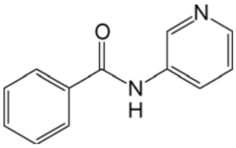
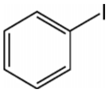
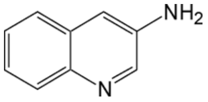
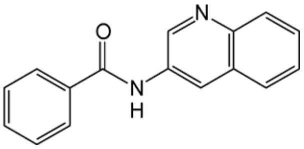
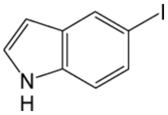
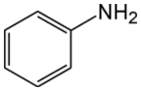
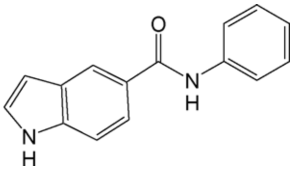
Entry	Aryl iodide	Amine	Product	Yield (%)[b]
1				90
2				88
3				79
4				94
5				90
6				87
7				80
8				89
9				78

Table 2 (*Continued*)

Entry	Aryl iodide	Amine	Product	Yield (%)[b]
10				14
11				72
12				82
13				75

[a] Reaction conditions = aryl iodide (1 mmol), amine (2 mmol), Na_2CO_3 (2 mmol), PS-Pd-NHC (50 mg, 14.2 μmol), water (10 mL), CO pressure (100 Psi), temperature (100 °C), time (8 h).

[b] Isolated yield.

over Na_2SO_4 and the solvent was evaporated under vacuum. The residue obtained was purified by column chromatography (silica gel, 60–120 mesh; PE-EtOAc, 90:10) to afford the desired aminocarbonylated product. All the products are well known and were confirmed by GC–MS analysis.

2.3. Recyclability study of PS-Pd-NHC complex for aminocarbonylation reaction of iodobenzene with aniline in water

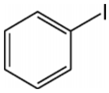
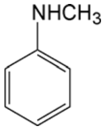
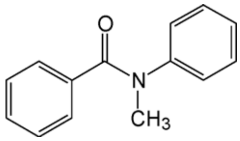
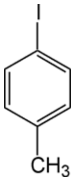
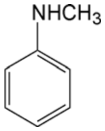
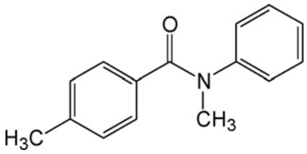
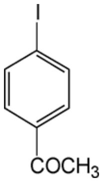
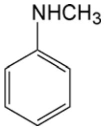
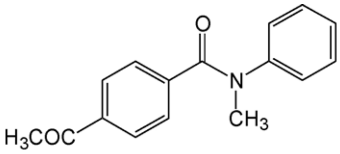
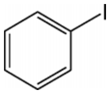
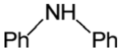
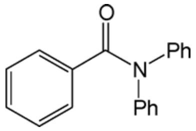
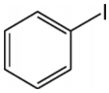
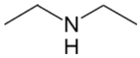
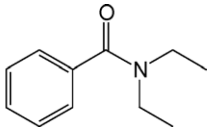
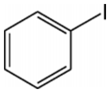
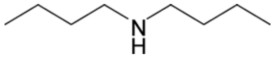
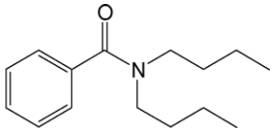
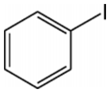
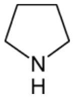
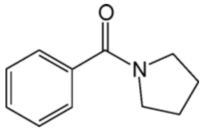
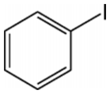
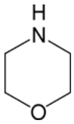
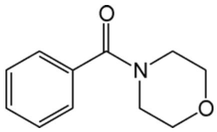
After completion of reaction, the reaction mixture was cooled to room temperature, and the catalyst was collected by filtration. The product was extracted in ethyl acetate and the aqueous layer containing catalyst was filtered (catalyst particles are suspended in aqueous layer), the filtered catalyst was washed vigorously with distilled water (3 × 10 mL) and methanol (3 × 10 mL) to remove all traces of product or reactant present. The filtered catalyst was then dried under reduced pressure and kept for activation at 80 °C for a period of 4 h prior to the next recycle. The dried catalyst was then used for catalyst recyclability experiment and it was observed that the recovered catalyst could be reused for four consecutive cycles for the aminocarbonylation reaction of iodobenzene with aniline (product yield = 92%, 90%, 90%, 88%, respectively Fig. 1). To check the palladium metal leaching, we performed the ICP-AES analysis of the 1st and 4th recycle run; where below detectable level (0.01 ppm) of palladium in solution was observed thus indicating no significant leaching of the palladium catalyst.

