Hydrocarbonylation of Enol Esters Catalyzed by a Palladium(II) Complex

Kiyoshi Kudo,* Yuji Oida, Koichi Mitsuhashi, Sadayuki Mori, Koichi Komatsu, and Nobuyuki Sugita

Institute for Chemical Research, