

A simple and efficient recyclable phosphine-free catalytic system for alkoxy carbonylation and carbonylative Sonogashira coupling reactions of aryl iodides

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Abstract

Using palladium on charcoal (Pd/C) and triethylamine as a novel, efficient, versatile, recyclable, and phosphine-free catalytic system, we carried out the alkoxy carbonylation of aryl iodides (alcohols or phenols as nucleophiles) and the carbonylative Sonogashira coupling reaction of aryl iodides with terminal alkynes, affording the corresponding aryl esters and α,β -alkynyl ketones in good to excellent yields under mild conditions. We found that both electron-withdrawing and electron-donating substituents on phenol enhanced the phenoxy carbonylation of iodobenzene. The recyclability of Pd/C was also demonstrated.

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Keywords: Palladium on charcoal; Alkoxy carbonylation; Carbonylative Sonogashira coupling; Aryl iodides; Aryl esters; α,β -Alkynyl ketones; Recycle

1. Introduction

The transition metal-catalyzed carbonylation of aryl halides in the presence of nucleophiles is an important methodology for the preparation of aromatic carbonyl compounds [1–3], including esters, acids, amides, ketones, and others. Of particular interest among these important carbonyl intermediates are the aryl esters and α,β -alkynyl ketones, because aryl esters (especially phenyl esters) are widely used in liquid crystals [4], photosensitizers [5], and biologically active compounds [6], whereas α,β -alkynyl ketones are crucial moieties in many biologically active molecules, natural products, and pharmaceuticals [7]. Traditionally, phenyl esters were obtained by the acylation of arenes by chloroformates, the acylation of phenols by anhydrides and acyl chlorides, or by acids themselves in the presence of dicyclohexylcarbodiimide [8]. The main drawbacks of the acylation technique are the harsh conditions, low yields, and serious environmental problems. α,β -Alkynyl ketones are generally synthesized via the coupling of alkynyl organometal-

lic reagents with acid chlorides [9]. Recently reported methods have used Pd- or Cu-catalyzed coupling reactions of acid halides and terminal alkynes [10]; however, these methods must be used in dry solvents under an inert atmosphere. Evidently, the conventional synthesis processes for these compounds are not so eco-friendly and atom-economical; thus, in this regard, the carbonylation of aryl halides with alcohol, phenol, or alkyne as a nucleophile provides an alternative approach to the synthesis of aryl esters and α,β -alkynyl ketones with atom economy.

Over the last decade, significant efforts have focused on the development of Pd-phosphine complexes for the one-step synthesis of phenyl esters [11,12] and α,β -alkynyl ketones [13–19] via carbonylation of aryl iodides under homogeneous conditions. However, as a result of the notorious phosphine degradation by P–C bond cleavage, an excess of phosphine is often necessary to avoid catalyst deactivation. Furthermore, homogeneous palladium catalysts usually are not reusable, and the products are frequently contaminated by residual palladium and toxic phosphine ligands, which can be difficult to separate from the products and starting materials in an efficient and simple manner. Recently, Leadbeater and Kormos [20] reported phosphine-free Pd(OAc)₂-catalyzed alkoxy carbony-

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lation of aryl iodides using heavy-walled quartz reaction vessels with CO in conjunction with microwave heating. But this requires special vessels with a microwave oven specifically designed for this purpose, which is a particular problem if the reaction is to be realized on an industrial scale.

Several approaches [21] to overcome the inherent difficulty of separating and recycling homogeneous palladium catalysts have been developed. Multiphasic systems [22], such as fluoruous-biphasic, ionic liquids, *sc*CO₂, and a combination of the latter two, show very promising results, but their high cost has restricted their commercial application. Anchoring the catalyst on a solid support allows separation of the catalyst by filtration or by using a fixed catalyst bed and continuous operation. One of the most common heterogeneous supported palladium catalysts, Pd/C has been widely used in hydrogenation processes [23], carbon–carbon bond forming reactions [24–26], and some carbonylation reactions [27–33]. It is especially noteworthy that Kotschy and co-workers [34] established that only a minor portion of the bound palladium (<2%) is released into the solution in the Pd/C-catalyzed Sonogashira coupling of aryl halides in aqueous dimethyl acetamide. These authors also suggested that by using solid-supported palladium in coupling reactions, one might be able to exploit the benefits of homogeneous catalysis but still retain the ease of heterogeneous catalyst separation. Recently, we reported a mild protocol for the oxidative cyclocarbonylation of β -aminoalcohols and 2-aminophenol to synthesize corresponding 2-oxazolidinones [27] with high turnover frequency (TOF) using a Pd/C-I₂ heterogeneous catalytic system.

