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A Convenient Route to *β*,*γ*-Unsaturated Esters without Formation of the *α*,*β*-Isomers. Palladium-Catalyzed Alkoxycarbonylation of Allylic Halides under Alcohol–Potassium Carbonate Tow-Phase Conditions

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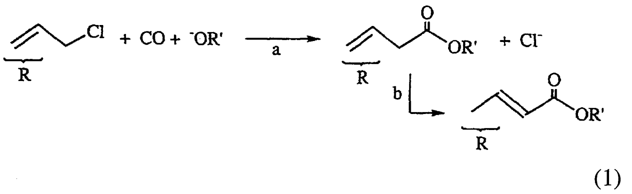
Palladium-catalyzed, atmospheric pressure carbonylation of allylic halides under alcohol-potassium carbonate (liquid–solid) two-phase conditions affords *β*,*γ*-unsaturated esters without formation of the *α*,*β*-isomers. Phosphine-free palladium compounds such as $Pd(OAc)_2$ (**1**) and $Na_2[PdCl_4]$ (**2**) are a convenient catalyst for this reaction. Presence of triphenylphosphine retards the carbonylation. A mixture of $Pd(OAc)_2$-PPh_3 or $[PdCl_2(PPh_3)_2]$ (**3**) catalyzes the carbonylation under pressure.

Palladium-catalyzed carbonylation of allylic halides in ethanol has a disadvantage that it requires a carbon monoxide pressure higher than 100 kg cm^{-2}. [1,2] In 1982 Tsuji and co-workers[3] have reported that *β*,*γ*-unsaturated esters can be obtained easily by the palladium-catalyzed carbonylation of allyl alkyl carbonates under mild conditions. Though this carbonylation occurs virtually under atmospheric pressure of carbon monoxide, higher pressure results in higher yields of esters in most cases. Additionally, it has been pointed out that the most crucial reaction variable is temperature. The reaction takes place at very limited ranges of temperature, namely, around 50 °C.[4] At 80 °C, exclusive ether formation takes place without carbonylation.

Several years ago we have succeeded in atmospheric-pressure carbonylation of allyl halides and their substituted derivatives in the presence of bases such as aqueous sodium hydroxide[5] or alkoxide[6] at room temperature (Eq. 1).[7]



(1)

In this reaction the solution is so strongly basic that the *β*,*γ*-unsaturated esters are very susceptible to the base-catalyzed isomerization (step b). This is a major disadvantage of this reaction. In order to prevent this isomerization, the base was added dropwise to the solution. But this procedure was somewhat troublesome and the isomerization still occurred to some extent. Hence, a more convenient method has been desired.

In these years two-phase systems such as aqueous/organic or solid/liquid systems attract attention in catalysis, where simple and complete separation of the catalyst from the product is required.[8—11] In the course of the study on two-phase catalysis, it has now been found that an ethanol–potassium carbonate liquid–solid two-phase system is very convenient for the synthesis of *β*,*γ*-unsaturated esters from allylic halides. Details of this reaction will be presented in this paper.

Results and Discussion

Initially, a systematic investigation was undertaken with cinnamyl chloride to define the reaction, since cinnamyl chloride is more liable to coupling or hydrolysis of the allylic moiety than other allylic halides and the analysis of the products is easy. The results are summarized in Table 1. Generally, a heterogeneous reaction like this is a diffusion-controlled reaction and is strongly influenced by stirring and by the shape of the reaction vessel. Thus, all reactions of the present study were carried out in the same vessel using the same stirring bar. The atmospheric-pressure reaction was followed by the measurement of the absorption of carbon monoxide by a burette. This carbonylation is characterized by the rapid absorption of carbon monoxide. A mixture of ethanol, cinnamyl chloride (5 mmols), K_2CO_3, and $Pd(OAc)_2$ (**1**) (1%) absorbed carbon monoxide immediately when it was stirred under carbon monoxide at 20 °C. During the first 10 min, the absorption was a little slow (on average, ca. 1.3 ml min^{-1}). After 10 min, the rate increased to ca. 2.7 ml min^{-1}. Within 50 min, the absorption was completed (Entry 1). Ethyl 4-phenyl-3-butenoate was obtained in a 94.1% yield. Sodium tetrachloropalladate, $Na_2[PdCl_4]$ (**2**) catalyzed the reaction. But the absorption rate was on average 0.8 ml min^{-1} during the first 2 hours (Entry 2).

