Studies Relevant to Palladium-Catalyzed Carbonylation Processes. Mechanisms of Formation of Esters and Amides from Benzylpalladium and (Phenylacetyl)palladium Complexes on Reactions with Alcohols and Amines

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Benzylpalladium and (phenylacetyl)palladium complexes having two PMe_3 or PPh_3 ligands or a dppe ligand (P2-type complexes) have been prepared as models to study the mechanisms of carbonylation reactions to convert benzyl halides into single and double carbonylation products. Removal of one of the tertiary phosphine ligands in the P2-type monophosphine complexes, *trans*-$PdCl(COCH_2Ph)(PR_3)_2$ (R = Ph, Me), by treatment with $PdCl_2(PhCN)_2$ led to the P1-type chloride-bridged dimers $[PdCl(COCH_2Ph)(PR_3)]_2$, which were split on interaction with secondary amines to give amine-coordinated complexes, $PdCl(COCH_2Ph)(PR_3)(NHEt_2)$. Examination of the reactions of the (phenylacetyl)palladium complexes with secondary amines and alcohols provided evidence for operation of different types of mechanisms for yielding amides and esters. The amide formation proceeds faster when more basic secondary amine is used. The process is proposed to proceed through coordination of the amine to palladium followed by its nucleophilic attack on the acyl group aided by a base. On the other hand, the ester formation from the (phenylacetyl)palladium complex proceeds more readily when more acidic alcohols were used. The formation of the ester is compatible with the reaction mechanism proceeding through an intermediate acyl−alkoxide complex. For the amide formation from the benzylpalladium complexes on reactions with secondary amines *under CO pressure*, operation of two routes has been revealed; one involves the attack of an amine on the CO-coordinated benzylpalladium species to give a benzyl(carbamoyl)palladium intermediate, and the other involves (phenylacetyl)(amine)palladium species, each giving the amide on reductive elimination or amine migration to the acyl ligand. Competition reactions using mixtures of secondary amines and alcohols toward the acylpalladium complexes furnished the supporting evidence for the reaction mechanisms to give esters involving the reductive elimination of phenylacetyl−alkoxide intermediates.

Introduction

Palladium-catalyzed carbonylation of organic halides to give carboxylic acids, esters, and amides has been extensively used for production of carbonyl-containing compounds in laboratory synthesis as well as in industrial processes.[1] Aryl halides have been used most extensively, whereas successful catalytic carbonylation of aliphatic halides are limited to allylic halides[2,3] and fluorinated alkyl halides.[4] To expand the scope of application of the carbonylation process, it is necessary to explore the possibility of utilizing aliphatic substrates on the basis of information regarding the reactivities of model organopalladium complexes that are considered to be involved in the possible catalytic processes.

From the mechanistic studies reported so far, it is generally accepted that an organopalladium halide (**B**) is produced by oxidative addition of an organic halide to a Pd(0) species (**A**) formed in the catalytic system (Scheme 1) but the later course of the catalytic reaction may vary depending on the nucleophiles and reaction conditions employed.

The most often assumed process involves migratory insertion of a coordinated carbon monoxide ligand in **C** to give an acylpalladium halide (**D**), which reacts further with a nucleophile (NuH) and a base to liberate RCONu

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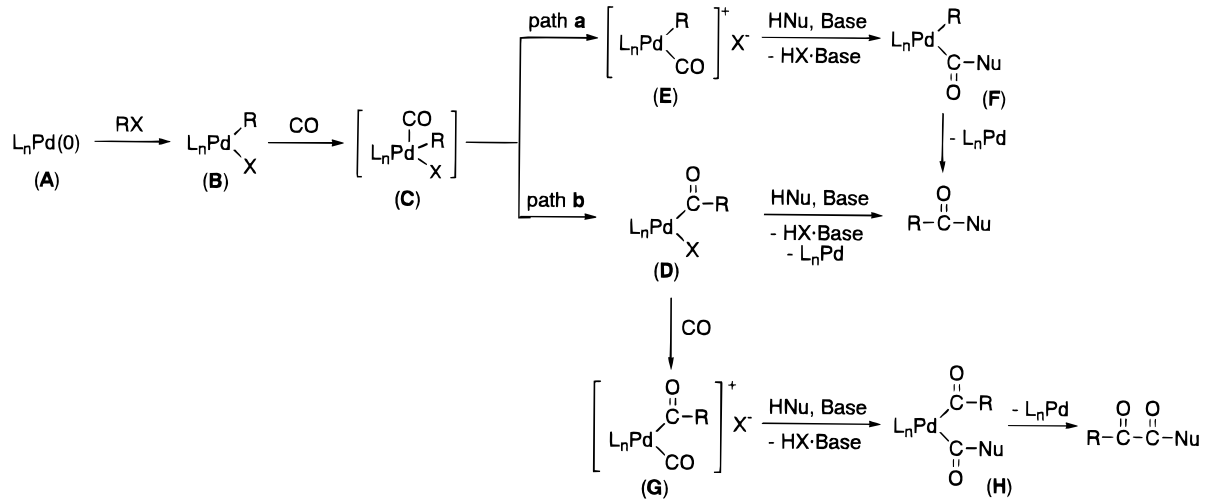
Scheme 1[a]



[a] L = tertiary phosphine, X = halide, HNu = HNR_2, HOR, or H_2O.

as carboxylic acid, ester, or amide, depending on the nucleophile (path **b**, Scheme 1).[1] The alternative route to path **b** is displacement of the halide ligand in **C** by CO to give a CO-coordinated cationic organopalladium species (**E**)[5] that undergoes the nucleophilic attack in the presence of a base to give an organo(acyl)palladium species (**F**).[6] Reductive elimination from **F** liberates RCONu as the carboxylic acid or its derivatives (path **a**, Scheme 1). A previous study using trimethylphosphine-coordinated phenylpalladium complexes, which gave phenyl(carbamoyl)palladium complexes on treatment with diethylamine under CO, provided the supporting evidence for path **a** involving the reductive elimination of the aryl and carbamoyl ligands.[6a] It was further demonstrated that combination of the CO insertion into the organopalladium bond to give the acylpalladium complex **D** with attack of a nucleophile on the coordinated CO in **G** to give a bis(acyl)-type palladium complex (**H**) provides the route to α-keto amides and esters, respectively, by reductive elimination of the acyl and the carbamoyl or of the acyl and alkoxycarbonyl ligands (Scheme 1).[6a,7] However, very few reports have been made to support the operation of path **a**, whereas operation of path **b** involving the acyl intermediate has been implicitly assumed in most of the catalytic carbonylation processes without sound experimental evidence supporting the mechanism.

In our attempts to achieve catalytic double carbonylation of aliphatic substrates, we have found that allylic chlorides can be successfully double-carbonylated to give α-keto amides[3] whereas attempts of palladium-catalyzed carbonylation of alkyl halides have, so far, been unsuccessful because of the direct conversion of alkyl halides with secondary amines to tertiary amines.

Benzyl halides are considered as the next candidates after allylic halides to examine their reactivities for achieving the carbonylation of aryl-substituted aliphatic compounds, since benzylic compounds have an allylic nature and are situated between the purely aromatic and aliphatic compounds. Since Heck,[8] Stille,[9] and Hidai[10] first reported that benzyl chloride and bromide were converted into phenylacetates under CO pressure in the presence of palladium catalysts in alcohols, many studies have been made on the single carbonylation of benzyl halides catalyzed by palladium complexes.[1a,c] Milstein presented the evidence to support operation of the mechanism proceeding through CO insertion into the benzyl−palladium bond followed by alcoholysis.[11] However, no detailed analysis of the *alcoholysis* process has been provided.

Concerning the formation of methyl benzoate from bromobenzene and CO in the presence of methanol and bases, Moser proposed a mechanism involving formation of a methoxide anion that attacks the benzoylpalladium complex.[12] On the other hand, Alper has reported a dimeric acylpalladium complex as an intermediate for

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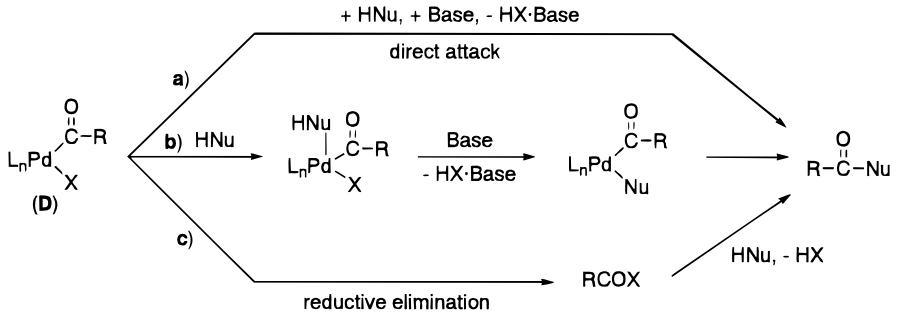
Scheme 2[a]



[a] L = tertiary phosphine; X = halide; HNu = HOR′, HNR_2'', and HOH.

the formation of carboxylic acid anion in the presence of an alkali.[13]

Our preliminary examination of the catalytic carbonylation of benzyl halides with methanol and a base showed that methyl phenylacetate was obtained as a single carbonylation product, but no double carbonylation product was formed.[14] On the other hand, our recent study showed that benzyl alcohol and its analogues can be catalytically converted into phenylacetic acid and its analogues by a palladium-catalyzed carbonylation in the presence of hydrogen iodide.[15] Detailed studies on the reaction mechanism revealed that benzyl iodide, produced in situ from benzyl alcohol and HI, forms a benzylpalladium iodide and that the subsequent CO insertion affords (phenylacetyl)palladium iodide. Phenylacetyl halides were found to be liberated from the (phenylacetyl)palladium halides by reductive elimination, and its subsequent hydrolysis under acidic conditions gave phenylacetic acid and hydrogen halides.[15b]

This finding prompted us to examine the behavior of the benzylpalladium halide and (phenylacetyl)palladium halide complexes toward CO and various nucleophiles for gaining further information to achieve catalytic carbonylation and, if possible, double carbonylation of benzylic substrates.

There are three possible paths that should be considered for formation of the carbonylation products from an acylpalladium complex, as shown in Scheme 2. The first is the direct attack of a nucleophile NuH on the acyl group in the acylpalladium intermediate **D** (route **a**). This is the process intuitively assumed in analogy with the behavior of simple carbonyl-containing organic compounds. The second possible route involves coordination of a nucleophile to the palladium center followed by deprotonation of the precoordinated nucleophile HNu by a base. The process is followed by reductive elimination of the acyl and Nu ligands to give acid derivatives, RCONu (route **b**). The third possibility is direct reductive elimination of an acyl halide, which is subsequently attacked by the nucleophile to give amide, ester, or carboxylic acid (route **c**).