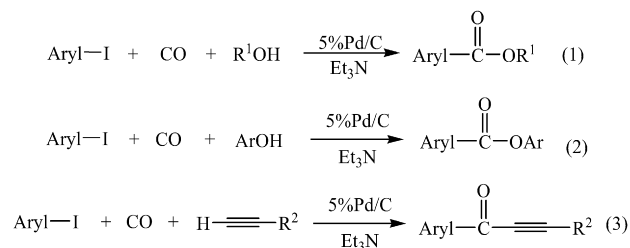
Up to now, only one report has described the use of heterogeneous catalyst (Pd/C) in the alkoxy carbonylation of aryl iodides. But in that work, the reaction required using carcinogenic benzene as a solvent, and the aryloxy carbonylation reaction has low nucleophile availability [28]. To the best of our knowledge, no heterogeneous catalyst systems have been investigated in the carbonylative Sonogashira coupling reaction of aryl halides with alkynes. 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, recyclable, versatile, and environmentally benign catalyst system for those interesting reactions.

As a part of our ongoing efforts to extend the scope of the use of Pd/C in carbonylation reactions, we report Pd/C-catalyzed alkoxy carbonylation and carbonylative Sonogashira coupling reactions of aryl iodides (Scheme 1) in the absence of copper and phosphine under mild conditions to afford aryl esters and α,β -alkynyl ketones efficiently. The recyclability of the catalyst also was investigated.

2. Experimental

2.1. Materials

The catalyst, consisting of 5% Pd/C, was purchased from Shanghai Sinopham Chemical Reagent Co. Ltd. (China); aryl iodides and alkynes were purchased from Aldrich, Fluka, or Alfa Aesar and used as received; other reagents were of analyt-



Scheme 1. Alkoxy carbonylation and carbonylative Sonogashira reactions of aryl iodides.

tical grade. Anhydrous methanol, triethylamine (Et₃N), toluene, and other solvents were freshly distilled from appropriate drying agents under an argon atmosphere before use. CO with a purity of 99.99% was commercially available.

2.2. General procedures for the carbonylation reactions

2.2.1. General procedure for the alkoxy carbonylation reaction [Scheme 1, Eq. (1)]

A magnetic stirring bar, aryl iodide (2.5 mmol), alcohol (4.0 mL), 5% Pd/C (5 mg), and Et₃N (7.2 mmol, 1 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.2 MPa of CO, pressurized to 0.5 MPa with CO, and then stirred at 130 °C for 2 h. After the reaction, the autoclave was cooled, and excess CO was discharged at room temperature. The reaction mixture was then analyzed by gas chromatography (GC) with biphenyl as the internal standard, using an Agilent 6820 gas chromatograph equipped with a SE-54 capillary column and a flame ionization detector, along with GC/mass spectroscopy (GC-MS). The crude product was purified by column chromatography on silica gel (eluting solvent, petroleum ether:ethyl acetate = 20:1) to give the desired product.

2.2.2. Recycling of Pd/C in the methoxy carbonylation of iodobenzene in methanol

A magnetic stirring bar, iodobenzene (2.5 mmol, 510 mg), CH₃OH (4.0 mL), 5% Pd/C (10 mg), and Et₃N (7.2 mmol, 1 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.2 MPa of CO, pressurized to 0.5 MPa with CO, and then stirred at 130 °C for 2 h.

After the reaction, the reaction mixture was separated by centrifugation. The liquid was transferred by a syringe; any Pd/C remaining in the vessel was washed with anhydrous methanol (2 × 2 mL). Then the combined liquid was qualitatively and quantitatively analyzed by GC-MS (Agilent 6890/5973) and GC (Agilent 6820), respectively, using biphenyl as the internal standard. The Pd/C was used in the next run under the same conditions.

2.3. General procedure for the phenoxy carbonylation reaction [Scheme 1, Eq. (2)]

A magnetic stirring bar, aryl iodide (2.5 mmol), ArOH (3.0 mmol), 5% Pd/C (30 mg), Et₃N (7.2 mmol, 1 mL), and

toluene (4.0 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.5 MPa of CO, pressurized to 2.0 MPa with CO, and then stirred at 130 °C for 8 h. After the reaction, the autoclave was cooled, excess CO was discharged at room temperature. The reaction mixture was qualitatively and quantitatively analyzed by GC-MS (Agilent 6890/5973) and GC (Agilent 6820), respectively, using biphenyl as the internal standard. The crude product was purified by column chromatography on silica gel (eluting solvent hexane:ethyl acetate = 10:1) to give the desired product.

2.3.1. Recycling of Pd/C in the phenoxycarbonylation of iodobenzene

A magnetic stirring bar, iodobenzene (2.5 mmol, 510 mg), phenol (3.0 mmol, 282 mg), 5% Pd/C (30 mg), Et₃N (7.2 mmol, 1 mL), and toluene (4.0 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.5 MPa of CO, pressurized to 2.0 MPa with CO, and then stirred at 130 °C for 8 h.

After the reaction, the reaction mixture was separated by centrifugation. The liquid was transferred by a syringe. The solid residue remaining in the vessel was washed with toluene (2 × 2 mL). Then the combined liquid was qualitatively and quantitatively analyzed by Agilent 6890/5973 GC-MS and Agilent 6820 GC, respectively, using biphenyl as the internal standard. The solid residue was used in the next run under the same conditions.