3. Results and discussion

In concern to development of efficient, phosphine free and heterogeneous protocol for aminocarbonylation, the reaction of iodobenzene with amines in the presence of PS-Pd-NHC as a catalyst was chosen as a model reaction, and the influence of various reaction parameters such as nature of solvent, base, temperature, CO pressure and time were studied (Table 1).

Firstly, the influence of solvents on aminocarbonylation reaction was investigated (entries 1–4). Non-polar solvent like toluene furnishes lower yield of desired product (entry 1). Whereas polar aprotic solvent like THF provides excellent yield (90%) of desired product (entry 2). With this observation, to make a synthetic protocol greener we screened water as a reaction solvent and it provided excellent yield of desired product (entry 4). To confirm the role of solvent in reaction outcome, we attempted reaction in neat condition, but poor yield of corresponding product was observed (entry 3). Therefore further reactions were carried out using water as a solvent. To check the activity of developed catalytic system, TOF values of PS-Pd-NHC is compared with homogeneous Palladium catalyst ($Pd(OAc)_2$) (entries 5 and 6) and it was observed that homogeneous catalyst gave somewhat higher TOF i.e. 8.5 h^{-1} than that of PS-Pd-NHC catalyst which gave TOF of 8.2 h^{-1}. This is observed due to the soluble nature of homogeneous catalyst. Also it should be noted that PS-Pd-NHC catalyst is giving nearly similar performance with additional benefit of catalyst product separation and recycle. Heterogeneous catalyst like Pd/C (5%) was also screened for aminocarbonylation reaction but it gave lower yield of desired product (entry 6) as compared to both of above mentioned catalysts. To confirm the influence of base in reaction progress, initially reaction was tried in absence of base, but no desired product was observed that indicates vital role of base in the reaction (entry 7). Consequently inorganic and organic bases were screened, and Na_2CO_3 was found to be best base for reaction (entries 4, 8–9). In order to examine the effect of temperature, reactions were carried out at different temperatures ranging from 80 to 110 °C (entries 4, 10–11). At 100 °C maximum yield of expected product was observed. The influence of CO pressure was also studied and 100 psi of CO pressure was found to be optimum for the reaction (entries 3, 12–13). When reaction was carried out for 6 h lower yield of corresponding product was observed (entry 14), while with the increase in reaction time improved yield of corresponding amide was observed (entries 3, 15).

Table 3
Aminocarbonylation of aryl iodides with various secondary amines.[a]

Entry	Aryl iodide	Amine	Product	Yield (%)[b]
1				91
2				88
3				81
4				–
5				88
6				91
7				86
8				79

[a] Reaction conditions = aryl iodide (1 mmol), amine (2 mmol), Na_2CO_3 (2 mmol), PS-Pd-NHC (50 mg, 14.2 μmol), water (10 mL), CO pressure (100 Psi), temperature (100 °C), time (8 h).

[b] Isolated yield.

Hence the optimized reaction conditions were, iodobenzene (1 mmol), amine (2 mmol), CO pressure (100 psi), PS-Pd-NHC (2 mol%), Na_2CO_3 (2 mmol) in water (10 mL) at 100 °C for 8 h.

These optimized reaction conditions were then used for aminocarbonylation of various aryl iodides with different aliphatic and aromatic primary amines results obtained are summarized in Table 2.