There are limited reports of organometallic studies on the formation of ester via a reductive elimination from an acyl(alkoxy)palladium complex. An acyl(aryloxy)palladium(II) complex has been prepared, and its reductive elimination to give an ester has been studied.[16] The mechanism for the formation of ester from a three-coordinate benzoylpalladium alkoxide has been proposed based on the kinetic studies.[7a] In this paper, we report the results of detailed studies of the courses of the reactions of nucleophiles with benzyl and (phenylacetyl)palladium complexes that are regarded as catalyst models of palladium-catalyzed carbonylation reactions of benzylic compounds.

Results

Preparation of Benzyl- and (Phenylacetyl)palladium Complexes Having Mono- and Bis-Phosphine Ligands. Chart 1 summarizes the benzyl- and (phenylacetyl)palladium complexes prepared in the present study for examining their properties relevant to carbonylation processes. The complexes include those prepared specifically for the present study as well as some of the reported complexes and their analogues having different tertiary phosphine ligands. To understand the effect of the tertiary phosphine ligands, we have prepared the benzyl- and (phenylacetyl)palladium complexes having two (P2-type) and one (P1-type) tertiary phosphine ligand(s), respectively.

The P2-type *trans*-(η^1-benzyl)bis(triphenylphosphine)-palladium(II) halides (**1**) were prepared by oxidative addition of benzyl halides to $Pd(PPh_3)_4$.[17] Their analogous complex (**2**) having two PMe_3 ligands was synthesized by the reaction of $Pd(PMe_3)_2$(styrene) with benzyl chloride.[15b]

Since the η^1-benzylpalladium halide complexes can be isomerized into η^3-type isomers with dissociation of the halide ligands, it is necessary to understand the behavior of the η^3-benzylpalladium complexes. Thus, cationic η^3-type complexes **3** and **4** were prepared by treating **1a** and **2** with $AgPF_6$.[15b]

Whereas the insertion of CO into the benzyl−palladium bond gives the (phenylacetyl)palladium complexes, pure (phenylacetyl)palladium chloride complex **8** was prepared by an independent route involving oxidative addition of $PhCH_2COCl$ with $Pd(PPh_3)_4$.[18]

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(14) For example, carbonylation of benzyl bromide catalyzed by $PdCl_2(PPh_3)_2$ (2 mol %) in the presence of proton sponge in methanol under high CO pressure (100 atm) at 60 °C gave methyl phenylacetate in 70% yield together with methyl benzyl ether (28%): Lin, Y.-S.; Yamamoto, A. Unpublished results.

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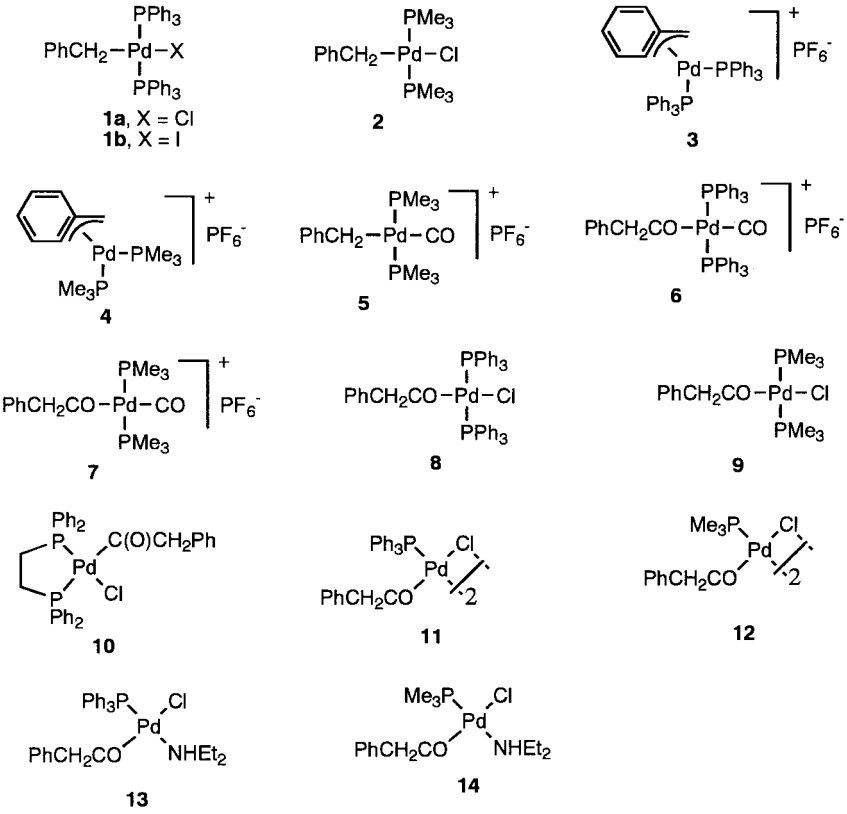
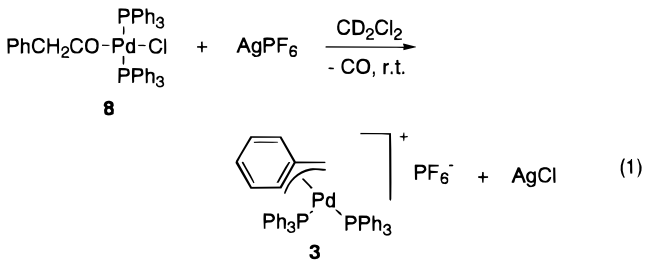
Chart 1. Benzyl- and (Phenylacetyl)palladium Complexes



Analogues of **8** having PMe_3 and dppe (dppe = 1,2-bis(diphenylphosphino)ethane) ligands, **9** and **10**, were prepared by replacement of the PPh_3 ligands in **8** with PMe_3 and dppe ligands, respectively (see Experimental Section).

The CO-coordinated η^1-benzylpalladium complex **5** can be prepared by treatment of the η^3-benzylpalladium complex **4** with CO (10 atm) at −80 °C.[15b] The subsequent increase in the temperature above −40 °C leads to CO insertion into the benzyl−palladium bond to give the CO-coordinated (phenylacetyl)palladium complex **7**. The corresponding PPh_3-coordinated cationic η^3-benzylpalladium complex **3** undergoes the CO insertion more readily than the PMe_3-coordinated analogue **4** to give the CO-coordinated cationic (phenylacetyl)palladium complex **6** without showing the sign of formation of a CO-coodinated η^1-benzylpalladium intermediate corresponding to **5**.[19] Release of CO gas from solutions containing **6** and **7** yields the starting cationic η^3-benzylpalladium complexes **3** and **4** with a faster decarbonylation rate for the PPh_3-coordinated complex **6**.[19] The neutral *trans*-(phenylacetyl)palladium chloride complex **8** also shows a trend to decarbonylate and to be converted into the η^3-benzylpalladium complex. Addition of an equilmolar amount of $AgPF_6$ to a CD_2Cl_2 solution of **8** at room temperature immediately gave the decarbonylation product **3**, as observed by ^1H and ^{31}P NMR and IR (eq 1). The result suggests that creation



(1)

of a vacant site on the palladium center accelerates the decarbonylation. Acceleration of the decarbonylation of the 3-butenoylpalladium bromide complex by removal of the halide with $AgBF_4$ was previously reported.[20]

For evaluation of the effect of tertiary phosphine ligands, it was necessary to prepare the (phenylacetyl)palladium complexes having one phosphine ligand per palladium. The chloride-bridged P1-type complexes **11** and **12** were prepared as dimers by treatment of the P2-type (phenylacetyl)palladium complexes **8** and **9** with $PdCl_2(PhCN)_2$ in a way similar to the preparation of the corresponding $[PdCl(CH_2Ph)(PPh_3)]_2$,[21] as shown in eq 2.[22]

Amine-coordinated complexes of the P1 type, **13** and **14**, can be obtained by addition of 2 mol of Et_2NH per 1 mol of the corresponding dimeric complexes **11** and **12** (eq 3).

(19) The reactions of complexes **3** and **4** with ^{13}CO (10 atm) were performed as described in ref 15b. At −80 °C, the reaction of the trimethylphosphine-coordinated complex **4** with ^{13}CO (10 atm) to give CO-coordinated complex **5** was first order in **4** ($k_{obs}^{-80°C} = (3.2 \pm 0.1) \times 10^{-5}$ s^{-1}). The first-order rate law was also obeyed in the conversion of complex **5** to **7** at −40 °C ($k_{obs}^{-40°C} = (3.3 \pm 0.2) \times 10^{-4}$ s^{-1}). On the other hand, conversion of complex **4** to **7** was also found to be a first-order process at −40 °C ($k_{obs}^{-40°C} = (7.7 \pm 0.1) \times 10^{-5}$ s^{-1}). The reaction of **3** with ^{13}CO to give **6** at −40 °C was first order ($k_{obs}^{-40°C} = (1.9 \pm 0.1) \times 10^{-4}$ s^{-1}) and faster than that of **4** with ^{13}CO. NMR data assigned for **6**: ^1H NMR (270 MHz, δ, CD_2Cl_2, 233 K) 7.6−7.2 (m, 30H, PPh_3), 6.73 (t, J = 8 Hz, 3H, Ph), 5.77 (s br, 2H, Ph), 3.34 (s, 2H, PhCH_2−). ^{13}C NMR (67.9 MHz, δ, CD_2Cl_2, 233 K): 227.5 (s br, $^{13}COCH_2Ph$), 179.6 (s br, ^{13}CO). ^{31}P NMR (109.4 MHz, δ, CD_2Cl_2, 233 K): 17.3 (s), −144.3 (sept, J = 710 Hz).

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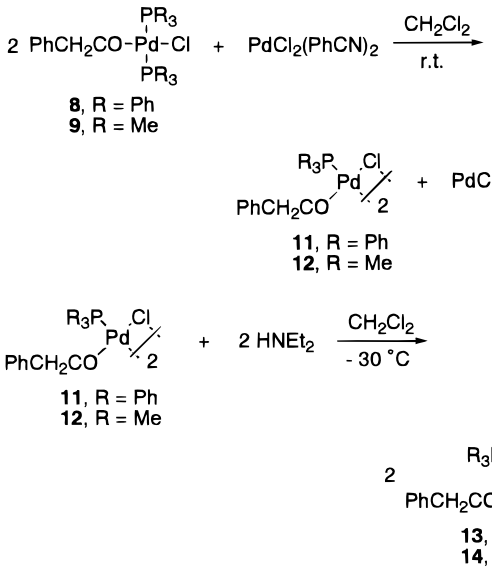


Both complexes can be isolated almost quantitatively at low temperature. However, they are slowly decomposed at room temperature. In the solid state, both **13** and **14** are gradually decomposed at room temperature in air in several days, releasing $HNEt_2$ and generating an unidentified black solid and the amine-free dimer **12**. The decomposition of **13** is faster than that of **14**. In solution, $PhCH_2CONEt_2$ (**15**) was formed on decomposition of **13** and **14** (see below). Coordination of amine to the palladium atom in complexes **13** and **14** was confirmed by ^1H NMR. Proton signals of the ethyl groups in Et_2NH were observed at lower field than that in free Et_2NH, and the protons in the methylene moiety in Et_2NH exhibited two different resonances at lower temperatures, at δ 2.63 and 2.52 as broad singlets at −50 °C for **13** and at δ 2.65 and 2.47 as broad singlets at −80 °C for **14**, respectively. The cis arrangement of the phenylacetyl group and the phosphine ligand in complex **13** was concluded by observation of the coupling of the methylene carbon in the benzylic group with phosphorus with a coupling constant of 21 Hz in the $^{13}C\{H\}$ NMR spectrum of **13**. The coupling constant is reasonable for the cis configuration by comparison with $^3J_{C-P}$ values in the dppe-coordinated complex **10**, $^3J_{C-P(cis)} = 19$ Hz and $^3J_{C-P(trans)} = 37$ Hz. With reference to the previously reported arylpalladium complexes having one phosphine and one amine ligand,[23] the trans disposition of the PR_3 (R = Ph and Me) and Et_2NH ligands in complexes **13** and **14**, as represented in Chart 1, was deduced. Various amine-coordinated (β-aminoacyl)-palladium complexes have been previously prepared, and mutual cis arrangement of the coordinated amine and the acyl groups has been confirmed.[24]

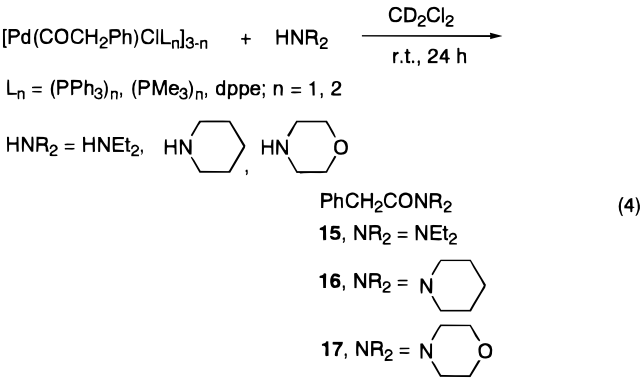
Table 1. Reaction of (Phenylacetyl)palladium(II) Complexes with Secondary Amines[a]

entry	complex	amine	$PhCH_2CONR_2$ (mol %/Pd)[b]
1	**8**	Et_2NH	88[c]
2	**9**	Et_2NH	0[d]
3	**11**	Et_2NH	76[c]
4	**12**	Et_2NH	4[d]
5	**10**	Et_2NH	82[c]
6	**8**	piperidine	84
7	**8**	morpholine	68[e]

[a] Reaction conditions: palladium complex (0.04 mmol in Pd) in CD_2Cl_2 (0.6 mL) was treated with amine (0.4 mmol) at room temperature. [b] Determined by ^1H NMR after 1 day ($PhSiMe_3$ as an internal reference). [c] A trace of $PhCH_2COO^-$ was detected. [d] $(PhCH_2)_2$ was detected in 3 days in entries 2 (10 mol %) and 4 (6 mol %). [e] 22% of **8** unreacted.

When the P1-type, diethylamine-coordinated complex **13** was treated with an equilmolar amount of PPh_3 in CD_2Cl_2, instant formation of *trans*-$PdCl(COCH_2Ph)(PPh_3)_2$ (**8**) and release of a quantitative amount of Et_2NH occurred, as confirmed by the analysis of ^1H and ^{31}P NMR spectra.

Reactions of the (Phenylacetyl)palladium Complexes with Nucleophiles in the Absence of CO. (1) Reactions with Secondary Amines. To examine the reaction courses of (phenylacetyl)palladium complexes toward various nucleophiles, the neutral, mono-phosphine-coordinated (phenylacetyl)palladium complexes, **8**, **9**, **11**, and **12**, and the dppe-coordinated complex, **10**, were subjected to reactions with Et_2NH, piperidine, and morpholine (eq 4 and Table 1). The results show a



marked influence of the tertiary phosphine ligands employed. The PPh_3-coordinated complexes **8** (entry 1) and **11** (entry 3) produced amide **15** in high yields, whereas the less electrophilic PMe_3-coordinated complexes **9** and **12** were found to be much less reactive (entries 2 and 4).

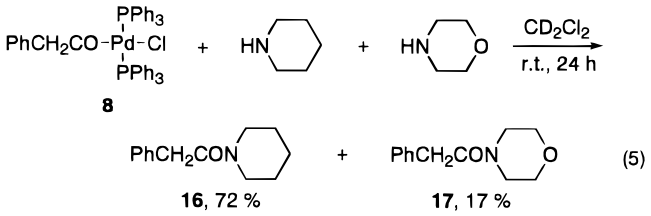
On the other hand, the dppe-coordinated complex **10** exhibited a reactivity similar to complexes **8** and **11** having the PPh_3 ligand(s). The results suggest that the basicity of the tertiary phosphine ligands has a decisive influence on the reactivity of the (phenylacetyl)palladium complexes toward $HNEt_2$. A decrease in the reactivity of benzoylpalladium complexes, *trans*-$PdX(COPh)(PR_3)_2$ (X = Cl and Br), on replacement of the PPh_3 with $PMePh_2$ was previously noted.[6b]

(22) Two types of isomers arising from a different arrangement of the two (phenylacetyl)palladium moieties in the dimers **11** and **12** can be observed in the ^{31}P NMR at −40 °C as two singlets at 27.3 and 26.6 ppm in a 3:1 ratio for **11** and at −5.8 and −6.4 ppm in a 2:3 ratio for **12**. At higher temperatures, these peaks coalesce to a broad singlet at − 9 °C for **11** and at 2 °C for **12**. From the Eyring equation, $\Delta G^{\ddagger}_{264K} = 50.5 \pm 0.2$ kJ/mol for **11** and $\Delta G^{\ddagger}_{275K} = 52.7 \pm 0.2$ kJ/mol for **12** were derived. The values indicate easier interconversion between the trans and cis isomers for the PPh_3-coordinated complex **11** than for the PMe_3-coordinated complex **12**.

(23) (a) Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030. (b) Widenhoefer, R. A.; Zhong, H. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 2745.

(24) (a) Hegedus, L. S.; Siirala-Hansén, K. *J. Am. Chem. Soc.* **1975**, *97*, 1184. (b) Hegedus, L. S.; Anderson, O. P.; Zetterberg, K.; Allen, G.; Siirala-Hansén, K.; Olsen, D. J.; Packard, A. B. *Inorg. Chem.* **1977**, *16*, 1887. (c) Ozawa, F.; Nakano, M.; Aoyama, I.; Yamamoto, T.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1986**, 382.

The nature of the secondary amine as a nucleophile also affects the reaction. Piperidine, having a pK_a value (of its conjugate acid in aqueous solution)[25] of 11.123 similar to 11.02 of $HNEt_2$, reacts with **8** in 1 day at room temperature, giving the phenylacetyl piperidine (**16**) in 84 mol %/Pd (entry 6, Table 1), whereas less basic morpholine (pK_a = 8.33) yields phenylacetyl morpholine (**17**) in 68 mol %/Pd in 1 day, leaving 22 mol % of **8** unreacted (entry 7). When an equimolar mixture of piperidine and morpholine was allowed to react with **8**, the reactivity of piperidine was found to be higher than that of morpholine, giving **16** as the major product (eq 5).



(5)

In the course of reaction of the P2-type (phenylacetyl)-palladium halide complexes with secondary amines, displacement of part of the phosphine ligands with the secondary amine is a probable process. In fact, formation of the amine-coordinated complex **13** as a transient intermediate was observed in the reaction of the P2-type complex **8** with $HNEt_2$.

The amine-coordinated complex **13** was found to be decomposed in CD_2Cl_2 at room temperature to give amide **15** in 41 mol %/Pd in 3 days. The reaction was accompanied by formation of $(PhCH_2)_2$ (8 mol %), indicating occurrence of decarbonylation from **13** followed by coupling of the benzyl moiety. When 10 mol of NEt_3 was added per 1 mol of palladium in **13**, the yield of the amide was increased to 80 mol %/Pd. On the other hand, employment of a more bulky proton sponge proved to be less effective, giving 43 mol % of the amide/Pd. Complex **14**, the PMe_3-coordinated analogue of **13**, was less susceptible to decomposition and released the amide in 15 mol %/Pd in 3 days at room temperature with 45 mol % of **14** remaining undecomposed. In addition to the amide, $(PhCH_2)_2$ (6 mol %/Pd) and $PhCH_2Cl$ (8 mol %/Pd) together with the P2-type complex **9** (6 mol %/Pd) were formed in the reaction system.

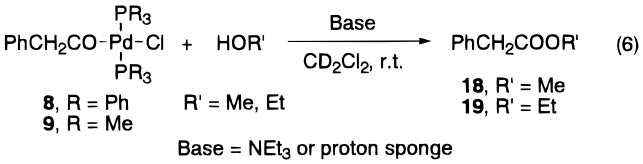
(2) Reactions with Alcohols in the Presence of Tertiary Amines. Table 2 summarizes the results of the reactions of the acylpalladium complexes **8** and **9** with mixtures of alcohols and tertiary amines. The treatment of the PPh_3-coordinated P2-type complex **8** with methanol and ethanol, respectively, in combination with NEt_3 afforded the methyl and ethyl phenylacetates (**18** and **19**) in high yields (eq 6 and entries 1 and 2 in Table 2). In contrast, the reactivity of the PMe_3-coordinated acylpalladium complex **9** toward the alcohols and NEt_3 was much less (entries 4 and 5).[26]

In contrast to NEt_3, which proved effective as a base in the reactions of **8** with alcohols, the proton sponge, a strongly basic but bulkier tertiary amine, proved to be much less effective (entry 3).