2.4. General procedure for the carbonylative Sonogashira coupling reaction [Scheme 1, Eq. (3)]

A magnetic stirring bar, aryl iodide (2.5 mmol), alkyne (3.0 mmol), 5% Pd/C (10 mg), Et₃N (7.2 mmol, 1 mL), and toluene (4.0 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.5 MPa of CO, pressurized to 2.0 MPa with CO, and then stirred for 4 h at 130 °C. After the reaction, the autoclave was cooled, and excess CO was discharged at room temperature. The reaction mixture was then qualitatively and quantitatively analyzed by Agilent 6890/5973 GC-MS and Agilent 6820 GC, respectively, using biphenyl as the internal standard. The crude product was purified by column chromatography on silica gel (eluting solvent hexane:ethyl acetate = 10:1) to give the desired product.

2.4.1. Recycling of Pd/C in the carbonylative Sonogashira coupling reaction

A magnetic stirring bar, iodobenzene (2.5 mmol, 510 mg), phenylacetylene (3.0 mmol, 306 mg), 5% Pd/C (10 mg), Et₃N (7.2 mmol, 1 mL), and toluene (4.0 mL) were placed in a 35-mL stainless autoclave. The autoclave was closed, purged three times with 0.5 MPa of CO, pressurized to 2.0 MPa with CO, and then stirred for 4 h at 130 °C.

After the reaction, the reaction mixture was separated by centrifugation. The liquid was transferred by a syringe. The solid residue remaining the vessel was washed with toluene

(2 × 2 mL). Then the combined liquid was qualitatively and quantitatively analyzed by Agilent 6890/5973 GC-MS and Agilent 6820 GC, respectively, using biphenyl as the internal standard. The solid residue was used in the next run under the same conditions.

3. Results and discussion

3.1. Pd/C-catalyzed alkoxycarbonylation reaction

For the optimization of the reaction conditions, we chose the methoxycarbonylation of iodobenzene (1a) as the model reaction, and examined the effects of different parameters on the reaction; the results are given in Table 1. First, the comparison experiments were carried out using Pd/C as catalyst with and without base, Et₃N (Table 1, entries 1 and 2). It was observed that in the absence of Et₃N, only a 22.8% yield of methyl benzoate (2a) was obtained, whereas with Et₃N, a 94.2% yield of 2a was seen. To further evaluate the effects of bases on the reaction, various other organic bases, including pyridine, 2,6-lutidine, and 4-dimethylaminopyridine (DMAP), also were investigated and were all found to be less effective than Et₃N with regard to the yields (Table 1, entries 3–5). CO pressure was found to play an important role in the reaction; increasing the CO pressure from 0.1 MPa to 0.5 MPa did significantly increase the yield of the desired product (Table 1, entries 2, 6, and 7), but, there was a slight increase in the yield of 2a when the reaction was operated at 1.0 MPa (Table 1, entry 8). Increasing the reaction temperature had a positive effect on the catalytic activity (Table 1, entries 9–12). When the quantity of iodobenzene was increased to 5.0 mmol (i.e., a molar ratio of

Table 1
Pd/C-catalyzed methoxycarbonylation of iodobenzene under different conditions^a

Entry	Base	Temperature (°C)	Pressure (MPa)	Yield of 2a (%) ^b
1	None	130	0.5	22.8
2	Et ₃ N	130	0.5	94.4
3	Pyridine	130	0.5	26.0
4	2,6-Lutidine	130	0.5	26.9
5	DMAP	130	0.5	72.4
6	Et ₃ N	130	0.1	37.6
7	Et ₃ N	130	0.25	79.7
8	Et ₃ N	130	1.0	95.5
9	Et ₃ N	100	0.5	73.6
10	Et ₃ N	110	0.5	82.2
11	Et ₃ N	120	0.5	93.5
12	Et ₃ N	140	0.5	96.9
13 ^c	Et ₃ N	130	0.5	88.7
14 ^d	Et ₃ N	130	0.5	96.6

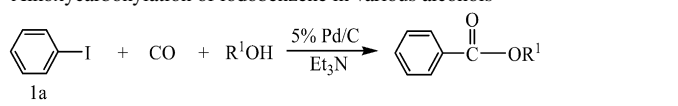
^a Reaction conditions: iodobenzene: 2.5 mmol, 5% Pd/C: 5 mg (2.4 × 10⁻³ mmol), base: 7.2 mmol, CH₃OH: 4 mL, reaction time: 2 h.

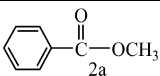
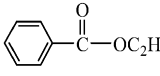
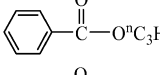
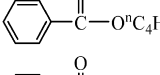
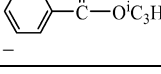
^b Determined by GC using biphenyl as internal standard.

^c 5.0 mmol iodobenzene was used.

^d 10 mg 5% Pd/C was used.

