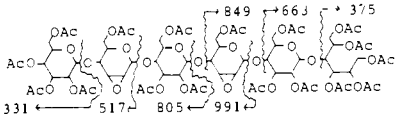
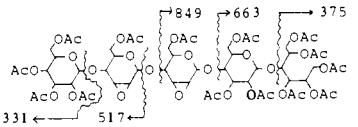
15 followed by complete acetylation with acetic anhydride in pyridine to give **16** and **17**, respectively. While FABMS spectra of **14** and **15** and FDMS[9] spectra of **16** and **17** showed the correct molecular ions of them, EIMS[9] fragmentations of **16** and **17** demonstrated that the epoxides were located on the second and fourth glucose units from the nonreducing end of **16** and on the second and third units for **17**.[16] Therefore, **8** and **9** are assigned to AC and AB isomers, respectively. In conclusion, the disulfonates **4**–**6** are assigned to 2A2D, 2A2C, and 2A2B isomers, respectively.

Thus, we could find highly regiospecific sulfonating reagents for secondary hydroxyls of α-cyclodextrin and obtain disulfonates of the secondary C-2-hydroxyls and the di-*manno*-epoxides, which will develop a new aspect of studies on construction of artificial enzymes and receptors having novel properties of molecular recognition and catalysis. Also, the present study suggests the wide application of Taka amylolysis to isomer determination of various polysubstituted cyclodextrins.

(16) The following fragmentation ions were observed.



16



17

Acknowledgment. We are indebted to Japan Maise Products Co. Ltd. for generous gift of α-cyclodextrin.

Registry No. **1a**, 95784-30-8; **1b**, 95784-31-9; **1c**, 95784-32-0; **1d**, 95784-33-1; **2a**, 95784-34-2; **2b**, 95784-35-3; **2c**, 95784-36-4; **2d**, 95784-37-5; **3a**, 95784-38-6; **3b**, 95784-39-7; **3c**, 95784-40-0; **3d**, 95784-41-1; **4**, 95784-42-2; **5**, 95784-43-3; 6, 95784-44-4; **7**, 95784-45-5; **8**, 95797-81-2; **9**, 95797-82-3; **12**, 95784-46-6; **13**, 95784-47-7; **14**, 95784-48-8; **15**, 95784-49-9; **16**, 95784-50-2; **17**, 95784-51-3; *m*-NBsCl, 121-51-7; *p*-NBsCl, 98-74-8; α-NsCl, 85-46-1; β-NsCl, 93-11-8; α-cyclodextrin, 10016-20-3.

Supplementary Material Available: Experimental data for α-cyclodextrins (8 pages). Ordering information given on any current masthead page.

Palladium-Catalyzed Double Carbonylation of Aryl Halides To Give α-Keto Amides. Mechanistic Studies

Fumiyuki Ozawa,[†] Hidehiko Soyama,[†] Hisayoshi Yanagihara,[†] Issei Aoyama,[†] Hiroaki Takino,[‡] Kunisuke Izawa,[‡] Takakazu Yamamoto,[†] and Akio Yamamoto*[†]

Contribution from the Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 227, and Central Research Laboratories, Ajinomoto Co., Inc., Suzuki-Chyo 1-1, Kawasaki-ku, Kawasaki 210, Japan.
Received September 11, 1984

Abstract: Various aryl halides are catalytically converted into α-keto amides and amides on treatment with secondary amines and carbon monoxide. Palladium complexes containing tertiary phosphine ligands, particularly diphenylmethylphosphine and 1,4-bis(diphenylphosphino)butane, are most effective among other transition-metal complexes. Detailed examination of factors controlling the reaction rates and selectivity for α-keto amide formation revealed the following characteristics of the reactions. (a) Reactivity of phenyl halide decreases in the order PhI > PhBr ≫ PhCl. (b) Oxidative addition of phenyl bromide constitutes the rate-determining step in double carbonylation of phenyl bromide, whereas in the reaction of phenyl iodide the rate-determining step is associated with the reaction of a catalytically active palladium species with carbon monoxide. (c) Introduction of an electron-withdrawing substituent into the para position of phenyl halide enhances the reactivity but decreases the selectivity for α-keto amide. (d) Employment of amines of high basicity ($pK_b \leq 4$) is essential for accomplishing the catalytic double carbonylation. (e) When highly basic secondary amines are used, less sterically demanding amines seem to favor the formation of amide. Decrease of selectivity for the α-keto amide formation in the order Pr_2NH > Et_2NH > piperidine > hexamethyleneimine > Me_2NH > pyrrolidine probably reflects the decrease in steric bulkiness of amines. (f) Although primary amines are in general not suitable for the double carbonylation, *tert*-butylamine can be used because of its inertness to the product α-keto amide. Reactivity of *trans*-PdPh(I) $(PMePh_2)_2$ and *trans*-Pd(COPh)I$(PMePh_2)_2$, supposed intermediates in the catalytic reaction of PhI, toward amines and CO was examined. The relative reactivity of six secondary amines with the benzoylpalladium complex increasing in the order Pr_2NH < Et_2NH < piperidine < Me_2NH < hexamethyleneimine < pyrrolidine was found to be inversely correlated with decreasing selectivity order for α-keto amide formation in the catalytic systems. On the basis of the experimental results, a mechanism consisting of two catalytic cycles to produce α-keto amides and amides has been proposed.

The recently discovered double-carbonylation reaction of aryl halides catalyzed by palladium complexes provides synthetic means useful for introducing two carbonyl groups into organic compounds[1,2]

$$ArX + 2HNR_2' + 2CO \xrightarrow{[Pd]} ArCOCONR_2' + R_2'NH_2X \quad (1)$$

The α-keto amides prepared by this method have potential applications to synthesis of a variety of useful products including α-amino acids, α-hydroxy acids, and heterocyclic compounds.

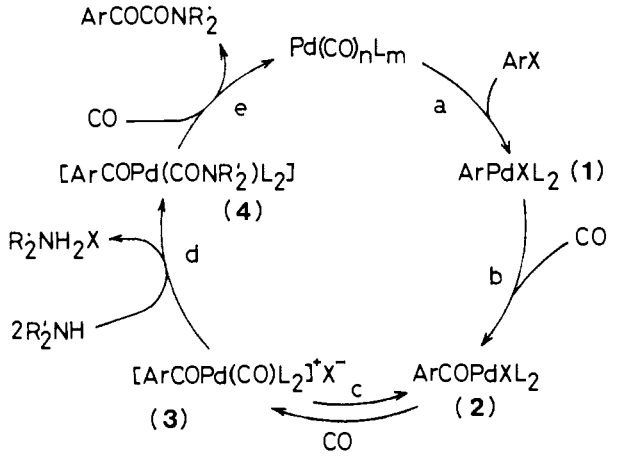
Previous papers[3,4] focused on stoichiometric reactions of aryl- and alkylpalladium halides with carbon monoxide, and amines indicated involvement of elementary processes in the double-

[†] Tokyo Institute of Technology.
[‡] Ajinomoto Co., Inc.

(1) Ozawa, F.; Soyama, H.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1982**, *23*, 3383.
(2) Kobayashi, T.; Tanaka, M. *J. Organomet. Chem.* **1982**, *233*, C64.
(3) Ozawa, F.; Yamamoto, A. *Chem. Lett.* **1982**, 865.
(4) (a) Ozawa, F.; Sugimoto, T.; Yuasa, Y.; Santra, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 683. (b) Ozawa, F.; Sugimoto, T.; Yamamoto, T.; Yamamoto, A. *Ibid.* **1984**, *3*, 692.

0002-7863/85/1507-3235$01.50/0

Scheme I. Proposed Mechanism for Catalytic Conversion of Aryl Halides into α-Keto Amides Promoted by Palladium Complexes



carbonylation reaction as shown in Scheme I. The elementary processes inferred in the study are (a) oxidative addition of aryl halide to a Pd(0) species formed in situ from catalyst precursors such as $PdCl_2L_2$ to give arylpalladium halide (**1**), (b) CO insertion into the Pd–C bond in the arylpalladium intermediate to give aroylpalladium species (**2**), (c) replacement of the halide ligand in **2** by CO to give an ionic intermediate (**3**), (d) attack of amine on the CO ligand in **3** to give an aroyl–carbamoyl species (**4**), and (e) reductive elimination of the aroyl and carbamoyl groups to liberate α-keto amides and to regenerate the Pd(0) species as a carrier of the subsequent catalytic cycle. An alternative mechanism involving double CO insertion into the Ar–Pd bond in **1** was excluded on the basis of the reactivity of $PhCOCOPdCl(PMePh_2)_2$.[4b,5]

In the present paper, we report full details of our study on the catalytic double-carbonylation reactions of aryl halides. In addition to α-keto amides, amides are produced as byproducts in the double-carbonylation reaction. We examined the factors to improve the selectivity for α-keto amide formation and propose here a mechanism accounting for production of amides as well as α-keto amides.

Results

Factors Influencing the Double-Carbonylation Reactions. Yields of α-keto amides are influenced by various factors including the nature of catalyst, substrate (organic moiety in the aryl halides as well as the kind of halogen atom), amine, CO pressure, solvent, and temperature. We now examine each of these factors.

(a) Catalyst. Among various transition-metal complexes examined as catalysts, palladium complexes having tertiary phosphine ligands proved to serve by far as the most effective catalysts for the double-carbonylation reaction. Table I summarizes catalytic activities of various transition-metal complexes in reactions of phenyl bromide with diethylamine under CO pressure at 100 °C.

The presence of tertiary phosphine ligands is required for developing the catalytic activities. Unidentate phosphines as well as bidentate phosphines are effective. The best yield of α-keto amide seems to be obtained when a suitable balance is achieved in the coordinating ability of the tertiary phosphine ligand; namely neither too strongly coordinating ligand nor too weakly bonding one is suitable for obtaining α-keto amide in the highest yield. Strongly coordinating phosphines with high basicity and limited bulkiness like PEt_3 gave the poorest yield. Selectivity for α-keto amide formation was not high when a triphenylphosphine-coordinated complex was used. High selectivity was achieved when dialkylphenylphosphine-coordinated complexes were employed although the yield was low. Among unidentate tertiary phosphines examined, methyldiphenylphosphine gave the most satisfactory result regarding the selectivity and yield. 1,4-Bis(diphenylphosphino)butane (dppb) was found to be a better ligand than 1,2-bis(diphenylphosphino)ethane (dppe) to give higher selectivity

Table I. Catalytic Activities of Various Transition-Metal Complexes in Reactions of PhBr, Et_2NH, and CO[a]

run	catalyst[b]	reaction time, h	product ratio: PhCO-$CONEt_2$	product ratio: PhCON-Et_2	tot[c] yield, %
1	$PhPd(Br)(PPh_3)_2$	35	47	53	87
2	$PhPd(Br)(PMePh_2)_2$	35	80	20	70
3	$PdCl_2(PMePh_2)_2$	40	86	14	95
4	$PdCl_2(PEt_2Ph)_2$	42	84	16	50
5	$PdCl_2(PMe_2Ph)_2$	42	89	11	19
6	$PdCl_2(PEt_3)_2$	42	77	23	9
7	$PdCl_2$(dppe)	40	49	51	100
8	$PdCl_2$(dppb)	48	71	29	100
9	$PdCl_2$	43			0
10	$PdCl_2$(bpy)	43			0
11	$Pd(OAc)_2$	43			0
12	$CuBr(PPh_3)_3$	40	58	42	0.8[d]
13	$NiCl_2(PEt_3)_2$	40	0	100	1.3[e]
14	$RhCl(PPh_3)_3$	70			0
15	$CoCl(PPh_3)_3$	70	29	71	9
16	$CoH(N_2)(PPh_3)_3$	48	22	78	7
17	$CoCl_2(PEtPh_2)_2$	61			0

[a] Reactions were carried out by using 10 mmol of PhBr witout solvent at 100 °C PhBr/Et_2NH/catalyst ≃ 1/3/0.01 (molar ratio). p-(CO) = 10 atm (initial value at room temperature). [b] dppe = $Ph_2P(CH_2)_2PPh_2$, dppb = $Ph_2P(CH_2)_4PPh_2$, bpy = 2,2′-bipyridine. [c] Based on PhBr. Determined by GLC. [d] 100% Cu. [e] 73% Ni.

