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Palladium-catalyzed phenoxycarbonylation of aryl iodides: electronic effect of the substituents on phenol

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Abstract

Carbonylation of 4-iodotoluene in the presence of a series of 3- or 4-substituted phenols as nucleophiles using a catalytic amount of $PdCl_2(PPh_3)_2$ and tributylamine as base to give aryl 4-methylbenzoates has been carried out. It was found that both electron-withdrawing and donating substituents on phenol enhance the reaction, while the latter ones are relatively more influential. Similar substituent electronic effects were also observed in the stoichiometric reaction of 4-methylbenzoylpalladium complex, *trans*-4-$MeC_6H_4COPdI(PPh_3)_2$, which may correspond to the key intermediate in the catalytic reaction, with the phenols.

Keywords: Phenoxycarbonylation; Substituted phenols; Aryl iodides; Palladium; Copper

1. Introduction

Palladium-catalyzed carbonylation of aryl halides is a useful tool for the preparation of a variety of aromatic carbonyl compounds: the reaction of intermediary aroylpalladium complexes with various nucleophiles and organometallic reagents gives the products [1,2]. In the context of our study of palladium-catalyzed synthetic reactions [3–8], we have recently reported that the reaction of aryl iodides in the presence of some nucleophiles such as ethanol, phenol and diethylamine using $PdCl_2(PPh_3)_2$ as catalyst precursor can be promoted by addition of copper(I) salt as cocatalyst and the role of the additive has also been discussed [8]. During a further study of the carbonylation, we observed that in the reaction with phenol, both electron-withdrawing and donating substituents on the nucleophile may interestingly enhance the reaction. While the phenoxycarbonylation has been utilized in organic synthesis [5,8–11], it has been less explored regarding the mechanism compared to the corresponding alkoxycarbonylation [1,2,12,13]. Consequently, (a) catalytic carbonylation of 4-iodotoluene with a series of 3- or 4-substituted phenols in the presence of $PdCl_2(PPh_3)_2$ and tributylamine as the representative, and (b) stoichiometric reaction of a 4-methylbenzoylpalladium complex, which may correspond to the key intermediate in the catalytic reaction, with the phenols have been carried out with or with-

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out addition of CuI. In addition, carbonylative polyester formation, using bis(4-iodophenyl) ether and three kinds of bisphenols having different acidities as the substrates, has been investigated. Careful examination of the results may provide further insight into the mechanism of the carbonylation.

2. Results and discussion

2.1. Catalytic phenoxycarbonylation of 4-iodotoluene

The reaction of iodide **1** (2 mmol) with a number of 3- or 4-substituted phenols **2a**–**2e** (2 mmol) was carried out in the presence of $PdCl_2(PPh_3)_2$ (0.06 mmol) and NBu^n_3 (2.4 mmol) in DMF under CO (1 atm) at 90°C (Eq. 1). The corresponding aryl 4-methylbenzoates **3a**–**3e** were formed

$$\underset{\mathbf{1}}{4\text{-MeC}_6\text{H}_4\text{I}} + \underset{\mathbf{2}}{\text{ArOH}} \xrightarrow[\text{NBu}^n_3/\text{DMF}]{\text{CO/PdCl}_2(\text{PPh}_3)_2/(\text{CuI})} \underset{\mathbf{3}}{4\text{-MeC}_6\text{H}_4\text{COOAr}} \quad (1)$$

in 76–100% (Table 1). Under the reaction conditions employed, each reaction followed second-order kinetics with dependence on the concentrations of both **2** and NBu^n_3 up to ca. 60% conversion of **1** [8]. Plots of the rate constants (k_{obsd}) versus the Hammett σ values for the substituents are shown in Fig. 1. It can be seen that the reactivity of phenol is enhanced by both the electron-donating (4-MeO, 4-Me) and withdrawing substituents (4-Cl, 3-CF_3), and the latter ones affect it more significantly. Thus, the reaction with **2e** proceeded 4.7 times more rapidly than that with **2a**. It should also be noted that in each case, addition of CuI (0.2 mmol) considerably increased the reaction rate.

Table 1
Catalytic carbonylation of 4-iodotoluene **1** using ArOH **2** and NBu^n_3 [a]

ArOH	CuI [b]	$k_{obsd} \times 10$ (M^{-1} h^{-1})	Yield of **3** (%) [c]
PhOH (**2a**)		2.9	76
	+	5.7	81
4-MeC_6H_4OH (**2b**)		4.6	84
	+	6.8	92
4-MeOC_6H_4OH (**2c**)		6.4	78
	+	8.9	78
4-ClC_6H_4OH (**2d**)		9.3	90
	+	16	94
$3\text{-CF}_3C_6H_4OH$ (**2e**)		13	~ 100
	+	21	~ 100

[a] The reaction was carried out under the following conditions: **1** (2 mmol), ArOH (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), CuI (0.2 mmol) and NBu^n_3 (2.4 mmol) in DMF under CO (1 atm) at 90°C for 22–24 h.