Table 2
Alkoxy carbonylation of iodobenzene in various alcohols^a



Entry	R ¹ OH	Product	Yield (%) ^b
1	CH ₃ OH		82
2	C ₂ H ₅ OH		89 (95) ^c
3	<i>n</i> -C ₃ H ₇ OH		92 (32) ^d
4	<i>n</i> -C ₄ H ₉ OH		89 (32) ^d
5	<i>i</i> -C ₃ H ₇ OH		75
6	<i>t</i> -C ₄ H ₉ OH	–	0

^a Reaction conditions: iodobenzene: 2.5 mmol, 5% Pd/C: 5 mg, Et₃N: 7.2 mmol, alcohol: 4 mL, 0.5 MPa of CO, 130 °C, 2 h.

^b Isolated yield after silica gel chromatography.

^c Determined by GC using biphenyl as internal standard.

^d Determined by GC, 3 mmol alcohol, 4 mL toluene was used as solvent.

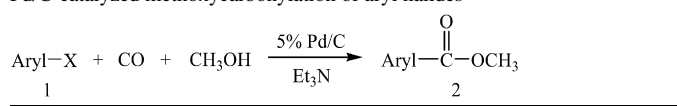
substrate/catalyst of 2128), only a 88.7% yield of methyl benzoate was obtained under the same reaction conditions (Table 1, entry 13).




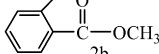

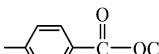

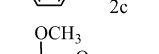

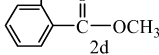

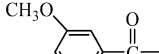

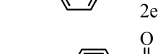

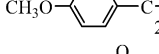

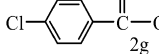
To determine the scope of this process, various aryl iodides and diverse alcohols were used as substrates; the results are summarized in Tables 2 and 3. The results of alkoxy carbonylation of iodobenzene (Table 2) demonstrate that changing the alcohol substrate from methanol to *n*-butanol had no significant effect on product yield (Table 2, entries 1–4). But with a secondary alcohol (2-propanol), a lower yield (75%) of carbonylation product was obtained (Table 2, entry 5). Unfortunately, when *tert*-butanol was used as a nucleophile, no desired product was detected by GC-MS, presumably due to steric bulk (Table 2, entry 6).

As shown in Table 3, a wide range of aryl iodides bearing an electron-withdrawing group or an electron-donating group were clearly carbonylated in methanol providing that the ester products, bromobenzene and chlorobenzene, were unreactive (Table 3, entries 1 and 2). Iodobenzenes containing substituents at the 2-position gave poorer results because of the steric influence (Table 3, entries 3 and 5). 2-Iodoanisole (1d), 3-iodoanisole (1e), and 4-iodoanisole (1f) were converted smoothly to the corresponding products 2d, 2e, and 2f in 77%, 96%, 98% yields, respectively (Table 3, entries 5–7). Remarkably, 4-chloriodobenzene (1g) was subjected to the methoxycarbonylation reaction to produce selectively methyl 4-chlorobenzoate (2g) at a 94% yield (Table 3, entry 8). The carbonylation of 1-iodonaphthalene (1h) and 4-iodoacetophenone (1i) also gave corresponding carbonylated products in excellent yields (Table 3, entries 9 and 10).

In addition to the high activity, the Pd/C-Et₃N catalytic system also demonstrated good stability in the methoxycar-

Table 3
Pd/C-catalyzed methoxycarbonylation of aryl halides^a



Entry	Aryl-X	Product	Yield (%) ^b
1		–	0
2		–	0
3			69
4			89
5			77
6			96
7			98
8			94
9			92
10			99

^a Reaction conditions: aryl halide: 2.5 mmol, 5% Pd/C: 5 mg, Et₃N: 7.2 mmol, CH₃OH: 4 mL, 0.5 MPa of CO, 130 °C, 2 h.

^b Isolated yield after silica gel chromatography.

bonylation of iodobenzene (reaction conditions: iodobenzene, 2.5 mmol; 5% Pd/C, 10 mg, Et₃N, 7.2 mmol; CH₃OH, 4 mL; 0.5 MPa of CO; temperature, 130 °C; time, 2 h), after the completion the catalyst was recovered by centrifugation and reused for the next reaction under the same reaction condition; no significant loss of catalytic activity and selectivity were found even after 10 reuses.

3.2. Pd/C-catalyzed phenoxycarbonylation reaction

Successful application of Pd/C in the alkoxy carbonylation of aryl iodides has inspired us to explore its use in the phenoxycarbonylation reaction. Initially, the influence of critical reaction parameters (i.e., base, temperature, CO pressure, solvent) on the carbonylation of iodobenzene using phenol as a nucleophile had been investigated for reaction optimization (Table 4). It was noteworthy that in all cases, >99% selectivity of phenyl benzoate was observed. A survey of various bases determined that Et₃N provided the highest conversion (Table 4, entries 1–4). The conversion of iodobenzene increased with increasing CO

Table 4
Phenoxycarbonylation of iodobenzene under different conditions^a

Entry	Solvent	Base	Temperature (°C)	Pressure (MPa)	Conversion of 1a (%) ^b
1	Toluene	Et ₃ N	130	2.0	96.9
2	Toluene	Pyridine	130	2.0	36.0
3	Toluene	2,6-lutidine	130	2.0	30.7
4	Toluene	HCO ₂ Na·2H ₂ O	130	2.0	49.9
5	Toluene	Et ₃ N	130	1.0	70.1
6	Toluene	Et ₃ N	130	2.5	98.2
7	Toluene	Et ₃ N	120	2.0	89.0
8	Toluene	Et ₃ N	100	2.0	56.3
9	Toluene	Et ₃ N	90	2.0	39.6
10 ^c	Toluene	Et ₃ N	130	2.0	83.9
11 ^d	Toluene	Et ₃ N	130	2.0	66.6
12	Et ₃ N	Et ₃ N	130	2.0	84.8
13	THF	Et ₃ N	130	2.0	100
14	DMF	Et ₃ N	130	2.0	100
15	DCM	Et ₃ N	130	2.0	29.6

^a Reaction conditions: iodobenzene: 2.5 mmol, phenol: 3 mmol, 5% Pd/C: 30 mg (0.0141 mmol), base: 7.2 mmol, solvent: 4 mL, reaction time: 8 h.

^b Determined by GC using biphenyl as internal standard.

^c 20 mg 5% Pd/C was used.

^d 10 mg 5% Pd/C was used.

pressure (Table 4, entries 1, 5, and 6). The catalyst system was sensitive to reaction temperature; conversion decreased dramatically when the temperature was decreased from 130 to 90 °C (Table 4, entries 7–9). Decreasing the amount of Pd/C resulted in a lower conversion (Table 4, entries 10 and 11). Besides these conditions, a series of solvents were also examined using Et₃N as a base and solvent, and only 84.8% conversion was achieved (Table 4, entry 12). Quantitative conversion of iodobenzene was observed when the reaction was performed in tetrahydrofuran (THF) or *N,N*-dimethylformamide (DMF) (Table 4, entries 13 and 14). However, poor result was obtained when the reaction was carried out in dichloromethane (DCM) (Table 4, entry 15). Considering the solvent cost as well as the subsequent handling, toluene may be the appropriate reaction medium.

To determine the scope and limitation of this reaction, the phenoxycarbonylation of iodobenzene using substituted phenol as the nucleophile, as well as the reaction of various aryl halides, was studied. The results are given in Tables 5 and 6, respectively.

As shown in Table 5, Pd/C-Et₃N as the catalytic system for the phenoxycarbonylation reactions of iodobenzene with phenols proved exceptionally active. Obviously, both electron-withdrawing and electron-donating substituents on the nucleophile may enhance the reaction, giving the desired products in excellent yields. It is possibly reasonable to consider that a phenol exists in an acid–base dissociation equilibrium in the presence of Et₃N in the reaction medium. An electron-withdrawing substituent attached to phenol may enhance its acidity; on the other hand, an electron-donating substituent may increase electron density on the O atom of phenol to enhance the reactivity.

Table 5
Effects of substituted phenol on phenoxycarbonylation of iodobenzene^a

Entry	Ar	Conversion of PhI (%) ^b	Product	Yield (%) ^c
1	Ph	96.9	3a	96
2	2-CH ₃ C ₆ H ₄	100	3b	93
3	3-CH ₃ C ₆ H ₄	100	3c	96
4	4-CH ₃ C ₆ H ₄	100	3d	97
5	4-(CH ₃) ₃ C-C ₆ H ₄	100	3e	95
6	4-(CH ₃) ₃ C-2-CH ₃ C ₆ H ₃	100	3f	97
7	2-(CH ₃) ₃ C-4-CH ₃ C ₆ H ₃	98.6	3g	97
8	4-CH ₃ OC ₆ H ₄	100	3h	94
9	4-ClC ₆ H ₄	100	3i	94

^a Reaction conditions: iodobenzene: 2.5 mmol, ArOH: 3 mmol, 5% Pd/C: 30 mg, Et₃N: 7.2 mmol, toluene: 4 mL, 2.0 MPa of CO, 130 °C, 8 h.

^b Determined by GC using biphenyl as internal standard.

^c Isolated yield after silica gel chromatography.

Table 6
Pd/C-catalyzed phenoxycarbonylation of aryl iodides^a

Entry	Aryl-I	Product	Yield (%) ^b
1	1b	4b	87
2	1c	4c	95
3	1d	4d	95
4	1e	4e	95
5	1f	4f	95
6	1g	4g	94
7	1h	4h	98

^a Reaction conditions: aryl iodide: 2.5 mmol, phenol: 3 mmol, 5% Pd/C: 30 mg, Et₃N: 7.2 mmol, toluene: 4 mL, 2.0 MPa of CO, 130 °C, 8 h.

^b Isolated yield after silica gel chromatography.

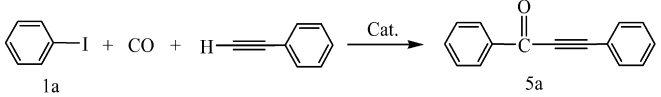
As shown in Table 6, the phenoxycarbonylation of various aryl iodides proceeded well and led to the corresponding carbonylated product in high yields.

3.3. Pd/C-catalyzed carbonylative Sonogashira coupling reaction

To further expand the scope of carbonylation reactions using Pd/C as a catalyst, we also evaluated the carbonylative Sonogashira coupling reaction of aryl halides with terminal alkynes. First, we examined effects of different parameters on the carbonylative Sonogashira coupling reaction of iodobenzene with phenylacetylene to optimize reaction conditions (Table 7). When using Pd/C as the sole catalyst, the carbonylative Sonogashira coupling reaction did not occur (Table 7, entry 1). Most strikingly, a 95.9% conversion of iodobenzene was obtained when 7.2 mmol Et₃N was added to the reaction system (Table 7, entry 2); decreasing the amount of Et₃N decreased the conversion (Table 7, entry 3). As in the methoxycarbonylation and phenoxycarbonylation of iodobenzene, pyridine and

Table 7

Pd/C-catalyzed carbonylative coupling of iodobenzene with phenylacetylene under different conditions^a



Entry	Solvent	Base	T (°C)/ P (MPa)	Conversion of 1a (%) ^b	Selectivity of 5a (%) ^b
1	Toluene	None	130/2.0	–	–
2	Toluene	Et ₃ N	130/2.0	95.9	>99
3 ^c	Toluene	Et ₃ N	130/2.0	85.7	>99
4	Toluene	Pyridine	130/2.0	27.6	>99
5	Toluene	2,6-Lutidine	130/2.0	17.6	>99
6	Toluene	Et ₃ N	100/2.0	50.9	>99
7	Toluene	Et ₃ N	110/2.0	68.0	>99
8	Toluene	Et ₃ N	120/2.0	82.4	>99
9	Toluene	Et ₃ N	130/1.0	67.3	>99
10	Toluene	Et ₃ N	130/3.0	99.4	>99
11	Et ₃ N	Et ₃ N	130/2.0	85.8	93.0
12	THF	Et ₃ N	130/2.0	91.8	>99
13	DMF	Et ₃ N	130/2.0	100	91.2
14	DCM	Et ₃ N	130/2.0	41.4	96.8

^a Reaction conditions: iodobenzene: 2.5 mmol, phenylacetylene: 3 mmol, 5% Pd/C: 10 mg, base: 7.2 mmol, solvent: 4 mL, reaction time: 4 h.

^b Determined by GC using biphenyl as internal standard.

^c 3.6 mmol Et₃N was used.

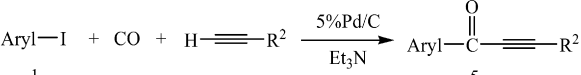
2,6-lutidine also did not work well (Table 7, entries 4 and 5). Increasing both the reaction temperature and CO pressure had a pronounced positive effect on the catalytic activity (Table 7, entries 6–10).

We also investigated the effects of different solvents on the reaction with Pd/C-Et₃N as the catalytic system (Table 7, entries 3, 11–14). The solvent was found to play an important role in activity and selectivity. DMF displayed excellent performance in the conversion of iodobenzene, while affording a lower selectivity of 1,3-diphenylprop-2-yn-1-one (5a) (Table 7, entry 13). Thus, from a practical standpoint, toluene was determined to be the best choice.

To explore the generality and scope of the carbonylative three-component coupling reaction, we also evaluated various aryl iodides and terminal alkynes as substrates. Some results are given in Table 8. It is noteworthy that only small percentage (not above 1%) of the noncarbonylative coupling products was observed; we reasoned that in the absence of copper, the less reactive alkyne (compared with its corresponding alkynyl copper gate complex) would easily react with the electron-deficient acylpalladium (II) rather than its precursor aryl palladium iodide species (I) derived from the oxidative addition of aryl iodide to Pd(0) [16,17] (Scheme 2). As a result, the carbonylative coupling reaction product was obtained through (III_A). Alternatively, insertion of an arylalkyne to the acylpalladium species giving (III_B), followed by β -hydrogen elimination, might be a plausible pathway [35]. It should be pointed out that the carbonylative coupling reaction of chlorobenzene (or bromobenzene) with phenylacetylene did not occur, because the dissociation energy of the sp²-C–Cl or sp²-C–Br bond is comparatively high (402, 339, and 272 kJ mol⁻¹ for PhCl, PhBr,

