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Journal of Catalysis 227 (2004) 542–546
JOURNAL OF CATALYSIS
www.elsevier.com/locate/jcat

Research Note

Synthesis of 2-oxazolidinone catalyzed by palladium on charcoal: a novel and highly effective heterogeneous catalytic system for oxidative cyclocarbonylation of β-aminoalcohols and 2-aminophenol

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Received 9 May 2004; revised 12 July 2004; accepted 18 July 2004

Available online 21 August 2004

Abstract

Oxidative cyclocarbonylation of β-aminoalcohols and 2-aminophenol to synthesize corresponding 2-oxazolidinones catalyzed by a Pd/C–I_2 heterogeneous catalytic system has been developed which gave excellent selectivity and high turnover frequency (TOF) values 15 times larger than the best results previously reported. The catalyst could be reused for five times almost without losing its catalytic activity and selectivity. The effects of promoters, pretreatment, solvents, and reaction conditions have been investigated.

Keywords: Palladium on charcoal; Oxidative cyclocarbonylation; β-Aminoalcohol; 2-Aminophenol; 2-Oxazolidinone; Reuse of the catalyst; TOF

1. Introduction

2-Oxazolidinones have found extensive applications as intermediates for fine chemicals, pharmaceuticals, cosmetics, pesticides, and so on. Especially, the chiral 2-oxazolidinones have been used as chiral auxiliaries in a wide range of asymmetric syntheses [1,2]. 2-Oxazolidinones are usually prepared by phosgenation of the corresponding 1,2-aminoalcohols with toxic phosgene or its derivatives [3], which may cause serious environmental pollution and equipment corrosion. Nowadays, as an alternative, the use of diethyl carbonate as a phosgene substitute is relatively expensive for commercial application [4]. It should be noted that dialkyl carbonates are currently produced via similar hazardous phosgenation routes [5]. Because of environmental concerns, there is a great demand for finding some highly efficient and environmentally benign methods in place of such toxic and dangerous reagents.

The intramolecular oxidative cyclocarbonylation of β-aminoalcohols or its derivatives catalyzed by transition metal is an attractive and effective way to produce these heterocyclic compounds (Scheme 1). To our knowledge, only few reports have been described using this catalytic process [6]. Although some advancements have been made, the corresponding catalytic turnover frequency (moles of oxazolidinones produced per mole of Pd atoms per hour, TOF) is still too low, the reaction conditions are stern, and the reaction time is too long (15 h). The most restricting aspect of these studies is that they were focused on the homogeneous catalytic systems, wherein the expensive palladium catalysts are difficult to be separated and reused. Until now, no heterogeneous catalyst systems have been studied in the direct oxidative cyclocarbonylation of β-aminoalcohols to synthesize the corresponding 2-oxazolidinones. In view of the importance and applications of palladium-catalyzed carbonylation reactions from industrial as well as academic viewpoints, it is urgent to find an efficient, inexpensive, and recyclable catalyst system for this interesting reaction.

Herein, we report a highly efficient oxidative cyclocarbonylation process for synthesis of 2-oxazolidinones

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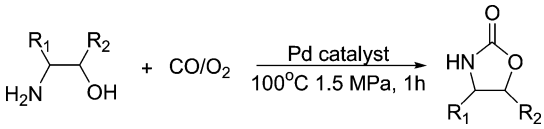
0021-9517/$ – see front matter
doi:10.1016/j.jcat.2004.07.019



Scheme 1.

from various aliphatic β-aminoalcohols and 2-aminophenol catalyzed by the Pd/C–I_2 catalytic system with excellent turnover frequency under mild conditions. The catalyst could be easily separated from the reactant and significant loss of catalytic activity and selectivity was not found even after recycling five times.

2. Experimental

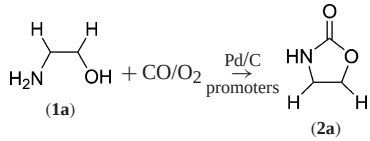
The catalyst, consisting of 10% Pd/C, was purchased from Fluka; aminoalcohols and solvents were freshly distilled and used. Carbon monoxide and oxygen with a purity of 99.99% were commercially available. Other reagents were of analytical grade and were used as received.