[b] Plus sign indicates that the cocatalyst was added.

[c] Yield based on the amount of **1** used was determined by GLC.

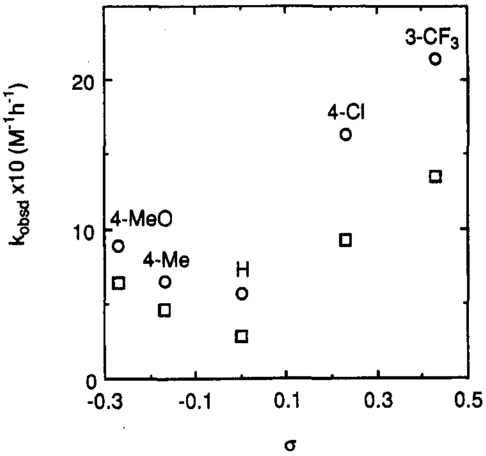
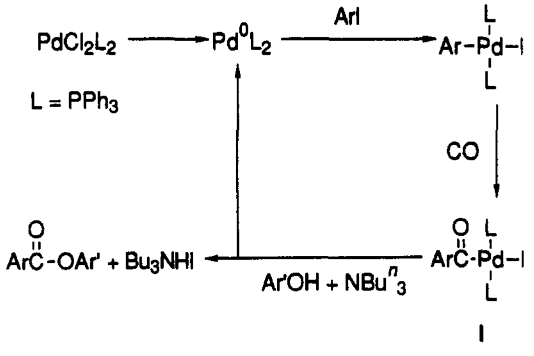


Fig. 1. Plots of k_{obsd} versus the Hammett σ values for the substituents on phenol in the catalytic carbonylation of **1** in the presence (○) and absence (□) of CuI.

The mechanism which may account for the phenoxycarbonylation is illustrated in Scheme 1 [1,12,13]. Oxidative addition of **1** to Pd(0) species generated in situ followed by insertion



Scheme 1.

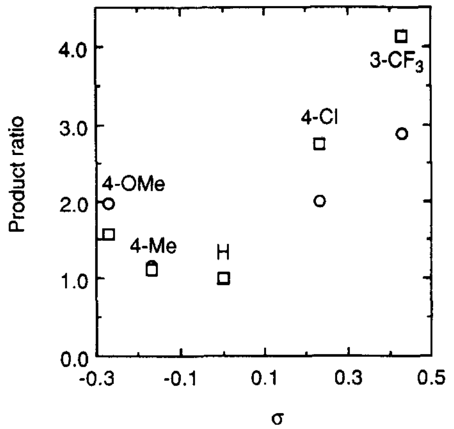


Fig. 2. Plots of relative reactivities of ArOH toward complex **4** versus the Hammett σ values for the substituents on phenol in the presence (○) and absence (□) of CuI.

of carbon monoxide affords the key intermediate, 4-methylbenzoylpalladium complex **I** (Ar = 4-MeC_6H_4). Subsequently, **I** reacts with **2** to give the corresponding product ester **3** and to regenerate Pd(0) species. The reaction kinetics may suggest that the rate-determining step is in the reaction sequence after the formation of **I**, as for alkoxycarbonylation of aryl iodides [12]. Therefore, the effect of the substituents of phenol on the stoichiometric reaction of *trans*-4-$MeC_6H_4COPdI(PPh_3)_2$ **4**, which may correspond to the intermediate **I** in the catalytic reaction, was examined.

*2.2. Stoichiometric reaction of trans-4-$MeC_6H_4COPdI(PPh_3)_2$ with phenols **2a–2e***

The reaction of complex **4** with phenols **2** was carried out under pseudo-first-order conditions using 10 equiv. of each of a phenolic substrate and NBu^n_3 at 50°C in DMF. While the pseudo-first-order rate constants were found to be 1.1–4.2 h^{-1} without addition of CuI, the reaction with CuI proceeded too rapidly to determine the rate accurately ($> 10\ h^{-1}$). Therefore, competitive reaction using equimolar mixtures of **2a** and one of the substituted phenols **2b–2e** was carried out to measure the relative reactivity of the phenols toward **4** (Eq. 2).

$$\underset{\mathbf{4}}{4\text{-}MeC_6H_4COPdI(PPh_3)_2} + PhOH + ArOH \xrightarrow[NBu^n_3/DMF]{(CuI)} 4\text{-}MeC_6H_4COOPh + 4\text{-}MeC_6H_4COOAr \qquad (2)$$

The observed reactivity order of the phenols was found to be the same with that observed in the catalytic reaction (Table 2 and Fig. 2). This is in harmony with the consideration that the rate-determining step of the catalytic reaction (Scheme 1) is the reaction of the intermediate **I** with **2** to give **3**.