The aminocarbonylation of iodobenzene with aniline provided the corresponding amide product in good yields (entry 1) and it was observed that both electron-donating and electron-withdrawing groups under present reaction conditions smoothly underwent aminocarbonylation reaction giving desired products with appreciable yields. In all cases, we observed that aryl halide consumes completely giving amide and benzene (to small extent as a dehalogenation product). There was no other side product was observed. Primary aromatic amines such as 4-methyl and 4-chloro aniline were found to react with iodobenzene providing 88% and 79% yield of respective amides products (entries 2–3). The reaction of aryl iodide bearing strong electron-withdrawing group such as COMe permits the aminocarbonylative coupling reaction with aniline giving 4-acetyl-*N*-phenyl-benzamide (94%) in excellent yield (entry 4). Aminocarbonylation of aliphatic primary amine such as benzylamine was found to react smoothly with iodobenezene and 4-iodotoluene providing 90% and 87% yields of respective *N*-benzylbenzamides (entries 5–6). Furthermore different aliphatic primary amines such as cyclohexylamine and butylamine were found to undergo the aminocarbonylation reaction with different substituted aryl iodides giving

78–89% yields of amide products (entries 7–9). Encouraged with these results, the PS-Pd-NHC complex was then subjected for aminocarbonylation reaction of heterocyclic primary amines such as 2-aminopyridine, 3-aminopyridine, 3-aminoquinoline with iodobenezene affording moderate to good yield of desired amides (entries 10–12). It was noticed that bicyclic heteroaryl iodide such as 5-iodoindole smoothly undergoes aminocarbonylative coupling reaction with aniline, providing 75% yield of expected amide (entry 13).

Moreover, the generality of our catalytic system (PS-Pd-NHC) under the present reaction conditions was further explored for the aminocarbonylation of secondary amines (Table 3). The aminocarbonylation of iodobenzene with *N*-methyl aniline provided the corresponding *N*-methyl-*N*-phenyl-benzamide product in good yield (entry 1). The aminocarbonylation coupling reaction of 4-iodotoluene and 4-acetyl iodobenzene with *N*-methyl aniline using PS-Pd-NHC complex as a catalyst provides 88% and 81% yield, respectively, of the desired products (entries 2–3). Unfortunately, aromatic secondary amine, i.e. biphenyl amine was not compatible with this aminocarbonylation coupling reaction (entry 4). The aminocarbonylation of iodobenzene with aliphatic secondary amines such as diethyl amine and dibutyl amine was also found to provide excellent yields of amide products (entries 5–6). The present catalytic system also worked very well for the aminocarbonylation reaction of iodobenzene with aliphatic cyclic secondary amines (pyrrolidine and morpholine) providing 91% and 79% yield, respectively (entries 7–8).

Thus the developed protocol is found to be general for the aminocarbonylation coupling reaction of various structurally and electronically different aryl iodides with aliphatic/aromatic primary and secondary amines providing good to excellent yield of the desired amides, illustrates broad application of the developed methodology and its remarkable functional group compatibility on both reagent was observed.

4. Conclusion

In conclusion, an efficient, phosphine-free protocol for the aminocarbonylation reaction of aryl iodides with primary and secondary amines in aqueous medium using PS-Pd-NHC complex as a heterogeneous and recyclable catalyst has been developed. The reaction was optimized with respect to various parameters and enabled aminocarbonylation reaction of different aryl iodides with variety of primary and secondary amines affording good to excellent yield of desired products thus illustrating broad application of the methodology. The catalyst can be easily recycled by simple filtration process up to four consecutive recycle without loss in any activity and selectivity. The developed protocol with use of water as a solvent and recyclable catalytic system introduces a success toward green approach in organic synthesis.

Acknowledgement

The financial assistance from Indira Gandhi Centre for Atomic Research (IGCAR) Kalpakkam, India is kindly acknowledged.

References

[1] (a) D. Valenline Jr., J.W. Tilley, R.A. LeMahieu, The Journal of Organic Chemistry 46 (1981) 4614;
(b) L. Classar, M. Foa, A. Gardano, Journal of Organometallic Chemistry 121 (1976) 55;
(c) V.V. Grushin, H.J. Alper, Journal of Chemical Society, Chemical Communications (1992) 611;
(d) I.P. Beletskaya, A.L. Lapidas, K.B. Petrovskii, Russian Journal of Organic Chemistry 34 (1998) 1464;
(e) Y.S. Lin, A. Yamamoto, Journal of Organometallic Chemistry 645 (2002) 152.

[2] (a) A. Schoenberg, R.F. Heck, Journal of Organometallic Chemistry 39 (1974) 3327;
(b) R.J. Perry, B.D. Wilson, Organometallics 13 (1994) 3346;
(c) T. Takahashi, H. Inoue, S. Tomida, T. Doi, A.M. Bray, Tetrahedron Letters 40 (1999) 7843;
(d) W. Magerlei, A.F. Indolesi, M. Beller, Journal of Organometallic Chemistry 641 (2002) 30.