Table 2. Reactions of Alcohols toward 8 and 9 in the Presence of Tertiary Amines[a]

		additives (10 mol/Pd)		$PhCH_2COOR$
entry	complex	HOR	NR_3	(mol %/Pd)[b]
1	**8**	HOMe	NEt_3	87[c]
2	**8**	HOEt	NEt_3	79[d]
3	**8**	HOEt	proton sponge	6
4	**9**	HOMe	NEt_3	trace(43)[c,e]
5	**9**	HOEt	NEt_3	0(10)[c,e]

[a] Reaction conditions: the palladium complex (0.03 mmol) in CD_2Cl_2 was treated with alcohol (0.30 mmol) and amine (0.30 mmol) at room temperature. [b] Determined by ^1H NMR after 24 h ($PhSiMe_3$ as an internal reference). [c] A trace of $PhCH_2COO^-$ was detected. [d] $PhCH_2COO^-$ (5%) was detected. [e] The data in the parentheses are the yields measured after the reaction for 3 days at room temperature.



(6)

(3) Competitive Reactions of Secondary Amines and Alcohols toward (Phenylacetyl)palladium Complexes. To compare the relative abilities of secondary amines and alcohols toward (phenylacetyl)-palladium halides, we have treated the P1- and P2-type acylpalladium complexes with mixtures of EtOH and $HNEt_2$ at room temperature for 1 day in the absence and presence of added PPh_3 (Table 3).

The reaction of the 1:1 EtOH/Et_2NH mixture with the P1-type bridged dimer **11** gave ethyl phenylacetate **19** in 74 mol %, affording only a trace of the amide **15** (entry 1, Table 3). Addition of 1 mol of PPh_3/Pd to **11** caused an increase in the yield of the amide at the cost of the ester (entry 2). A higher yield of the amide was obtained on treatment of the P2-type complex **8** without additional PPh_3 at the cost of the ester (entry 3). A further increase in the amount of extra PPh_3 added led to production of the amide as the predominant product, yielding only minor amounts of the ester (entries 4−6).

A plot of the respective yields of the ester and amide against the molar ratio of the PPh_3 ligands to palladium is given in Figure 1, which clearly shows that an increase in the P2-type complex hinders the formation of the ester and favors the formation of the amide. A retardation effect in the production of an ester by addition of free phosphine was previously observed in the Pd-catalyzed carbonylation of aryl iodides in the presence of alcohol and tertiary amine[7a] and in the reductive elimination of aryl esters from acyl(aryloxy)-palladium complexes.[16a]

The PMe_3-coordinated P2-type (phenylacetyl)palladium halide was found to be quite inactive, and the reaction of **9** with the 1:1 mixture of EtOH/Et_2NH gave only a small amount of the ester in 3 days (entry 7, Table 3), whereas the P1-type complex **12** gave the ester

(25) Lide, D. R. *CRC Handbook of Chemistry and Physics*, 76th ed.; CRC Press: New York, 1995; pp 8−47.

(26) While the present results show the much lower reactivity of the PMe_3-coordinated (phenylacetyl)palladium complex **9** than the PPh_3-coordinated complex **8** with the alcohols and NEt_3 at room temperature, the yields can be increased on prolonged reaction time. Quantitative ester formation was reported on heating **9** with MeOH and NEt_3 at 80 °C for 1 h, see ref 11a.

Table 3. Reactions of (Phenylacetyl)palladium Complexes with 1:1 Mixtures of Et_2NH and EtOH in the Presence and Absence of PPh_3[a]

entry	complex	PPh_3 added (mol/Pd)	molar ratio P/Pd	products (mol %/Pd)[b] $PhCH_2COOEt$ (**19**)	$PhCH_2CONEt_2$ (**15**)
1	**11**	0	1	74	trace
2	**11**	1	1.5	60	17
3	**8**	0	2	56	38[c]
4	**8**	2	4	26	60[c]
5	**8**	4	6	18	67[c]
6	**8**	10	12	10	75[c]
7	**9**	0	2	trace(5)	0(0)[d,e]
8	**12**	0	1	47(62)	0(0)[d,f]
9	**10**	0	2	76	9

[a] Reaction conditions: the palladium complex (0.04 mmol in Pd) in CD_2Cl_2 (0.5 mL) was treated with a 1:1 mixture of Et_2NH (0.40 mmol) and EtOH (0.40 mmol) at room temperature. [b] Determined by ^1H NMR after 24 h ($PhSiMe_3$ as an internal reference). [c] A trace of $PhCH_2COO^-$ was detected. [d] The data in the parentheses are the yields measured after the reaction for 3 days at room temperature. [e] $(PhCH_2)_2$ (3%) was detected after 3 days. [f] *trans*-$PdCl(COCH_2Ph)(PMe_3)_2$ (**9**) was formed (26 mol %) in 3 days.

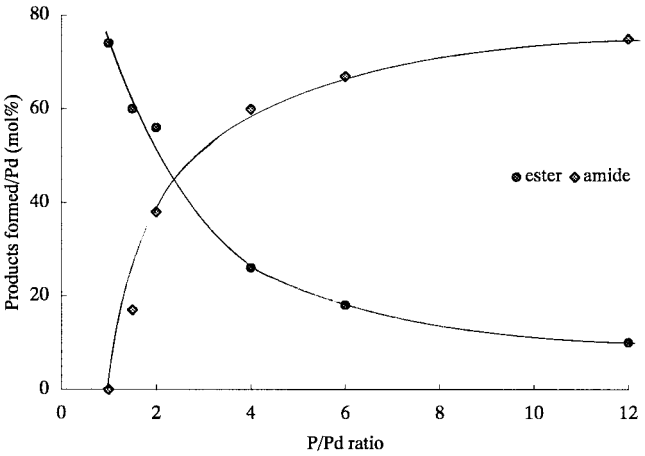


Figure 1. Effect of the PPh_3 ligands on the relative amounts of the ester and amide formed in reactions of 1:1 mixtures of Et_2NH and EtOH with (phenylacetyl)palladium complexes

in 47 mol % yield in a day and 62 mol % in 3 days (entry 8). The dppe-coordinated complex **10** behaved differently from the PMe_3-coordinated complex and yielded the ester as the major product (entry 9).

Not only the product ratios of the ester/amide were changed on addition of the free PPh_3 to the acylpalladium complexes, but also the rate of reaction was considerably decreased by addition of PPh_3 to **8**. The rate of the reaction of **8** with 10 equiv each of EtOH and Et_2NH was found to be first order in **8**. In the absence of added PPh_3, the reaction proceeds rapidly and is complete in 100 min, with the rate constant being $k_{obs}^{20°C} = (2.4 \pm 0.1) \times 10^{-4}$ s^{-1} based on complex **8**. During the course of the reaction of **8**, the Et_2NH-coordinated P1-type complex was observed as a transient intermediate by NMR.

When 2 mol of PPh_3 per 1 mol of palladium was added to the reaction system containing **8** and 10 mol each of EtOH and Et_2NH, the rate constant of the reaction of **8** with EtOH/Et_2NH at room temperature to give ester and amide was dropped to $(5.4 \pm 0.1) \times 10^{-5}$ s^{-1} compared to the case without added PPh_3. The NMR signals arising from the transient intermediate Et_2NH-coordinated species **13** were negligibly small. The reactions monitored by NMR indicated that both formation of ester and amide were slowed by addition of 2 mol extra of PPh_3 to the system, with retardation of formation of ester being more severe than that of amide.

Table 4. Competitive Reaction of Amines and Alcohols toward *trans*-$PdCl(COCH_2Ph)(PPh_3)_2$ (8)[a]

entry	additives (10 mol/Pd) HOR[1]	HNR_2[2]	products (mol %/Pd)[b] $PhCH_2COOR$[1]	$PhCH_2CONR_2$[2]
1	HOMe	$HNEt_2$	80	trace[c]
2	HOEt	$HNEt_2$	56	38[c]
3	HOPr	$HNEt_2$	52	42[c]
4	HO^{i}Pr	$HNEt_2$	6	81[c]
5	$HOCH_2CF_3$	$HNEt_2$	87	5[c]
6	HOPh	$HNEt_2$	86	7[c]
7	HOEt	$HNPr_2$	51	28[c]
8	HOEt	HN^iPr_2	60	20[c]
9	HO^{i}Pr	HN^iPr_2	11	71[c]
10	HOEt	piperidine	59	40[c]
11	HOEt	morpholine	16	60[c,d]
12	HOEt	$HNPh_2$	0	0

[a] Reaction conditions: the palladium complex **8** (0.03 mmol) in CD_2Cl_2 was treated with amine (0.30 mmol) and alcohol (0.30 mmol) at room temperature. [b] Determined by ^1H NMR after 24 h ($PhSiMe_3$ as an internal reference). [c] A trace of $PhCH_2COO^-$ was detected. [d] Unreacted **8** (6 mol %) was found.

We have further examined the reactions of the P2-type complex **8** toward 1:1 mixtures of various alcohols and amines at room temperature in CD_2Cl_2. The results summarized in Table 4 show that acidic alcohols such as trifluoroethanol and phenol give higher ester yields and that usage of bulkier alcohols such as isopropyl alcohol is less favorable for the ester formation in comparison with less bulky alcohols such as methanol, ethanol, and *n*-propyl alcohol.

In the competition of an alcohol and a secondary amine for the (phenylacetyl)palladium complex **8**, the nature of the secondary amines also affect the reaction. Comparison of the effect of piperidine with that of less basic morpholine, both having a similar steric bulkiness, showed that more basic piperidine is favored for the ester formation (entries 10 and 11, Table 4). Less basic diphenylamine proved to be inactive for the formation of the ester and the amide (entry 12). Employment of the bulkier *i*-Pr_2NH somewhat disfavored the amide formation and favored the formation of the ethyl ester than less bulky *n*-Pr_2NH (entries 7 and 8).

Reactions of the Benzyl- and (Phenylacetyl)-palladium Complexes with $HNEt_2$ under CO Pressure. To examine the feasibility of achieving catalytic carbonylation and double carbonylation of benzylic substrates in the presence of a secondary amine and to get information concerning the reaction mechanism of formation of amide, reactions of the benzyl- and (phenylacetyl)palladium halide complexes **1a**, **1b**, and **8** having the PPh_3 ligands toward $HNEt_2$ were conducted under various CO pressures (Table 5).