Anhydrous K_2CO_3 is practically insoluble in ethanol. During the rapid absorption of carbon monoxide, the suspension

Table 1. Carbonylation of Cinnamyl Chloride in C_2H_5OH–K_2CO_3 Two-Phase System[c)]

$$C_6H_5CH{=}CH{-}CH_2Cl \xrightarrow[C_2H_5OH/K_2CO_3]{CO} C_6H_5CH{=}CH{-}CH_2CO_2C_2H_5$$

Entry	Pd	PPh$_3$	Conditions			Yield[a)]
	Compd	Added (P/Pd)	kg cm^{-2} [b)]	°C	min	%
1	Pd(OAc)$_2$ (**1**)	No	1	20	50	94.1
2	Na$_2$[PdCl$_4$] (**2**)	No	1	20	180	83.2
3	**1**	Yes (1/1)	1	20	220	25.8
4	**1**	Yes (1/1)	50	50	180	93.2
5	**2**	Yes (1/1)	1	20	240	38.0
6	**2**	Yes (1/1)	50	50	180	95.0
7	[PdCl$_2$(PPh$_3$)$_2$] (**3**)	No	1	20	24(h)	13.1
8	**3**	No	10	50	30	34.9
9	**3**	No	30	50	30	54.5
10	**3**	No	50	50	30	82.1
11	**3**	No	50	50	60	94.3

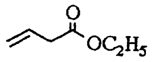
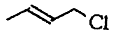
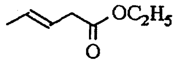
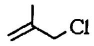
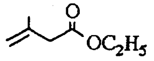
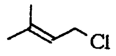
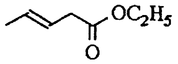
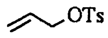
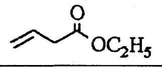
a) Ethyl 4-phenyl-3-butenoate. b) CO pressure. c) Cinnamyl chloride, 5 mmol; catalyst, 1 mol%; K_2CO_3, 15 mmol; ethanol, 5 ml.

had a color varying from pale yellow to off-white at the end. After the carbon monoxide absorption stopped, the suspension turned gray to black, liberating palladium as a black precipitate. To avoid precipitation of metallic palladium, one equivalent of triphenylphosphine was added to Pd(OAc)$_2$ (Entry 3). In this case, however, the absorption was very slow (ca. 0.2 ml min^{-1}) and the yield of the ester was below 30% for 220 min. These results show that even the addition of one equivalent of triphenylphosphine results in marked decrease of the absorption rate of carbon monoxide. A large amount of cinnamyl chloride remained unchanged. Triphenylphosphine complex, [PdCl$_2$(PPh$_3$)$_2$] (**3**), catalyzed the reaction with difficulty under atmospheric pressure (Entry 7). In ethanol–K_2CO_3 system, it can be assumed that allylic carbonate is formed as an intermediate. The allylic carbonate thus formed would be carbonylated at atmospheric pressure, as reported by Tsuji et al.[4)] However, it is difficult to explain why this pathway would be favored under the present biphasic conditions. As described in the previous paper,[7)] phosphine-free palladium compounds are preferable to phosphine-modified ones in the present two-phase reaction. This is a marked contrast to the decarbonylation–carbonylation of allylic carbonates, where Pd(OAc)$_2$ alone has on catalytic activity and phosphine as a ligand must be added. The effect of triphenylphosphine in the present reactions is not clear. But the negative effect of adding it as the auxiliary ligand is not ascribed to the difficulty in the formation of a zero valent catalytic species, from the following evidence: 1) Pd(OAc)$_2$ reacts with triphenylphosphine to give triphenylphosphine oxide and a zero valent palladium species,[12)] and 2) the reduction is also promoted by adding a small amount of water.[13)] Water is not completely excluded from this C_2H_5–OH–K_2CO_3 two-phase system discussed below. Under pressure, however, [PdCl$_2$(PPh$_3$)$_2$] catalyzed the carbonylation and the formation of metallic palladium as a precipitate was not observed. Thus, cinnamyl chloride was readily carbonylated under 50 atm at 50 °C. The ester was obtained in a 94.3% yield within 1 h (Entry 11). It is likely that triphenylphosphine exerts its effect either on the CO insertion step or on the reductive elimination to ester.

Though the carbonylation of allyl and methallyl chlorides in alcohol-alkoxide homogeneous system failed to give the corresponding β,γ-unsaturated esters selectively due to the base-catalyzed isomerization,[6)] all reactions with various allylic halides proceeded satisfactorily under the solid–liquid two-phase conditions except for the carbonylation of 1-chloro-3-methyl-2-butene, which gave the ester in a 28.8% yield (Entry 15) (Table 2). The corresponding bromo analogue, 1-bromo-3-methyl-1-butene, gives the acid or ester in a moderate yield in an aqueous NaOH/organic solvent two-phase system or homogeneous alcoholic/alkoxide system, respectively.[7)] These results show that the bulky end of allylic group hinders the carbonylation appreciably.

Allyl tosylate was carbonylated similarly. Allyl acetate and alcohol were not carbonylated under atmospheric pressure, while they afford ethyl 3-butenoate in 40—80% yields

Table 2. Atmospheric Pressure Carbonylation of Allylic Compounds by Pd(OAc)$_2$ in C_2H_5OH–K_2CO_3 Two-Phase System at 20 °C[a)]

Entry	Allylic Compd	Time / min	Ester (Yield/%)	
12		35		(67.1)
13		55		(63.0)
14		50		(98.9)
15		60		(28.8)
16		50		(71.8)

a) Conditions were same as those in Table 1.

in ethanol without K_2CO_3 under 100 atmospheres at 100 °C.

