 © 1988 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 61, 1251—1258 (1988)

Palladium-Catalyzed Double-Carbonylation of Alkenyl Halides with Secondary Amines To Give α-Keto Amides

Tae-il Son, Hisayoshi Yanagihara, Fumiyuki Ozawa, and Akio Yamamoto*
Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227
(Received September 28, 1987)

The double-carbonylation reaction of alkenyl halides with diethylamine in the presence of palladium catalysts has been examined in detail. The reaction gives α-keto amide together with amide, the single-carbonylation by-product. The yield of α-keto amide is strongly dependent on the nature of alkenyl halide. Alkenyl bromides or iodides having phenyl group(s) as substituent(s) on the vinyl group are successfully double-carbonylated under appropriate reaction conditions and the corresponding α-keto amides are obtained in good to modest yields together with amides. In contrast, the reactions of alkenyl halides without a phenyl group give amides exclusively. In order to clarify the reason for the substrate-specificity in the reaction, series of alkenyl- and alkenoylpalladium(II) complexes, the presumed intermediates in the catalytic reactions, have been prepared and their reactions with secondary amines, carbon monoxide, and alkenyl halides were examined. The study suggests the operation of three types of processes for amide formation in the catalytic reactions. Possible mechanisms for amide as well as α-keto amide formation are discussed.

Recently novel double-carbonylation reactions of organic halides catalyzed by palladium complexes have been discovered.[1-3]

$$RX + 2CO + 2R'_2NH \xrightarrow{[Pd]} RCOCONR'_2 + R'_2NH_2X \quad (R = \text{aryl, alkenyl; } X = Br, I; R' = \text{alkyl}) \quad (1)$$

$$ArX + 2CO + ROH + Et_3N \xrightarrow{[Pd]} ArCOCOOR + Et_3NHX \quad (Ar = \text{aryl; } X = I, (Br); R = \text{alkyl}) \quad (2)$$

$$ArI + 2CO + H_2O + Base \xrightarrow{[Pd]} ArCOCOOH + Base \cdot HI \quad (Base = Et_3N, Ca(OH)_2) \quad (3)$$

Double-carbonylation reactions of aryl halides have been extensively examined and a variety of aryl bromides and iodides were shown to be converted into α-keto amides,[1] α-keto esters,[2] and α-keto acids[3] in good to modest yields by proper choice of nucleophiles used in the catalytic systems. On the other hand, double-carbonylation reactions of other types of organic halides have been explored less extensively.

In this study we examined the double-carbonylation reaction of alkenyl halides in detail. Alkenyl halides can be successfully double-carbonylated only by process (1) using secondary amines. Further study has revealed that yield of α-keto amide in process (1) is strongly dependent on the kind of alkenyl halide. Namely, alkenyl halides having phenyl group(s) as substituent(s) on the vinyl group give α-keto amides together with amides, whereas in the reactions of alkenyl halides without phenyl groups, only amides are formed without any α-keto amide formation. For getting information regarding the substrate-specificity in the double-carbonylation, we prepared alkenyl- and alkenoylpalladium(II) complexes as models of intermediates assumed in the catalytic reactions and examined their reactivity toward secondary amines, carbon monoxide, and alkenyl halides.

Results

Catalytic Reaction. First we sought appropriate conditions for double-carbonylation of alkenyl halides by using styryl bromide and diethylamine as starting materials. Based on the previous results regarding the double-carbonylation of aryl halides,[1] diethylamine was chosen as the most suitable secondary amine for getting α-keto amides. Table 1 summarizes catalytic activities of palladium complexes having several kinds of tertiary phosphine ligands. No product other than α-keto amide and amide was observed in the reactions as confirmed by GLC. Among the complexes examined, the palladium complex coordinated with 1,4-bis(diphenylphosphino)butane (dppb) was found to serve as the most effective catalyst regarding the selectivity for α-keto amide formation as well as conversion of the bromide.

The highest selectivity for α-keto amide formation was achieved at moderate reaction temperatures of 50 °C (Table 1, Runs 5, 8, and 9). Higher CO pressure caused increase in selectivity for α-keto amide formation but significantly retarded the progress of reaction (Runs 5—7). The similar trend of the effect of CO pressure has been observed in the double-carbonylation of aryl bromides and secondary amines.

Although styryl bromide was used as a mixture of *Z* and *E* isomers, only (*E*)-α-keto amide was obtained as double-carbonylation product, presumably for a thermodynamic reason. In contrast, amide, the single-carbonylation by-product, was formed as a mixture of the both isomers.[4]

Table 2 summarizes the results of double carbonylation of various alkenyl halides. In the double-carbonylation of alkenyl bromides and iodides having phenyl group(s), α-keto amides were formed in good to modest selectivities (Runs 1—6). In contrast, no α-keto amide formation was observed when alkenyl halides without phenyl group were employed as starting materials (Runs 7—12).

Table 1. Double-Carbonylation of Styryl Bromide and Et_2NH Promoted by Palladium Catalysts[a]

Run	Catalyst[b]	p(CO)/atm[c]	Temp/°C	Time/h	Product ratio		Conversion of RBr/%
					α-keto amide	amide	
1	$PdCl_2(PMePh_2)_2$	50	50	40	44[d]	56[e]	91
2	$PdCl_2(PEtPh_2)_2$	50	50	67	27[d]	73[f]	100
3	$PdCl_2(PMe_2Ph)_2$	50	50	67	70[d]	30[g]	76
4	$PdCl_2(PEt_2Ph)_2$	50	50	67	50[d]	50[h]	100
5	$PdCl_2$(dppb)	50	50	67	70[d]	30[i]	100
6	$PdCl_2$(dppb)	25	50	24	58[d]	42[j]	97
7	$PdCl_2$(dppb)	10	50	16	14[d]	86[k]	96
8	$PdCl_2$(dppb)	50	40	40	49[d]	51[j]	45
9	$PdCl_2$(dppb)	50	100	20	3[d]	97[l]	100

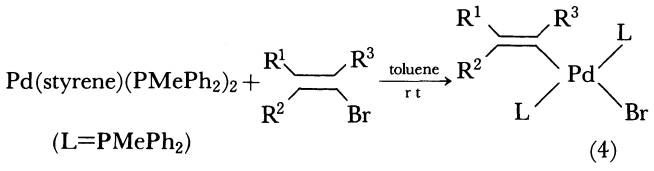
a) Reactions were carried out by using 6 mmol of styryl bromide (Z/E=1/6.5) without solvent. PhCH=CHBr/Et_2NH/catalyst=1/6/0.01 (molar ratio). b) dppb=$Ph_2P(CH_2)_4PPh_2$. c) Initial value measured at room temperature. Z/E ratio: d) E only; e), 1/5.1; f), 1/8.7; g), 1/5.8; h), 1/3.4; i), 1/9.9; j), 1/6.5; k), 1/7; l), 1/9.6.