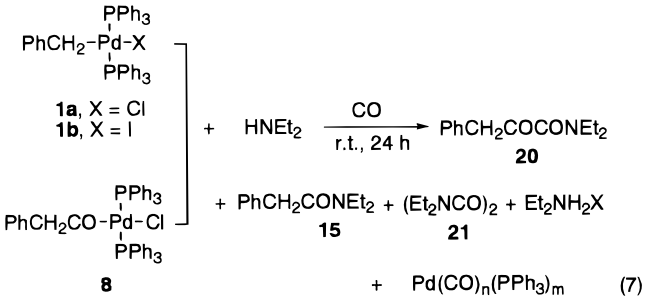
On reactions with $HNEt_2$ (10 mol/Pd) in the presence of CO, these complexes were smoothly transformed into amide **15** and *N*,*N*-diethylphenylpyruvamide (**20**) at room temperature in 1 day (eq 7).

For the three complexes examined, an increase in the CO pressure led to an increase in the yield of the α-keto amide **20** at the cost of the amide **15**. The relative yields of the α-keto amide to the amide are listed in the last column in Table 5, which clearly indicates that higher

Table 5. Reaction of Benzyl- and (Phenylacetyl)palladium Complexes with CO in the Presence of Et_2NH[a]

				products (%)[b,c]			
entry	complex	CO (atm)	solvent	**20**	**15**	**21**	ratio **20**/**15**
1	**1a**	10	THF	49	25	27	2.0
2	**1a**	20	THF	54	21	24	2.6
3	**1a**	40	THF	60	19	20	3.2
4	**1a**	60	THF	67	17	19	3.9
5	**1a**	20	$CHCl_3$	61	30	26	2.0
6	**1a**	60	$CHCl_3$	77	15	15	5.1
7	**1b**	20	$CHCl_3$	53	43	trace	1.2
8	**1b**	60	$CHCl_3$	63	33	6	1.9
9	**8**	20	$CHCl_3$	64	31	32	2.1
10	**8**	60	$CHCl_3$	75	17	13	4.4
11	**1a**	20	none[d]	6	73	21	0.1
12	**8**	20	none[d]	54	10	19	5.4

[a] Reaction conditions: a mixture of the palladium complex (0.13 mmol), solvent (2 mL), and Et_2NH (1.30 mmol) under CO pressure was stirred at room temperature for 24 h. [b] Respective yields in mol %/Pd were determined by ^1H NMR and GC ($PhSiMe_3$ as an internal reference). [c] $Et_2NH_2^+X^-$ was found in the reaction mixtures as identified by ^1H NMR. The amount of $Et_2NH_2^+I^-$ was smaller than that of $Et_2NH_2^+Cl^-$. [d] The reaction was carried out in neat Et_2NH (26.0 mmol).



CO pressure favors the α-keto amide formation. The benzyl- and (phenylacetyl)palladium complexes show a similar reactivity pattern in giving the α-keto amide and amide (entries 5, 6 vs 9, 10). The results suggest that the reactions proceed through a common (phenylacetyl)-palladium species regardless of the starting complex, whether it is benzyl or phenylacetyl. The amount of *N*,*N*-diethyloxamide (**21**) produced as the byproduct was found to decrease upon increasing the CO pressure.

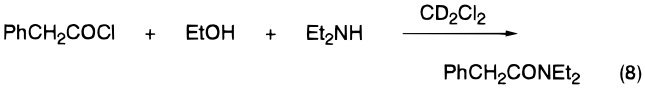
Quite different results were obtained when the carbonylation was carried out in $HNEt_2$ without using any other solvent. In neat $HNEt_2$, the amide **15** was obtained as the major product when the benzylpalladium complex was carbonylated, whereas the α-keto amide **20** was the predominant product in the treatment of the (phenylacetyl)palladium complex (entries 11 and 12).

For gaining information concerning the mechanism of the formation of α-keto amide and comparing the reactivities of the phenylacetyl and CO ligands toward nucleophiles, the reaction of $HNEt_2$ (10 mol/Pd) with the cationic CO-coordinated (phenylacetyl)palladium complex **7** at room temperature under 10 atm of CO was examined. The reaction released the α-keto amide **20** and amide **15** in a molar ratio of 2.5:1, accompanied by formation of a black precipitate of Pd metal and $Et_2NH_2^+PF_6^-$, as confirmed by NMR. The results indicate that the amide as well as the α-keto amide can be produced from the CO-coordinated (phenylacetyl)-palladium complex.

Discussion

Reaction Courses of (Phenylacetyl)palladium Complexes with Secondary Amines and Alcohols in the Absence of CO. In the Introduction we discussed the possible reaction courses of the acylpalladium complexes with nucleophiles to produce amides or esters in Scheme 2. Among the three courses we considered, course **c** involving the direct reductive elimination of phenylacetyl halide from the (phenylacetyl)palladium halide was found operative in the HI-promoted palladium-catalyzed carbonylation to liberate phenylacetic acid.[15] However, the operation of this course is unlikely in the reactions of (phenylacetyl)-palladium halide with nucleophiles under basic conditions on the following grounds. First, if phenylacetyl chloride is produced on reductive elimination, amides should be formed in preference to esters in the competitive reactions of alcohols and secondary amines with the acyl halide whereas esters were in fact formed as the main reaction product at lower PPh_3/Pd ratios (Figure 1). Second, if the direct reductive elimination of acyl halide is operative, the influence of added phosphine ligands on relative yields of amides and esters would not be observed.

To unequivocally establish the reaction course of the liberated acyl chloride with a mixture of nucleophiles, we have examined the reaction of 0.04 mmol of phenylacetyl chloride with a mixture of 0.4 mol each of ethanol and diethylamine (eq 8). The reaction gave only amide

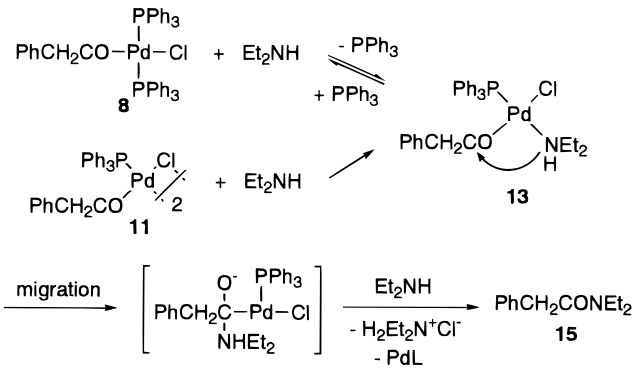


without giving any ester, excluding the possibility of liberation of phenylacetyl chloride by reductive elimination from the (phenylacetyl)palladium chloride complex.

Course **a** involving the direct attack of the nucleophile on the phenylacetyl ligand is the generally accepted course and is compatible with the intuitive reasoning based on the knowledge of organic chemistry without involvement of a transition-metal catalyst. However, if this reaction is operative, we would expect formation of the amide as the predominant product in the competitive reaction of the (phenylacetyl)palladium complex with a 1:1 mixture of alcohol and secondary amine. Formation of the ester as the main product is difficult to explain, if we assume that the simple competition of free secondary amine and alcohol toward the carbonyl group in the phenylacetyl ligand determines the product ratio. The assumption of formation of a minute amount of a free alkoxide anion having a much greater nucleophilicity toward the acyl carbonyl group than free amine is not reasonable either on the basis of the experiment in eq 8.

On the other hand, formation of a free alkoxide on interaction of an alcohol with a tertiary amine and the subsequent attack of the alkoxide on the acylpalladium complex, as proposed by Moser et al. in the reaction of a benzoylpalladium complex with mixtures of methanol and various tertiary amines, is a process worth consideration.[12] However, employment of a proton sponge, the highly efficient deprotonation agent having a great bulkiness, proved to be much less effective than that of

Scheme 3. Proposed Mechanism for the Formation of Amide



triethylamine (entry 3 in Table 2). The result is not compatible with the idea of simple deprotonation of methanol by tertiary amines and suggests that consideration of a steric effect is necessary to account for the striking ineffectiveness of the proton sponge. The effect of suppression of formation of carboxylic esters on increase of the amount of triphenylphosphine added to the (phenylacetyl)palladium complex resulting in an increase of the amount of amide is also difficult to explain by the mechanism involving the attack of free alkoxide on the carbonyl group in the (phenylacetyl)-palladium complex.

Since both routes **a** and **c** in Scheme 2 do not seem to accommodate a reasonable explanation of the experimental results, we now discuss the mechanisms of *aminolysis* and *alcoholysis* (course **b** in Scheme 2) in the reactions of the (phenylacetyl)palladium complexes with secondary amines or alcohols. Both processes should involve deprotonation from the neutral nucleophile HNu at a certain stage to give the esters and the amides. The results shown in Tables 1, 3, and 4 on the reactions of the (phenylacetyl)palladium complexes with secondary amines and alcohols suggest that the mechanism to give amides is different from the mechanism to give esters; a more basic amine is preferred to give the amides, whereas a less basic alcohol is favored for giving the esters.

For the amide formation from the (phenylacetyl)-palladium chloride **8** and **11** on reaction with diethylamine, we propose the mechanism shown in Scheme 3.

From either the P2- or P1-type complexes **8** or **11**, the monoamine-coordinated complex **13** is formed first, as observed experimentally. Direct deprotonation from the coordinated $HNEt_2$ to give (phenylacetyl)palladium amide is not the likely course to give phenylacetamide, since the less basic morpholine is less reactive than piperidine (eq 5). Therefore, migration of the amine to the carbonyl group in the phenylacetyl ligand is assumed to take place with the resultant formation of the amide **15** by deprotonation with the aid of a base.

In the ester formation from the (phenylacetyl)palladium complexes on reaction with alcohols and a tertiary amine (Table 2), the palladium complexes will also be coordinated by the amine first. Trogler prepared various amine-coordinated cationic methylpalladium complexes and measured the binding constants of the amines.[27] Coordination of the alcohol will follow, and deprotonation of the coordinated alcohol by the base gives the (phenylacetyl)palladium alkoxide that reductively eliminates the ester (Scheme 4). The ineffectiveness of the strongly basic proton sponge for the ester formation may be an indication that too bulky base is not a suitable agent for the deprotonation. A similar mechanism was proposed previously to account for the formation of esters in the reaction of benzoylpalladium complexes with alcohols and amine bases.[7a]

In the competitive reactions of alcohols and secondary amines with **8** and **11** in the absence of added triphenylphosphine to give esters as the main product, a similar mechanism may be operative (Scheme 5).

In the reaction of the triphenylphosphine-coordinated acylpalladium complexes **8** and **11**, coordination of diethylamine will take place first to give the amine-coordinated P1-type complex **13**.

The alcohol and the amine will coordinate to complex **13** to form an equilibrium mixture of the amine- and alcohol-coordinated complexes. Deprotonation of the coordinated alcohol from the alcohol-coordinated species (**I**) will give the acylpalladium ethoxide intermediate (**II**) that produces the ester **19** on reductive elimination, whereas migration of the coordinated amine to the acyl ligand as discussed in Scheme 3 will give the amide **15**. If deprotonation from the coordinated alcohol is favored over the migration of the coordinated amine to the phenylacetyl ligand, the ester will be produced through the (phenylacetyl)palladium alkoxide intermediate (**II**).

A difficulty in the present mechanism is in assuming the coordination of alcohol forming a five-coordinate complex in Schemes 4 and 5. It is not unreasonable, however, to assume the coordination of alcohol to the Pd(II) center and the subsequent slow deprotonation process to give the alkoxide intermediate. In fact, the formation of ester in a high yield in the reaction of the dppe-coordinated complex **10** with ethanol and Et_2NH seems to support the involvement of a five-coordinate intermediate. Examples of alcohol coordination to tertiary phosphine-coordinated palladium complexes are known.[28] Furthermore, the result that the bulky isopropyl alcohol is less favorable than linear alcohols for the ester formation may reflect the difficulty in coordination of a sterically demanding alcohol (entries 4 and 9, Table 4).

The higher yields of esters with alcohols of higher acidities are compatible with the mechanism where deprotonation is a key step in the ester formation. The route through formation of a free alkoxide is not compatible with the results that employment of a bulky base such as a proton sponge is ineffective in giving the esters as we previously discussed.

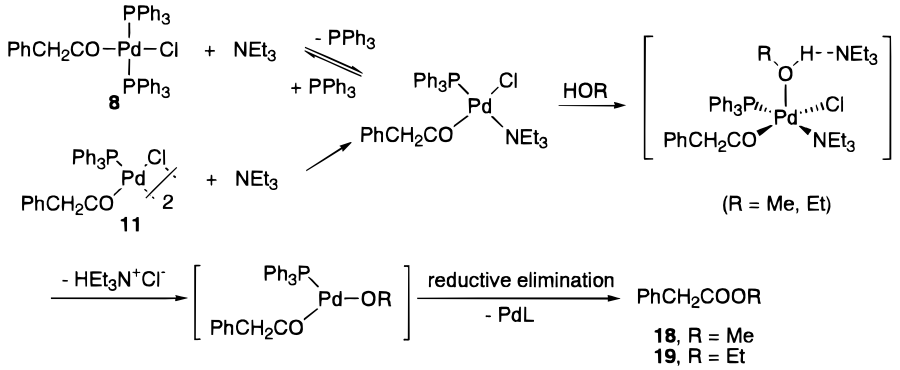
In the presence of added phosphine to form the P2-type complexes, the coordination site for the nucleophile to palladium is blocked and the nucleophile will approach from the fifth coordination site. In this case, the competition for coordination to the palladium center between the amine and alcohol to be followed by deprotonation is favorable for the amine to yield the amide **15** preferentially.

The much lower reactivity of the PMe_3-coordinated P1- and P2-type (phenylacetyl)palladium complexes

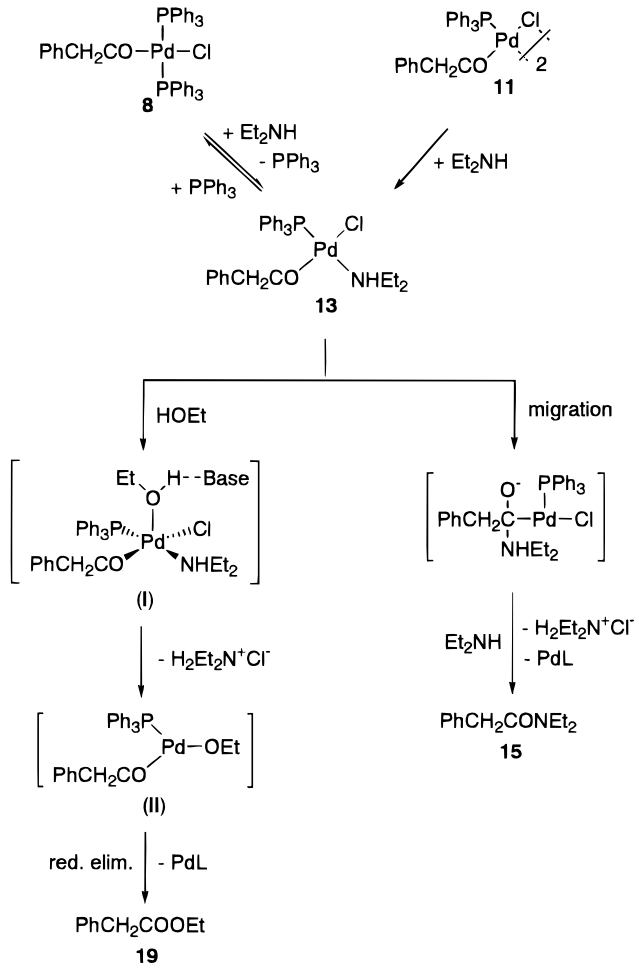
(27) Seligson, A. L.; Trogler, W. C. *J. Am. Chem. Soc.* **1991**, *113*, 2520.

(28) Davies, J. A.; Hartley, F. R.; Murray, S. G. *J. Chem. Soc., Dalton Trans.* **1980**, 2246.

Scheme 4. Proposed Mechanism for the Formation of Ester in the Presence of Tertiary Amine



Scheme 5. Proposed Mechanism for the Formation of Ester in the Presence of $HNEt_2$



than the PPh_3- and dppe-coordinated complexes toward Et_2NH (Table 1) and alcohol mixed with tertiary amine base (Table 2) suggests that the electrophilicity of the acylpalladium center toward a nucleophile is very important in determining the production of the organic carbonylation product. The result that the dppe-coordinated (phenylacetyl)palladium chloride complex **10** reacted smoothly with $HNEt_2$ to give the amide as well as the reaction of **10** with a 1:1 mixture of EtOH and $HNEt_2$ to give the ester as the main product implies that the assumption of the approach of a nucleophile from the fifth coordination site is not unreasonable.

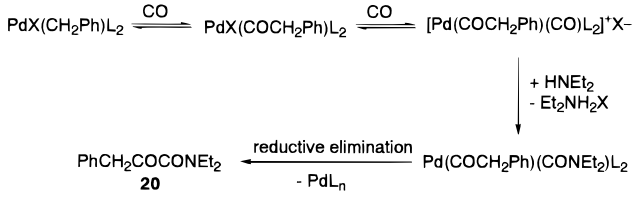
Reactions of Benzyl- and (Phenylacetyl)palladium Halide Complexes with Et_2NH in the Presence of CO. On the basis of the fundamental information on the reactivities of the (phenylacetyl)palladium complexes with various nucleophiles, we now discuss the reactivities of the benzyl- and (phenylacetyl)palladium complexes toward Et_2NH under CO pressures.

As shown in Table 5, upon increasing the CO pressure from 20 to 60 atm in $CHCl_3$, a similar increase in the amount of the α-keto amide **20** at the cost of the amide **15** and oxamide **21** was observed for the both benzyl- and (phenylacetyl)palladium complexes. The results may be taken as an indication that under CO pressure all of the benzylpalladium complexes are converted into (phenylacetyl)palladium prior to the reaction of the CO-coordinated benzylpalladium complex with the amine and that the α-keto amide and amide may arise from the common (phenylacetyl)palladium complex. Previously, arylpalladium complexes have been converted into α-keto amides and amides under CO pressure on reaction with secondary amines.[29] The enhancement in the selectivity of α−keto amide over amide on increasing the CO pressure was ascribed to promotion of the course through path **b** and the intermediate **G** in Scheme 1 with suppression of the reaction course through path **a** involving the aryl(carbamoyl)palladium complex.[29] The difference of the previous results on the arylpalladium complex from the present one is partly ascribed to the difference in the reactivities between the aryl- and benzylpalladium complexes toward CO insertion and toward the attack of a nucleophile at the coordinated CO. The other important factor is that the reaction of the arylpalladium complex with the amine under CO to give the amide was carried out in neat amine. The presence of the large excess of the amine in the system would favor its attack on the coordinated CO before the CO insertion occurs. In fact, in the present study, the reaction of the benzylpalladium complex **1a** with CO (20 atm) in neat Et_2NH at room temperature also produced the amide **15** as the major product (entry 11 in Table 5), indicating the occurrence of the attack of amine on the CO coordinated to the benzylpalladium species. On the other hand, the reaction of the (phenylacetyl)-palladium complex **8** in neat Et_2NH under similar conditions produced the α-keto amide **20** as the main product.

The proposed course of α-keto amide formation from the benzyl- and (phenylacetyl)palladium complexes is shown in Scheme 6, which is comprised of (a) CO

(29) Ozawa, F.; Sugimoto, T.; Yusas, Y.; Santra, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1984**, *3*, 683.

Scheme 6. Proposed Mechanism for the Formation of α-Keto Amide[a]



[a] L = tertiary phosphine; X = halide.

insertion into the benzyl−Pd bond; (b) CO coordination to the phenylacetyl complex; (c) attack of Et_2NH on the coordinated CO to give (phenylacetyl)(carbamoyl)palladium species; and (d) the reductive elimination of the phenylacetyl and carbamoyl groups to give **20** after trans to cis isomerization. The amide **15** may be formed by the reaction of the (phenylacetyl)palladium complex with Et_2NH as we previously discussed.

These results suggest that employment of a high CO pressure and a limited amount of a secondary amine is favorable for achieving double carbonylation to give an α-keto amide. In fact, the palladium-catalyzed double carbonylation was realized using allylic chlorides, high CO pressure, and a limited amount of Et_2NH.[3]

Conclusion

Examination of the reactivities of benzyl- and (phenylacetyl)palladium complexes toward various nucleophiles has shed light on the detailed courses of the reactions of these complexes with amines and alcohols. More acidic and less bulky alcohols have been found to be more favorable to give esters in reactions of the (phenylacetyl)palladium complexes in the presence of a base. On the other hand, operation of two processes to give the phenylacetamide has been established. One involves formation of an amine-coordinated (phenylacetyl)palladium complex in which amine migration to the acyl group takes place in the absence of CO, whereas the other involves the nucleophilic attack of an excess of Et_2NH on the coordinated CO to give benzyl(carbamoyl)palladium, which liberates amide on reductive elimination. The α-keto amide formation is considered to proceed via the route involving nucleophilic attack of amine on the CO-coordinated (phenylacetyl)palladium complex followed by reductive elimination of the phenylacetyl and the carbamoyl ligands. The attempted catalytic double carbonylation of benzylic substrates has not been realized yet, but various pieces of fundamental information obtained in the present study should provide a basis to eventually realize the catalytic processes.

Experimental Section

All manipulations were carried out under an atmosphere of argon. Infrared spectra were recorded on a Hitachi 295 spectrometer using KBr pellets. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a JEOL EX-270 spectrometer. Chemical shifts are reported in δ units (parts per million, ppm) downfield from Me_4Si for ^1H and ^{13}C and H_3PO_4 (85% in aqueous solution, external reference) for ^{31}P. Carbon, hydrogen, and nitrogen analyses were carried out on a Perkin-Elmer PE 2400II Elemental Analyzer. Mass spectra were analyzed on a JEOL AUTOMASS spectrometer. Gas chromatographic (GC) analyses were performed on a Hitachi 263-50 equipped with an SE-30 column, using N_2 as the carrier gas.

Solvents were dried and distilled before use by standard methods. Amines and alcohols were commercially available and dried by MS 4A before use. Benzyl iodide was prepared by the reaction of benzyl chloride with excess of LiI. The palladium complexes, $Pd(PPh_3)_4$,[30] $Pd(CH_2Ph)Cl(PPh_3)_2$ (**1a**),[17] $Pd(CH_2Ph)I(PPh_3)_2$ (**1b**),[15b] $Pd(CH_2Ph)Cl(PMe_3)_2$ (**2**),[15b] (η^3-benzyl)bis(triphenylphosphine)palladium hexafluorophosphate (**3**),[15b] (η^3-benzyl)bis(trimethylphosphine)palladium hexafluorophosphate (**4**),[15b] and $Pd(COCH_2Ph)Cl(PPh_3)_2$ (**8**),[18] were synthesized as reported in the literature.

Preparation of *trans*-Pd(COCH$_2$Ph)Cl(PMe$_3$)$_2$ (9). To a white turbid mixture of *trans*-$PdCl(COCH_2Ph)(PPh_3)_2$ (1.0 g, 1.27 mmol) and toluene (30 mL) was added PMe_3 (0.394 mL, 3.81 mmol) at room temperature under an atmosphere of argon. After the mixture was stirred for 20 min at room temperature, it was concentrated to 5 mL. Ether (30 mL) was added to the solution to yield a white precipitate, which was filtered, washed with ether, and dried. Recrystallization of the above solid from CH_2Cl_2/Et_2O gave a white powder of **9** (0.41 g, 78%). ^1H NMR (CD_2Cl_2, δ, 270 MHz, 298 K): 7.3 (m, 5H, Ph), 3.86 (s, 2H, PhCH_2), 1.24 (s br, 18H, PMe_3). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 298 K): −18.7 (s). $\nu_{C=O}$ 1661 cm^{-1}. Anal. Calcd for $C_{14}H_{25}ClOP_2Pd$: C, 40.70; H, 6.10. Found: C, 40.52; H, 6.07.

Preparation of PdCl(COCH$_2$Ph)(dppe) (10). To a suspension of *trans*-$PdCl(COCH_2Ph)(PPh_3)_2$ (0.079 g, 0.1 mmol) in CH_2Cl_2 (5 mL) was added dppe (0.080 g, 0.2 mmol). The mixture was stirred for 1 h at room temperature under an atmosphere of argon. Addition of ether (20 mL) to the mixture gave a white precipitate, which was filtered and recrystallized from CH_2Cl_2 (2 mL)−Et_2O (4 mL) twice to give a white powder of **10** (0.040 g, 61%). ^1H NMR (CD_2Cl_2, δ, 270 MHz, 298 K): 7.82 (dd, J = 7, 3 Hz, 4H, *Ph*$_2$PCH$_2$CH$_2$PPh$_2$), 7.61 (dd, J = 11, 7 Hz, 4H, Ph$_2$PCH$_2$CH$_2$P*Ph*$_2$), 7.45 (s br, 12H, *Ph*$_2$PCH$_2$-CH$_2$P*Ph*$_2$), 7.05 (s br, 3H, Ph), 6.68 (s br, 2H, Ph), 3.85 (s, 2H, PhCH_2), 2.45 (dm, J = 26, 6 Hz, 2H, Ph$_2$P*CH*$_2$CH$_2$PPh$_2$), 2.09 (ddt, J = 26, 13, 6 Hz, 2H, Ph$_2$PCH$_2$*CH*$_2$PPh$_2$). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 298 K): 38.5 (d, J = 44, Ph$_2$*P*CH$_2$CH$_2$PPh$_2$), 22.7 (d, J = 44, Ph$_2$PCH$_2$CH$_2$*P*Ph$_2$). ^{13}C NMR (CD_2Cl_2, 67.9 MHz, δ, 298 K): 238.2 (d br, J = 12 Hz, *C*OCH$_2$Ph), 58.7 (dd, J = 37, 19 Hz, CO*C*H$_2$Ph), 29.4 (dd, J = 33, 22 Hz, Ph$_2$P*C*H$_2$-CH$_2$PPh$_2$), 22.6 (dd, J = 24, 11 Hz, Ph$_2$PCH$_2$*C*H$_2$PPh$_2$). $\nu_{C=O}$ 1693 cm^{-1}. Anal. Calcd for $C_{34}H_{31}ClOP_2Pd$: C, 61.93; H, 4.74. Found: C, 61.66; H, 4.75.

Preparation of [PdCl(COCH$_2$Ph)(PPh$_3$)]$_2$ (11). To a CH_2Cl_2 (20 mL) solution of *trans*-$PdCl(COCH_2Ph)(PPh_3)_2$ (0.800 g, 1.018 mmol) was added $PdCl_2(PhCN)_2$ (0.195 g, 0.509 mmol). Immediately, a yellow precipitate was formed. After the mixture was stirred for 20 min at room temperature, the precipitate was filtered off and the filtrate was concentrated to give an orange residue. Addition of ether followed by filtration and drying gave a yellowish-orange solid of **11** (0.46 g, 86%). Purification can be achieved by recrystallization from CH_2Cl_2−Et_2O. ^1H NMR (CD_2Cl_2, δ, 270 MHz, 298 K): 7.67 (m, 12H, P*Ph*$_3$), 7.40 (m, 18H, P*Ph*$_3$), 7.10 (d, J = 6 Hz, 6H, *m*-, *p*-Ph), 6.64 (d, J = 6 Hz, 4H, *o*-Ph), 3.76 (s, 4H, PhCH_2). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 298 K): 27.0 (s). ^{13}C NMR (CD_2Cl_2, 67.9 MHz, 298 K): δ 219.2 (s br, *C*OCH$_2$Ph), 57.5 (d, J = 24, CO*C*H$_2$Ph). $\nu_{C=O}$ 1712 cm^{-1}. Anal. Calcd for $C_{52}H_{44}Cl_2O_2P_2Pd_2$: C, 59.68; H, 4.24. Found: C, 59.78; H, 4.22.

Preparation of [PdCl(COCH$_2$Ph)(PMe$_3$)]$_2$ (12). To a CH_2Cl_2 (10 mL) solution of *trans*-$PdCl(COCH_2Ph)(PMe_3)_2$ (0.280 g, 0.678 mmol) was added $PdCl_2(PhCN)_2$ (0.130 g, 0.339 mmol). Immediately, a white precipitate was formed. After the mixture was stirred for 20 min at room temperature, ether (ca. 30 mL) was added to the mixture until no more precipitate

(30) Hegedus, L. S. In *Organometallics in Synthesis: A Manual*; Schlosser, M., Ed.; Wiley: New York, 1994; p 383.

formed. Filtration gave a white solid and a pale yellow filtrate. The white solid was dissolved in CH_2Cl_2 (10 mL), and ether was added to the mixture until no more precipitate formed. After filtration, the white solid was repeatedly recrystallized from CH_2Cl_2 and ether. The filtrates and washings were combined and concentrated to give a white precipitate, which was filtered, washed with ether, and dried to afford a white powder of **12** (0.14 g, 56%). ^{1}H NMR (CD_2Cl_2, δ, 270 MHz, 298 K): 7.41 (d, J = 7 Hz, 4H, *o*-Ph), 7.34 (t, J = 7 Hz, 4H, *m*-Ph), 7.25 (t, J = 7 Hz, 2H, *p*-Ph), 4.02 (s, 4H, PhCH_2), 1.16 (d, J = 11 Hz, 18H, PMe_3). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 298 K): −6.8 (s). $\upsilon_{C=O}$ 1696 cm^{-1}. Anal. Calcd for $C_{22}H_{32}Cl_2O_2P_2Pd_2$: C, 39.20; H, 4.78. Found: C, 38.93; H, 4.76.

Synthesis of PdCl(COCH$_2$Ph)(PPh$_3$)(NHEt$_2$) (13). To a CH_2Cl_2 solution (8 mL) of [PdCl(COCH$_2$Ph)(PPh$_3$)]$_2$ (0.105 g, 0.10 mmol) cooled to −20 °C was added $HNEt_2$ (0.026 mL, 0.25 mmol) under an atmosphere of argon. After the mixture was stirred at −20 °C for 20 min, a light-yellow solution was obtained, which was concentrated under reduced pressure at −20 °C to give a pale yellow residue. Addition of pentane (10 mL) gave a pale yellow precipitate. After filtration, washing with cooled pentane (2 × 10 mL), and careful vacuum-drying at low temperature (−30 °C), a pale yellow solid of **13** was obtained (0.107 g, 90%), which was stored in a refrigerator (−30 °C). ^{1}H NMR (CD_2Cl_2, δ, 270 MHz, 253 K): 7.68 (m, 6H, PPh_3), 7.41 (m, 9H, PPh_3), 7.09 (s br, 3H, Ph), 6.40 (s br, 2H, Ph), 3.60 (s br, 1H, *H*NEt$_2$), 3.57 (s, 2H, PhCH_2), 2.63 (s br, 4H, HN(CH_2CH$_3$)$_2$), 1.62 (t, J = 7 Hz, 6H, HN(CH$_2$CH_3)$_2$). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 253 K): 26.9 (s). ^{13}C NMR (CD_2Cl_2, δ, 67.9 MHz, 253 K): 231.3 (d, J = 3 Hz, *C*OCH$_2$Ph), 57.7 (d, J = 21 Hz, CO*C*H$_2$Ph), 47.0 (d, J = 8 Hz, HN(*C*H$_2$CH$_3$)$_2$)), 15.9 (s, HN(CH$_2$*C*H$_3$)$_2$). IR: 3216, 1671 cm^{-1}. Anal. Calcd for $C_{30}H_{33}ClNOPPd$: C, 60.41; H, 5.58; N, 2.35. Found: C, 59.49; H, 5.56; N, 2.19.

