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Effect of Copper and Iron Cocatalysts on the Palladium-Catalyzed Carbonylation Reaction of Iodobenzene

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It has been found that carbonylation of iodobenzene using $PdCl_2(PPh_3)_2$ as a catalyst precursor in the presence of a number of nucleophiles, including ethanol, phenol, and diethylamine, can be promoted by the addition of copper halides or $Fe(CO)_5$ as cocatalysts. To clarify the effect of the cocatalysts, kinetic investigations into not only the catalytic reaction but also the stoichiometric reactions of the corresponding two intermediary complexes, *trans*-$PdPh(I)(PPh_3)_2$ (**6a**) and *trans*-$Pd(COPh)(I)(PPh_3)_2$ (**7a**), have been carried out. Consequently, it has been revealed that both the CO insertion into **6a** to give **7a** and the subsequent reaction with the nucleophiles are enhanced by the cocatalysts. The possible role of the cocatalysts has also been discussed.

Introduction

The palladium-catalyzed carbonylation of aryl halides in the presence of nucleophiles and organometallic reagents is a highly useful tool for the preparation of a variety of aromatic carbonyl compounds such as esters, amides, aldehydes, carboxylic acids, and ketones.[1] In the case of amines or alcohols as the nucleophiles, Yamamoto's and Tanaka's groups have reported that two CO molecules can also be incorporated into the substrates under pressurized conditions to afford α-keto amides[2] or α-keto esters[3] along with normal amides or esters.

We have recently reported that arenesulfonyl chlorides also undergo palladium-catalyzed alkoxycarbonylation in the presence of titanium(IV) tetraalkoxides accompanied by desulfonylation to give the corresponding esters along with diaryl disulfides (eq 1).[4] Interestingly, it was observed that addition of CuI to the reaction as a cocatalyst considerably increased the yield of the carbonylation products, suppressing the formation of the disulfides.[5] We have suggested that one of the possible roles of added CuI might be acceleration of the catalytic step(s) after the arylpalladium intermediate formation, i.e. the CO insertion into the intermediate and/or the reaction of the resulting aroylpalladium species with the nucleophiles (eq 2). During a further study of the effect of copper salts in the palladium-catalyzed carbonylation reactions, it was found that CuI could also promote the carbonylation of aryl iodides using ethanol, phenol, and diethylamine as the nucleophiles (eq 3). Particularly, in the reaction using diethylamine, the corresponding α-keto amides were formed in enhanced yields in the presence of CuI even under 1 atm of CO.

$$\mathrm{ArSO_2Cl} \xrightarrow[\mathrm{Ti(OR)_4}]{\mathrm{CO/Pd\text{-}cat.}} \mathrm{ArCOOR} + \mathrm{ArSSAr} \qquad (1)$$

$$\mathrm{PdPh(I)L_2} \xrightarrow{\mathrm{CO}} \mathrm{Pd(COPh)(I)L_2} \xrightarrow{\mathrm{Nu}} \mathrm{PhCONu} + \mathrm{Pd^0} \qquad (2)$$

$$\mathrm{ArI} + \mathrm{NuH} \xrightarrow[\mathrm{base}]{\mathrm{CO/PdCl_2(PPh_3)_2/CuI/(LiX)}} \mathrm{ArCONu}\ (+\mathrm{ArCOCONR_2}) \qquad (3)$$

$$\mathrm{NuH} = \mathrm{ROH},\ \mathrm{R_2NH}$$

It is known that copper salts can act as cocatalysts in palladium-catalyzed carbonylations of alcohols,[6] alkenes,[7] and alkynes[8] under oxidative conditions using molecular oxygen to give oxalates, saturated carboxylic acid esters, and unsaturated dicarboxylic acids, respectively. However, to our knowledge, copper species have never been effectively used under reductive carbonylation conditions. Consequently, we have made a detailed investigation of the carbonylation of iodobenzene by using a combination of $PdCl_2(PPh_3)_2$ and CuI in the presence of three kinds of nucleophiles. Other metal species in place of CuI have also been tested; $Fe(CO)_5$ has been found to be capable of being used, as well as copper halides.

Results and Discussion

Ethoxy- and Phenoxycarbonylations of Iodobenzene. When iodobenzene (**1a**; 2 mmol) was treated

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Table 1. Ethoxy- and Phenoxycarbonylations of Iodobenzene (1a)[a]

ROH	conditions[b]	CuI	LiX	conversn of **1a**/%[c]	yield of ester/%[c]
EtOH	A			45	26
		+		65	34
		+	+	78	47
PhOH	B			18	15
		+	+	60	60

[a] Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), CuI (0.2 mmol), in 2-methoxyethyl ether (5 mL). The + sign indicates that the catalyst was added. [b] A: LiCl (0.4 mmol), EtOH (2.4 mmol), NEt_3 (2.4 mmol), uner CO (10 atm) at 110 °C for 15 h. B: LiI (0.4 mmol), PhOH (4 mmol), NEt_3 (4 mmol), under CO (1 atm) at 60 °C for 5 h. [c] Determined by GLC based on **1a** used.