All oxidative cyclocarbonylation experiments were carried out in a 100-ml autoclave equipped with magnetic stirring and automatic temperature control. In a typical experiment, known quantities of β-aminoalcohols (10 mmol), catalyst: 10% Pd/C (0.01 mmol), I_2 (0.036 mmol), and solvent (DME, 8 ml) were charged into the reactor. Then the autoclave was pressurized with carbon monoxide and oxygen to a total pressure of 1.25 MPa (CO 1.0 MPa and O_2 0.25 MPa). The autoclave was placed in oil bath preheated at 100 °C, and the whole reaction mixture was stirred for only 1 h. After the reaction, the autoclave was cooled, excess gas was purged, and the reaction mixture was filtered. The catalyst could be directly reused for the next run without any treatment and the promoters should be freshly added before the new carbonylation. Qualitative analyses were conducted with a HP 6890/5973 GC-MS and quantitative analyses were carried out over a HP 5890 GC.

3. Results and discussion

Iodine compounds (e.g., iodine, sodium iodide) have been employed in recent years as promoters for a number of reactions. It should be noted that a heterogeneous iodide-promoted oxidative carbonylation of amines to carbamate esters or diphenylureas has been described by Fukuoka and co-workers and Chaudhari and co-workers [7]. During the investigation of our catalyst system, the effects of promoters were examined under the typical reaction conditions (Table 1). Initially, the comparison experiments of oxidative carbonylation of ethanolamine (**1a**) were carried out using Pd/C as catalyst with and without promoter, I_2 (Table 1, entries 1 and 3). It was observed that in the absence of I_2, only 43% conversion and 57% selectivity of 2-oxazolidinone were obtained, while with I_2, quantitive conversion of ethanolamine

Table 1
Oxidative cyclocarbonylation of ethanolamine (**1a**) to 2-oxazolindinone (**2a**): effect of iodide promoters[a]



(**1a**) (**2a**)

Entry	Promoter	Conversion (%)	Selectivity (%)	TOF (h^{-1})
1[b]	–	43	57	245
2[c]	I_2	–	–	–
3	I_2	100	99	990
4	NaI	100	99	990
5	CuI	99	99	980
6	C_4H_9I	98	99	970
7	LiI	98	98	960
8	KI	76	96	730

[a] Reaction conditions: Pd/C 0.01 mmol; ethanolamine 10 mmol; promoter 0.036 mmol; temperature 100 °C, solvent (DME) 8 ml; P_{CO} 1.0 MPa; P_{O_2} 0.25 MPa; time 1 h.

[b] Only Pd/C was used.

[c] Only I_2 was used.

is observed. Another experiment using only I_2 in the absence of Pd/C catalyst gave no conversion of **1a** (Table 1, entry 2). These results suggested that neither Pd/C nor I_2 could act as an efficient catalyst for oxidative cyclocarbonylation of ethanolamine. It was shown that promoters containing iodide were absolutely necessary in this oxidative cyclocarbonylation catalyst system. Therefore, the effects of a variety of iodide-containing promoters, particularly I_2, NaI, C_4H_9I, CuI, LiI, and KI were studied. The data in Table 1 showed that all the employed iodide compounds besides KI were very efficient promoters. Furthermore, the selectivities of **2a** were all excellent (> 96%).

Catalyst pretreatment can play an important role in the activity and selectivity of catalytic reactions and it is necessary to learn the intrinsic activity of catalyst from the pretreatment information. Therefore, some experiments were conducted to investigate the effect of pretreatment of Pd/C catalyst with CO, O_2, and aminoalcohol. In these experiments, the catalyst system with solvent was pretreated with CO, O_2, or aminoalcohol individually and then the oxidative cyclocarbonylation was carried out. The results are presented in Table 2 along with the conditions of pretreatment. It was seen that treatment of Pd/C with all the reactants had almost no effect on the catalytic activity and selectivity. If there were some effects obtained in the pretreatment catalyst system, the more or less similar results would probably appear in the fresh catalyst system. It was because that they reacted under the same reaction conditions and it was unsure which reactant would first act on the catalyst. Though a detailed mechanism for pretreatment effects has not been studied here, the reported data showed that there was no need to conduct catalyst pretreatment with reactants; therefore, all further experiments were carried out without any pretreatment.