Table 2. Reactions of Alkenyl Halides (R^1R^2C=CR^3X) and Et_2NH under CO Pressure in the Presence of Palladium Catalyst[a]

Run	Alkenyl halide				Catalyst[b]	p(CO)[c]	Temp	Time	Conversion[d] of RX (%)	Yield (%/RX)[d]	
	R^1	R^2	R^3	X		atm	°C	h		α-keto amide	amide
1	Ph	H	H	Br[g]	A	50	50	67	100	70[h]	30[j]
2	Ph	H	H	I[h]	B	70	25	70	100	93[h]	7[h]
3	Ph	Ph	H	Br	A	25	60	67	80	51	29
4	Ph	Ph	H	Br	C	40	80	18	100	43	54
5	Ph	Ph	Ph	Br	A	30	100	67	93	33	55
6	Ph	Me	H	Br[h]	A	10	60	164	98	32[h]	54[h]
7	H	H	H	Br	A	40	60	96	100	0	100[f]
8	Me	H	H	Br[i]	A	10	60	115	e)	0	50[k]
9	Me	Me	Me	Br	A	10	100	45	0	0	0
10	H	H	Bu	Br	A	10	60	67	48	0	48
11	H	H	Bu	I	A	40	40	67	100	0	100
12	COOH	Me	H	Br	A	10	60	67	79	0	30

a) Reactions were carried out by using 6 mmol of alkenyl halides without solvent; alkenyl halide/Et_2NH/catalyst=1/6/0.01 (molar ratio). b) A, $PdCl_2(Ph_2P(CH_2)_4PPh_2)$; B, $PdMe_2(PMePh_2)_2$; C, $PdCl_2(PMePh_2)_2$. c) Initial value measured at room temperature. d) Confirmed by means of GLC. e) Not measured. f) Obtained as $Et_2NCH_2CH_2CONEt_2$. Z/E ratio: g), 1/6.5; h), E only; i), 1/3; j), 1/9.9; k), 1/6.1.

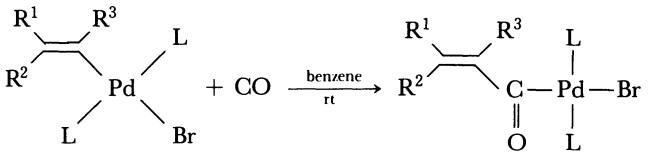
Preparation of Alkenyl- and Alkenoylpalladium(II) Complexes. Series of alkenylpalladium(II) complexes having $PMePh_2$ ligands **1a—1d** were prepared as possible intermediates in the catalytic systems.



1a: R^1=R^2=R^3=H
1b: R^1=Me, R^2=R^3=H
1c: R^1=Ph, R^2=R^3=H
1d: R^1=R^2=Ph, R^3=H

Reactions of Pd(styrene)$(PMePh_2)_2$[5] with phenyl-substituted vinyl bromides proceeded smoothly in toluene at room temperature to give alkenyl complexes **1c**[6] and **1d** in good yields. In contrast, treatment of Pd(styrene)$(PMePh_2)_2$ with vinyl bromide or 1-propenyl bromide under the same conditions gave $PdBr_2(PMePh_2)_2$ instead of the desired alkenyl complex **1a** or **1b**. Formation of butadiene and 2,4-hexadiene was also noted in the reactions. The reactions may involve the alkenyl complexes **1a** and **1b** as intermediates, which undergo further interaction with alkenyl bromides to give dibromopalladium and butadiene derivatives. Indeed, the reaction of isolated **1b** with 1-propenyl bromide in toluene at room temperature afforded $PdBr_2(PMePh_2)_2$ and 2,4-hexadiene. Addition of free $PMePh_2$ to the reaction systems containing Pd(styrene) $(PMePh_2)_2$ and the alkenyl halides, effectively retarded the formation of the dibromide complex, and **1a** and **1b** could be isolated in good yields.

The alkenyl complexes thus prepared underwent CO insertion into the Pd-C bond in solution to form corresponding alkenoylpalladium complexes **2a—2d** with retention of the trans configuration.



(L=$PMePh_2$)

2a: $R^1=R^2=R^3=H$
2b: $R^1=Me$, $R^2=R^3=H$
2c: $R^1=Ph$, $R^2=R^3=H$
2d: $R^1=R^2=Ph$, $R^3=H$ (5)

The alkenyl- and alkenoylpalladium(II) complexes were characterized by means of elemental analysis and spectroscopy (see Experimental section).

Reactions of the Alkenyl- and Alkenoylpalladium(II) Complexes with Secondary Amines under CO Pressure. 1. Effect of Amine. Reactions of the isolated alkenyl- and alkenoylpalladium(II) complexes with secondary amines under CO pressure smoothly proceeded in solution at room temperature to give corresponding α-keto amides and amides together with ammonium salts. The relative yields of α-keto amide and amide markedly varied with the nature of amine employed for the reaction.

Table 3. Reactions of the Styrylpalladium Complex **1c** with Various Secondary Amines under CO Pressure[a)]

Run	Amine	Product ratio		Total yield (%/Pd)
		α-keto amide	amide	
1	Pr_2NH	51	49	26
2	Et_2NH	87	13	55
3	piperidine	25	75	100
4	pyrrolidine	2	98	100

a) Reactions were carried out by using **1c** (0.05 mmol) and amine (1 mmol) in benzene (3 cm^3) under 50 atm of CO at room temperature for 2 h.

Table 4. Reactions of the Cinnamoylpalladium Complex **2c** with Various Secondary Amines under CO Pressure

Run	Amine	Product ratio		Total yield (%/Pd)
		α-keto amide	amide	
1	Pr_2NH	46	54	30
2	Et_2NH	87	13	46
3	piperidine	100	0	100
4	pyrrolidine	99	1	80

a) Reactions were carried out by using **2c** (0.05 mmol) and amine (1 mmol) in benzene (3 cm^3) under 50 atm of CO at room temperature for 2 h.