with ethanol (2.4 mmol) in the presence of $PdCl_2(PPh_3)_2$ (0.06 mmol) and NEt_3 (2.4 mmol) in 2-methoxyethyl ether (5 mL) under CO (10 atm) at 110 °C for 15 h, ethyl benzoate (**2a**) was formed in a yield of 26%, the conversion of **1a** being 45% (eq 4 (R = Et) and Table 1).

$$\underset{\textbf{1a}}{\mathrm{PhI}} + \mathrm{HOR} \xrightarrow[\mathrm{NEt_3/(CH_3OCH_2CH_2)_2O}]{\mathrm{CO/PdCl_2(PPh_3)_2/CuI/LiX}} \mathrm{PhCOOR} \quad (4)$$

Addition of CuI (0.2 mmol) together with LiCl (0.4 mmol) to the reaction significantly increased the conversion of **1a** and the yield of **2a**. In the absence of LiCl the increase in the ester yield was reduced. The role of the lithium salt may be that it effectively solubilizes CuI.[9] In each reaction, a trace amount of *N,N*-diethylbenzamide (1−3%) was also formed as a byproduct.

In the carbonylation reaction of **1a** with phenol in place of ethanol under CO (1 atm) at 60 °C for 5 h, phenyl benzoate (**3a**) was formed as the sole carbonylation product. The reaction also was remarkably promoted by CuI•2LiCl. Since the reaction with phenol proceeded smoothly and quantitatively under 1 atm of CO, its kinetic analysis was carried out. It has been recognized that alkoxycarbonylation of active halides such as aryl iodides catalyzed by palladium−phosphine complexes involves rate-determining alcoholysis of intermediary aroylpalladium complexes.[3b,10] Consistent with this, when the time course of the reaction with 1 10-fold excess of both phenol and NEt_3 in the presence or absence of the cocatalyst was monitored by GLC, the yield of the ester was found to increase linearly with the reaction time up to ca. 70% conversion of **1a** (Figure 1). With 2 equiv each of phenol and NEt_3, the plot of $1/c$ (c = [PhOH] = [NEt_3]) vs time was linear with a slope which may correspond to a second-order rate constant. By using this constant, the effect of the ratio of copper to palladium on the reaction rate was examined (Figure 2). The rate constant increased significantly up to Cu:Pd = 0.5:1; when the ratio was increased further, it was almost invariant.

(Diethylamino)carbonylation of 1a. It is known that aryl bromides and iodides undergo carbonylation in the presence of palladium catalysts and secondary amines under pressurized conditions to produce the corresponding mixtures of mono- and dicarbonylated products, i.e. amides and α-keto amides.[2] To examine the effect of copper iodide on the product composition as well as the reaction rate, the reaction of **1a** (2 mmol) using $PdCl_2(PPh_3)_2$ (0.06 mmol) and diethylamine (6 mmol) in the presence or absence of CuI (0.2 mmol) was performed (eq 5). It was found that the reaction

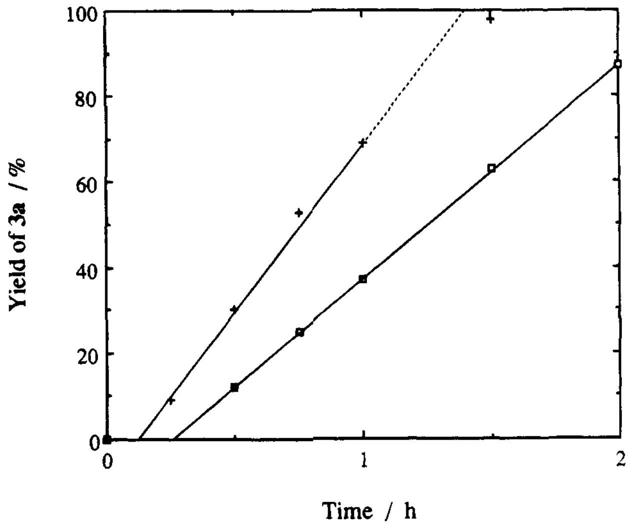

Figure 1. Time course of the reaction of **1a** with an excess amount of both PhOH and NEt_3: reaction in the presence (+) and absence (□) of CuI•2LiI. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), CuI (0.2 mmol), LiI (0.4 mmol), PhOH (20 mmol), NEt_3 (20 mmol).