Table 2
Effect of CO, O_2, and ethanolamine pretreatment on activity of a 10% Pd/C–I_2 catalyst system[a]

Pretreatment	Pretreatment conditions			Conversion (%)	Selectivity (%)
	Duration (min)	Temperature (°C)	Pretreatment (MPa)		
Fresh catalyst	–	–	–	100	99
CO	60	100	2	100	99
Pretreatment O_2	60	100	2	98	98
Pretreatment ethanolamine (under N_2)	60	100	2	99	98

[a] Pretreated catalyst reaction conditions: Pd/C 0.01 mmol; ethanolamine 10 mmol; promoter 0.036 mmol; temperature 100 °C; P_{CO} 1.0 MPa; P_{O_2} 0.25 MPa; DME 8 ml; time 1 h.

Table 3
Oxidative cyclocarbonylation of ethanolamine (**1a**) to 2-oxazolindinone (**2a**): effects of different solvents on the reaction

Entry	Solvent	Conversion (%)	Selectivity (%)	TOF (h^{-1})
1	DME	100	99	990
2	DMF	100	100	1000
3	DMSO	100	98	980
4	CH_3OH	58	96	557
5	C_2H_5OH	52	96	499
6	THF	40	100	400

Reaction conditions: Pd/C 0.01 mmol; ethanolamine 10 mmol; promoter 0.036 mmol; temperature 100 °C; P_{CO} 1.0 MPa; P_{O_2} 0.25 MPa; solvent 8 ml; time 1 h.

Reaction solvents play a key role in the activity and selectivity of catalysts during the catalytic reactions. The effects of different solvents on the reaction were also investigated at 100 °C, 1.25 MPa with Pd/C–I_2 as the catalytic system. The results are presented in Table 3. High catalytic activities were obtained when DME acted as the reaction media. However, when other polar solvents (methanol, ethanol) were used in the reaction, the catalyst showed comparatively poor catalytic activity. This phenomenon was the same as that reported by Gabriele and co-workers, which explained it as follows: the polarity of is higher in CH_3OH than in DME and it is well established that the basicity of amines is significantly reduced in low-polar aprotic solvents with respect to polar protic solvents [6c,6d,8]. That is, the high polarity is disadvantageous to the oxidative carbonylation. However, when the more polar DMF and DMSO act as the solvents, as high as 1000 TOF was obtained with absolute conversion of substrate. Therefore, the protic/aprotic nature of the solvent alone is not enough to explain the observed change in activity of the catalyst.

A significant drawback associated with using CO/O_2 as the reagent in organic synthesis is the potential dangers operating at high reaction temperatures and pressures. Thus, we were gratified to discover that our catalyst system could operate at low reaction pressures and temperatures. The quantitative transformation of reactant could also be obtained under considerable mild reaction conditions (Table 4, entry 1). Decreasing the temperature below the optimal level (100 °C) resulted in a dramatic decrease in catalytic activity (Table 4, entries 2 and 3), which indicated that the catalyst system was sensitive to the reaction temperature. Besides, the mol ratio of I_2 the Pd/C catalyst was also examined. In comparison

Table 4
Oxidative cyclocarbonylation of ethanolamine (**1a**) to 2-oxazolindinone (**2a**): effects of various reaction conditions[a]

Entry	Temperature (°C)	P_{CO/O_2} (MPa)	Conversion (%)	Selectivity (%)	TOF
1	100	1.0/0.25	100	99	990
2	80	1.0/0.25	54	98	530
3	60	1.0/0.25	43	96	413
4[b]	100	1.0/0.25	100	99	990
5[c]	100	2.0/0.5	52	99	1030
6[c]	120	2.0/0.5	72	100	1440
7[d]	100	2.0/0.5	58	100	1160
8[e]	100	2.0/0.5	81	100	1620
9[e]	120	2.0/0.5	98	98	1921