Table 2
Stoichiometric reaction of *trans*-4-$MeC_6H_4COPdI(PPh_3)_2$ **4** with a mixture of PhOH and ArOH [a]

ArOH	Product ratio of 4-MeC_6H_4COOAr/4-MeC_6H_4COOPh (total yield, %) [b]	
	without CuI	with CuI
4-$MeOC_6H_4OH$ (**2c**)	1.6 (82)	2.0 (89)
4-MeC_6H_4OH (**2b**)	1.1 (97)	1.2 (~ 100)
4-ClC_6H_4OH (**2d**)	2.8 (79)	2.0 (99)
3-$CF_3C_6H_4OH$ (**2e**)	4.1 (~ 100)	2.9 (~ 100)

[a] The reaction was carried out under the following conditions: **4** (0.1 mmol), PhOH **2a** (1 mmol), ArOH (1 mmol), NBu^n_3 (2.4 mmol), dimethylmaleate (0.4 mmol) and CuI (0.1 mmol) in DMF under N_2 at 50°C for 1 h.

[b] Yield based on the amount of **4** used was determined by GLC.

2.3. Mechanistic implication

It may be reasonable to consider that the reaction of the intermediate **I** or complex **4** with phenols **2** to give **3** proceeds via formation of aryloxy(4-methylbenzoyl)palladium species and the subsequent reductive elimination of the ester [12]. While the possibility that another route to **3** involving direct attack of **2** on the carbonyl carbon of **I** or **4** also participates can not be excluded [14], the present results seems to be compatible with the two-step mechanism (vide infra).

Taking account of the observed substituent effect and the reported fact that in the reductive elimination of aryl ester from the palladium complex, 4-X-$C_6H_4OPd(COMe)L_2$, an electron-withdrawing substituent retards the reaction [15], the rate determining step of the reaction of **1** with **2** does not seem to include the final reductive elimination in the catalytic sequence, but it may be the formation of the aryloxypalladium species. We have proposed that the role of CuI as the cocatalyst in the catalytic carbonylation may be to remove one PPh_3 ligand from intermediary palladium complexes, i.e. aryl and aroylpalladium species to form relatively more reactive intermediates in which the cocatalyst itself may be involved in the palladium coordination sphere [8]. Thus, the addition of the copper species to the reactions of **1** and **4** appears to promote the formation of the aryloxypalladium species.

Meanwhile, it is also be reasonable to consider that a phenol exists in an acid–base dissociation equilibrium in the presence of NBu^n_3 in the reaction medium as shown in Eq. 3.

$$\underset{\mathbf{2}}{\mathrm{ArOH}} + \mathrm{NBu}^n_3 \rightleftharpoons \underset{\mathbf{II}}{\mathrm{ArO}\cdot\cdot\mathrm{H}\cdot\cdot\cdot\mathrm{NBu}^n_3} \rightleftharpoons \underset{\mathbf{5}}{\mathrm{ArO}^-} + \mathrm{HN}^+\mathrm{Bu}^n_3 \qquad (3)$$

An electron-withdrawing substituent attached to phenol may enhance its acidity to shift the equilibrium toward ionization. Due to the higher concentration of phenoxide anion, the reaction of such a phenol with aroylpalladium intermediate **I** or complex **4** seems to proceed more readily than that using **2a** itself. On the other hand, an electron-donating substituent may increase electron density on the O atom of phenol to enhance the reactivity of its complex with NBu^n_3 (i.e. **II** in Eq. 3) toward **I** or **4**. The fact that the catalytic and stoichiometric reactions using **2e** were considerably faster than those using **2c** may imply that ionization, i.e. deprotonation, is relatively more influential to enhance the reactivity of the phenolic oxygen.