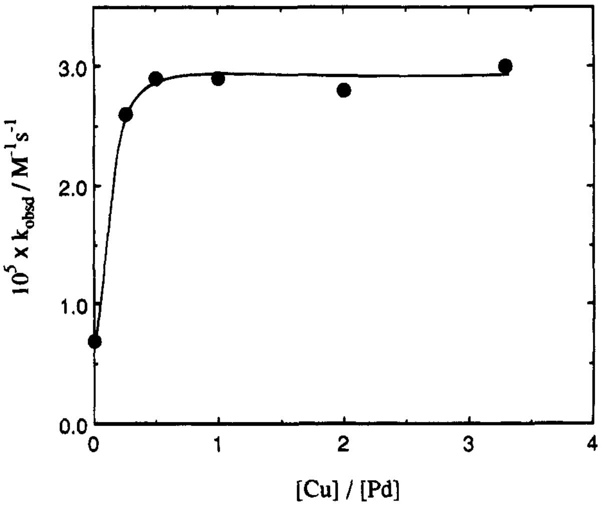

Figure 2. Effect of the Cu:Pd ratio on the reaction of **1a** with phenol. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), LiI (0.4 mmol), PhOH (4 mmol), NEt_3 (4 mmol), in 2-methoxyethyl ether under CO (1 atm) at 60 °C.

$$\underset{\textbf{1}}{\mathrm{ArI}} + \mathrm{HNEt_2} \xrightarrow[\mathrm{DMF}]{\mathrm{CO/PdCl_2(PPh_3)_2/cocat.}} \underset{\textbf{4}}{\mathrm{ArCOCONEt_2}} + \underset{\textbf{5}}{\mathrm{ArCONEt_2}} \quad (5)$$

proceeded efficiently at 50 °C even at 1 atm to give *N,N*-diethyl-2-phenylglyoxylamide (**4a**) as the major product along with *N,N*-diethylbenzamide (**5a**) (Table 2), while it was very slow in 2-methoxyethyl ether. Under the conditions employed, the plot of the recovery of **1a** vs time was linear up to ca. 50% conversion of **1a**, suggesting that the rate-determining step does not involve the oxidative addition of **1a** to the catalyst, as has been suggested previously.[2b] This reaction, as well as that with phenol, was enhanced by the CuI addition. In this case, the reaction was conducted without using lithium

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Table 2. (Diethylamino)carbonylation of 1[a]

ArI	cocat.	10^4V_{max}[c]/(mol h^{-1})	**4**:**5**[b]	yield of **4** + **5**/%[b]
1a		2.4	71:29	~100
1a[d]		3.9	78:22	~100
1a	CuI	4.1	87:13	~100
1a[d]	CuI	6.0	89:11	~100
1a	CuBr	3.9	85:15	~100
1a	CuCl	3.3	84:16	~100
1a	$Fe(CO)_5$	4.5	85:15	91
1a	$Fe_3(CO)_{12}$	2.9	62:38	95
1a	$Co_2(CO)_8$	1.8	70:30	97
1a	$Mn_2(CO)_{10}$	6.1	53:47	89
1a	$Mo(CO)_6$	3.5	81:19	85
1a	$Cr(CO)_6$	2.3	75:25	83
1b		*e*	11:85	~100
1b	CuI	*e*	51:47	~100
1c		*e*	68:30	~100
1c	CuI	*e*	83:17	~100

[a] Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), cocatalyst (0.2 mmol), Et_2NH (6 mmol), in DMF (5 mL) under CO (1 atm) at 50 °C. [b] Determined by GLC based on **1a**. [c] Maximum reaction rate. [d] Et_2NH (10 mmol). [e] Not determined.

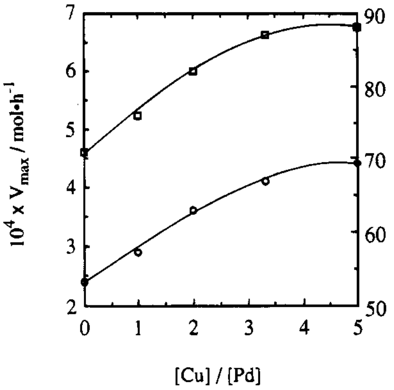


Figure 3. Effect of the Cu:Pd ratio on V_{max} (○) and selectivity of **4a** (□) in the reaction of **1a** with diethylamine. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), Et_2NH (6 mmol), in DMF (5 mL) under CO (1 atm) at 50 °C.

salt, since CuI is completely solubilized under the conditions employed. It should be noted that the product ratio of **4a** to **5a** was essentially constant, irrespective of the conversion of **1a**. It was also of interest that the CuI addition considerably increased the selectivity of α-keto amide **4a**. When the reaction was examined using 5 equiv of diethylamine, the corresponding plot of the conversion vs time was linear up to ca. 95% conversion of **1a**, and even in this case, the addition of CuI affected both the reaction rate and the selectivity of **4a** (Table 2). Figure 3 indicates the effect of the Cu:Pd ratio on the reaction. When the amount of CuI was increased up to 0.2 mmol, the reaction rate increased monotonously.