Tables 3 and 4 show effects of amines on the reactions of styryl and cinnamoyl complexes **1c** and **2c**. The reactions listed in the tables were carried out for 2 h under the same reaction conditions. In the reactions of the styryl complex **1c** (Table 3), selectivity for α-keto amide formation decreased in the order of diethylamine > dipropylamine > piperidine > pyrrolidine. The order is approximately similar to the selectivity order of these amines in the catalytic double-carbonylation of aryl halides to the α-keto amides except for the reversal of the order of diethylamine and dipropylamine. The selectivity order is inversely related with the previously observed reactivity order of the secondary amines in the reaction of *trans*-$PhCOPdI(PMePh_2)_2$ with the amines under CO.[1a)] The reactivity order of the amines is also reflected in the values of the total yields in Table 3,[7)] namely the reaction proceeds at higher rate with the more compact and reactive amines, such as piperidine and pyrrolidine, to give more amides rather than α-keto amides. However, examination of the reaction of the amines with the cinnamoylpalladium complex **2c** (Table 4) revealed that the reactivity of the alkenoyl complex differs from that of the aroyl complex.[1a,8)] Whereas the reaction of the benzoylpalladium complex with the amines and CO gave only α-keto amides, the reactions of the cinnamoylpalladium complex **2c** afforded also considerable amounts of amides when less reactive diethylamine and dipropylamine were used even under 50 atm of CO, although at higher pressure over 70 atm of CO the amide formation from **2c** became negligible.

2. Effect of Alkenyl Halide. Similarly to the reactions of **1c** and **2c**, reactions of 1-propenyl- and crotonoylpalladium complexes **1b** and **2b** derived from 1-propenyl bromide with diethylamine were found to give α-keto amide in relatively high selectivity under CO pressure (Table 5, Runs 1 and 4). These results are in contrast with those obtained in the catalytic reactions of 1-propenyl bromide, where no α-keto amide formation was observed (Table 2). Since the difference

Table 5. Reactions of Propenyl (**1b**) and Crotonoylpalladium Complex **2b** with Et_2NH under CO Pressure in the Absence and Presence of Propenyl Halides[a)]

Run	Complex	Additive (equiv/Pd)	Product ratio		Total yield (%/Pd)
			α-keto amide	amide	
1	**1b**	—	65	35	45
2	**1b**	MeCH=CHBr (50)	0	100	88
3	**1b**	MeCH=CHI (10)	0	100	250
4	**2b**	—	62	38	43
5	**2b**	MeCH=CHBr (50)	0	100	41

a) Reactions were carried in benzene under 50 atm of CO at room temperature for 2 h. Initial conditions: complex (ca. 0.05 mmol), Et_2NH (1 mmol), and benzene (3 cm^3).

in the reaction conditions between the stoichiometric and the catalytic reactions is the presence of the excess amount of 1-propenyl bromide in the catalytic systems, we next examined effect of 1-propenyl bromide on the reactions of **1b** and **2b** with diethylamine under CO pressure.

As seen from Table 5, in the presence of 1-propenyl bromide, the α-keto amide formation was completely suppressed and only amide was produced (Runs 2 and 5). Furthermore, in the presence of 1-propenyl iodide, **1b** yielded more than a stoichiometric amount of amide without formation of α-keto amide. The observation strongly suggests that 1-propenyl halides may interact with an intermediate species for α-keto amide formation derived from **2b**, carbon monoxide, and diethylamine to alter the reaction course into amide formation.

Kinetic Study on Amide Formation from Cinnamoylpalladium Complex 2c and Diethylamine in the Absence of Carbon Monoxide. The alkenoyl complexes prepared in the present study were found to have higher tendency to afford amides on interaction with amines than the previously reported aroylpalladium complexes.[1a,8] Therefore, we carried out kinetic examination of the amide formation process using cinnamoyl complex **2c** and diethylamine to get further information on the reaction mechanism.

$$\underset{(\mathbf{2c})}{PhCH=CHCOPd(Br)L_2} + 2HNEt_2 \xrightarrow[\text{toluene}]{\text{dmm}} PhCH=CHCONEt_2 + Pd(dmm)L_2 + H_2NEt_2Br \quad (6)$$

(L=$PMePh_2$, dmm=dimethyl maleate[9])

The reaction of **2c** and diethylamine in toluene containing dimethyl maleate[9] under N_2 atmosphere at 40 °C proceeded obeying the first-order kinetics up to 80% conversion of **2c** and gave a quantitative amount of amide. The first-order rate constant (k_{obsd}) increased with increase in the concentration of Et_2NH, while the reaction was effectively retarded by addition of free $PMePh_2$ to the system (Table 6). The k_{obsd} value was inversely proportional to [$PMePh_2$], the concentration of added $PMePh_2$ (Fig. 1).

Table 6. First-Order Rate Constants (k_{obsd}) for the Reaction of *trans*-Pd(COCH=CHPh)Br($PMePh_2$)$_2$ (**2c**) and Et_2NH in Toluene Containing Dimethyl Maleate at 40 °C[a]

Run	[$HNEt_2$]/ mol l^{-1}	[$PMePh_2$]/ mol l^{-1}	$10^4\,k_{obsd}$/s^{-1}	r[b]
1	0.097	0.0	0.68	0.999
2	0.17	0.0	1.05	0.997
3	0.24	0.0	1.43	0.997
4	0.48	0.0	1.73	0.990
5	0.48	0.0011	0.55	0.993
6	0.48	0.0021	0.32	0.999
7	0.48	0.0053	0.27	1.000
8	0.48	0.016	0.19	0.999
9	0.48	0.027	0.15	0.996

a) Initial conditions: [**2c**]=0.025 mol l^{-1}, [dimethyl maleate]=0.20 mol l^{-1}. b) Correlation coefficient for the first-order plot up to 70% conversion of **2c**.

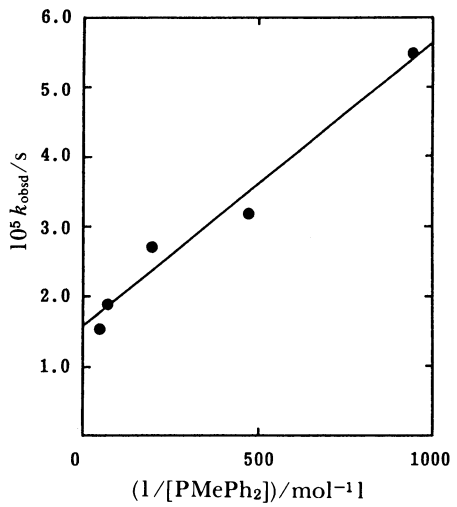


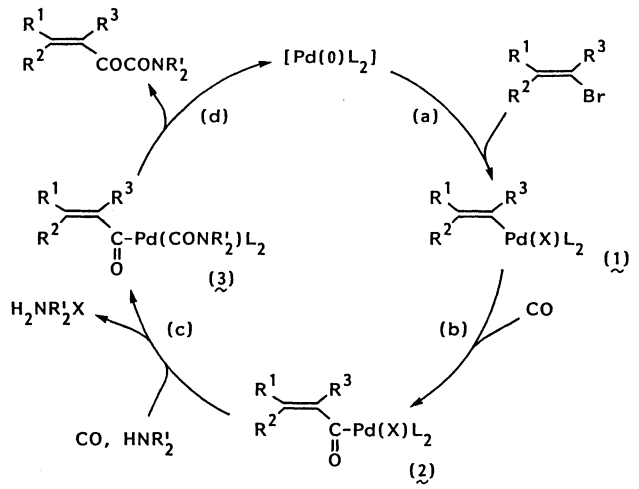
Fig. 1. Plot of k_{obsd} vs. 1/[$PMePh_2$] in the reaction of *trans*-Pd(COCH=CHPh)Br($PMePh_2$)$_2$ (**2c**) and Et_2NH to give amide.

Discussion

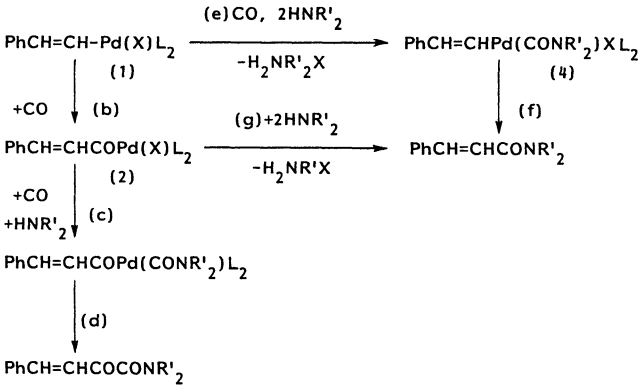
The results obtained in the present study regarding reactivity of the isolated alkenyl- and alkenoylpalladium complexes toward CO and amines support the involvement of these organopalladium species as intermediates in the catalytic system for the α-keto amide formation. Scheme 1 represents a catalytic cycle for the α-keto amide formation proposed on the basis of the present study together with information derived in the previous studies.

The alkenyl complex **1**, which is formed by oxidative addition of alkenyl halide to a [Pd(0)L_2] species, undergoes CO insertion into the Pd-C bond to give an alkenoyl complex **2**. Interaction of **2** with CO and amine gives an alkenoyl(carbamoyl)palladium species **3**, which reductively eliminates α-keto amide accompanied by reproduction of a [Pd(0)L_2] species as a carrier of the subsequent catalytic cycle. Since the oxidative addition of alkenyl halide (process (a) in Scheme 1) and the CO insertion (process (b)) are known to proceed with retention of the original configuration at the alkenyl group,[10] the *Z* to *E* isomerization of the alkenyl group observed in the doublecarbonylation of styryl bromide should occur after formation of **3**. It is likely that the highly electron-withdrawing COCONR′$_2$ group induces the *Z* to *E* isomerization after formation of the α-keto amide.

In the previous studies where the aryl halides have been carbonylated in the presence of CO and amines to give α-keto amides and amides, the formation of α-keto amide was accounted for by a scheme analogous to Scheme 1, whereas the formation of amide was accounted for most reasonably by assuming the reac-



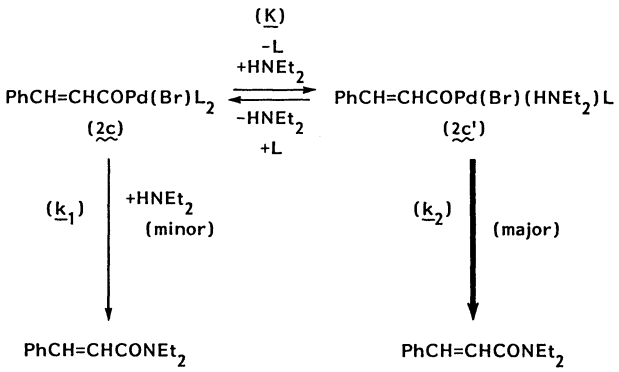
Scheme 1. Proposed mechanism for the palladium-catalyzed double-carbonylation of alkenyl halides and secondary amines to give α-keto amides.



Scheme 2. Possible processes for amide formation in the reaction of alkenylpalladium with secondary amine.

tion of a CO-coordinated arylpalladium complex with amine to give an aryl-carbamoylpalladium complex that subsequently reductively eliminates amide. The results shown in Table 3 regarding the reaction of the styrylpalladium complex **1c** with various amines and CO suggest the operation of similar two routes to give α-keto amide (route b→c→d in Scheme 2) and amide (route e→f).

The formation of α-keto amides in higher yields in the reactions of styryl complex **1c** with amines and CO when less reactive amines are used can be accounted for reasonably by assuming the competitive two routes as in the reaction of the corresponding arylpalladium complexes with CO and the amines. When the reactive amine such as piperidine and pyrrolidine is employed the reaction of the styrylpalladium complex gives amide through the reaction paths (e) and (f), whereas the less reactive amine such as diethylamine and dipropylamine allows the CO insertion to take place through path (b) giving the cinnamoyl complex. Then the reaction of amine with the cinnamoyl complex under CO gives the α-keto amide through paths



Scheme 3. Proposed mechanism for the amide formation in the reaction of *trans*-Pd(COCH=CHPh)-Br(PMePh$_2$)$_2$ (**2c**) and Et$_2$NH.

(c) and (d) as shown in Scheme 2.

However, the results shown in Table 4 and the kinetic studies of the cinnamoylpalladium complex **2c** with the secondary amines indicate that the amides can be formed by the reaction of the cinnamoyl complex with amines, whereas the corresponding reaction of the benzoylpalladium complex with amines and CO gave α-keto amides exclusively.[1a,8] Thus we have to consider another pathway to give amide from the cinnamoyl complex reacting with the amines as shown by path (g) included in Scheme 2.

In fact the kinetic study of the reaction of the cinnamoyl complex **2c** with diethylamine showed that amide can be readily formed in the reaction of **2c** with diethylamine in the absence of CO, the reaction being retarded in the presence of tertiary phosphine. The results of the kinetic study can be accounted for by assuming Scheme 3 where partial dissociation of the tertiary phosphine ligand from **2c** is involved.

In the major path to give the cinnamoyl amide from **2c** on reaction with HNEt$_2$, participation of an amine-coordinated species **2c′** is assumed. The retardation of the amide formation by addition of L suggests that one of the two tertiary phosphine ligands in **2c** is dissociated. The amide formation from the amine-coordinated intermediate complex **2c′** constitutes the main pathway. As indicated by observation of the intercept in Fig. 1, addition of an excess of L does not inhibit the amide formation completely. Thus we have to assume the presence of a minor pathway to give the amide directly from **2c** without partial dissociation of L.

Assumption of a rapid equilibrium between **2c** and **2c′** [11] and the rate-determining formation of amide from **2c** and **2c′** in Scheme 3 leads to the kinetic expressions given by Eqs. 7 and 8, where $K=[\mathbf{2c'}][L]/[\mathbf{2c}][HNEt_2]$ and $[PdCOR]=[\mathbf{2c}]+[\mathbf{2c'}]$.

$$\frac{d[\text{amide}]}{dt} = \frac{k_1[L]+k_2[K]}{[L]+K[HNEt_2]}[HNEt_2][PdCOR] \quad (7)$$

$$k_{obsd} = \frac{k_1[L]+k_2[K]}{[L]+K[HNEt_2]}[HNEt_2] \quad (8)$$

If one can assume [**2c**]≫[**2c'**] in the reaction solution containing an excess amount of added L, k_{obsd} value should be expressed by Eq. 9, because $[L]+K[HNEt_2]=[L](1+[\mathbf{2c'}]/[\mathbf{2c}])\approx[L]$.

$$k_{obsd} = k_1[HNEt_2] + \frac{k_2 K[HNEt_2]}{[L]} \quad (9)$$

Equation 9 is compatible with the kinetic observation as shown in Fig. 1.

The behavior of the crotonoylpalladium complex **2b** with CO and Et_2NH shows a striking difference from that of the cinnamoyl complex as shown in Table 5 in that addition of propenyl halides to the reaction of **2b** with CO and Et_2NH completely inhibits the formation of α-keto amide.

$$\text{MeCH=CHCOPd(X)L}_2 \xrightarrow{+\text{CO, HNEt}_2} \text{MeCH=CHCOCONEt}_2 + \text{MeCH=CHCONEt}_2$$
$$\text{MeCH=CHCOPd(X)L}_2 \xrightarrow[+\text{MeCH=CHX (X=Br, I)}]{+\text{CO, HNEt}_2} \text{only MeCH=CHCONEt}_2 \quad (10)$$

Exclusive formation of amide in the catalytic conversion of alkenyl halides without a phenyl substituent (Table 2) is compatible with the behavior of the alkenoyl complex with CO and $HNEt_2$ in the presence of alkenyl halide. The exact reason for diversion of the reaction course that gives considerable amount of α-keto amide in the reaction of the alkenoyl complex with CO and $HNEt_2$ in the absence of alkenyl halide to that giving only amide is presently unclear and merits the further study.

Experimental

Infrared spectra were measured on a Hitachi 295 spectrometer by using KBr pellets for solid and KBr plates for liquid samples. NMR spectra were measured on JEOL FX-100 and PS-100 spectrometers by Dr. Y. Nakamura and Ms. R. Ito of our laboratory. ^1H NMR signals are referred to Me_4Si as internal standard and $^{31}P\{^1H\}$ NMR signals to PPh_3 as external standard. Microanalysis (C, H, N, and halogen) was carried out by Mr. T. Saito and Dr. M. Tanaka of our laboratory by using Yanagimoto CHN Autocorder Type MT-2 and Yazawa Halogen Analyzer. Mass spectra were measured on a Hitachi M-80 GC-mass spectrometer.

Solvents and amines were dried in the usual manner, distilled, and stored under a nitrogen atmosphere. Vinyl bromide, 1-propenyl bromide, and styryl bromide were used as purchased without further purification. $Ph_2C=CHBr$,[12] $Ph_2C=C(Ph)Br$,[13] $Ph(Me)C=CHBr$,[14] $Me_2C=C(Me)Br$,[15] $CH_2=C(Bu)I$,[16] $CH_2=C(Bu)Br$,[16] $BrCH=C(Me)COOH$,[17] $PhCH=CHI$,[18] $MeCH=CHI$[18] were prepared according to the methods in literature. Dichlorobis(tertiary phosphine)-palladium(II) complexes were prepared by the reactions of $PdCl_2(PhCN)_2$ with corresponding tertiary phosphines.

Catalytic Double-Carbonylation Reactions. A typical procedure (Table 1, Run 5) is as follows: styryl bromide (*Z*/*E*)=1/6.5; (1.0 g, 5.6 mmol) and diethylamine (3.6 cm^3, 34 mmol) were added to a 100 cm^3 stainless steel pressure bottle containing $PdCl_2(Ph_2P(CH_2)_4PPh_2)$ (0.034 g, 0.057 mmol) under nitrogen atmosphere. After evacuation of the system, 50 atm of CO gas was introduced at room temperature, and the mixture was magnetically stirred at 50 °C for 67 h. After purging the CO gas, the reaction solution was analyzed by means of GLC (Shimadzu GC-6A; column, PEG 20M 1 m) by using *o*-terphenyl as internal standard. The GLC analysis revealed the formation of $PhCH=CHCOCONEt_2$ (*E*-form; 70%/styryl bromide) and $PhCH=CHCONEt_2$ (*Z*/*E*=1/10; 30%) at 100% conversion of styryl bromide. 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 catalyst by bulb-to-bulb distillation (Shibata GTO-250R), and identified by means of elemental analysis, IR and NMR spectroscopy, and mass spectrometry. (*E*)-$PhCH=CHCOCONEt_2$: IR (KBr plate) 1640 cm^{-1} (vs); ^1H NMR ($CDCl_3$) δ=1.19 (3H, t, *J*=7 Hz, CH_3), 1.24 (3H, t, *J*=7 Hz, CH'_3), 3.28 (2H, q, *J*=7 Hz, CH_2), 3.25 (2H, q, *J*=7 Hz, CH'_2), 6.85 (1H, d, *J*=16 Hz, =CH), 7.58 (1H, d, *J*=16 Hz, =CH'), and 7.2—7.6 (5H, m, Ph). Found: C, 72.6; H, 7.4; N, 6.0%; M^+, 231. Calcd for $C_{14}H_{17}NO_2$. C, 72.7; H, 7.4; N, 6.1%; M, 231. $PhCH=CHCONEt_2$: Found: C, 76.7; H, 8.5; N, 6.8%; M^+, 203. Calcd for $C_{13}H_{17}NO$: C, 76.8; H, 8.4; N, 6.9%; M, 203.

α-Keto amides and amides prepared in this study gave satisfactory analytical and spectroscopic data. The data for α-keto amides are as follows. $Ph_2C=CHCOCONEt_2$: mp 80 °C; IR (KBr disk) 1640 cm^{-1} (vs); ^1H NMR (CCl_4) δ=0.89 (3H, t, *J*=7 Hz, CH_3), 1.16 (3H, t, *J*=7 Hz, CH'_3), 3.08 (2H, q, *J*=7 Hz, CH_2), 3.11 (2H, q, *J*=7 Hz, CH'_2), 6.72 (1H, s, =CH), and 7.1—7.4 (10H, m, Ph). Found: C, 78.2; H, 6.8; N, 4.6%; M^+, 307. Calcd for $C_{20}H_{21}NO_2$: C, 78.1; H, 6.9; N, 4.6%; M^+, 307. $Ph_2C=C(Ph)COCONEt_2$: mp 118—120 °C; IR (KBr disk) 1680 (s) and 1640 cm^{-1} (vs); ^1H NMR (CCl_4) δ=0.64 (3H, t, *J*=7 Hz, CH_3), 1.16 (3H, t, *J*=7 Hz, CH'_3), 2.98 (2H, q, *J*=7 Hz, CH_2), 3.05 (2H, q, *J*=7 Hz, CH'_2), and 7.0—7.4 (15H, m, Ph). Found: C, 81.5; H, 6.4; N, 3.7%; M^+, 383. Calcd for $C_{26}H_{25}NO_2$: C, 81.4; H, 6.4; N, 3.7%; M^+, 383. (*E*)-$Ph(Me)C=CHCOCONEt_2$: IR (KBr plate) 1680 (s) and 1650 cm^{-1} (vs); ^1H NMR (CCl_4) δ=1.18 (3H, t, *J*=7 Hz, CH_3), 1.23 (3H, t, *J*=7 Hz, CH'_3), 2.61 (3H, s, $=CCH_3$), 3.33 (2H, q, *J*=7 Hz, CH_2), 3.42 (2H, q, *J*=7 Hz, CH'_2), 6.74 (1H, s, =CH), 7.1—7.6 (5H, m, Ph). Found: C, 72.5; H, 7.9; N, 5.6%; M^+, 245. Calcd for $C_{15}H_{19}NO_2$: C, 73.4; H, 7.8; N, 5.7%; M, 245.

Preparation of *trans*-Pd(CH=CH$_2$)Br(PMePh$_2$)$_2$ (la). To a Schlenk tube containing *trans*-$PdEt_2(PMePh_2)_2$[19] (2.12 g, 3.75 mmol) were added toluene (3 cm^3) and styrene (1.7 cm^3, 15 mmol) at −30 °C under nitrogen atmosphere. The heterogeneous white mixture was stirred at 30 °C for 2 h to give a homogeneous pale yellow solution of $Pd(styrene)(PMePh_2)_2$ with evolution of quantitative amounts of ethane and ethene.[5] After cooling the system to −30 °C, $PMePh_2$(0.34 cm^3, 3.75 mmol) and vinyl bromide (1 cm^3, 15 mmol) were added to the solution. On stirring the system at room temperature, a white precipitate was gradually formed from the solution. After 3 h the system was concentrated to almost dryness and 15 cm^3 of Et_2O was added at −30 °C to give a white solid. The solid formed was recrystallized from CH_2Cl_2-Et_2O to yield a white crystalline powder of **la** (2.03 g, 88%): decomp 122—124 °C; ^1H NMR ($CDCl_3$, −40 °C) δ=2.13 (6H, t(br), PCH_3), 4.43 (1H, dt, $^3J_{HH}$=16.6 Hz, $^4J_{HP}$=2.5 Hz, =CH cis to Pd), 5.03 (1H, dt, $^3J_{HH}$=8.8 Hz, $^4J_{HP}$=6.1 Hz, =CH trans to Pd), 5.98 (1H, ddt, $^3J_{HH}$=16.6 and

8.8 Hz, $^3J_{HP}$=10.3 Hz, =CH geminal to Pd), 7.3—7.7 (20H, m, PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, −40 °C) 15.1 ppm (s). Found: C, 54.9; H, 4.9; Br, 12.5%. Calcd for $C_{28}H_{29}P_2BrPd$: C, 54.8; H, 4.8; Br, 13.0%.

Complex **1b** was similarly prepared by using 1-propenyl bromide instead of vinyl bromide (54%): decomp 117—120 °C; ^1H NMR ($CDCl_3$, −50 °C) δ=2.14 (6H, t(br), PMe), 1.06 (3H, m, =CMe), 4.43 (1H, m, =CH cis to Pd), 5.10 (1H, dtq, $^3J_{HH}$=14.9 Hz, $^3J_{HP}$=10.3 Hz, $^4J_{HH}$=1 Hz), 7.3—7.8 (20H, m, PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, −50 °C) 15.8 ppm (s). Found: C, 55.4; H, 4.5; Br, 12.2%. Calcd for $C_{29}H_{31}P_2BrPd$: C, 55.5; H, 5.0; Br, 12.7%.