Table 8

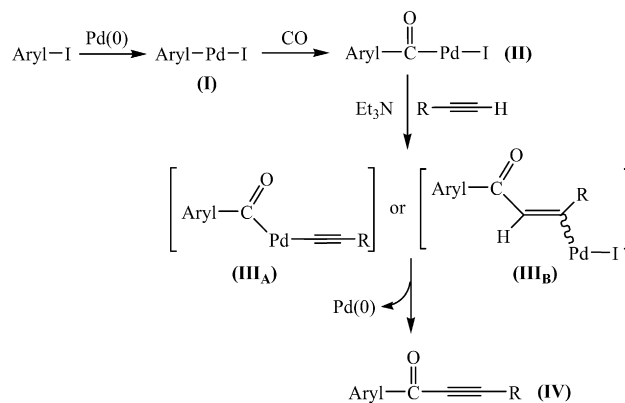
Pd/C-catalyzed carbonylative coupling of aryl iodides with terminal alkynes in the presence Et₃N^a



Entry	Aryl-I	R ²	Product	Yield (%) ^b
1	1a	Ph	5a	84
2	1b	Ph	5b	93
3	1c	Ph	5c	96
4	1d	Ph	5d	80
5	1e	Ph	5e	90
6	1f	Ph	5f	97
7	1g	Ph	5g	91
8	1h	Ph	5h	94
9	1a	4-(CH ₃) ₃ CC ₆ H ₄	5i	83
10	1a	CH ₃ (CH ₂) ₃	5j	63

^a Reaction conditions: aryl iodide: 2.5 mmol, alkyne: 3 mmol, 5% Pd/C: 10 mg, Et₃N: 7.2 mmol, toluene: 4 mL, 2.0 MPa of CO, 130 °C, 4 h.

^b Isolated yield after silica gel chromatography.



Scheme 2. Possible explanation for carbonylative coupling reactions.

and PhI, respectively, at 298 K) [36]. The reaction of substituted aryl iodides gave the corresponding alkynyl ketones in good to excellent yields. When the terminal alkyne bearing an alkyl substituent was used (Table 8, entry 10), the reaction was found to be slower than that of arylalkynes, whose relative reactivity was similar to the noncarbonylative coupling reactions.

3.4. Recyclability of Pd/C in the phenoxycarbonylation and carbonylative three-component coupling reactions

The key property of heterogeneous catalysts is their recovery and reuse, an essential perspective for green chemistry involving both ecologic and economic considerations. As mentioned above, Pd/C could be reused at least 10 times in the methoxy-carbonylation of iodobenzene with only a slight decrease in efficiency; the slight change may be due to the loss of catalyst during handling and transferring of catalyst. We also evaluated the activity and recyclability of Pd/C in the phenoxycarbonylation of iodobenzene and the carbonylative three-component coupling reaction of iodobenzene with phenylacetylene; the re-

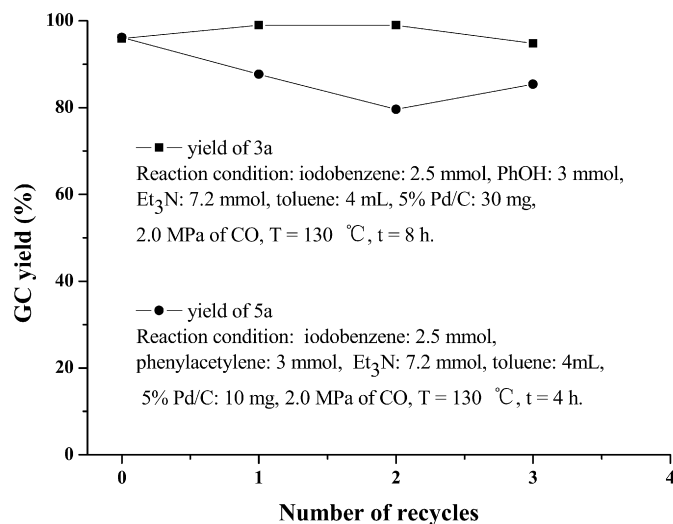


Fig. 1. Recyclability of Pd/C in the phenoxycarbonylation of iodobenzene and the carbonylative Sonogashira coupling of iodobenzene with phenylacetylene.

sults are presented in Fig. 1. Obviously, the reuse of Pd/C was viable in both the phenoxycarbonylation and carbonylative Sonogashira coupling reactions; the two reactions were repeated three times with no significant loss of catalytic activity. But after the third cycle, the reuse of Pd/C became difficult, because the increase in the byproduct triethylammonium iodide after each cycle due to increasing viscosity of the reaction medium prevented further reaction.

4. Conclusion

In summary, a highly efficient and recyclable Pd/C-Et₃N system for the alkoxycarbonylation of aryl iodides and the carbonylative Sonogashira coupling reaction of aryl iodides with terminal alkynes has been developed. These reactions can be carried out under mild conditions to afford the corresponding aryl esters (especially phenyl esters) and α,β -alkynyl ketones in good to excellent yields. Obviously, this novel and versatile catalyst system has competitive advantages, including no need to add toxic phosphine ligands and easy catalyst recycling, allowing several reuses with no significant loss in catalytic activity and selectivity. This inexpensive and effective catalyst system is particularly attractive and should have a bright future in industrial-scale applications.