Table II. Dependence of the Yield of $PhCOCONEt_2$ on Concentration of Palladium Catalyst in Double Carbonylation of PhI in the Presence of Et_2NH[a]

catal concn, mol L^{-1}	$PhCOCONEt_2$ yield,[b] %	turnover no.
0.0082[c]	9	16
0.016[d]	16	15
0.032[e]	30	16

[a] Carried out at 60 °C for 80 min using PhI (2 mmol) and Et_2NH (10 mmol). Catalyst: $PdCl_2(PMePh_2)_2$. p(CO) = 20 atm (initial value at room temperature). [b] Based on PhI. Catalyst/PhI are as follows. [c] 0.005. [d] 0.01. [e] 0.02.

of the α-keto amide. Tertiary phosphine-coordinated palladium chlorides were as effective as organopalladium(II) complexes in the catalytic reactions. Dichloropalladium(II) complexes are conisdered to serve as catalyst precursors which are reduced to catalytically active Pd(0) species in the presence of CO and amine.

Among other transition-metal complexes examined, cobalt complexes having PPh_3 ligands such as $CoCl(PPh_3)_3$ and $CoH(N_2)(PPh_3)_3$ showed mild catalytic activities. Stoichiometric conversion of PhBr into $PhCOCONEt_2$ was promoted by $CuBr(PPh_3)_3$. On the other hand, $CoCl_2(PEtPh_2)_2$, $PtCl_2(PPh_3)_2$, and $RhCl(PPh_3)_3$ were inactive while $NiCl_2(PEt_3)_2$ showed a low activity for stoichiometric conversion of PhBr into $PhCONEt_2$. In addition, $Co_2(CO)_8$ showed a mild catalytic activity for double carbonylation of PhI in the presence of additives such as LiCl and $PhCH_2NEt_3Cl$.

Based on these results, most of catalytic reactions were performed by using $PdCl_2(PMePh_2)_2$ which shows the highest catalytic activity for production of α-keto amide among the monotertiary phosphine-coordinated palladium complexes. Table II shows the effect of concentration of the palladium catalyst on the yield of $PhCOCONEt_2$ in the reaction of PhI and Et_2NH under a constant CO pressure. The results indicate that the rate of the α-keto amide formation is first order in the concentration of the palladium complex with the turnover number almost constant. In the reaction of PhI and Et_2NH catalyzed by the same catalyst under the same pressure of CO, the yield of $PhCOCONEt_2$ was observed to increase linearly with time independently of the concentration of PhI up to 70% conversion of PhI as shown in Figure 1. Thus, the rate of formation of α-keto amide can be expressed by

$$\frac{d[PhCOCONEt_2]}{dt} = k_{obsd}[\text{catalyst}] \qquad (2)$$

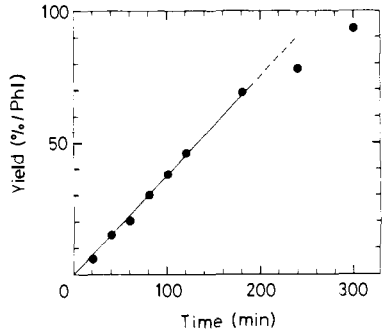


Figure 1. Time–yield curve of $PhCOCONEt_2$ in the double carbonylation of PhI and Et_2NH catalyzed by $PdCl_2(PMePh_2)_2$ at 60 °C. Initial conditions: PhI (2 mmol), Et_2NH (10 mmol), $PdCl_2(PMePh_2)_2$ (0.04 mmol), $p(CO)$ = 20 atm (the value at room temperature).

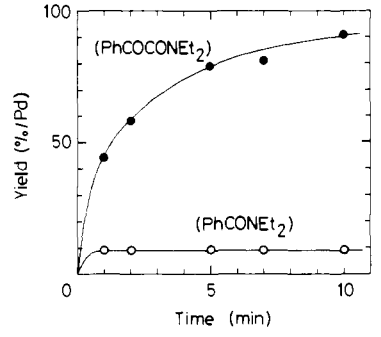
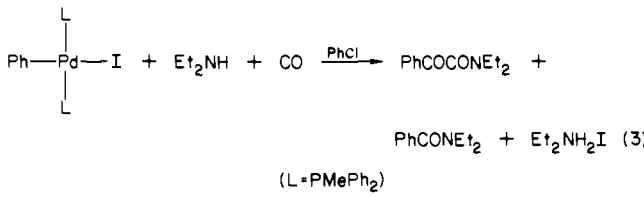


Figure 2. Time–yield curves of $PhCOCONEt_2$ and $PhCONEt_2$ in the reaction of *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**) and CO in the presence of Et_2NH and PhCl at 60 °C. Reaction conditions: **1a** (0.08 mmol), Et_2NH (20 mmol), PhCl (500 μL), $p(CO)$ = 20 atm (the value at room temperature).

The k_{obsd} value of 3.4×10^3 s^{-1} was obtained from Figure 1 by dividing the slope of the line by concentration of the catalyst. Since the rate of α-keto amide formation increases with increase in the CO pressure in the reaction of PhI (vide infra), the k_{obsd} value includes the term regarding the CO pressure. It may well contain also the term regarding the amine concentration. However, we have not further pursued the effect of the concentration of amine since the reaction was carried out in amine without using other solvent.

For getting more information on the reactivity of the putative reaction intermediate **1** in the catalytic cycle, *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**) was prepared independently and its stoichiometric reaction with CO and Et_2NH was examined. Reaction 3 was carried out in unreactive phenyl chloride instead of phenyl iodide for comparing the stoichiometric process with the catalytic one under similar conditions. As will be discussed later, phenyl



chloride is unreactive under the reaction conditions. The results shown in Figure 2 reveal intriguing reaction behavior of the phenylpalladium(II) iodide complex. In contrast to the gradual formation of α-keto amide, formation of benzamide occurs only in the initial period. The conversion of **1a** into $PhCOCONEt_2$ was found to be first order in the concentration of **1a** with the first-order rate constant of 4.3×10^{-3} s^{-1}.

(b) Effects of Substrates and CO Pressure. Table III compares reactions of various phenyl halides with CO in the presence of Et_2NH. The reactivity of the phenyl halide decreases in the order of PhI > PhBr ≫ PhCl. Phenyl chloride is so unreactive that it did not react even at 200 °C. In the double carbonylation of phenyl iodide, raising the temperature accelerates the reaction rate at the expense of selectivity for α-keto amide. The reactivity order shown in Table III parallels the known reactivity order of phenyl halides with $Pd(PPh_3)_4$.[6] Thus, the reactivity order most likely reflects the ease of oxidative addition of phenyl halides to Pd(0) species in the catalytic double-carbonylation process.

For the reaction of phenyl iodide, higher CO pressure enhances both the reaction rate and the selectivity for α-keto amide formation. On the other hand, an increase in the CO pressure retards the reaction of phenyl bromide, while the selectivity for double carbonylation is somewhat enhanced. These results suggest that the rate-determining step in the reaction of PhBr differs from that of PhI. The rate-determining step in the system of PhBr may be in the oxidative addition of PhBr to Pd(0) species (Scheme I, step a).[7] Under higher CO pressure, the Pd(0) species will be coordinated by a greater number of CO molecules and its nucleophilicity will be reduced. Since oxidative addition of aryl halide to the Pd(0) species can be regarded to proceed through nucleophilic attack of palladium on the halogen-bonded carbon,[6,8] the higher pressure of CO retards the reaction with PhBr. On the other hand, the rate-determining step of the PhI system seems to be in a later stage than the formation of the phenylpalladium complex. The higher rate in catalytic double carbonylation of phenyl iodide under higher CO pressure should be associated with the higher stoichiometric double-carbonylation rate of isolated phenylpalladium complexes under higher CO pressure.[4a]

Introduction of substituents into the phenyl group varied the reactivity of phenyl halides. Table IV shows the influence of

Table III. Double Carbonylation of Various Phenyl Halides in the Presence of Et_2NH[a]

run	PhX	CO,[b] atm	reaction temp, °C	reaction time, h	product ratio: PhCO-$CONEt_2$	product ratio: PhCON-Et_2	tot[c] yield, %
1	PhI	20	60	5	93	7	100
2	PhI	5	100	2	48	52	33
3	PhI	10	100	2	61	39	43
4	PhI	47	100	2	83	17	100
5	PhBr	10	50	24			0
6	PhBr	10	100	24	82	18	73
7	PhBr	24	100	24	91	9	27
8	PhCl	10	100	46			0
9	PhCl	10	200	12			0

[a] Reactions were carried out in a 5 mmol scale using $PdCl_2(PMePh_2)_2$ as catalyst without solvent. $PhX/Et_2NH/catalyst \simeq 1/5/0.02$ (molar ratio). [b] Initial value at room temperature. [c] Based on PhX by GLC.

Table IV. Double Carbonylation of Various Para-Substituted Phenyl Bromides in the Presence of Et_2NH Catalyzed by $PdCl_2(PMePh_2)_2$[a]

run	subst	Hammett σ_p	reaction time, h	product ratio: α-keto amide	product ratio: amide	tot[b] yield, %
1	CN	0.63	24	35	65	98
2	CF_3	0.55	50	63	37	89
3	Ac	0.50	50	67	33	100
4	Cl	0.30	50	69	31	91
5	H	0	50	90	10	80
6	OPh	−0.03	50	91	9	89
7	Me	−0.17	45	84	16	84
8	OMe	−0.32	50	92	8	22
9	NMe_2	−0.60	50	86	14	26

[a] Reaction conditions: $bromide/Et_2NH/catalyst \simeq 1/3/0.01$, at 100 °C, $p(CO)$ = 10 atm (initial value at room temperature). [b] Based on phenyl bromides.

(5) Chen, J.; Sen, A. *J. Am. Chem. Soc.* **1984**, *106*, 1506.
(6) Fitton, P. F.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287.
(7) α-Keto amide formation in the system of PhBr and Et_2NH was confirmed to be first order in the concentration of PhBr in contrast with the system of PhI and Et_2NH (Figure 1).
(8) Fauvarque, J. F.; Pfluger, F.; Troupel, M. *J. Organomet. Chem.* **1981**, *208*, 419.

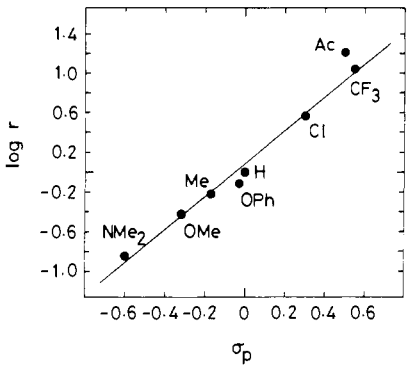


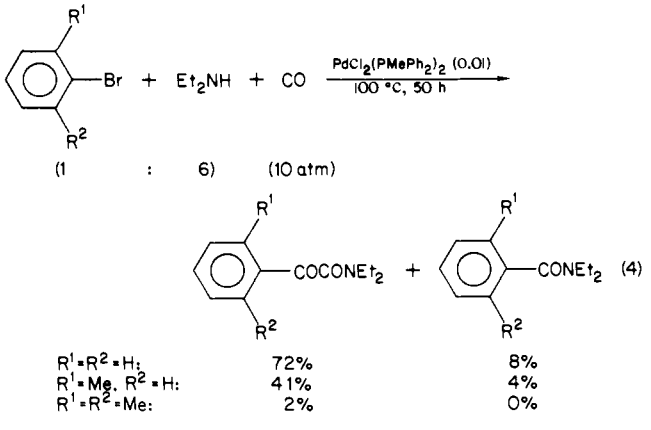
Figure 3. Hammett plot for the relative reactivities (r) of various para-substituted phenyl bromides to phenyl bromide in the catalytic double carbonylation in the presence of Et_2NH. Carried out at 100 °C for 6 h; $p(CO)$ = 10 atm (initial value at room temperature).

substituents at the para position of phenyl bromide on the reactivity for double carbonylation. Introduction of electron-withdrawing substituents such as CN and CF_3 groups at the para position increases the reactivity but decreases the selectivity for α-keto amide formation. Introduction of electron-donating para substituents, on the other hand, causes a decrease in reactivity.

More direct comparison of the reactivity can be achieved by carrying out competition experiments by using equimolar mixtures of phenyl bromide and various para-substituted phenyl bromides. Figure 3 demonstrates the result of competition experiments using seven para-substituted phenyl bromides carried out at 100 °C in the presence of Et_2NH with $PdCl_2(PMePh_2)_2$ as the catalyst. The plot of logarithms of the relative conversions of the bromides against Hammett σ_p constants showed a reasonably good linear relationship with a ρ value of 1.7. The value may be compared with the ρ value of 2.0 determined in oxidative addition of para-substituted phenyl iodides to $Pd(PPh_3)_4$ reported by Fauvarque.[8]

Table V compares the time required to complete the reactions of various para-substituted phenyl iodides with CO and Et_2NH and selectivities of α-keto amides. The effect of the para substituents on the relative reactivities and selectivities in the double carbonylation is seen to be similar to that for para-substituted phenyl bromides.

Introduction of methyl group(s) at the ortho position(s) of phenyl bromides strongly retards the reaction. Monosubstitution at the ortho position with a methyl group caused the drop of the reaction rate to nearly half of that for the unsubstituted phenyl bromide, and substitution with two methyl groups at the ortho positions almost blocked the reaction as indicated in eq 4 below.



Steric hindrance of the ortho methyl group(s) on the reaction is evident.

(c) Effect of Amine. Amines used in the double carbonylation have a considerable influence on the yields of α-keto amides and amides as summarized in Tables VI and VII. Trends are similar in both reactions of phenyl bromide (Table VI) and iodide (Table VII). Secondary amines of high basicities are suitable for the reactions but steric bulkiness of the amines has a great influence on the yields of α-keto amides. Of eight amines having similar basicities (pK_b = ca. 3; runs 1–8 in Table VI), the bulkiest amine i-Bu_2NH was totally inactive and i-Pr_2NH gave only a low yield of amide, whereas less bulky amines proved to be effective for carbonylation reactions with different selectivities for the double carbonylation. Comparison of the relative yields of α-keto amides and amides in runs 1–3 and 6–8 in Table VI reveals that the selectivity decreases in the order of Pr_2NH > Et_2NH > hexamethyleneimine > piperidine > Me_2NH > pyrrolidine. The result suggests that sterically more demanding secondary amines, within a certain limit, give α-keto amides in higher selectivities. Among these secondary amines, Pr_2NH gave the highest selectivity for the α-keto amide formation, although the total yield of the α-keto amide and amide was lower than that given by using Et_2NH.

Table V. Double Carbonylation of Various Para-Substituted Phenyl Iodides in the Presence of Et_2NH Catalyzed by $PdCl_2(PMePh_2)_2$[a]

run	subst	Hammett σ_p	product ratio: α-keto amide	product ratio: amide	reaction[b] time, min
1	CN	0.63	15	85	15
2	Cl	0.30	77	23	60
3	H	0	91	9	45
4	Me	−0.17	96	4	120
5	OMe	−0.32	97	3	90

[a] Initial conditions: iodide/Et_2NH/catalyst ≃ 1/8/0.01, at 80 °C. $p(CO)$ = 50 atm (at room temperature). [b] Time to complete the reaction; confirmed by following a decrease of CO pressure. Total yield of α-keto amide and amide in each run was confirmed to be 100% iodide.

Table VI. Double Carbonylation of PhBr Catalyzed by $PdCl_2(PMePh_2)_2$ in the Presence of Various *sec*-Amines[a]

run	amine (pK_b)	product yield: α-keto amide	product yield: amide	tot[b] yield, %	turnover no.
1	Me_2NH (3.28)	7	93	73	34
2	Et_2NH (2.90)	75	25	78	30
3	Pr_2NH (3.02)	91	9	33	15
4	i-Pr_2NH (2.95)	0	100	4	2
5	i-Bu_2NH (2.65)			0	0
6	pyrrolidine (2.89)	0	100	95	36
7	piperidine (2.80)	21	79	83	33
8	hexamethyleneimine	24	76	71	31
9	$PhCH_2(Me)NH$ (4.15)	77	23	39	18
10[c]	$PhCH_2(Me)NH$	68	32	79	38
11	Ph(Me)NH (5.39)			0	0
12[d]	Ph(Me)NH	0	100	8	4
13	$(PhCH_2)_2NH$ (4.80)			0	0
14	diallylamine			0	0

[a] Reaction conditions: PhBr/amine/catalyst ≃ 1/5/0.02, at 100 °C, for 24 h. $p(CO)$ = 10 atm (initial value at room temperature). [b] Based on PhBr. [c] For 72 h, Et_3N was added. [d] For 48 h, Et_3N was added.

Table VII. Double Carbonylation of PhI Catalyzed by $PdCl_2(PMePh_2)_2$ in the Presence of Various *sec*-Amines[a]

run	amine	product ratio: α-keto amide	product ratio: amide	tot[b] yield, %	turnover no.
1	Me_2NH	10	90	100	46
2	Et_2NH	61	39	43	21
3	Pr_2NH	72	28	47	18
4	i-Pr_2NH	0	100	4	2
5	i-Bu_2NH			0	0
6	$PhCH_2(Me)NH$	66	34	35	18
7	Ph(Me)NH			0	0
8	$(PhCH_2)_2NH$			0	0
9	diallylamine			0	0

[a] Reaction conditions: PhI/amine/catalyst ≃ 1/5/0.02, at 100 °C, for 2 h. $p(CO)$ = 10 atm (initial value at room temperature). [b] Based on PhI.

Table VIII. Relative Reactivities of Amines toward *trans*-Pd(COPh)I($PMePh_2$)$_2$ (2a) under CO as Revealed by Competitive Reactions Using Equimolar Mixtures of Amines[a]

amine pair		product ratio		tot yield of α-keto amides
HNR_2^1	HNR_2^2	$PhCOCONR_2^1$	$PhCOCONR_2^2$	(% Pd)
$HNPr_2$	$HNEt_2$	0.75	1	100
$HNEt_2$		1	11	99
		1	2.4	95
	$HNMe_2$	1	1.9	100
$HNMe_2$		1	4.7	96

[a] Reactions were carried out by using 2a (0.1 mmol), R_1^1NH (10 mmol), and R_2^2NH (10 mmol) in the presence of PhCl (500 μL) under 20 atm of CO at room temperature for 20–60 min.

Pyrrolidine, which is considered to be the most compact amine among the examined secondary amines, showed the highest activity for the monocarbonylation but gave no α-keto amide.

The influence of the steric bulkiness of the secondary amines on selectivity in the catalytic reactions is associated with the reactivity difference of the amines in stoichiometric reactions of *trans*-Pd(COPh)X($PMePh_2$)$_2$ (X = Cl, Br, and ClO_4) with CO and the amines.[4a] The benzoyl complexes, which are probable intermediates in the catalytic double carbonylation (**2** in Scheme I), afforded predominantly α-keto amides on reactions with secondary amines in the presence of CO. The reactivity of amines was found to decrease in the order of $Me_2NH \geq$ piperidine > $Et_2NH > Pr_2NH$. The trend was reasoned to reflect the reactivity of the amines toward the CO-coordinated intermediate **3** in Scheme I, and the steric bulkiness was inferred as the prime reason for the difference in reactivity of the amines. A somewhat related steric influence on rates of nucleophilic attack of alcohols on coordinated CO in $[PtCl(PPh_3)_2(CO)]^+$ has been reported by Halpern.[9]

For further comparison of relative reactivities of amines toward the aroylpalladium complexes in the presence of carbon monoxide, relative yields of α-keto amides produced in competitive reactions of *trans*-Pd(COPh)I($PMePh_2$)$_2$ (**2a**) with equimolar mixtures of different pairs of amines were determined. The results are summarized in Table VIII. Relative reactivities (r) of the six secondary amines referred to the reactivity of Et_2NH decrease in the order pyrrolidine (r = 98) > hexamethyleneimine (26) > Me_2NH (21) > piperidine (11) > Et_2NH (1) > Pr_2NH (0.75). The relative reactivity order is in agreement with the previously obtained qualitative reactivity order estimated from yields of α-keto amides in separate reactions of benzoylpalladium complexes with CO and amines.

Comparison of the results of stoichiometric reactions of the benzoylpalladium complexes with CO and the amines and of catalytic reactions in Tables VI and VII suggests that the selectivity for α-keto amide formation is closely associated with the reactivity of amines, among which less bulky amines have higher reactivities than bulkier ones.

Relative reactivities of amines were compared by competitive experiments in actual catalytic systems containing pairs of amines with different reactivities. Table IX shows product distributions in two competitive reactions catalyzed by $PdCl_2(PMePh_2)_2$ using a pair of amines of similar reactivities and another pair of amines with considerably different reactivities. In the first experiment using the pair of diethylamine and dipropylamine of slightly different reactivities, the reactivity ratio based on relative yield of amides of dipropylamine to that of diethylamine was 0.74 (after correction of the difference in ratio of the amines fed into the reaction) whereas the reactivity ratio for α-keto amide formation was 0.78. These reactivity ratios are close to the value of 0.75 obtained in competitive reaction of the same amines with the benzoylpalladium iodide complex **2a** and CO (Table VIII). In the other experiment using the pair of piperidine and diethylamine, of which the former amine is much more reactive than the latter, *N*-benzoylpiperidine was formed as the dominant product. Reactivity ratios of piperidine to diethylamine, after correction of the relative amounts of amines fed to the catalytic system, was 25 for formation of amides and 8 for α-keto amides. Because of the big difference in reactivities of the two amines, $PhCONEt_2$ and $PhCOCONEt_2$ are produced in only small quantities and the accuracy in determination of the reactivity ratios of the two amines is not high. Nevertheless, these values may be compared with the relative reactivity ratio of 11 of piperidine to diethylamine in the competitive reaction of these amines with **2a** and CO (Table VIII).

The reactivities of less basic amines were smaller than basic amines (compare runs 9–14 with 1–8 in Table VI and runs 6–9 with 1–4 in Table VII).