Table 2 also summarizes the reaction rate and the ratio of **4a** to **5a** in the presence of several copper salts and metal carbonyls. The other copper salts as well as CuI could also increase both the reaction rate and the ratio of **4a** to **5a**. Among the metal carbonyls tested, $Fe(CO)_5$ was found to be as effective as CuI. It is noted that in the examination of the effect of the ratio of iron to palladium on both the reaction rate and the selectivity of **4a**, the maximum effect was obtained when 2 equiv of $Fe(CO)_5$ was used (Figure 4). Although $Mn_2(CO)_{10}$ increased the reaction rate, the selectivity of **4a** was detrimentally decreased.

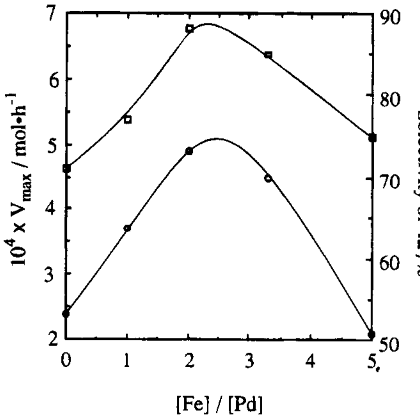
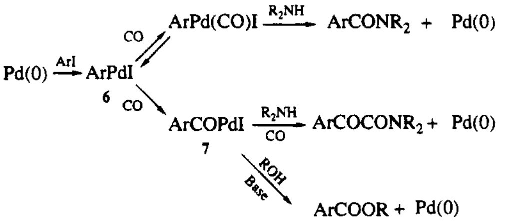


Figure 4. Effect of the Fe:Pd ratio on V_{max} (○) and selectivity of **4a** (□) in the reaction of **1a** with diethylamine. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.06 mmol), Et_2NH (6 mmol), in DMF (5 mL) under CO (1 atm) at 50 °C.

Scheme 1



The CuI addition also increased the selectivity of the corresponding α-keto amides in the reactions of *p*-chloroiodobenzene (**1b**) and *p*-iodotoluene (**1c**) (Table 2).

The mechanism to account for the mono- and dicarbonylations of aryl halides in the presence of secondary amines, which has been proposed previously,[2b] is illustrated in Scheme 1, where phosphine ligands are omitted. When the arylpalladium intermediate **6** undergoes CO insertion to give the aroylpalladium species **7**, an α-keto amide is formed. On the other hand, coordination of CO to **6** followed by reaction with amine affords the simple amide. It has also been suggested that (a) the selectivity of α-keto amide increases when the CO insertion of **6** to **7** is enhanced by an electron-donating substituent on the aryl halide and (b) the rate-determining step in the transformation of aryl iodides into the corresponding α-keto amides is in the reaction sequence after the formation of **7**, as is alkoxycarbonylation. Therefore, the observed effects of copper halides and $Fe(CO)_5$ on the overall reaction rate and on the selectivity of α-keto amide indicate that the cocatalysts may enhance both the CO insertion into **6** to give **7** and the subsequent step. To confirm this, kinetic investigations into the stoichiometric reactions of *trans*-$PdPh(I)(PPh_3)_2$ (**6a**) and *trans*-$Pd(COPh)(I)(PPh_3)_2$ (**7a**) as the intermediates in the catalytic reaction were performed in the presence or absence of CuI.

Stoichiometric Reactions of 6a and 7a.[11] When **6a** (0.09 mmol) was dissolved in DMF (15 mL) at 19 °C under 1 atm of CO, CO was consumed with a pseudo-first-order rate constant (k_{obsd}) of 2.5×10^{-3} s^{-1} (eq 6, Table 3, and Figure 5). As expected, addition of CuI (0.3 mmol) with LiCl (0.6 mmol) enhanced the CO uptake, k_{obsd} being 4.5×10^{-3} s^{-1}. It should be noted

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Table 3. Pseudo-First-Order Rate Constants of CO Uptake by 6a[a]

CuI·2LiCl	10^3k_{obsd}/s^{-1}	CuI·2LiCl	10^3k_{obsd}/s^{-1}
	2.5	*b*	0.61
+	4.5	+[b]	1.3

[a] Reaction conditions: **6a** (0.09 mmol), CuI (0.3 mmol). LiCl (0.6 mmol), in DMF (15 mL) under CO (1 atm) at 19 ± 1 °C. The + sign indicates that the catalyst was added. [b] Reaction in 2-methoxyethyl ether (15 mL).