[a] Reaction conditions: Pd/C 0.01 mmol; ethanolamine 10 mmol; I_2 0.036 mmol; solvent (DME) 8 ml; time 1 h.
[b] Only 0.018 mmol I_2 was added.
[c] The mol ratio of **1a**/catalyst = 2000.
[d] The mol ratio of **1a**/catalyst = 2000, I_2, 0.05 mmol.
[e] The mol ratio of **1a**/catalyst = 2000, I_2, 0.036 mmol, the reaction solvent is DMF.

with the results of Gabriele and co-workers, which need a large excess of promoter (10 or more mole KI per mole of PdI_2) to obtain the optimal catalyst efficiency, the reaction could be effectively performed using only 1.8 eq of I_2 with respect to Pd/C catalyst under the same conditions (Table 4, entry 4) [6d]. When the quantity of ethanolamine was increased to 20 mmol, i.e., the mole ratio of substrate/catalyst is 2000, only 52% yield of 2-oxazolidinone was obtained under the same reaction conditions (Table 4, entry 5). Neither increasing the quantity of promoter nor improving the reaction temperature could enhance the yield of product greatly. However, if the solvent was replaced with DMF, the yield of 2-oxazolidinone was accordingly increased to 81%, and almost quantitative transformation of **1a** was achieved with the reaction temperature increasing to 120 °C (Table 4, entry 9). It is important to note that the reaction TOF value obtained in our catalytic system is 15 times larger than the highest result previously reported (TOF = 128 h^{-1}).

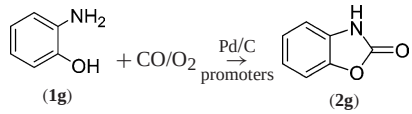
In addition to the high activity and selectivity, the Pd/C–I_2 catalytic system also showed good stability. After the completion of the oxidative cyclocarbonylation of ethanolamine, the catalyst was recovered and recycled for the next reaction with the fresh promoter added under the same reaction condition; any significant loss of catalytic activity and selectivity were not found even after being reused for five times.

Table 5
Oxidative cyclocarbonylation of different β-aminoalcohols (**1b–1f**) to synthesize corresponding 2-oxazolidinone (**2b–2f**) using the Pd/C–I_2 catalytic system[a]

Sub.	R_1	R_2	Conversion (%)	Selectivity (%)	TOF (h^{-1})
1b	H	CH_3	100	100	1000
1c	CH_3	H	99	99	980
1d	CH_3CH_2	H	99	98	970
1e[b]	$(CH_3)_2CH$	H	98	98	960
1f[c]	$(CH_3)_2CH$	H	96	98	941

[a] Reaction conditions: the mol ratio of substrates/catalyst = 1000; promoter (I_2) 0.036 mmol; temperature 100 °C; $P_{CO/O_2} = 1.0/0.25$; solvent (DME) 8 ml; time 1 h.
[b] Racemic.
[c] L enantiomer.

Table 6
Oxidative carbonylation of 2-aminophenol (**1g**) to produce 2-benzoxazolinone (**2g**)[a]



(**1g**) (**2g**)

Sub.	Solvent	Promoter	Conversion (%)	Selectivity (%)	TOF
1g	DME	NaI	60	96	576
1g	DMF	NaI	64	97	621
1g	DMF	I_2	100	100	1000

[a] Reaction conditions: the mol ratio of **1g**/Pd/C = 1000; promoter 0.036 mmol; temperature 100 °C; $P_{CO/O_2} = 1.0/0.25$; solvent 10 ml; time 1 h.

It was found that the high efficiency of the Pd/C–iodine promoter catalytic system was applicable to the oxidative carbonylation of other β-aminoalcohols (**1b–1f**) under the optimal reaction conditions (the molar ratio of substrates/catalyst = 1000, temperature 100 °C, $P_{CO/O_2} = 1.0/0.25$, time 1 h). The results are summarized in Table 5. As can be seen, the Pd/C–I_2 catalyst system showed excellent catalytic activity to almost all the employed β-aminoalcohols under the optimal reaction conditions, providing the corresponding 2-oxazolidinones in high TOF and selectivity (> 98%).