Primary amines also serve as reagents for the double carbonylation to give α-keto amides.[2] Generally further reaction of the primary amines with the α-keto amides produced in the double carbonylation leads to secondary reaction of the α-keto group with the primary amines to afford Shiff bases of α-keto amides. Among primary amines, *tert*-butylamine is exceptional and serves as a suitable reagent for producing α-keto amides in excellent yields.

$$\underset{(1}{ArI} + \underset{:\ 7)}{t\text{-}BuNH_2} + \underset{(20\ atm)}{CO} \xrightarrow[60\ ^\circ C,\ 6\text{-}8\ h]{PdCl_2(PMePh_2)_2\ (0.02)} ArCOCONH\text{-}t\text{-}Bu \quad (5)$$

yields: 96% (Ar = Ph)
92% (*m*-tolyl)
97% (*p*-tolyl)

Aniline, being the least basic amine among the amines examined, afforded only amide on reaction with PhI and CO even under the pressure of 10 atm.

$$\underset{(1}{PhI} + \underset{:\ 4)}{PhNH_2} + \underset{(10\ atm)}{CO} \xrightarrow[Bu_3N,\ 100\ ^\circ C,\ 2\ h]{PdCl_2(PMePh_2)_2\ (0.02)} PhCONHPh \quad (6)$$

(73%)

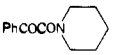
(d) Effect of Other Factors. In the reactions of *trans*-Pd(COPh)X($PMePh_2$)$_2$ (X = Br and I) with CO and Et_2NH, solvents of higher dielectric constants favored the formation of α-keto amides.[4a] In the catalytic reactions of PhI, Et_2NH, and CO, solvents of higher dielectric constants had favorable effects on reaction rate, but solvent effect on the selectivity was not marked in comparison with the results carried out without added solvent. In the catalytic reactions, where amines are usually used in excess compared to aryl halides, amines are thought to serve as good solvent for promoting the reactions.

Addition of $PMePh_2$ in a 1:1 ratio to the palladium catalyst, $PdCl_2(PMePh_2)_2$, in a reaction of PhI and Et_2NH at 100 °C under CO pressure of 10 atm suppressed the reaction rate to one-eight of the reaction rate without the added ligand.

Attempt to Characterize Reaction Intermediates in Catalytic Systems. In order to characterize possible reaction intermediates involved in the catalytic formation process of α-keto amide (Scheme I), a reactive catalyst precursor, *trans*-$PdMe_2(PMePh_2)_2$ (1 mmol) was treated with PhI (10 mmol), Et_2NH (67 mmol), and CO (10 atm) at room temperature for 5 h, and products were examined. The reaction gave predominantly $PhCOCONEt_2$ (227%/Pd) together with small amounts of benzamide (19%/Pd) and tetraethyloxamide (19%/Pd). Examination of the reaction systems, after purging the CO gas, with $^{31}P\{^1H\}$ NMR spectroscopy revealed the formation of three species observed as singlets at 11.3, 6.7, and 5.9 ppm (relative to PPh_3, downfield positive) in a ratio of 2:5:3. The former two singlets are assignable to *trans*-PdPh(I)($PMePh_2$)$_2$ (**1a**) and *trans*-Pd(COPh)I($PMePh_2$)$_2$ (**2a**), respectively. The complex corresponding to the latter singlet

(9) Byrd, J. F.; Halpern, J. *J. Am. Chem. Soc.* **1971**, *93*, 1634.

Table IX. Distribution of Amides and α-Keto Amides Produced in Competitive Reactions of Amines with PhI and CO Catalyzed by $PdCl_2(PMePh_2)_2$ [a]

run	amine pair (molar ratio)	reaction time, min	yield (% PhI) amide	yield (% PhI) α-keto amide
1	$HNEt_2$ (1.5 : 1) $HNPr_2$	100	$PhCONEt_2$ (1.7) $PhCONPr_2$ (0.84)	$PhCOCONEt_2$ (7.3) $PhCOCONPr_2$ (3.8)
2	 $HNEt_2$ (1.1 : 1)	30	$PhCONEt_2$ (0.53)  (14.5)	 (1.0)

[a] Reactions were carried out by using PhI (4.5 mmol), amines (totally ca. 20 mmol), and 2 mol % PhI of $PdCl_2(PMePh_2)_2$ under 20 atm of CO at 40 °C.

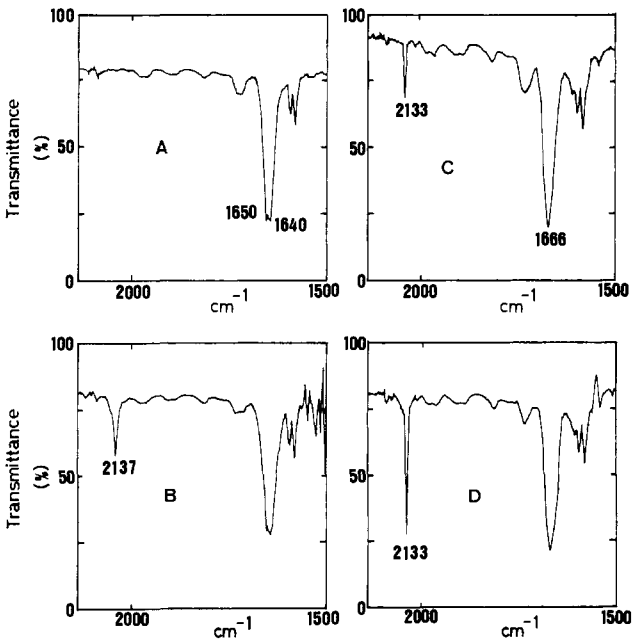


Figure 4. IR spectra of benzoylpalladium complexes in solution under CO pressure. (A) *trans*-$Pd(COPh)I(PMePh_2)_2$ (**2a**) in CH_2Cl_2, $p(CO)$ = 20 atm; (B) **2a** in CH_2Cl_2–MeOH (9:1), $p(CO)$ = 20 atm; (C, D) *trans*-$Pd(COPh)(PMePh_2)_2ClO_4$ in CH_2Cl_2, $p(CO)$ = 1 (C) and 20 atm (D).

at 5.9 ppm was isolated from the reaction mixture and characterized as carbamoylpalladium iodide complex, *trans*-$Pd(CONEt_2)I(PMePh_2)_2$ (**5**).

$$PhI + Et_2NH + CO \xrightarrow[\text{room temp, 5 h}]{\textit{trans}\text{-}PdMe_2(PMePh_2)_2\ (0.1)} \underset{(1\ :\ 7)}{} \underset{(10\ atm)}{}$$

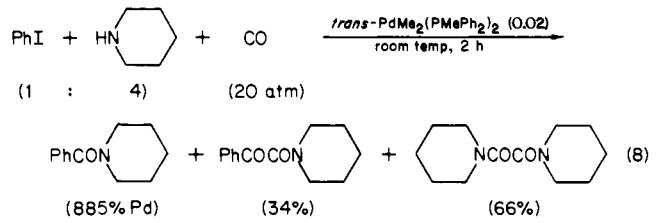
$$PhCOCONEt_2 + PhCONEt_2 + Et_2NCOCONEt_2 +$$
(227% Pd) (19%) (19%)

$$\textit{trans}\text{-}Pd(COPh)I(PMePh_2)_2 + \textit{trans}\text{-}PdPh(I)(PMePh_2)_2 +$$
(5 : 2 :

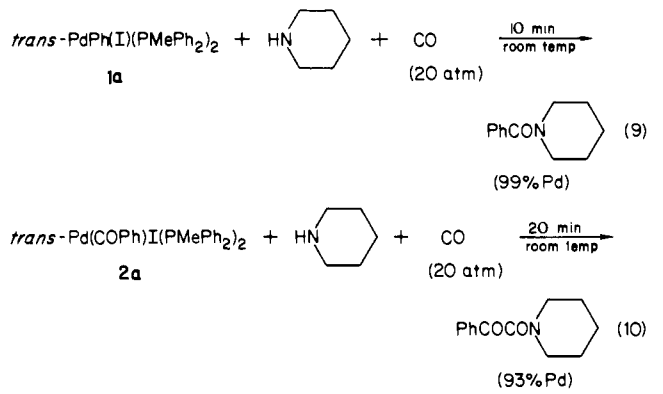
$$\textit{trans}\text{-}Pd(CONEt_2)I(PMePh_2)_2 \quad (7)$$
3)

The isolated carbamoyl complex **5** was totally inactive to PhI in the presence of CO (20 atm) and Et_3N at room temperature, and no α-keto amide, amide, or oxamide was formed after the reaction for 6 h. On the other hand, the reaction of **5** with CO (20 atm) and Et_2NH (3 mL) in chlorobenzene (0.5 mL) at room temperature for 6 h gave $Et_2NCOCONEt_2$ (75%/Pd) and $Et_2NCONEt_2$ (18%). Complex **5** did not react with benzoyl complex **2a** and CO in solution at room temperature for 6 h.

A similar examination was made for the system affording predominantly monocarbonylation product. The reaction of phenyl iodide and piperidine under CO pressure of 20 atm gave benzamide as a principal product in the presence of a catalytic amount of *trans*-$PdMe_2(PMePh_2)_2$. Examination of the reaction system after

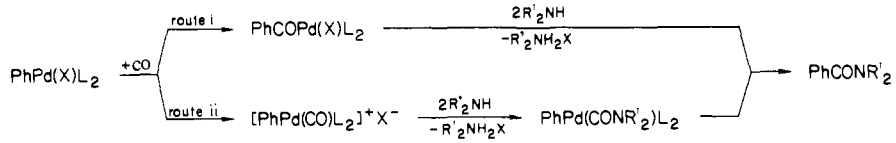


removal of CO gas with $^{31}P\{^1H\}$ NMR spectroscopy indicated formation of the phenyl complex **1a** together with the unidentified species which may be ascribed to a Pd(0) complex. A signal corresponding to benzoyl complex **2a** was negligible in contrast with the system of Et_2NH, yielding mainly α-keto amide. This observation suggests that amide is afforded from phenylpalladium complex on interaction with CO and piperidine without participation of benzoylpalladium species. This assumption was further supported by the following reactions of isolated phenyl- and benzoylpalladium complexes with CO and piperidine. The reaction of phenyl complex **1a** with piperidine under CO pressure actually afforded amide selectively, while the benzoyl complex **2a** produced only α-keto amide in the reaction with piperidine and CO under similar conditions.



In Scheme I we assumed the participation of a cationic benzoylcarbonylpalladium species **3** as the key reaction intermediate for formation of α-keto amide. For getting direct information of a CO-coordinated benzoylpalladium species, infrared spectra of benzoylpalladium complexes in solution were examined under CO pressure at room temperature. Figure 4 shows the IR spectra of the benzoylpalladium iodide complex **2a** and the ionic benzoylpalladium complex *trans*-$Pd(COPh)(PMePh_2)_2ClO_4$. Complex **2a** in CH_2Cl_2 showed acyl ν(C=O) bands at 1640 and 1650 cm^{-1}, but no peak due to the coordinated CO was observed even under the CO pressure of 20 atm (A). On addition of a small amount of methanol (CH_2Cl_2:MeOH = 9:1), a new peak at 2137 cm^{-1} arising from the coordinated CO ligand appeared (B). The ionic benzoylpalladium complex, on the other hand, showed a peak due to the coordinated CO ligand at 2133 cm^{-1} in addition to the benzoyl ν(C=O) band at 1666 cm^{-1} even under 1 atm of CO (C).