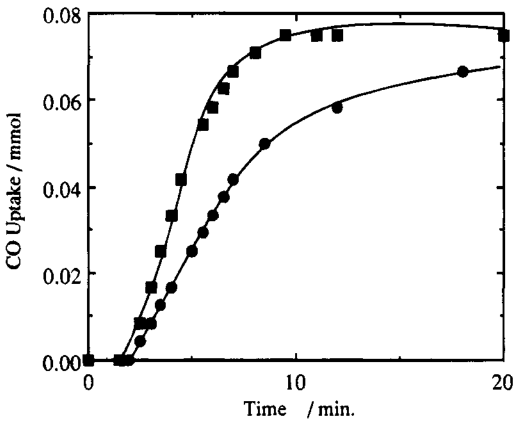


Figure 5. Time course of the CO uptake of **6a**: reaction in the presence (■) or absence (●) of CuI·2LiCl. Reaction conditions: **6a** (0.09 mmol), CuI (0.3 mmol), LiCl (0.6 mmol), in DMF (15 mL) under CO (1 atm) at 19 ± 1 °C.

$$\underset{\textbf{6a}}{\mathrm{PdPh(I)(PPh_3)_2}} + \mathrm{CO} \xrightarrow[\mathrm{DMF\ or\ (CH_3OCH_2CH_2)O}]{\mathrm{(CuI\cdot 2LiCl)}} \underset{\textbf{7a}}{\mathrm{Pd(COPh)(I)(PPh_3)_2}} \quad (6)$$

that in the presence of CuI without LiCl, more than a stoichiometric amount of CO (ca. 1.3 equiv based on Pd) was absorbed at a greater rate. This appeared to be due to the fact that CuI itself could absorb CO under the reaction conditions. It was indeed confirmed that CuI in DMF absorbed ca. 0.1 equiv of CO based on Cu, whereas in the presence of LiCl, CuI did not react with CO. The CO uptake by **6a** in 2-methoxyethyl ether was also promoted by the addition of CuI·2LiCl (Table 3).

The reaction of **7a** with ethanol, phenol, and diethylamine was examined under pseudo-first-order conditions using 10 equiv of these nucleophiles in DMF (eq 7 and Table 4). The reaction with diethylamine under

$$\underset{\textbf{7a}}{\mathrm{Pd(COPh)(I)(PPh_3)_2}} + \mathrm{NuH} \xrightarrow[\mathrm{(NEt_3)/DMF}]{\mathrm{CO\ or\ N_2/CuI}} \mathrm{PhCONu\ or\ PhCOCONEt_2} \quad (7)$$

1 atm of CO proceeded quantitatively, giving the α-keto amide **4a** as a single product.[2b] It was also found that the pseudo-first-order rate constant of this reaction, which may correspond to the rate-determining step of the double-carbonylation reaction of **1a** with diethylamine as described above, increased in the presence of CuI.

Similarly, the reactions with ethanol and phenol under nitrogen were promoted by the addition of CuI. It is noted that, in these reactions, dimethyl maleate was added to prevent interference by the Pd(0) species formed according to the previous report.[3b] These reactions in the presence of CuI terminated within 30 min, giving ethyl and phenyl benzoates in 67% and 97% yields. Thus, the reaction with ethanol is not quantitative and, in contrast, that with phenol is smooth and fast. To determine the exact rate of the formation of these esters, analytical techniques other than GLC should be examined.

Table 4. Reaction of 7a with Et_2NH, EtOH, and PhOH[a]

	10^4k_{obsd}/s^{-1}		
CuI	Et_2NH[b]	EtOH[c,d]	PhOH[c]
+	9.7	>6.5	>10
	2.4	0.082	4.3

[a] Reaction conditions: **7a** (0.1 mmol), CuI (0.1 mmol), NuH (1 mmol), in DMF (5 mL) at 20 °C. The + sign indicates that the catalyst was added. [b] Under CO (1 atm). [c] Under N_2 in the presence of NEt_3 (1 mmol) and dimethyl maleate (0.4 mmol). [d] At 30 °C.

Table 5. IR Data for Benzoylpalladium Species in the Presence or Absence of CuI or $Fe(CO)_5$

	ν(CO)/cm^{-1}	
complex	Pd(CO)Ph	Fe(CO)
$Pd(COPh)(I)(PPh_3)_2$	1636	
$PdPh(I)(PPh_3)_2$ + CuI[a]	1673	
$Pd(COPh)(I)(PPh_3)_2$ + CuI[a]	1673	
$PdPh(I)(PPh_3)_2$ + $Fe(CO)_5$[b]	1669	1931, 1973
$Pd(COPh)(I)(PPh_3)_2$ + $Fe(CO)_5$[b]	1669	1931, 1973
$Fe(CO)_5$		1999, 2022
$Fe(CO)_3(PPh_3)_2$		1873, 1887

[a] Dark brown solid formed when a mixture of Pd complex and CuI·2LiCl (Pd:Cu = 1:1) was stirred under CO at room temperature for 1 h followed by elimination of the solvent under vacuum. [b] Dark brown solid formed when a mixture of complexes (Pd:Fe = 1:2), NEt_3, and THF was stirred under nitrogen at 50 °C for 1 h followed by elimination of the solvent under vacuum.