[3] (a) A. Schoenberg, I. Barrolatti, R.F. Heck, Journal of Organometallic Chemistry 39 (1974) 3318;
(b) Y. Ben-David, M. Portnoy, D. Milstein, Journal of the American Chemical Society 111 (1989) 8742;
(c) J. Yang, A. Haynes, P.M. Maitlis, Chemical Communications (1999) 179;
(d) V. Calo, P. Giannoccaro, A. Nacci, A. Monopoli, Tetrahedron Letters 42 (2001) 3299;
(e) W. Magerlein, M. Beller, A.F. Indolese, Journal of Molecular Catalysis A: Chemical 156 (2000) 213.

[4] (a) Y. Ben-David, M. Portnoy, D. Milstein, Journal of the American Chemical Society (Commununication) (1989) 1816;
(b) T. Okano, N. Harada, J. Kiji, Bulletin of the Chemical Society of Japan 67 (1994) 2329.

[5] J.K. Stille, Pure Applied Chemistry 57 (1985) 1771.

[6] (a) H.M. Colquhoun, D.H. Thompson, M.V. Twigg, Carbolylation Direct Synthesis of Carbonyl Compounds, Plenum Press, New York, 1991;
(b) J. Tsuji, Palladium Reagents and Catalysis, Wiley, Chichester, 1995;
(c) R.F. Heck, Palladium Reagents in Organic Synthesis, Academic Press, New York, 1985.

[7] A. Schoenberg, R.F. Heck, Journal of Organic Chemistry 39 (1974) 3327.

[8] M. Cai, Y. Huang, R. Hu, C. Song, Journal of Molecular Catalysis A: Chemical 212 (2004) 151.

[9] M. Cai, H. Zhao, Y. Huang, Journal of Molecular Catalysis A: Chemical 238 (2005) 41.

[10] R. Skoda-Foldes, E. Takacs, J. Horvath, Z. Tuba, L. Kollar, Green Chemistry 5 (2003) 643.

[11] (a) W. Herrmann, Angewandte Chemie, International Edition 41 (2002) 1290;
(b) K. Ofele, Journal of Organometallic Chemistry 12 (1968) 42;
(c) H. Wanzlick, H. Schonherr, Angewandte Chemie, International Edition 80 (1968) 154.

[12] (a) J.W. Sprengers, J. Wassenaar, N.D. Clement, K.J. Cavell, C.J. Elsevier, Angewandte Chemie, International Edition 44 (2005) 2026;
(b) P. Hauwert, R. Boerleider, S. Warsink, J.J. Weigand, C.J. Elsevier, Journal of American Chemical Society 132 (2010) 16900.

[13] (a) Z.S. Qureshi, K.M. Deshmukh, P.J. Tambade, B.M. Bhanage, Synthesis (2011) 243;
(b) J. Byun, Y. Lee, Tetrahedron Letters 45 (2004) 1837;
(c) J. Kim, B. Jun, J. Byun, Y. Lee, Tetrahedron Letters 45 (2004) 5827.

[14] (a) M.V. Khedkar, S.R. Khan, D.N. Sawant, D.B. Bagal, B.M. Bhanage, Advanced Synthesis & Catalysis 353 (2011) 3415;
(b) M.V. Khedkar, P.J. Tambade, Z.S. Qureshi, B.M. Bhanage, European Journal of Organic Chemistry 6981 (2010);
(c) P.J. Tambade, Y.P. Patil, B.M. Bhanage, Applied Organometallic Chemistry 23 (2009) 235;
(d) P.J. Tambade, Y.P. Patil, M.J. Bhanushali, B.M. Bhanage, Synthesis 2347 (2008);
(e) P.J. Tambade, Y.P. Patil, M.J. Bhanushali, B.M. Bhanage, Tetrahedron Letters 49 (2008) 2221;
(f) P.J. Tambade, Y.P. Patil, A.G. Panda, B.M. Bhanage, European Journal of Organic Chemistry (2009) 3022.

[15] D.B. Bagal, Z.S. Qureshi, K.P. Dhake, S.R. Khan, B.M. Bhanage, Green Chemistry 13 (2011) 1490.