Scheme II. Two Possible Routes for Benzamide Formation



When the CO pressure was increased to 20 atm, the peak due to the coordinated CO ligand increased considerably (D). These results are considered to support the presence of the following equilibrium which is shifted toward the right-hand side under CO pressure in the presence of a protic solvent such as methanol.

$$trans\text{-Pd(COPh)I(PMePh}_2)_2 + CO \rightleftarrows trans\text{-[Pd(COPh)(CO)(PMePh}_2)_2]^+I^- \quad (11)$$

Although it is likely that secondary amines favor the shift of the equilibrium toward the right-hand side, actual observation of the IR spectrum in the presence of secondary amine was not feasible because it rapidly reacts with the benzoyl complex under pressurized CO atmosphere.

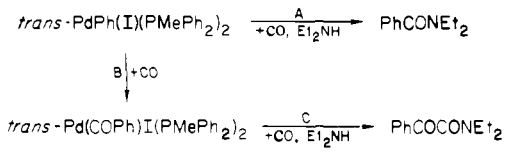
Discussion

Main features of the catalytic processes are consistent with the elementary processes involved in Scheme I. The rate-determining step in the catalytic cycle is noted to vary depending on the aryl halide used for the reaction and by change of other experimental conditions. In the reaction of phenyl bromide with Et_2NH and CO catalyzed by the palladium complexes, the rate of formation of the α-keto amide was confirmed to be first order in the concentration of PhBr. Suppression of the reaction rate upon increase of the CO pressure also suggests that the rate-determining step is in the oxidative addition process in Scheme I.

For phenyl iodide, on the other hand, oxidative addition to the Pd(0) complex takes place more easily than phenyl bromide. Figure 1 clearly shows that the catalytic rate of conversion of PhI into α-keto amide is independent of concentration of PhI over the most of the reaction time. It is further demonstrated that the rate constant of 3.4×10^{-3} s^{-1} for conversion of PhI into α-keto amide derived from Figure 1 by dividing the slope by concentration of the catalyst agrees with the first-order rate constant of 4.3×10^{-3} s^{-1} for formation of α-keto amide from the isolated phenylpalladium complex (**1a**) obtained from Figure 2. These results clearly indicate that the rate-determining step is in the process *after* formation of the phenylpalladium species. The rate-determining step in the conversion of PhI into α-keto amide is likely to be in the attack of the coordinated CO ligand in **3** in Scheme I by amine to give **4**. However, since various factors can influence the catalytic process composed of several elementary steps as shown in Scheme I, further discussion on the rate-determining step is to be deferred.

One of the central issues in the double-carbonylation reaction is the factor controlling the selectivity for α-keto amide and amide formation. Through the present and previous[4] studies, soundness of the proposed mechanism as represented in Scheme I for accounting for the α-keto amide formation has been established. The remaining issue is the mechanism of amide formation. Two routes are conceivable for benzamide formation. One is the attack of amine on a benzoyl group bonded to palladium and the other is attack of amine on the CO ligand bound to a phenylpalladium species to give a carbamoylphenylpalladium species, which reductively eliminates benzamide (Scheme II). Attack of amine on the benzoyl group (route i) is certainly a viable process at least in slow stoichiometric reactions of benzoylpalladium complexes under vacuum or low CO pressure.[10] However, the situation

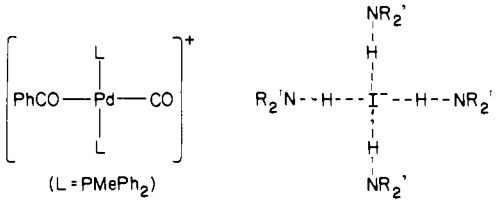
Scheme III



seems to be different in a catalytic process, and we favor route ii as a likely process. The striking difference in the behavior of the phenylpalladium and benzoylpalladium complexes in the reactions with CO and piperidine (eq 9 and 10), each giving the amide and α-keto amide quite selectively, provides a strong support for the amide formation process of route ii.

By assuming route ii for the monocarbonylation process and steps b–e in Scheme I for the double-carbonylation process, the result in Figure 2 concerning reaction of phenylpalladium complex **1a** with CO and Et_2NH is explicable reasonably as shown in Scheme III. Under the reaction conditions (60 °C, 20 atm), the reaction yielding benzamide goes to completion quite rapidly whereas the α-keto amide formation proceeds gradually. In the initial period of the reaction, phenyl complex **1a** may undergo two parallel reaction processes, amide formation (path A) and CO insertion (path B), simultaneously. Since ^{13}C-enriched benzoyl complex *trans*-Pd(^{13}COPh)I(PMePh$_2$)$_2$ affords Ph^{13}CO^{12}CONEt$_2$, selectively, on the reaction with ^{12}CO and Et_2NH (see Experimental Section), CO insertion reaction (path B) can be regarded as an irreversible process. Thus, after all the **1a** is converted into **2a** in the initial period of the reaction, the system will exclusibly afford α-keto amide according to path C. The result of Figure 2, on the other hand, is cleary incompatible with the mechanism involving the amide formation process of route i in Scheme II, in which benzamide is produced by the interaction of benzoylpalladium complex with amine.

The results of the IR studies, which indicate that the CO-coordinated benzoylpalladium species is favored in a protic solvent such as methanol, suggest presence of the following CO-coordinated ionized species in the environment of secondary amines as well. The trend of decrease of relative reactivities of amines



toward *trans*-Pd(COPh)I(PMePh$_2$)$_2$ and CO (Table VIII) may reflect the increase in the steric interaction between the ionic benzoylcarbonyl species and amines. In order to examine the steric environment about palladium in the ionic benzoylcarbonyl species, a CPK molecular model of *trans*-[Pd(COPh)(PMePh$_2$)$_2$(CO)]$^+$I$^-$ was inspected. The space left for attack of amine on the CO ligand in the ionic complex having two PMePh$_2$ ligands, each having a cone angle of 136°,[11] was found to be limited. Thus, decrease in the reaction rate with increase in the steric bulkiness of the attacking amine is understandable. Similar restriction of space should be present in the attack of the amine on the CO ligand for the phenylpalladium species. Direct comparison of the relative reactivities of amines toward the CO-coordinated phenylpalladium species is not feasible because of occurrence of the CO insertion into the phenyl–palladium bond. However, the trend of relative

(10) The reactions of *trans*-Pd(COPh)X(PMePh$_2$)$_2$ (X = Cl and Br) with Et_2NH under vacuum actually gave benzamide.[4a] However, the reaction rate is very slow. For example, the reaction of bromo complex under vacuum at room temperature for 1 day gave benzamide only in a 4% yield per complex. On the other hand, under 40 atm of CO the same complex afforded almost a quantitative yield of α-keto amide in an excellent selectivity under the same conditions.

(11) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.

Table X. IR and ^{1}H NMR Data of α-Keto Amides (A) and Analytical and Mass Spectroscopic Data of α-Keto Amides (B)

ArCOCONR$_2$'		IR,[a] ν(CO)		^{1}H NMR[b]	
Ar	NR$_2$'	α-keto CO	amide CO	NR$_2$'	Ar
Ph[c]	NEt_2	1685	1640	1.13 (t, J = 7 Hz, 3 H, CH_3), 1.27 (t, J = 7 Hz, 3 H, CH_3'), 3.25 (q, J = 7 Hz, 2 H, CH_2), 3.57 (q, J = 7 Hz, 2 H, CH_2')	7.3–7.7 (m, 3 H, m,p-Ph), 7.92 (m, 2 H, o-Ph)
Ph[d]	NPr_2	1685	1640	0.78 (t, J = 7 Hz, 3 H, CH_3), 0.99 (t, J = 7 Hz, 3 H, CH_3'), 1.64 (m, 4 H, NCCH_2), 3.10 (t, J = 8 Hz, 2 H, NCH_2), 3.40 (t, J = 8 Hz, 2 H, NCH_2')	7.2–7.5 (m, 3 H, m,p-Ph), 7.78 (m, 2 H, o-Ph)
Ph[d]		1685	1640	1.66 (br, 6 H, N–C–(CH_2)$_3$–C), 3.26 (br, 2 H, NCH_2), 3.64 (br, 2 H, NCH_2')	7.2–7.6 (m, 3 H, m,p-Ph), 7.78 (m, 2 H, o-Ph)
Ph[d]		1685	1640	1.64 (br, 8 H, N–C–(CH_2)$_4$–C), 3.30 (br, 2 H, NCH_2), 3.60 (br, 2 H, NCH_2')	7.2–7.6 (m, 3 H, m,p-Ph), 7.90 (m, 2 H, o-Ph)
Ph[d]	NMe(CH_2Ph)	1690	1650	2.74 (s) and 2.87 (s) (total 3 H, NCH_3), 4.29 (s) and 4.63 (s) (total 2 H, NCH_2), 7.2–8.0 (m, 5 H, Ph)	7.2–8.0 (m, 5 H, Ph)
p-NCC_6H_4[c]	NEt_2	1680	1640	1.17 (t, J = 7 Hz, 3 H, CH_3), 1.29 (t, J = 7 Hz, 3 H, CH_3'), 3.29 (q, J = 7 Hz, 2 H, CH_2), 3.62 (q, J = 7 Hz, 2 H, CH_2')	7.81 (d, J = 9 Hz, 2 H, o-Ph), 8.09 (d, J = 9 Hz, 2 H, m-Ph)
p-$CF_3C_6H_4$[e]	NEt_2	1695	1645	1.12 (t, J = 7 Hz, 3 H, CH_3), 1.26 (t, J = 7 Hz, 3 H, CH_3'), 3.28 (q, J = 7 Hz, 2 H, CH_2), 3.57 (q, J = 7 Hz, 2 H, CH_2')	7.81 (d, J = 9 Hz, 2 H, o-Ph), 8.14 (d, J = 9 Hz, 2 H, m-Ph)
p-AcC_6H_4[d]	NEt_2	1685	1640	1.20 (t, J = 8 Hz, 3 H, CH_3), 1.32 (t, J = 8 Hz, 3 H, CH_3'), 3.29 (q, J = 8 Hz, 2 H, CH_2), 3.61 (q, J = 8 Hz, 2 H, CH_2')	7.96 (s, 4 H, o,m-Ph), 2.68 (s, 3 H, $COCH_3$)
p-ClC_6H_4[c]	NEt_2	1685	1640	1.15 (t, J = 8 Hz, 3 H, CH_3), 1.25 (t, J = 8 Hz, 3 H, CH_3'), 3.21 (q, J = 8 Hz, 2 H, CH_2), 3.49 (q, J = 8 Hz, 2 H, CH_2')	7.37 (d, J = 8 Hz, 2 H, m-Ph), 7.75 (d, J = 8 Hz, 2 H, o-Ph)
p-PhOC_6H_4[e]	NEt_2	1680	1640	1.07 (t, J = 7 Hz, 3 H, CH_3), 1.21 (t, J = 7 Hz, 3 H, CH_3'), 3.22 (q, J = 7 Hz, 2 H, CH_2), 3.51 (q, J = 7 Hz, 2 H, CH_2')	~7.2,[f] 7.86 (d, J = 9 Hz, 2 H, o-Ph), 6.8–7.6 (m, 5 H, OPh)
p-MeC_6H_4[c]	NEt_2	1680	1640	1.15 (t, J = 7 Hz, 3 H, CH_3), 1.29 (t, J = 7 Hz, 3 H, CH_3'), 3.27 (q, J = 7 Hz, 2 H, CH_2), 3.59 (q, J = 7 Hz, 2 H, CH_2')	7.30 (d, J = 8 Hz, 2 H, m-Ph), 7.83 (d, J = 8 Hz, 2 H, o-Ph), 2.44 (s, 3 H, CH_3)
p-MeOC_6H_4[c]	NEt_2	1685	1650	1.14 (t, J = 7 Hz, 3 H, CH_3), 1.27 (t, J = 7 Hz, 3 H, CH_3'), 3.24 (q, J = 7 Hz, 2 H, CH_2), 3.54 (q, J = 7 Hz, 2 H, CH_2')	6.95 (d, J = 9 Hz, 2 H, m-Ph), 7.87 (d, J = 9 Hz, 2 H, o-Ph), 3.87 (s, 3 H, OCH_3)
p-$Me_2NC_6H_4$[e]	NEt_2	1640	1580	1.11 (t, J = 7 Hz, 3 H, CH_3), 1.30 (t, J = 7 Hz, 3 H, CH_3'), 3.24 (q, J = 7 Hz, 2 H, CH_2), 3.52 (q, J = 7 Hz, 2 H, CH_2')	6.60 (d, J = 11 Hz, 2 H, m-Ph), 7.64 (d, J = 11 Hz, 2 H, o-Ph), 3.09 (s, 6 H, NCH_3)
o-MeC_6H_4[d]	NEt_2	1675	1640	1.12 (t, J = 7 Hz, 3 H, CH_3), 1.22 (t, J = 7 Hz, 3 H, CH_3'), 3.20 (q, J = 7 Hz, 2 H, CH_2), 3.48 (q, J = 7 Hz, 2 H, CH_2')	7.1–7.6 (m, 4 H, C_6H_4), 2.61 (s, 3 H, CH_3)
Ph[c]	NH-t-Bu	1690	1650	1.46 (s) and 1.73 (s) (total 9 H, C(CH_3)$_3$), 6.7–7.2 (br, 1 H, NH)	7.4–7.7 (m, 3 H, m,p-Ph), 8.4 (m, 2 H, o-Ph)
p-MeC_6H_4[c]	NH-t-Bu	1690	1655	1.45 (s) and 1.84 (s) (total 9 H, C(CH_3)$_3$), 6.6–7.2 (br, 1 H, NH)	7.27 (d, J = 8 Hz, 2 H, m-Ph), 8.27 (d, J = 8 Hz, 2 H, o-Ph), 2.42 (s, 3 H, CH_3)
m-MeC_6H_4[c]	NH-t-Bu	1690	1660	1.40 (s, 9 H, C(CH_3)$_3$), 6.7–7.2 (br, 1 H, NH)	7.3–7.5 (m, 2 H, m,p-Ph), 8.0–8.3 (m, 2 H, o-Ph), 2.35 (s, 3 H, CH_3)