Preparation of *trans*-Pd(CH=CHPh)Br(PMePh$_2$)$_2$ (1c). To a homogeneous toluene solution of Pd(styrene)-(PMePh$_2$)$_2$ (3.50 mmol, 3 cm^3)[5] was added (*E*)-styryl bromide (1.8 cm^3, 14 mmol)[6] at −30 °C under nitrogen atmosphere. On stirring the system at room temperature, a white precipitate was gradually formed from the solution. After 2 h 10 cm^3 of hexane was added to the system, and the white precipitate formed was collected by filtration, washed with hexane (10 cm^3) and then Et_2O (10 cm^3), and dried in vacuo. The crude product was recrystallized from CH_2Cl_2-Et_2O to yield white crystals of **1c** (2.0 g, 84%): decomp 132—134 °C; ^1H NMR ($CDCl_3$, −40 °C) δ=2.12 (6H, t, *J*=3.4 Hz, PMe), 5.51 (1H, dt, $^3J_{HH}$=15.9 Hz, $^4J_{HP}$=2 Hz, =CH cis to Pd), 6.41 (1H, dt, $^3J_{HH}$=15.9 Hz, $^3J_{HP}$=9.6 Hz, =CH geminal to Pd), 6.3—6.4 (2H, m, =CPh), 7.0—7.1 (3H, m, =CPh), 7.3—7.7 (20H, m, PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, −40 °C) 15.5 ppm (s). Found: C, 58.9; H, 4.9; Br, 12.4%. Calcd for $C_{34}H_{33}P_2BrPd$: C, 59.2; H, 4.8; Br, 11.6%.

Complex **1d** was similarly prepared by using Ph_2C=CHBr instead of styryl bromide (81%): decomp 178—182 °C; ^1H NMR ($CDCl_3$, −40 °C) δ=2.00 (6H, t(br), PMe), 6.62 (1H, t, $^3J_{HP}$=9.4 Hz, =CH), 6.4—6.5 (2H, m, =CPh), 7.0—7.6 (28H, m, PPh and =CPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, =40 °C) 14.6 ppm (s). Found: C, 62.0; H, 5.1; Br, 11.1%. Calcd for $C_{40}H_{37}P_2BrPd$: C, 62.7; H, 4.9; Br, 10.4%.

Preparation of *trans*-Pd(COCH=CH$_2$)Br(PMePh$_2$)$_2$ (2a). To a Schlenk tube containing *trans*-Pd(CH=CH$_2$)Br(PMe-Ph$_2$)$_2$(**1a**; 0.27 g, 0.45 mmol) was added benzene (3 cm^3) under nitrogen atmosphere. After evacuating the system, atmospheric pressure of CO gas was introduced, and the resulted colorless solution was magnetically stirred at room temperature. The color of the solution was quickly changed into yellow. After 2 h, the CO gas was purged and the system was concentrated to almost dryness. Addition of 20 cm^3 of Et_2O to the system at −30 °C gave a yellow precipitate, which was collected by filtration, washed with Et_2O (15 cm^3×3), and dried in vacuo. The yellow powder thus obtained was recrystallized from CH_2Cl_2-Et_2O to yield yellow crystals of **2a** (0.21 g, 67%): decomp 122—125 °C; IR (KBr) 1635 cm^{-1} (vs), ^1H NMR ($CDCl_3$, room temperature) δ=2.11 (6H, t, *J*=3.7 Hz, PMe), 5.19 (1H, ddt, $^3J_{HH}$=17 and 8 Hz, $^4J_{HP}$=1 Hz, =CH geminal to CO), 5.46 (1H, dd, $^3J_{HH}$=8 Hz, $^2J_{HH}$=1 Hz, =CH trans to CO), 6.08 (1H, dd, $^3J_{HH}$=17 Hz, $^2J_{HH}$=1 Hz, =CH cis to CO), 7.2—7.8 (20H, m PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, room temperature) 8.9 ppm (s). Found: C, 53.7; H, 4.6; Br, 13.5%. Calcd for $C_{29}H_{29}OP_2BrPd$: C, 54.3; H, 4.6; Br, 12.5%.

Similarly prepared were *trans*-Pd(COCH=CHMe)Br-(PMePh$_2$)$_2$ (**2b**; 53%) and *trans*-Pd(COCH=CHPh)Br-(PMePh$_2$)$_2$ (**2c**; 75%). **2b**: decomp 131—135 °C; IR (KBr) 1633 cm^{-1} (vs); ^1H NMR ($CDCl_3$, room temperature) δ=2.10 (6H, t, *J*=3.4 Hz, PMe), 1.34 (3H, dd, $^3J_{HH}$=6.8 Hz, $^4J_{HH}$=1.5 Hz, =CMe), 4.91 (1H, dq, $^3J_{HH}$=15.4 Hz, $^4J_{HH}$=1.5 Hz, =CH geminal to CO), 6.68 (1H, dq, $^3J_{HH}$=15.4 Hz, $^3J_{HH}$=6.8 Hz, =CH trans to CO), 7.2—7.9 (20H, m, PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, room temperature) 8.7 ppm (s). Found: C, 55.6; H, 4.9; Br, 12.9%. Calcd for $C_{30}H_{31}OP_2BrPd$: C, 54.9; H, 4.8; Br, 12.2%. **2c**: decomp 132—134 °C; IR (KBr) 1640 cm^{-1} (vs); ^1H NMR ($CDCl_3$, room temperature) δ=2.12 (6H, t, *J*=3.5 Hz, PMe), 5.48 (1H, dt, $^3J_{HH}$=15.9 Hz, $^4J_{HP}$=1.5 Hz, =CH geminal to CO), 7.1—7.2 (2H, m, =CPh), 7.3—8.1 (24H, m, PPh, =CPh, and =CH cis to CO); $^{31}P\{^1H\}$ NMR ($CDCl_3$, room temperature) 9.0 ppm (s). Found: C, 57.9; H, 4.6; Br, 11.2%. Calcd for $C_{35}H_{33}OP_2BrPd$: C, 58.6; H, 4.6; Br, 11.1%.

Preparation of *trans*-Pd(COCH=CPh$_2$)Br(PMePh$_2$)$_2$ (2d). To a test tube containing *trans*-Pd(CH=CPh$_2$)Br(PMePh$_2$)$_2$ (**1d**; 0.21 g, 0.28 mmol) was added 3 cm^3 of benzene under nitrogen atmosphere. The test tube was placed in a 100 cm^3 stainless steel pressure bottle, and 10 atm of CO gas was introduced at room temperature. After the system was stirred for 8 h at room temperature, the CO gas was purged and the resulted reddish yellow solution was replaced into a Schlenk tube. The solution was concentrated to ca. half in volume. Addition of 20 cm^3 of hexane to the system yielded a yellow powder, which was recrystallized from CH_2Cl_2-Et_2O to give yellow crystals of **2d** (0.43 g, 43%): decomp 179—183 °C; IR (KBr) 1651 cm^{-1}; ^1H NMR ($CDCl_3$, room temperature) δ= 2.12 (6H, t, *J*=3 Hz, PMe), 6.60 (1H, s, =CH), 6.33 (2H, dd, *J*= 8 and 1 Hz, =CPh), 6.72 (2H, dd, *J*=8 and 1 Hz, =CPh′), 6.9—7.8 (26H, m, =CPh, =CPh′ and PPh); $^{31}P\{^1H\}$ NMR ($CDCl_3$, room temperature) 7.7 ppm (s). Found: C, 62.0; H, 5.1; Br, 11.1%. Calcd for $C_{41}H_{37}OP_2BrPd$: C, 62.0; H, 4.7; Br, 10.1%.