Synthesis of PdCl(COCH$_2$Ph)(PMe$_3$)(NHEt$_2$) (14). To a CH_2Cl_2 solution (5 mL) of [PdCl(COCH$_2$Ph)(PMe$_3$)]$_2$ (0.067 g, 0.10 mmol) cooled to −30 °C was added $HNEt_2$ (0.026 mL, 0.25 mmol) under an atmosphere of argon. After the mixture was stirred at −30 °C for 20 min, the colorless solution obtained was concentrated under reduced pressure at −30 °C to give a pale yellow oily residue. Addition of pentane (5 mL) and $HNEt_2$ (0.026 mL) to the residue and stirring gave a white precipitate. After filtration and careful vacuum-drying at low temperature (−50 °C), a white solid of **14** was obtained (0.078 g, 95%), which was stored in a refrigerator (−30 °C). ^{1}H NMR (CD_2Cl_2, δ, 270 MHz, 253 K): 7.28 (t, J = 7 Hz, 2H, Ph), 7.23 (t, J = 7 Hz, 1H, Ph), 7.15 (d, J = 7 Hz, 2H, Ph), 3.96 (s, 2H, PhCH_2), 2.98 (s br, 1H, *H*NEt$_2$), 2.62 (m, 4H, HN(CH_2CH$_3$)$_2$), 1.47 (t, J = 7 Hz, 6H, HN(CH$_2$CH_3)$_2$), 1.26 (d, J = 11 Hz, 9H, PMe_3). ^{31}P NMR (CD_2Cl_2, δ, 109.4 MHz, 253 K): −7.4 (s). IR: 3232, 1680 cm^{-1}. Anal. Calcd for $C_{15}H_{27}ClNOPPd$: C, 43.92; H, 6.63; N, 3.41. Found: C, 43.57; H, 6.67; N, 3.60.

Reaction of 8 with AgPF$_6$. To a CD_2Cl_2 (2 mL) solution of $AgPF_6$ (0.036 g, 0.142 mmol) was added *trans*-PdCl(COCH$_2$Ph)(PPh$_3$)$_2$ (**8**) (0.112 g, 0.142 mmol) under an atmosphere of argon. A white precipitate formed immediately. After 10 min, the mixture was filtered through kieselgur to give a light yellow solution, which was analyzed by ^{1}H and ^{31}P NMR. The solution was found to contain only (η^3-benzyl)bis(triphenylphosphine)palladium hexafluorophosphate (**3**). Evaporation of the solvent and addition of ether gave a yellow solid. The infrared spectrum indicated the disappearance of the acyl υ(CO) band.

Reaction of 13 with PPh$_3$. To an NMR tube containing a CD_2Cl_2 solution (0.6 mL) of PdCl(COCH$_2$Ph)(PPh$_3$)(NHEt$_2$) (**13**) (0.020 g, 0.0335 mmol) cooled at −20 °C was added PPh_3 (0.009 g, 0.0335 mmol). The mixture was warmed to room temperature and analyzed by ^{1}H and ^{31}P NMR to indicate the quantitative formation of *trans*-PdCl(COCH$_2$Ph)(PPh$_3$)$_2$ (**8**) and free $HNEt_2$.

Reactions of Complexes 8−12 with Secondary Amines. To a CD_2Cl_2 (0.6 mL) solution of **8** (0.04 mmol) in an NMR tube was added $HNEt_2$ (0.041 mL, 0.40 mmol) and $PhSiMe_3$ (0.0068 mL, 0.04 mmol, as an internal reference) at room temperature under an atmosphere of argon. After 1 day, the reaction was analyzed by ^{1}H NMR and GC-MS (Table 1).

The same procedure as described above was used in the reactions of complexes **9**−**12** with $HNEt_2$, piperidine, and morpholine, respectively (Table 1).

Decomposition of PdCl(COCH$_2$Ph)(PR$_3$)(NHEt$_2$) (R = Ph, Me). A CD_2Cl_2 (0.6 mL) solution of **13** (0.024 g, 0.04 mmol) was placed in an NMR tube at room temperature under an atmosphere of argon. $PhSiMe_3$ (0.0068 mL, 0.04 mmol) was added as an internal reference. After 3 days at room temperature, the solution was analyzed by ^{1}H and ^{31}P NMR and GC-MS to reveal the formation of **15** (41%), (PhCH$_2$)$_2$ (8%), a small amount of phenylacetic acid anion, and an unidentified compound (6%).

The same procedure was used for the decomposition experiment of **14** (0.016 g, 0.04 mmol). After the CD_2Cl_2 solution of **14** was allowed to stand at room temperature for 3 days, the solution was found to be composed of a mixture of the undecomposed complex **14** (45 mol %/Pd), **15** (15 mol %/Pd), $PhCH_2Cl$ (8 mol %/Pd), (PhCH$_2$)$_2$ (6 mol %/Pd), **9** (6 mol %/Pd), and a small amount of phenylacetic acid anion.

Decomposition of 13 in the Presence of a Tertiary Amine. A CD_2Cl_2 (0.6 mL) solution of **13**, prepared in situ by mixing **11** (0.021 mg, 0.02 mmol) with $HNEt_2$ (0.0046 mL, 0.044 mmol), was placed in an NMR tube at room temperature under an atmosphere of argon. NEt_3 (0.055 mL, 0.4 mmol) or proton sponge (0.086 g, 0.4 mmol) and $PhSiMe_3$ (0.0068 mL, 0.04 mmol, as an internal reference) were added. The decomposition reaction was analyzed by ^{1}H NMR and GC-MS after 3 days to show the formation of **15** in a yield of 80 mol %/Pd (NEt_3) or 43 mol %/Pd (Proton Sponge).

Reactions of Complexes 8 and 9 with MeOH and EtOH in the Presence of Et$_3$N or Proton Sponge. To a CD_2Cl_2 (0.6 mL) solution of **8** (0.04 mmol) in an NMR tube was added alcohol (0.40 mmol), $PhSiMe_3$ (0.0068 mL, 0.04 mmol, as an internal reference), and a tertiary amine (0.40 mmol) at room temperature under an atmosphere of argon. After 1 day, the reaction was analyzed by ^{1}H NMR and GC-MS (Table 2).

The same procedure as described above was used in the reactions of complex **9** with alcohols (Table 2).

Reactions of Complexes 8−12 with HNEt$_2$/EtOH. To a CD_2Cl_2 (0.6 mL) solution of a (phenylacetyl)palladium complex (0.04 mmol/Pd) in an NMR tube was added a mixture of $HNEt_2$ (0.041 mL, 0.40 mmol) and EtOH (0.023 mL, 0.40 mmol), together with $PhSiMe_3$ (0.0068 mL, 0.04 mmol, as an internal reference) at room temperature under an atmosphere of argon. After 1 and 3 days, the reaction mixtures were analyzed by ^{1}H NMR and GC-MS (Table 3).

In the reaction of **8** with $HNEt_2$/EtOH, different ratios of free PPh_3 were added and the formation of ester **19** and amide **15** were analyzed by ^{1}H NMR after 1 day (Table 3). Kinetic studies on the reactions of **8** with $HNEt_2$/EtOH in the absence and presence of 2 equiv of PPh_3 were performed and monitored by ^{1}H NMR by observing the decay of the benzyl signals of complex **8** at room temperature.

Competitive Reactions of Complex 8 with Various Pairs of Alcohols and Secondary Amines. To a CD_2Cl_2 (0.6 mL) solution of **8** (0.03 mmol) in an NMR tube was added amine (0.30 mmol) and alcohol (0.30 mmol), together with $PhSiMe_3$ (0.0051 mL, 0.03 mmol, as an internal reference) at room temperature under an atmosphere of argon. After 1 day, the reaction was analyzed by ^{1}H NMR and GC-MS (Table 4).

Reactions of *trans*-PdX(CH$_2$Ph)(PPh$_3$)$_2$ (1a, X = Cl; 1b, X = I) and *trans*-PdCl(COCH$_2$Ph)(PPh$_3$)$_2$ (8) with CO and Et$_2$NH. General Procedure. In a typical experiment, a 100-mL stainless steel autoclave was charged with *trans*-PdCl(CH$_2$Ph)(PPh$_3$)$_2$ (**1a**) (0.100 g, 0.13 mmol), THF or $CHCl_3$ (2 mL), and Et_2NH (0.135 mL, 1.3 mmol) under an atmosphere of argon. Carbon monoxide was introduced into the system, and

the mixture was magnetically stirred at room temperature for 1 day. The yields of *N*,*N*-diethyl phenylacetamide (**15**), *N*,*N*-diethyl phenylpyruvamide (**20**), and *N*,*N*-diethyl oxamide (**21**) produced were measured using $PhSiMe_3$ as an internal standard by means of GC (Column: SE-30), GC-MS, and ^1H NMR after evaporation of solvent by comparison with authentic samples. In addition, $Et_2NH_2^+X^-$ was detected in the mixture. NMR data assigned for **20**: ^1H NMR (CD_2Cl_2, δ, 270 MHz, 298 K) 7.4−7.2 (m, 5H, Ph), 4.01 (s, 2H, PhCH_2), 3.29 (q, J = 7.3 Hz, 2H, N(CH_2CH$_3$)(CH$_2$′CH$_3$′)), 2.97 (q, J = 7.0 Hz, 2H, N(CH$_2$CH$_3$)(CH_2′CH$_3$′)), 1.03 (t, J = 7.3 Hz, 3H, N(CH$_2$CH_3)(CH$_2$′CH$_3$′)), 0.95 (t, J = 7.0 Hz, 3H, N(CH$_2$CH$_3$)-(CH$_2$′CH_3′)).

The same procedure as for the carbonylation of **1a** was employed for the carbonylation of **1b** and **8**. The results are summarized in Table 5.

Reaction of *trans*-[Pd(COCH$_2$Ph)(CO)(PMe$_3$)$_2$]PF$_6$ (7) with Et$_2$NH in the Presence of CO. A CD_2Cl_2 solution of **7** was prepared in situ by the reaction of **4** with ^{12}CO as described elsewhere.[15b] Et_2NH (0.042 mL, 0.4 mmol) was added to this solution at −20 °C under CO pressure by a syringe, and the mixture was allowed to stand at room temperature for 2 days. Compounds **15** and **20** were obtained in a ratio of 1 to 2.5, as identified by ^1H NMR and GC-MS. The formation of $Et_2NH_2^+PF_6^-$ was confirmed by ^1H and ^{31}P NMR, and a Pd metal black precipitate was found.

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