ArCOCONR$_2$'		anal. (%) found (calcd)				mass (m/e) (rel intensity)[g]			
Ar	NR$_2$'	C	H	N	Cl	M$^+$	ArCO$^+$	CONR$_2$'	other
Ph	NMe_2		h			177 (10)	105 (100)	77 (51)	
Ph	NEt_2	70.1 (70.2)	7.4 (7.3)	6.7 (6.8)		205 (4)	105 (70)	100 (100)	
Ph	NPr_2	71.9 (72.1)	8.3 (8.2)	5.9 (6.0)		233 (13)	105 (85)	128 (100)	
Ph			h			203 (0.6)	105 (15)	98 (91)	70 (100)
Ph		71.6 (71.9)	7.0 (7.0)	6.4 (6.5)		217 (14)	105 (57)	112 (100)	
Ph		72.8 (72.7)	7.7 (7.4)	6.1 (6.1)		231 (14)	105 (70)	126 (100)	
Ph	NMe(CH_2Ph)	75.7 (75.9)	5.9 (6.0)	5.6 (5.5)		253 (5)	105 (100)	148 (11)	
p-NCC_6H_4	NEt_2	67.9 (67.8)	6.1 (6.2)	12.5 (12.2)		230 (1)	130 (8)	100 (100)	
p-$CF_3C_6H_4$	NEt_2		h			273 (0.3)	173 (7)	100 (30)	43 (100)

p-AcC_6H_4	NEt_2	67.7 (68.0)	7.1 (6.9)	5.7 (5.7)		247 (15)	147 (31)	100 (100)
p-ClC_6H_4	NEt_2	59.8 (60.1)	5.9 (5.9)	5.8 (5.8)	14.5 (14.8)	239 (5)	139 (38)	100 (100)
						240 (1)	140 (3)	
						241 (2)	141 (12)	
p-$PhOC_6H_4$	NEt_2	72.1 (72.7)	6.3 (6.4)	4.6 (4.7)		297 (7)	197 (100)	100 (36)
p-MeC_6H_4	NEt_2	71.2 (71.2)	8.0 (7.8)	6.4 (6.4)		219 (7)	119 (100)	100 (53)
p-$MeOC_6H_4$	NEt_2	66.2 (66.4)	7.6 (7.3)	5.9 (5.9)		235 (3)	135 (100)	100 (11)
p-$Me_2NC_6H_4$	NEt_2	67.6 (67.7)	8.1 (8.2)	11.1 (11.3)		248 (8)	148 (100)	100 (1)
o-MeC_6H_4	NEt_2	71.0 (71.2)	7.9 (7.8)	6.2 (6.4)		219 (7)	119 (100)	100 (41)
2,6-$Me_2C_6H_3$	NEt_2		*h*			233 (2)	133 (100)	100 (9)
Ph	NH-*t*-Bu	70.2 (70.2)	7.7 (7.4)	7.0 (6.8)		205 (7)	105 (100)	100 (2)
p-MeC_6H_4	NH-*t*-Bu	71.3 (71.2)	8.1 (7.8)	6.4 (6.4)		219 (7)	119 (100)	100 (1)
m-MeC_6H_4	NH-*t*-Bu	71.1 (71.2)	8.1 (7.8)	6.4 (6.4)		219 (8)	119 (100)	100 (1)

[a] In cm^{-1}. [b] 100 MHz, at room temperature. Chemical shifts are in δ (ppm) with respect to Me_4Si as an internal standard. Multiplicity abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. NMR solvent are as follows. [c] $CDCl_3$. [d] CCl_4. [e] CD_2Cl_2. [f] Chemical shift is obscured due to the signals of OPh protons. [g] 70 eV. [h] Not measured. Others (Anal.) Found for Et_2NH_2Br: C, 31.0; H, 8.2; N, 9.0; Br, 51.8. Anal. Calcd for $C_4H_{12}NBr$: C, 31.2; H, 7.9; N, 9.1; Br, 51.9. Found for *trans*-$Pd(CONEt_2)I(PMePh_2)_2$ (5): C, 50.7; H, 5.0; N, 1.8; I, 17.3. Anal. Calcd for $C_{31}H_{36}NIOP_2Pd$: C, 50.7; H, 4.9; N, 1.9; I, 17.3.

reactivities of selected amines in competitive catalytic reactions (Table IX) indicates that the relative rate of formation of amides as well as α-keto amides is determined by relative reactivity of the amines toward the coordinated CO ligand.

Taking these experimental results obtained in the present as well as previous[4] studies into account, we propose the mechanism represented in Scheme IV to account for the double carbonylation and monocarbonylation of aryl halides catalyzed by the palladium-based catalysts.

This scheme consists of two catalytic cycles; cycle I produces α-keto amide whereas cycle II yields amide. The first step in the catalytic reactions is the oxidative addition of aryl halide to zero-valent palladium species to give the arylpalladium complex **1**,which is the common intermediate for the both cycles. When a very reactive amine such as sterically less demanding and nucleophilic pyrrolidine and piperidine is used under CO pressure, the amine attacks the coordinated CO in arylcarbonylpalladium species **6**. The reaction gives an arylcarbamoylspecies **7**, which reductively eliminates amide to generae the zero-valent palladium species as the carrier of the catalytic cycles. When less reactive amine is employed, the arylpalladium complex **1** undergoes the CO insertion, before the CO ligand in **6** is attacked by the amine, to give the aroylpalladium species **2**. Coordination of CO to **2** to give an ionic species **3** followed by attack of amine on the coordinated CO ligand gives an aroylcarbamoyl species **4**, which liberates α-keto amide on reductive elimination. The regenerated zero-valent palladium species further carries the catalytic cycles.

In this scheme, CO insertion into the aryl–palladium bond in **1** is considered to be an irreversible process as supported by the experiment using ^{13}C-enriched benzoyl complex (vide supra). Therefore, the relative ratio of α-keto amide and amide can be given by the 12, where r_1 represents the CO insertion rate into

$$\frac{\text{α-keto amide}}{\text{amide}} = \frac{r_1}{r_2} \qquad (12)$$

the aryl–palladium bond whereas r_2 stands for the rate of formation of amide on interaction of **1** with CO and amine. Since the rate of CO insertion would not vary very much depending on amine, the selectivity for α-keto amide formation is predominantly determined by reactivity of amine toward the CO-coordinated arylpalladium complex in agreement with experimental results. Thus, for piperidine having a large r_2 value, amide is preferentially produced, whereas for diethylamine having a smaller r_2 value than r_1, mainly α-keto amide is produced.

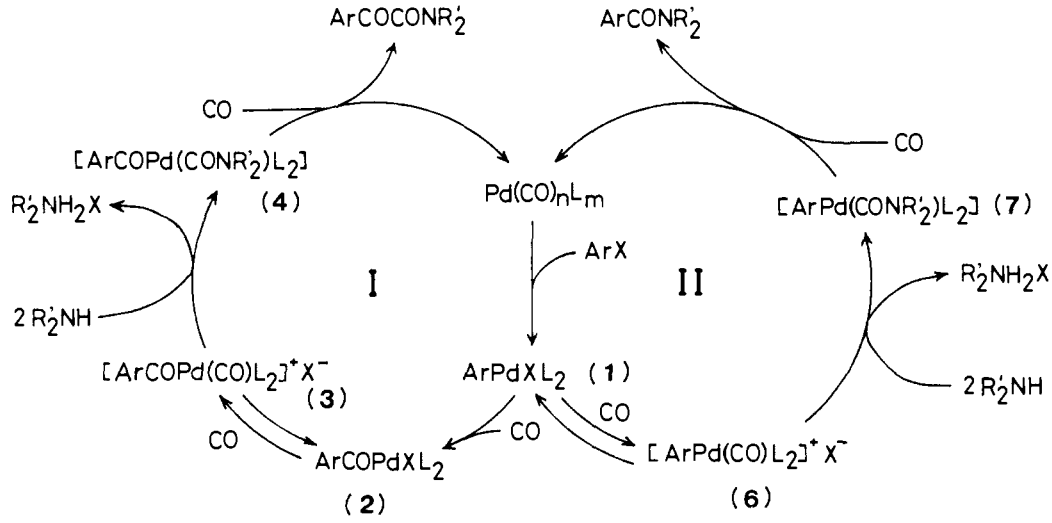
The effect of para substituent on the rate of catalytic reactions and selectivity can be accounted for by assuming Scheme IV and eq 12. Substitution of para hydrogen with an electron-withdrawing substituent enhances the oxidative addition rate[6,8] but decreases the CO insertion rate, r_1.[12] The electron-withdrawing substituent will enhance also the electrophilicity of the CO-coordinated arylpalladium species and increase r_2. Thus, the net result is decrease in selectivity for α-keto amide formation with increase in the reaction rate.

Our discussion above is restricted to the systems with reactive amines having high basicity and limited bulkiness. On the other hand, reactions with less basic amines such as aniline derivatives as well as alcohols give only monocarbonylation products even under pressurized conditions.[13] Since nucleophilicity of anilines and alcohols is much smaller than that of basic amines such as Et_2NH and Pr_2NH, r_2 values for these less reactive nucleophiles seem to be small. Thus the exclusive formation of monocarbonylation products in the systems with these less basic nucleophiles cannot be elucidated by Scheme IV. This problem is now under investigation.