Table 3
Catalytic carbonylation of 4-iodotoluene in the presence of a mixture of PhONa and ArONa [a]

ArONa	Product ratio of 4-MeC_6H_4COOAr/4-MeC_6H_4COOPh (total yield, %) [b]	
	without CuI	with CuI
4-$MeOC_6H_4ONa$	2.7 (67)	3.5 (67)
4-MeC_6H_4ONa	2.0 (85)	2.0 (68)
4-ClC_6H_4ONa	0.32 (71)	0.52 (79)
3-$CF_3C_6H_4ONa$	0.23 (74)	0.37 (85)

[a] The reaction was carried out under the following conditions: **1** (1 mmol), PhONa (1 mmol), ArONa (1 mmol), $PdCl_2(PPh_3)_2$ (0.03 mmol) and CuI (0.1 mmol) in DMF under CO (1 atm) at 50°C for 1 h.

[b] Yield based on the amount of **1** used was determined by GLC.

To support the above consideration, the catalytic carbonylation of **1** using sodium phenoxides (prepared from **2** and sodium hydride) in place of **2**–NBu^n_3 was carried out [9]. The relative reactivity of sodium phenoxides determined by the competition method are shown in Table 3. The phenoxides with electron-withdrawing substituents were found to become less reactive than those with electron-donating ones. This does not contradict that when NBu^n_3 is used as the base, the enhanced reactivity of the phenols having electron-withdrawing substituents may result from their higher ionization ability.

2.4. Carbonylation of bis(4-iodophenyl) ether in the presence of bisphenols 7a–7c

It has been recently demonstrated that palladium-catalyzed carbonylation may be applied to the synthesis of wholly aromatic heat resistant

Table 4
Carbonylation of bis(4-iodophenyl) ether in the presence of bisphenols **7** [a]

7	CuI [b]	Yield of **8** (%) [c]	$k_{obsd} \times 10$ (M^{-1} h^{-1})	M_w [d]	M_w / M_n [d]
7a		78	8.7	20000	1.7
7a	+	92	18	25000	1.8
7b		82	27	35000	2.4
7b	+	86	42	40000	2.6
7c		94	35	29000	2.1
7c	+	94	49	35000	2.3

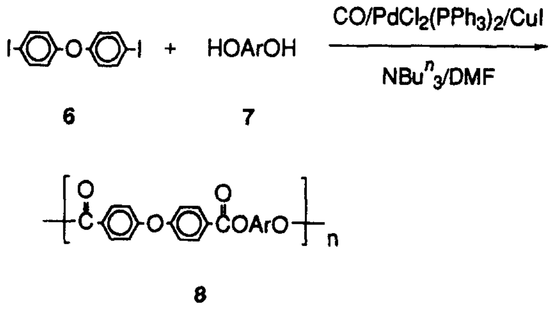
[a] The reaction was carried out under the following conditions: **6** (2 mmol), **7** (2 mmol), $PdCl_2(PPh_3)_2$ (0.12 mmol), CuI (0.4 mmol) and NBu^n_3 (4.8 mmol) in DMF under CO (1 atm) at 90°C for 22–30 h.

[b] Plus sign indicates that the cocatalyst was added.

[c] Yield (%) = 100 × {weight of product (mg)}/[2 × {(MW of **6**) + (MW of **7**) + 2 × 28 (CO) − 2 × 128 (HI)}] IR wave numbers ($\nu_{C=O}$) of **8a**, **8b**, and **8c** were 1735, 1743 and 1740 cm^{-1}, respectively.

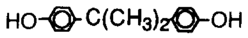
[d] Determined by GPC as polystyrene equivalent molecular weight.

polyesters by using aromatic dihalides and bisphenols as the substrates [10,11]. In the present work, it has been found that using an amine base which allows good product yield, electron-withdrawing substituents on phenol as well as addition of CuI can enhance the aryloxycarbonylation of **1**. Consequently, carbonylative polymerization reaction of diiodide **6** with bisphenols **7a**–**7c** having different acidities was examined with the catalyst system of $PdCl_2(PPh_3)_2$/CuI (Eq. 4 and Table 4).



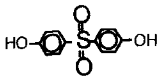
(4)

When the reaction of **6** (2 mmol) and bisphenol **7a** (2 mmol) using $PdCl_2(PPh_3)_2$ (0.12 mmol) and NBu^n_3 (4.8 mmol) in DMF under 1 atm of carbon monoxide at 90°C was carried out, polyester **8a** was formed in a yield of 78% (see Experimental). Gel permeation chromatogram of **8a** indicated that its number-average molecular weight (M_n) and weight-average molecular weight (M_w) values were 12000 and 20000, respectively, for standard polystyrene, the ratio M_w/M_n being 1.7. Interestingly, addition of CuI (0.4 mmol) was found to increase not only the rate of the substrate consumption but also the molecular weight of **8a** to some extent. As expected from the results for the reaction of **1** with **2**, the reaction using bisphenols containing electron-withdrawing bridges, 2,2-bis(4-hydoxyphenyl)-hexafluoropropane **7b** and 4,4′-bis(4-hydroxyphenyl)sulfone **7c** proceeded more readily than that with **7a** to afford the corresponding polyesters **8b** and **8c**. The addition of CuI also increased their molecular weight.