Role of the Cocatalysts. To characterize the product in the stoichiometric reaction of complex **6a** with CO in the presence of CuI·2LiCl, the reaction using **6a** (0.1 mmol), CuI (0.1 mmol), and LiCl (0.2 mmol) was carried out in a volatile solvent, THF. Evaporation of the solvent gave a dark brown solid powder. The IR spectrum of the solid showed a single peak at 1673 cm^{-1} in the carbonyl region, which may be characteristic of a benzoylpalladium species (Table 5). It should be noted that the wavenumber is considerably higher than that of a yellow sample of **7a** (1636 cm^{-1}) which was obtained without the cocatalyst. The ^{31}P NMR spectrum of the brown solid in d_8-THF exhibited two broad signals at 28.0 and 30.1 ppm (1:1) due to the PPh_3 ligands, the peaks appearing at lower field relative to a sharp singlet of **7a** (23.6 ppm), as shown in Figure 6. The brown material appeared to be able to be formed by mixing **7a** with CuI·2LiCl in THF. The IR spectrum of the powder obtained by this method was identical with that of the product obtained from **6a** and CuI·2LiCl under CO as described above. These results indicate that the benzoyl species formed in the presence of CuI·2LiCl is not a simple mixture of **7a** and the cocatalyst.

Reaction of **6a** in the presence of $Fe(CO)_5$ in THF gave a dark brown powder which showed an IR absorption band at 1669 cm^{-1}, as did the reaction with CuI. In this case, two major peaks, which may be due to the terminal CO molecules coordinated to the iron center, were also observed at 1931 and 1973 cm^{-1} along with two minor ones at 1900 and 2049 cm^{-1} (Table 5). The powder obtained by mixing **7a** and $Fe(CO)_5$ gave essentially the same IR spectrum. These major IR peaks

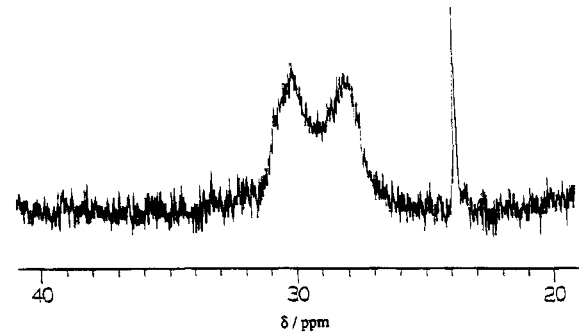


Figure 6. ^{31}P NMR spectrum of the benzoylpalladium species formed in the presence of CuI·2LiCl in d_8-THF at room temperature (161.9 MHz; chemical shifts are referenced to external PPh$_3$).

due to the terminal CO appear between those of Fe(CO)$_5$ itself (1999 and 2022 cm^{-1}) and of Fe(CO)$_3$(PPh$_3$)$_2$ (1873 and 1887 cm^{-1}). Furthermore, two carbonyl peaks at 1931 and 1973 cm^{-1} were again observed when Fe(CO)$_5$ and 1 equiv of PPh$_3$ were mixed in THF at room temperature. Under these conditions, Fe(CO)$_4$(PPh$_3$) may be expected to be generated. It should be noted that PhCOPd(I)PPh$_3$·(toluene) and (PhCOPd(μ-I)(PPh$_3$))$_2$ have been reported to show their IR absorption bands at 1660[12] and 1665 cm^{-1},[13] respectively. Thus, these results may suggest that the treatment of either **6a** or **7a** with Fe(CO)$_5$ involves transfer of one of the two phosphine ligands coordinated to the palladium complex to the iron center. In the treatment with CuI, a similar transfer of the ligand to the copper species seems to take place.

The above observations led us to deduce that the carbonylation of **1** in the presence of the cocatalysts involves intermediary palladium complexes having one PPh$_3$ ligand. Consequently, the carbonylation reaction of **1a** (2 mmol) with diethylamine (6 mmol) under CO (1 atm) in DMF at 50 °C was examined in the presence of 0.06 mmol of both PdCl$_2$(PhCN)$_2$ and PPh$_3$ (eq 8 and Table 6).

$$\underset{\mathbf{1a}}{\mathrm{PhI}} + \mathrm{HNEt_2} \xrightarrow[\mathrm{DMF}]{\mathrm{CO/PdCl_2(PhCN)_2} + n\mathrm{PPh_3/cocat.}} \underset{\mathbf{4a}}{\mathrm{PhCOCONEt_2}} + \underset{\mathbf{5a}}{\mathrm{PhCONEt_2}} \quad (8)$$

Under these conditions, a catalytically active species which contains 1 equiv of PPh$_3$ may be expected to be generated *in situ*. Addition of CuI (0.2 mmol) or Fe(CO)$_5$ (0.12 mmol) increased the reaction rate and the selectivity of **4a** in this reaction as well as in the reaction using 2 equiv of PPh$_3$ (0.12 mmol). It should be noted that a high selectivity of **4a** (more than 90%) was achieved concurrently with an enhanced rate by using the present catalyst system of PdCl$_2$(PhCN)$_2$–PPh$_3$–CuI or Fe(CO)$_5$ under 1 atm of CO. When the reaction using PdCl$_2$(PhCN)$_2$ without addition of PPh$_3$ was examined, the reaction mixture gradually darkened with the deposition of palladium black. Even in the presence of CuI or Fe(CO)$_5$, the reaction was not complete after 72 h.