It is to note that the most convenient and typical preparation method of a π-allyl complex of palladium, $[PdCl(\eta^3\text{-}C_3H_5)]_2$, is to bubble carbon monoxide into a wet methanol solution of $Na_2[PdCl_4]$.[14] As described earlier,[1] the carbonylation of allyl chloride in ethanol without K_2CO_3 required a high pressure of carbon monoxide and the yield of the esters (2- and 3-butenoate) was at the highest 50%. Addition of K_2CO_3 brings about a sudden change. The presence of K_2CO_3 is crucial for this atmospheric pressure carbonylation. Stille and co-workers[15] have reported that the palladium-catalyzed, atmospheric pressure carbonylation of *cis*-4-chloro-2-buten-1-ol by $[Pd(CO)(PPh_3)_3]$ in a K_2CO_3/DMF system at 25 °C for 72 h gives 2-methylene-3-propanolide in a 52% yield. The turnover number per hour is 0.18. The CO insertion into the Pd–O bond, namely hydroxide attack on a coordinated carbon monoxide, has been proposed. In the previous paper,[7] the possibility of an insertion of carbon monoxide into the Pd–alkoxide bond was also proposed in the carbonylation of allylic halides in the presence of alkoxide. Both solid–liquid two-phase carbonylation and Stille's lactone formation can be discussed in the same manner. The only difference is that the lactone formation is the intramolecular esterification. The K_2CO_3–ethanol system forms an alkoxide solution. The alcoholic solution is characterized by very limited concentration ranges of alkoxide, because K_2CO_3 is almost insoluble in alcohol. Consequently, the concentration of the base during the carbonylation is held so low that the base-catalyzed isomerization of β,γ- to α,β-isomer occurs with difficulty. The alkoxide attack on a coordinated carbon monoxide accounts nicely for the present two-phase carbonylation.

In the present study, commercially available, anhydrous K_2CO_3 was used without drying before use. Therefore, a very small amount of water was likely involved, because K_2CO_3 is hygroscopic. The use of sodium carbonate monohydrate instead of anhydrous K_2CO_3 resulted in the decrease of the ester yield (below 50%). These results show that even the addition of a small, controlled amount of water affects the reaction markedly. In this case the system is brought so close to the aqueous NaOH/organic two-phase conditions that its acid is formed at the expense of the ester. On the other hand, a very small amount of water absorbed in anhydrous K_2CO_3 does not affect the yield.

Sodium hydroxide gave similar results. But this is more hygroscopic than K_2CO_3. Therefore, the use of K_2CO_3 and $Pd(OAc)_2$ as the base and the catalyst, respectively, is a favorable choice for this carbonylation.

Experimental

General Remarks. Commercially available allylic chlorides, anhydrous potassium carbonate, and $Pd(OAc)_2$ were used without further purification. Sodium carbonate mono-hydrate was prepared by depositing from an aqueous solution around 50 °C and was dried under vacuum. $PdCl_2(PPh_3)_2$ was prepared by the known methods.[16] Ethanol was dried over magnesium, distilled and stored under an atmosphere of argon. The NMR spectra were recorded on a JEOL JMN-GX270 or JNM-PMX60 spectrometer. Gas chromatographic (GC) analysis was performed on a column, Silicone DC-560, 2 m×6 ϕ. The yields of esters were determined by GC, using naphthalene as an internal standard.

General Procedure for the Carbonylation. 1. Under Atmospheric Pressure. The reaction apparatus and procedure were similar to those of the alkoxycarbonylation in alcohol-alkoxide system. A round-bottom flask (30 ml) and a Teflon®-coated magnetic stirring bar were used. The catalyst, K_2CO_3, and a stirring bar were placed in the flask. The atmosphere was replaced with carbon monoxide and then alcohol and allylic compounds were added by a syringe under carbon monoxide. The reaction conditions are shown in Tables 1 and 2. The flask was thermostatted. After the reaction was started by magnetically stirring, the absorption rate of carbon monoxide was measured by a burette. The solids were filtered off and then the solution was subjected to GC and NMR analyses.

2. Under Pressure. In an stainless steel autoclave (50 ml) were placed a short and broad stirring bar, catalyst, and K_2CO_3. The atmosphere was replaced with carbon monoxide and then alcohol and allylic compounds were added under carbon monoxide. The autoclave was assembled and charged with carbon monoxide, placed in an oil bath, and heated with magnetically stirring. The conditions are shown in Table 1. After the reaction, the autoclave was disassembled and the reaction solution was filtered. The solution was subjected to GC analysis.

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