7a

7b



7c

The increased reaction rate by the CuI addition may result from the acceleration of the rate-determining phenolysis step. One of the possible reasons for the increase in the molecular weight of the polymers would be that the palladium intermediate formed in the presence of CuI tends to hold the polyester in its coordination sphere, so that the carbonylative condensation proceeds relatively more continuously on identical polyester molecule.

3. Experimental

GLC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm × 1.5 m) or with a CBP-1 capillary column (i.d. 0.5 mm × 25 m). The complexes $PdCl_2(PPh_3)_2$ [1] and *trans*-4-$MeC_6H_4COPdI(PPh_3)_2$ **4** [16] and bis(4-iodophenyl) ether **6** [17] were prepared by the methods reported previously.

3.1. Catalytic carbonylation of 4-iodotoluene using phenols and NBu^n_3

A mixture of **1** (436 mg, 2 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol), CuI (38 mg, 0.2 mmol), a phenol **2** (2 mmol), NBu^n_3 (0.57 cm^3, 2.4 mmol), and an appropriate amount of 1-methylnaphthalene as internal standard in DMF (5 cm^3) was stirred under CO (1 atm) at 90°C. The time course of the reaction was monitored by GLC. Product identification and quantification were made by GLC and GLC–MS. Each ester was also isolated by column chromatography on silica gel using hexane–CH_2Cl_2 as eluent and compared with the corresponding authentic sample.

3.2. Stoichiometric reaction of trans-4-$MeC_6H_4COPdI(PPh_3)_2$ with a mixture of **2a** and a substituted phenol

A mixture of **4** (88 mg, 0.1 mmol), CuI (19 mg, 0.1 mmol), **2a** (94 mg, 1 mmol), a substituted phenol **2** (1 mmol), NBu^n_3 (0.57 cm^3, 2.4 mmol), dimethyl maleate (58 mg, 0.4 mmol) as a trap for Pd^0 species formed during the reaction [12], and an appropriate amount of 1-methylnaphthalene as internal standard in DMF (5 cm^3) was stirred under nitrogen at 50°C. The yield of two product esters was determined by GLC analysis.

3.3. Catalytic carbonylation of 4-iodotoluene with a mixture of sodium salts of **2a** and a substituted phenol

A mixture of **2a** (94 mg, 1 mmol), a substituted phenol (1 mmol), and NaH (48 mg, 2 mmol) in DMF (3 cm^3) was stirred under nitrogen at room temperature for 5 min and then, $PdCl_2(PPh_3)_2$ (21 mg, 0.03 mmol), CuI (19 mg, 0.1 mmol), and DMF (3 cm^3) containing **1** (218 mg, 1 mmol) and 1-methylnaphthalene as internal standard were added. The resulting mixture was stirred under CO (1 atm) at 50°C for 1 h. The product mixture was analyzed by GLC.

3.4. Carbonylation of bis(4-iodophenyl) ether in the presence of bisphenols **7a–7c**

A mixture of **6** (844 mg, 2 mmol), **7** (2 mmol), $PdCl_2(PPh_3)_2$ (84 mg, 0.12 mmol), and CuI (76 mg, 0.4 mmol) in DMF (5 cm^3) was stirred under CO (1 atm) at 90°C for 5 min and then, a DMF (5 cm^3) solution containing NBu^n_3 (1.14 cm^3, 4.8 mmol) and 1-methylnaphthalene as internal standard was added. The resulting mixture was stirred at 90°C for 22 h. Irrespective of the bisphenol used, precipitation of the product polyester was not observed during the reaction. The time course of the substrate consumption was also monitored by GLC. After cooling, the reaction mixture was poured into methanol (100 cm^3). The precipitated polymer was filtered, washed with methanol (100 cm^3), and dried at room temperature in vacuo to give polyester **7**. The number-average molecular weight (M_n) and the weight-average molecular weight (M_w) of **7** were determined by means of gel permeation chromatography (GPC) using DMF containing 0.01 mol/dm^3 of LiBr as eluent on the basis of a polystyrene calibration.

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