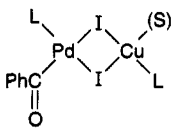
Table 6. (Diethylamino)carbonylation of 1a Using PdCl$_2$(PhCN)$_2$, *n* PPh$_3$, and Cocatalyst[a]

cat.	cocat.	$10^4V_{\max}$[b]/ (mol h^{-1})	**4a**:**5a**[c]	yield of **4a** + **5a**/%[c]
PdCl$_2$(PhCN)$_2$		1.5[d]	97:3	65
PdCl$_2$(PhCN)$_2$ + PPh$_3$		2.2	79:21	97
PdCl$_2$(PhCN)$_2$ + 2 PPh$_3$		1.6	75:25	92
PdCl$_2$(PhCN)$_2$	CuI	1.6[d]	97:3	75
PdCl$_2$(PhCN)$_2$ + PPh$_3$	CuI	4.0	92:8	94
PdCl$_2$(PhCN)$_2$ + 2 PPh$_3$	CuI	3.2	86:14	97
PdCl$_2$(PhCN)$_2$	Fe(CO)$_5$	1.6[d]	86:14	42
PdCl$_2$(PhCN)$_2$ + PPh$_3$	Fe(CO)$_5$	3.4	95:5	86
PdCl$_2$(PhCN)$_2$ + 2 PPh$_3$	Fe(CO)$_5$	4.1	84:16	81

[a] Reaction conditions: **1a** (2 mmol), PdCl$_2$(PPh$_3$)$_2$ (0.06 mmol), CuI (0.2 mmol) or Fe(CO)$_5$ (0.12 mmol), Et$_2$NH (6 mmol), in DMF (5 mL) under CO (1 atm) at 50 °C for 24 h. [b] Maximum reaction rate. [c] Determined by GLC. [d] The reaction was not complete even after 72 h.

There have been several reports that CuI can promote the Stille type reaction, i.e. the palladium-catalyzed cross-coupling reaction of aryl halides or triflates with organotin compounds, while the role of the copper species has not been well understood.[14] Liebeskind and Fengl[14a] suggested the possibility that added CuI facilitated the transmetalation step (Sn → Cu → Pd) in the cross-coupling of stannylcyclobutenediones with aryl iodides using a combination of (PhCH$_2$)(Cl)Pd(PPh$_3$)$_2$ and CuI. It is also known that the palladium-catalyzed reactions of aryl halides with terminal alkynes are enhanced by CuI.[15] A plausible explanation for this may be that copper(I) acetylides are generated in the reaction medium as the reaction intermediates. Hobbs[16] noted that in the alkynylation of iodo nucleosides using a catalyst system of Pd(PPh$_3$)$_4$–CuI, CuI might remove two PPh$_3$ ligands from the palladium complex to promote the reaction.

In the present carbonylation reaction, however, the results described above may suggest that the role of copper halides and Fe(CO)$_5$ is not only to remove one PPh$_3$ ligand from the intermediary palladium complexes **6a** and **7a** but also to form more reactive intermediates in which the cocatalysts coordinated by one PPh$_3$ ligand are involved in the palladium coordination sphere. Consequently, a further characterization of the brown solid obtained from the mixture of **7a**, CuI, and LiCl has been attempted. Since it was soluble in THF or methylene chloride, it was purified by recrystallization from THF–hexane. As a result, a dark brown solid powder which shows a benzoyl C=O band at 1673 cm^{-1} in the IR spectrum was obtained. Attempted further crystallization appropriate for X-ray structural analysis was unsuccessful, although quantitative XPS analysis of it indicated that it contained palladium, copper, and phosphorus atoms. Thus, the structure of this species has not yet been defined. However, the species



L = PPh$_3$; (S) = CO, amine, solvent, X$^-$, or other ligand

which is analogous to [(PhCO)Pd(PPh$_3$)(μ-I)]$_2$ previously

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isolated by Alper *et al.*,[13] might be postulated as one possible candidate for the solid obtained, because the ^{31}P NMR spectrum of the palladium dimer with two iodo bridges at room temperature was reported to exhibit similar two broad signals due to interconversion between the cis and trans isomers. The corresponding arylpalladium species may also be expected to be involved in the present catalytic carbonylation reactions. It is conceivable that these iodo bridges may be cleaved easily[13] to provide species relatively more reactive than the corresponding palladium species tightly coordinated by two PPh_3 ligands. Thus, the catalytic reaction involving these intermediates may be expected to proceed more efficiently. It should be pointed out that, in the catalytic phenoxycarbonylation, 0.5 equiv of CuI was sufficiently effective (Figure 2). Therefore, in a less polar solvent such as 2-methoxyethyl ether, it might also be possible to form intermediate(s) containing Pd and Cu in a 2:1 ratio. On the other hand, since addition of more than 1 equiv of CuI was more favorable in the (diethylamino)carbonylation in DMF as shown in Figure 3, an excess amount of CuI must be needed for the complete formation of the reactive species in the presence of the amine in the polar solvent.