(12) Garrou, P. E.; Heck, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 4115. Sugita, N.; Minkiewicz, J. V.; Heck, R. F. *Inorg. Chem.* **1978**, *17*, 2809. Anderson, G. K.; Cross, R. J. *Acc. Chem. Res.* **1984**, *17*, 67.

(13) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3327. Schoenberg, A.; Bartoletti, I.; Heck, R. F. *Ibid.* **1974**, *39*, 3318. Stille, J. K.; Wong, P. K. *Ibid.* **1975**, *40*, 532. Hidai, M.; Hikita, T.; Wada, Y.; Fujikura, Y.; Uchida, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2075.

Scheme IV. Proposed Mechanism for the Catalytic Double Carbonylation and Monocarbonylation of Aryl Halides Catalyzed by *tert*-Phosphine-Coordinated Palladium Complexes



Experimental Section

Infrared spectra were recorded on a Hitachi 295 spectrometer by using KBr pellets for solid and KBr plates for liquid materials. IR spectra of benzoylpalladium complexes in solution under CO pressure were obtained on a JASCO FT/IR-3 spectrometer. ^1H NMR spectra were measured on a JEOL PS-100 spectrometer. ^1H NMR signals are referred to Me_4Si as an internal standard. $^{31}P\{^1H\}$ NMR spectra were recorded on a JEOL FX-100 spectrometer by Dr. Y. Nakamura of our laboratory. Microanalyses (C, H, N, and halogen) were carried out by T. Saito of our laboratory by using Yanagimoto CHN Autocorder Type MT-2 and Yazawa Halogen Analyzer. Mass spectra were obtained on a Hitachi M-80 GC–mass spectrometer.

Solvents, amines, and aryl halides in the liquid state were dried in the usual manner, distilled, and stored under a nitrogen atmosphere. Aryl halides in the solid state were used as purchased without further purification. Dichlorobis(*tert*-phosphine)palladium(II) complexes were prepared by the reactions of $PdCl_2(PhCN)_2$ and corresponding tertiary phosphines. *trans*-$PdMe_2(PMePh_2)_2$, *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**), *trans*-$Pd(COPh)I(PMePh_2)_2$ (**2a**), and *trans*-$Pd(COPh)(PMePh_2)_2ClO_4$ were prepared as described previously.[4,14]

Catalytic Double-Carbonylation Reactions. A typical procedure (Table I, run 3) is as follows: PhBr (1 mL, 9.6 mmol) and Et_2NH (3 mL, 29 mmol) were added to a 100-mL stainless-steel pressure bottle containing $PdCl_2(PMePh_2)_2$ (0.049 g, 0.085 mmol) under nitrogen atmosphere. After evacuating the system, 10 atm of CO gas was introduced at room temperature, and the mixture was magnetically stirred at 100 °C for 40 h. After the CO gas was purged, the reaction mixture was extracted with Et_2O (10 mL × 2) and analyzed by means of GLC (Shimadzu GC-3BT; column, PEG 20M 1 m) by using Ph_2O as an internal reference. The GLC analysis revealed the formation of $PhCOCONEt_2$ (82% PhBr) and *N,N*-diethylbenzamide (13%). The remaining part, which could not be extracted with Et_2O, was white solid and characterized as Et_2NH_2Br by IR spectroscopy and elemental analysis (0.52 g, 35% PhBr). Anal. ($C_4H_{12}NBr$)C, H, N, Br. The α-keto amide and amide produced were isolated by column chromatography (Merck, Lobar column, LiChroprep Si 60; hexane–Et_2O) after removal of palladium complex by bulb-to-bulb distillation (Shibata GTO-250R).

α-Keto amides and amides isolated from catalytic double-carbonylation systems were characterized by means of elemental analysis (C, H, N, and/or Cl), IR and ^1H NMR spectroscopy, and mass spectrometry. Among the carbonylation products, $PhCOCONMe_2$, *N*-phenylglyoxylpyrrolidine, and *N,N*-diethyl-(2,6-dimethylphenyl)glyoxylamide were characterized only by GC–mass spectrometry since their yields in catalytic reactions were very low. The analytical and mass spectroscopic data agreed well with the calculated values. IR and ^1H NMR data of α-keto amides are summarized in Table X. IR spectra of α-keto amides show two ν(C=O) bands. The higher band is ascribable to α-keto carbonyl whereas the lower to amide carbonyl group.

Kinetics. (a) Catalytic Reaction of PhI, CO, and Et_2NH (Figure 1). Mixtures of $PdCl_2(PMePh_2)_2$ (0.040 ± 0.001 mmol), PhI (2.0 ± 0.1 mmol), and Et_2NH (1.0 mL) were placed in 100-mL stainless-steel pressure bottles under nitrogen atmosphere. After the systems were evacuated, CO gas (20 atm) was introduced at room temperature into each bottle. The reaction bottles were placed in a thermostated oil bath controlled at 60 ± 0.1 °C, and the reaction systems were magnetically stirred. At intervals, the bottles were removed, cooled to room temperature, and CO gas was purged immediately. The yield of $PhCOCONEt_2$ at each time was determined by means of GLC. The catalytic reaction at room temperature without CO pressure is slow, and the rate can be ignored. It was also confirmed that decrease of CO pressure under the reaction conditions was very small throughout the reaction (about 5% of pressure decreased at 100% conversion of PhI).

(b) Stoichiometric Reaction of *trans*-$PdPh(I)(PMePh_2)_2$ (1a), CO, and Et_2NH (Figure 2). Mixtures of **1a** (0.080 mmol), Et_2NH (2.0 mL), and PhCl (500 μL) were introduced into 100-mL stainless-steel pressure bottles under nitrogen atmosphere. After evacuation, 20 atm of CO was introduced to the systems at room temperature, and the bottles were placed in a thermostated bath (60 ± 0.1 °C). At each interval, the bottles were removed, cooled in an ice bath immediately, and CO gas was purged. Yields of reaction products at time were measured by GLC.

Competitive Reactions of Various Para-Substituted Phenyl Bromides and Phenyl Bromide in the Presence of Et_2NH under CO Pressure Catalyzed by $PdCl_2(PMePh_2)_2$ (Figure 3). As a typical example, PhBr (0.47 g, 3.0 mmol) and *p*-tolyl bromide (0.51 g, 3.0 mmol) were added to a 100-mL stainless-steel pressure bottle containing Et_2NH (3.8 mL, 36 mmol) and $PdCl_2(PMePh_2)_2$ (0.036 g, 0.063 mmol). After the system was evacuated, 10 atm of CO gas was introduced at room temperature, and the bottle was placed in an oil bath controlled at 100 °C. After the system was magnetically stirred for 6 h, CO gas was purged, and the reaction products were analyzed by GLC. The GLC analysis revealed that 13.9% of PhBr and 8.4% of *p*-tolyl bromide were consumed with formation of corresponding α-keto amides and amides: $PhCOCONEt_2$ (12.8% PhBr), $PhCONEt_2$ (1.1%), $p\text{-}MeC_6H_4COCONEt_2$ (7.6% *p*-tolyl bromide), and $p\text{-}MeC_6H_4CONEt_2$ (0.8%). On the basis of the conversions and the initial amounts of bromides, the relative reactivity of bromides was determined as *p*-tolyl bromide/PhBr = 0.60.

Competitive Reactions of Various Secondary Amines with *trans*-Pd(COPh)I($PMePh_2$)$_2$ (2a) in the Presence of PhCl and CO (Table VIII). For example, to a test tube containing *trans*-$Pd(COPh)I(PMePh_2)_2$ (0.059 g, 0.080 mmol) were added Et_2NH (0.76 g, 10.5 mmol), Pr_2NH (0.75 g, 7.4 mmol), and PhCl (500 μL) at −30 °C under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO gas was introduced at room temperature. After the system was stirred for 60 min at room temperature, CO gas was purged, and the reaction products were analyzed by GLC. Formation of $PhCOCONEt_2$ (0.053 mmol, 66%/Pd) and $PhCOCONPr_2$ (0.028 mmol, 35%) was confirmed, but amides could not be detected. Based on the yields of α-keto amides and the amounts of amines fed to the system, the relative reactivity of amines was determined as Pr_2NH/Et_2NH = 0.75.

$^{31}P\{^1H\}$ NMR Study. (a) On the Reaction of PhI, CO, and Et_2NH in the Presence of *trans*-$PdMe_2(PMePh_2)_2$. To a test tube containing *trans*-$PdMe_2(PMePh_2)_2$ (0.59 g, 1.1 mmol) were added PhI (2.1 g, 10 mmol) and Et_2NH (7.0 mL, 67 mmol) under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 10 atm of CO was introduced at room temperature. After the system was

(14) Ito, T.; Tsuchiya, H.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1319.

stirred for 5 h at the same temperature, CO gas was purged. The resulted orange solution was cooled to 0 °C and examined by means of GLC. The GLC analysis showed the formation of $PhCOCONEt_2$ (227% Pd), $PhCONEt_2$ (19%), and $Et_2NCOCONEt_2$ (19%). The solution was transferred into an NMR sample tube and examined by $^{31}P\{^1H\}$ NMR spectroscopy. The $^{31}P\{^1H\}$ NMR spectrum measured at room temperature exhibited three singlets at 11.3, 6.7, and 5.9 ppm (referred to PPh_3, downfield positive) in a ratio of 2:5:3. The former two peaks were assigned to *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**) and *trans*-$Pd(COPh)I(PMePh_2)_2$ (**2a**), respectively, by comparison with the spectra of authentic samples in PhI–Et_2NH solutions. The reaction solution was replaced in a Schlenk tube under a nitrogen atmosphere and concentrated to almost dryness by pumping. The resulted reddish-yellow solid was dissolved in CH_2Cl_2 and washed with water. A liquid chromatography of the dichloromethane solution (Merck, Lobar column, LiChroprep Si 60; hexane–Et_2O = 3/7) gave the mixture of **1a** and **2a** (with a total of 422 mg) and the pale yellow solid (185 mg) together with carbonylation products. The pale yellow solid isolated was recrystallized from CH_2Cl_2–Et_2O and characterized as *trans*-$Pd(CONEt_2)I(PMePh_2)_2$ (**5**) by means of IR and ^1H and $^{31}P\{^1H\}$ NMR spectroscopy and elemental analysis. Anal. ($C_{31}H_{36}NIOP_2Pd$) C, H, N, I. IR ν(C=O) 1580 cm^{-1}; ^1H NMR (CD_2Cl_2, room temperature) δ 0.47 (t, $^3J_{HH}$ = 8 Hz, 3 H, NCC*H*$_3$) 0.71 (t, $^3J_{HH}$ = 8 Hz, 3 H, NCC*H*$_3$) 2.27 (t, $^2J_{PH}$ = 4 Hz, 6 H, PC*H*$_3$) 2.59 (q, $^3J_{HH}$ = 8 Hz, 2 H, NC*H*$_2$) 3.61 (q, $^3J_{HH}$ = 8 Hz, 2 H, NC*H*$_2$) 7.3–8.0 (m, 20 H, P*Ph*); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, room temperature) 6.1 ppm (s; referred to PPh_3, downfield positive). $^{31}P\{^1H\}$ NMR spectrum of the isolated complex **5** in PhI–Et_2NH solution exhibited a singlet peak at 5.9 ppm.