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Supplementary material

The online version of this article contains additional supplementary material.

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References

- [1] H.M. Colguhoun, D.J. Thompson, M.V. Twigg, *Carbonylation. Direct Synthesis of Carbonyl Compounds*, Plenum Press, New York, 1991, p. 55.
- [2] J. Tsuji, *Palladium Reagents and Catalysts—New Perspectives for the 21st Century*, Wiley, New York, NY, 2004, p. 265.
- [3] R. Skoda-Földes, L. Kollár, *Curr. Org. Chem.* 6 (2002) 1097.
- [4] M.J.S. Dewar, P.S. Goldberg, *J. Org. Chem.* 35 (1970) 2711.
- [5] I.C. Khoo, P.H. Chen, M.V. Wood, M.-Y. Shih, *Chem. Phys.* 245 (1999) 517.
- [6] S. Neelakantan, R. Padmasani, T.R. Seshadri, *Tetrahedron* 21 (1965) 3531.
- [7] C. Chowdhury, N.G. Kundu, *Tetrahedron* 55 (1999) 7011.
- [8] D.A. Whiting, in: D. Barton, W.D. Ollis (Eds.), *Comprehensive Organic Chemistry*, Pergamon Press, Oxford, 1979, p. 734.
- [9] M.W. Logue, K. Teng, *J. Org. Chem.* 47 (1982) 2549.
- [10] D.A. Alonso, C. Najera, M.C. Pacheco, *J. Org. Chem.* 69 (2004) 1615.
- [11] Y. Kubota, T. Hanaoka, K. Takeuchi, Y. Sugi, *J. Chem. Soc. Chem. Commun.* (1994) 1553.
- [12] T. Satoh, M. Ikeda, M. Miura, M. Nomura, *J. Mol. Catal. A Chem.* 111 (1996) 25.
- [13] T. Kobayashi, M. Tanaka, *J. Chem. Soc. Chem. Commun.* (1981) 333.
- [14] A. Arcadi, S. Cacchi, F. Marinelli, P. Pace, G. Sanzi, *Synlett* (1995) 823.
- [15] L. Delaude, A.M. Masdeu, H. Alper, *Synthesis* (1994) 1149.
- [16] M.S. Mohamed Ahmed, A. Mori, *Org. Lett.* 5 (2003) 3057.
- [17] B. Liang, M. Huang, Z. You, Z. Xiong, K. Lu, R. Fathi, J. Chen, Z. Yang, *J. Org. Chem.* 70 (2005) 6097.
- [18] T. Fukuyama, R. Yamaura, I. Ryu, *Can. J. Chem.* 83 (2005) 711.
- [19] V. Sans, A.M. Trezeciak, S. Luis, J.J. Ziólkowski, *Catal. Lett.* 109 (2006) 37.
- [20] C.M. Kormos, N.E. Leadbeater, *Org. Biomol. Chem.* 5 (2007) 65.
- [21] D.J. Cole-Hamilton, R.P. Tooze, *Catalyst Separation, Recovery and Recycling: Chemistry and Process Design*, Springer, Dordrecht, 2005, p. 39.
- [22] B. Cornils, W.A. Herrmann, I.T. Horvath, W. Leitner, S. Mecking, H. Olivier-Bourbigou, D. Vogt, *Multiphase Homogeneous Catalysis*, Wiley-VCH, Weinheim, 2005, p. 309.
- [23] S. Nishimura, *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*, Wiley-VCH, New York, 2001, p. 64.
- [24] L. Yin, J. Liebscher, *Chem. Rev.* 107 (2007) 133.
- [25] F. Felpin, T. Ayad, S. Mitra, *Eur. J. Org. Chem.* 2006 (2006) 2679.
- [26] M. Seki, *Synthesis* (2006) 2975.
- [27] F. Li, C. Xia, *J. Catal.* 227 (2004) 542.
- [28] C. Ramesh, R. Nakamura, Y. Kubota, M. Miwa, Y. Sugi, *Synthesis* (2003) 501.
- [29] Y.S. Lin, H. Alper, *Angew. Chem. Int. Ed.* 40 (2001) 779.
- [30] H.Y. Song, E.D. Park, J.S. Lee, *J. Mol. Catal. A Chem.* 154 (2000) 243.
- [31] M. Beller, W.A. Moradi, M. Eckert, H. Neumann, *Tetrahedron Lett.* 40 (1999) 4523.
- [32] B. El Mi, G. Vasapollo, H. Alper, *J. Org. Chem.* 58 (1993) 4739.
- [33] K. Inomata, S. Toda, H. Kmoehita, *Chem. Lett.* 19 (1990) 1567.
- [34] Z. Novák, A. Szabó, J. Répási, A. Kotschy, *J. Org. Chem.* 68 (2003) 3327.
- [35] K. Sonogashira, *J. Organomet. Chem.* 653 (2002) 46.
- [36] W. Mägerlein, A.F. Indolese, M. Beller, *Angew. Chem. Int. Ed.* 40 (2001) 2856.