In the benzoylpalladium species formed in the presence of $Fe(CO)_5$, the mode of the interaction between palladium and iron species is difficult to describe: CO, PPh_3, and iodo-bridged species would be possible.

Experimental Section

Infrared spectra were obtained with a Shimadzu FTIR-8100M by using KBr pellets for solid samples and KRS-5 plates for liquid materials. ^{31}P NMR spectra were obtained with a JEOL JNM-GSX-400 spectrometer for d_8-THF solutions. The signals were referenced to PPh_3 as an external standard (downfield positive). GC−MS spectra were obtained with a Shimadzu GCMS-QP 2000A spectrometer. GLC analysis was carried out on a Shimadzu GC-8APF gas chromatograph with 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). XPS spectra were obtained on a VG ESCALAB 200i spectrometer with Mg Kα radiation (15 kV−20 mA).

The complexes $PdCl_2(PPh_3)_2$,[17] $PdCl_2(PhCN)_2$,[18] $PdPh(I)(PPh_3)_2$,[19] $Pd(COPh)(I)(PPh_3)_2$,[11] and $Fe(CO)_3(PPh_3)_2$[20] were prepared by the methods reported previously. Other starting materials were commercially available.

Ethoxycarbonylation of Iodobenzene (1a). A mixture of **1a** (408 mg, 2 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol), CuI (38 mg, 0.2 mmol), LiCl (17 mg, 0.4 mmol), ethanol (0.14 mL, 2.4 mmol), NEt_3 (0.33 mL, 2.4 mmol), and 2-methoxyethyl ether (5 mL) was placed in a 50 mL stainless steel autoclave with a glass tube. Then, carbon monoxide (10 atm at room temperature) was charged and the mixture was magnetically stirred at 110 °C for 15 h. After it was cooled, the reaction mixture was poured into water and extracted with ether. Product identification and quantification were made by GLC−MS and GLC analyses.

(Diethylamino)carbonylation of Aryl Iodides. A mixture of 1 (2 mmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol), CuI (38 mg, 0.2 mmol), diethylamine (0.62 mL, 6 mmol), 1-methylnaphthalene as an internal standard, and DMF (5 mL) was stirred under CO (1 atm) at 50 °C. The time course of the reaction was monitored by GLC.

Stoichiometric Reaction. (a) Reaction of $PdPh(I)(PPh_3)_2$ (6a) with CO. In a 100 mL two-necked flask equipped with a stirrer, a carbon monoxide inlet tube, and a dropping funnel containing DMF (15 mL), **6a** (75 mg, 0.09 mmol) and CuI (57 mg, 0.3 mmol) were placed. After the apparatus was flushed with carbon monoxide and allowed to come to equilibrium at 1 atm of pressure, DMF was injected into the reaction flask, and then the mixture was stirred at 19 ± 1 °C. The gas volume consumed with time was measured using a gas buret.

(b) Reaction of $Pd(COPh)(I)(PPh_3)_2$ (7a) with Diethylamine. After a mixture of **7a** (86 mg, 0.1 mmol), CuI (19 mg, 0.1 mmol), and DMF (3 mL) was stirred under CO (1 atm) at 20 °C for 9 min, resulting in a yellow homogeneous solution, a DMF (2 mL) solution containing diethylamine (0.10 mL, 1 mmol) and 1-methylnaphthalene as an internal standard was added; the mixture was then stirred at 20 °C. The amount of *N,N*-diethyl-2-phenylglyoxylamide (**4a**) produced was measured by means of GLC.

Characterization of Benzoylpalladium Species Formed in the Presence of the Cocatalysts. (a) With CuI·2LiCl. A mixture of **6a** (83 mg, 0.1 mmol), CuI (19 mg, 0.1 mmol), LiCl (8 mg, 0.2 mmol), and THF (5 mL) was stirred under CO (1 atm) at room temperature for 1 h. Evaporation of the solvent gave a dark brown solid powder. The results of the IR and ^{31}P NMR analyses are shown in Table 5 and Figure 6. After recrystallization of this solid from THF−hexane, its XPS spectrum was measured. It showed peaks due to Cu (2p 3/2), Pd (3d 5/2), and P (2p) at 935.5, 340.0, and 134.0 eV, respectively. Since the Cu (2p 3/2) peak was overlapped by a peak due to I (3p 1/2), quantitative analysis was unsuccessful.

(b) With $Fe(CO)_5$. A mixture of **6a** (83 mg, 0.1 mmol), $Fe(CO)_5$ (0.026 mL, 0.2 mmol), triethylamine (0.14 mL, 1 mmol), and THF (5 mL) was stirred under nitrogen at 50 °C for 1 h. Evaporation of the solvent gave a dark brown solid powder. The results of the IR analysis are shown in Table 5.

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