Reactions of Organopalladium Complexes with CO and Amines. General Procedure. To a test tube containing an organopalladium complex (ca. 0.05 mmol) were added benzene (3 cm^3), amine (1 mmol), and/or the additive under nitrogen atmosphere. The test tube was placed in a 100 cm^3 stainless steel pressure bottle, and CO gas was introduced at room temperature. After the system was magnetically stirred at room temperature for 2 h, the CO gas was quickly purged and the reaction solution was analyzed by means of GLC.

Kinetic Study on the Amide Formation from 2c and Et$_2$NH. To a Schlenk tube containing **2c** (ca. 25 mmol) and *o*-terphenyl (ca. 0.17 mmol) as an internal standard for GLC analysis, were added toluene (10 cm^3) and adequate amounts of Et_2NH and $PMePh_2$ under argon atmosphere. The Schlenk tube was placed in a thermostated bath (HAAKE F2) controlled to 40.0±0.5 °C. At intervals, a part of the reaction solution (ca. 0.1 cm^3) was sampled and quickly added into an aqueous HCl solution (ca. 1 mol dm^{-1}, 0.5 cm^3) for quenching the reaction. The organic layer separated out from the aqueous solution was analyzed by means of GLC.

The present work was supported by a Grant-in-Aid for Developmental Scientific Research from the Ministry of Education, Science and Culture (No. 62850147).

References

1) a) F. Ozawa, H. Soyama, H. Yanagihara, I. Aoyama, H. Takino, K. Izawa, T. Yamamoto, and A. Yamamoto, *J. Am. Chem. Soc.*, **107**, 3235 (1985); b) F. Ozawa, H. Yanagihara, and A. Yamamoto, *J. Org. Chem.*, **51**, 415 (1986); c) F. Ozawa, H. Soyama, T. Yamamoto, and A. Yamamoto, *Tetrahedron Lett.*, **23**, 3383 (1982); T. Kobayashi and M.

Tanaka, *J. Organomet. Chem.*, **233**, C64 (1982).

2) F. Ozawa, N. Kawasaki, H. Okamoto, T. Yamamoto, and A. Yamamoto, *Organometallics*, **6**, 1640 (1987); F. Ozawa, N. Kawasaki, T. Yamamoto, and A. Yamamoto, *Chem. Lett.*, **1985**, 567; M. Tanaka, T. Kobayashi, T. Sakakura, H. Itatani, S. Danno, and K. Zushi, *J. Mol. Catal.*, **32**, 115 (1985); B. Morin, A. Hirschauer, F. Hugues, D. Commereuc, and Y. Chauvin, *ibid.*, **34**, 317 (1986).

3) M. Tanaka, T. Kobayashi, and T. Sakakura, *J. Chem. Soc., Chem. Commun.*, **1985**, 837; T. Kobayashi, T. Sakakura, and M. Tanaka, *Tetrahedron Lett.*, **28**, 2721 (1987).

4) A. Schoenberg and R. F. Heck, *J. Org. Chem.*, **39**, 3327 (1974); A. Schoenberg, I. Bartoletti, and R. F. Heck, *ibid.*, **39**, 3318 (1974).

5) F. Ozawa, T. Ito, Y. Nakamura, and A. Yamamoto, *J. Organomet. Chem.*, **168**, 375 (1979).

6) M. K. Loar and J. K. Stille, *J. Am. Chem. Soc.*, **103**, 4174 (1981).

7) Since it has been confirmed that the reactions with less reactive Et_2NH and Pr_2NH yield quantitative amounts of α-keto amide and amide at extended reaction time, the values of total yields obtained after the reactions for 2 h at room temperature can be used as a measure of the reactivity of the amines.

8) F. Ozawa, T. Sugimoto, Y. Yuasa, M. Santra, T. Yamamoto, and A. Yamamoto, *Organometallics*, **3**, 683 (1984).

9) In the absence of dimethyl maleate (dmm), Reaction 6 did not proceed according to the first-order kinetics, probably due to interference by a $[Pd(0)L_2]$ species generated in the reaction. Since dmm serves as a good trapping agent of$[Pd(0)L_2]$ species to from stable $Pd(dmm)L_2$ complex,[5] the reaction was followed in the presence of dmm to get a well behaved kinetic results.

10) J. K. Stille and K. S. Y. Lau, *Acc. Chem. Soc.*, **10**, 434 (1977); T. C. Flood, "Stereochemistry of Reactions of Transition Metal-Carbon Sigma Bonds," in "Topics in Stereochemistry, Vol. 12," ed by G. L. Geoffroy, N. L. Allinger, and E. L. Eliel, Wiley, New York (1981), p. 37.

11) Occurrence of the rapid equilibrium between **2c** and **2c'** has been confirmed by observing the ^1H NMR spectrum of **2c** at room temperature in toluene-d_8. In the absence of Et_2NH, methyl protons of $PMePh_2$ ligands in **2c** gave a triplet due to virtual coupling of the phosphorus nuclei, while the PMe-protons were observed as a broad singlet in the presence of Et_2NH.

12) E. P. Kohler and M. Tishler, *J. Am. Chem. Soc.*, **57**, 217 (1935).

13) C. F. Koelsch, *J. Am. Chem. Soc.*, **54**, 2045 (1932).

14) D. R. Davis and J. R. Roberts, *J. Am. Chem. Soc.*, **84**, 2252 (1962).

15) J. I. Kim, B. A. Patel, and R. F. Heck, *J. Org. Chem.*, **46**, 1067 (1981).

16) B. A. Patel, J. I. Kim, D. D. Bender, L. C. Kao, and R. F. Heck, *J. Org. Chem.*, **46**, 1061 (1981).

17) C. Kolbe, *J. Prakt. Chem.*, **25**, 382 (1882).

18) K. Takagi, N. Hayama, and S. Inokawa, *Chem. Lett.*, **1978**, 1435.

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