The high efficiency of accomplishing the reaction under considerably mild oxidizing conditions has also permitted the application of this methodology to substrates particularly sensitive to oxidizing agents. When 2-aminophenol (**1g)** was used as the reaction substrate, 60% yield and 96% selectivity of 2-benzoxazolinone (**2g**) were obtained using Pd/C–NaI as the catalyst system and DME as the solvent in 1 h (Table 6). Based on the results of the effect of solvents, initially, we considered that the catalytic activity could be enhanced if the polarity of the reaction solvent were enhanced. Then the yield of **2g** was slightly increased to 64% with DMF as solvent. However, quantitative conversion of **1g** was attained using I_2 as the promoter under the same reaction conditions, which indicated that I_2 was the most efficient promoter in the oxidative cyclocarbonylation of 2-aminophenol (**1g**) to 2-benzoxazolinone (**2g**).

Untill now, the mechanism of oxidative carbonylation of amine was not well understood. However, all possible mechanisms proposed the assumption that a Pd–carbamoyl complex (Pd–CONHR) was formed as an intermediate species [6b,6c,8]. As can be seen from the results initially obtained, neither Pd/C nor I_2 alone could act as an efficient catalyst for the oxidative cyclocarbonylation of β-aminoalcohols and Pd/C catalyst combined with I_2 was an active catalytic system for this reaction. Based on the previous reports, a modified mechanism was proposed in Fig. 1. Active Pd–I species reacted with the NH_2 of the β-aminoalcohols and CO to produce the cabamoyl-type complexes (**I**), which further reacted with the OH of the β-

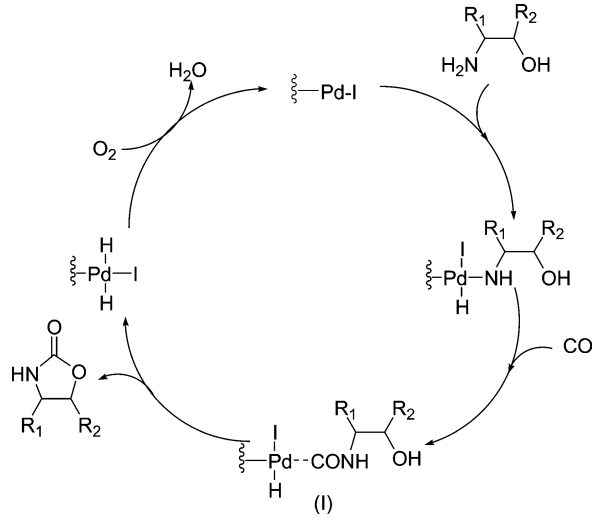


Fig. 1. Proposed mechanism for oxidative cyclocarbonylation of β-aminoalcohols to 2-oxazolidinones.

aminoalcohols and then produced stoichiometric quantities of 2-oxazolidinones. However, unlike the studies of Gabriele and co-workers, which need a large excess of iodide anions to ensure the reoxidation of the deactivated palladium catalyst, i.e., there are probably more catalytic steps in his catalytic cycle, then the catalytic activity was decreased accordingly. On the contrary, there was no reoxidation process in our catalytic cycle and only 1.8 eq of I_2 with respect to Pd/C catalyst could achieve a high catalytic turnover frequency. Furthermore, promoter, KI, employed in Gabriele and co-workers' research was the poorest promoter in our catalyst system. In addition, activated charcoal of a Pd/C catalyst would likely stabilize the active sites and favor the high catalytic activity.

4. Conclusion

In summary, we have found that Pd/C–I_2-catalyzed oxidative cyclocarbonylation of β-aminoalcohols and 2-aminophenol producing the corresponding 2-oxazolidinones could be performed with high yields and excellent catalytic efficiencies under considerably mild condition. The cata-

lyst could be reused five times without significant loss in catalytic activity and selectivity. The catalyst system not only solves the basic problems of catalyst separation and recovery but also avoids the use of phosphine ligands in comparison with homogeneous Pd catalyst systems. This atom-economical methodology represents a valuable and environmentally benign nonphosgene alternative to the use of toxic phosgene or expensive diethyl carbonate. These characteristics make Pd/C–I_2 an ideal catalyst system for the synthesis of these very important heterocyclic compounds.

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