(b) On the Reaction of PhI, CO, and Piperidine in the Presence of *trans*-$PdMe_2(PMePh_2)_2$. To a test tube containing *trans*-$PdMe_2(PMePh_2)_2$ (0.056 g, 0.10 mmol) were added PhI (500 μL, 4.5 mmol) and piperidine (2 mL, 20 mmol) at −30 °C under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO was introduced. After the system was stirred for 2 h at room temperature, the bottle was cooled to −30 °C, and CO gas was purged. GLC analysis of the orange reaction solution showed the formation of *N*-benzoylpiperidine (885% Pd), *N*-phenylglyoxylpiperidine (34%), and oxamide of piperidine (66%). The solution was transferred into an NMR sample tube and examined by $^{31}P\{^1H\}$ NMR spectroscopy. The NMR spectrum (at −30 °C) showed a singlet peak due to *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**) at 12.9 ppm and two broad peaks at 10.5 and 6.5 ppm in a ratio of 2:3:5. When the NMR sample was allowed to stand at room temperature, the color of the solution rapidly changed from orange to pale yellow (within 2 min). The $^{31}P\{^1H\}$ NMR spectrum of the resulted pale yellow solution exhibited almost one signal at 11.5 ppm (at room temperature) due to the phenyl complex (**1a**). These results suggested that the complexes corresponding to the signals at 10.5 and 6.6 ppm in the initial spectrum were converted into **1a** at room temperature. Thus the signals at 10.5 and 6.6 ppm may arise from Pd(0) complexes having carbonyl and $PMePh_2$ ligands, which were converted into **1a** by oxidative addition of PhI at room temperature.

Reactions of *trans*-$Pd(CONEt_2)I(PMePh_2)_2$ (5). (a) With CO and Et_2NH. To a test tube containing *trans*-$Pd(CONEt_2)I(PMePh_2)_2$ (**5**; 0.092 g, 0.13 mmol) were added Et_2NH (3 mL) and PhCl (1 mL) at −30 °C under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle and 20 atm of CO was introduced. The mixture was stirred for 6 h at room temperature. After the CO gas was purged, the reaction solution was analyzed by GLC and formation of $Et_2NCOCONEt_2$ (75% Pd) and $Et_2NCONEt_2$ (18%) was confirmed.

(b) With CO and PhI. To a test tube containing complex **5** (0.059 g, 0.13 mmol) were added PhI (1 mL) and Et_3N (3 mL) at −30 °C under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO was introduced. The system was stirred for 6 h at room temperature. After the CO gas was purged, the reaction solution was examined by GLC. Formation of carbonylation product such as α-keto amide, amide, and oxamide was not found.

(c) With *trans*-$Pd(COPh)I(PMePh_2)_2$ (2a) under CO Pressure. To a test tube containing the carbamoyl complex **5** (0.061 g, 0.083 mmol) and *trans*-$Pd(COPh)I(PMePh_2)_2$ (**2a**, 0.062 g, 0.083 mmol) were added PhCl (1 mL) and Et_3N (3 mL) under nitrogen atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO was introduced. After the system was stirred for 6 h at room temperature, CO gas was purged, and the reaction solution was examined by GLC. GLC analysis showed that the reaction gave no carbonylation product.

Reaction of *trans*-$PdPh(I)(PMePh_2)_2$ (1a) with Piperidine under CO Pressure. To a test tube containing *trans*-$PdPh(I)(PMePh_2)_2$ (**1a**; 0.058 g, 0.0815 mmol) were added piperidine (2.0 mL, 20 mmol) and PhCl (500 μL) under argon atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO was introduced. After the system was stirred for 10 min at room temperature, CO gas was purged, and the resulting red solution was examined by GLC. GLC analysis showed the formation of *N*-benzoylpiperidine (99% Pd).

Reaction of *trans*-$Pd(COPh)I(PMePh_2)_2$ (2a) with Piperidine under CO Pressure. To a test tube containing **2a** (0.057 g, 20 mmol) under nitrogen atmosphere at −30 °C. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of CO was introduced. After the system was stirred for 20 min at room temperature, the CO gas was purged, and the reaction solution was examined by GLC. Formation of *N*-phenylglyoxylpiperidine (93% Pd) was confirmed.

Preparation of *trans*-$Pd(^{13}COPh)I(PMePh_2)_2$ and Its Reaction with Et_2NH under CO Pressure. To a Schlenk tube containing *trans*-$PdPh(I)(PMePh_2)_2$ (1.17 g, 1.65 mmol) was added 8.8 mL of CH_2Cl_2 under nitrogen atmosphere. After the system was evacuated by pumping, an atmospheric pressure of ^{13}CO gas (90% isotopic purity) was introduced. On stirring the homogeneous reaction solution at room temperature, the color of the solution quickly changed from pale yellow to yellow. After the system was stirred for 14 h, the solvent was removed under reduced pressure. The resulted yellow precipitate was washed with Et_2O and recrystallized from CH_2Cl_2–hexane to yield yellow crystals of *trans*-$Pd(^{13}COPh)I(PMePh_2)_2$ (1.12 g, 92% yield). IR $\nu(^{13}C{=}O)$ 1604 cm^{-1} (cf. $\nu(^{12}C{=}O)$ 1640 cm^{-1}).[4a]

To a test tube containing *trans*-$Pd(^{13}COPh)I(PMePh_2)_2$ (0.12 g, 0.17 mmol) were added PhCl (1 mL) and Et_2NH (4.0 mL, 38 mmol) under argon atmosphere. The test tube was placed in a 100-mL stainless-steel pressure bottle, and 20 atm of nonlabeled CO gas was introduced. After the system was stirred for 10 min at 60 °C, the CO gas was purged, and the reaction products were analyzed by GC–mass spectrometry. The GC–mass analysis revealed the formation of $Ph^{13}CO^{12}CONEt_2$ and $Ph^{12}CO^{12}CONEt_2$ in a ratio of 13:1, suggesting the absence of decarbonylation reaction in the α-keto amide formation.

Acknowledgment. This work was supported by a Grant-in-Aid for Special Project Research from the Ministry of Education, Science and Culture, Japan.

Registry No. 1a, 68391-86-6; **2a**, 68391-88-8; **5**, 95725-13-6; PhBr, 108-86-1; Et_2NH, 109-89-7; $PhPd(Br)(PPh_3)_2$, 30643-33-5; $PhPd(Br)(PMePh_2)_2$, 84059-60-9; $PdCl_2(PMePh_2)_2$, 52611-08-2; $PdCl_2(PEt_2Ph)_2$, 40791-49-9; $PdCl_2(PMe_2Ph)_2$, 15616-85-0; $PdCl_2(PEt_3)_2$, 28425-04-9; $PdCl_2$(dppe), 19978-61-1; $PdCl_2$(dppb), 29964-62-3; $PdCl_2$, 7647-10-1; $PdCl_2$(bpy), 14871-92-2; $Pd(OAc)_2$, 33571-36-7; $CuBr(PPh_3)_3$, 15709-74-7; $NiCl_2(PEt_3)_2$, 17523-24-9; $RhCl(PPh_3)_3$, 14694-95-2; $CoCl(PPh_3)_3$, 26305-75-9; $CoH(N_2)(PPh_3)_3$, 16920-54-0; $CoCl_2(PEtPh_2)_2$, 14916-45-1; $PhC(O)C(O)NEt_2$, 34906-86-0; $PhC(O)NEt_2$, 1696-17-9; PhI, 591-50-4; PhCl, 108-90-7; *p*-CNC_6H_4Br, 623-00-7; *p*-$CF_3C_6H_4Br$, 402-43-7; *p*-AcC_6H_4Br, 99-90-1; *p*-ClC_6H_4Br, 106-39-8; *p*-$PhOC_6H_4Br$, 101-55-3; *p*-MeC_6H_4Br, 106-38-7; *p*-$MeOC_6H_4Br$, 104-92-7; *p*-$Me_2NC_6H_4Br$, 586-77-6; *p*-$CNC_6H_4C(O)C(O)NEt_2$, 95724-98-4; *p*-$CF_3C_6H_4C(O)C(O)NEt_2$, 95724-99-5; *p*-$AcC_6H_4C(O)C(O)NEt_2$, 95725-00-1; *p*-$ClC_6H_4C(O)C(O)NEt_2$, 84039-66-7; *p*-$PhOC_6H_4C(O)C(O)NEt_2$, 95725-01-2; *p*-$MeC_6H_4C(O)C(O)NEt_2$, 80120-40-7; *p*-$MeOC_6H_4C(O)C(O)NEt_2$, 80120-53-2; *p*-$Me_2NC_6H_4C(O)C(O)NEt_2$, 95725-02-3; *p*-$CNC_6H_4C(O)NEt_2$, 95725-03-4; *p*-$CF_3C_6H_4C(O)NEt_2$, 95725-04-5; *p*-$AcC_6H_4C(O)NEt_2$, 95725-05-6; *p*-$ClC_6H_4C(O)NEt_2$, 7461-38-3; *p*-$PhOC_6H_4C(O)NEt_2$, 95725-06-7; *p*-$MeC_6H_4C(O)NEt_2$, 2728-05-4; *p*-$MeOC_6H_4C(O)NEt_2$, 7465-86-3; *p*-$Me_2NC_6H_4C(O)NEt_2$, 95725-07-8; *p*-CNC_6H_4I, 3058-39-7; *p*-ClC_6H_4I, 637-87-6; *p*-MeC_6H_4I, 624-31-7; *p*-$MeOC_6H_4I$, 696-62-8; *i*-Pr_2NH, 108-18-9; *i*-Bu_2NH, 110-96-3; $PhCH_2(Me)NH$, 98-84-0; Ph(Me)NH, 100-61-8; $(PhCH_2)_2NH$, 103-49-1; $PhC(O)C(O)NMe_2$, 51579-87-4; $PhC(O)NMe_2$, 611-74-5; $PhC(O)C(O)NPr_2$, 84017-26-5; $PhC(O)NPr_2$, 14657-86-4; PhC(O)N-*i*-Pr_2, 20383-28-2; $PhC(O)C(O)N(Me)CH_2Ph$, 95725-09-0; $PhC(O)N(Me)CH_2Ph$, 61802-83-3; PhC(O)N(Me)Ph, 1934-92-5; $PhC(O)C(O)NH$-*t*-Bu, 21010-60-6; *p*-$MeC_6H_4C(O)C(O)NH$-*t*-Bu, 95725-10-3; *m*-$MeC_6H_4C(O)C(O)NH$-*t*-Bu, 95725-11-4; *trans*-$PdMe_2(PMePh_2)_2$, 74345-90-7; $Et_2NC(O)C(O)NEt_2$, 14288-05-2; $Et_2NC(O)NEt_2$, 1187-03-7; *trans*-$Pd(^{13}C(O)Ph)I(PMePh_2)_2$, 95725-14-7; $Ph^{13}C(O)C(O)NEt_2$, 95725-12-5; Me_2NH, 124-40-3; Pr_2NH, 142-84-7; pyrrolidine, 123-75-1; hexamethyleneimine, 111-49-9; piperidine, 110-89-4; diallylamine, 124-02-7; *N*-benzoylpyrroldine, 3389-54-6; *N*-(benzoylcarbonyl)piperidine, 14377-63-0; *N*-benzoylpiperidine, 776-75-0; *N*-(benzoylcarbonyl)-1*H*-hexahydroazepine, 95725-08-9; *N*-benzoyl-1*H*-hexahydroazepine, 3653-39-2; 1-[(piperidin-1-ylcarbonyl)carbonyl]piperidine, 17506-94-4.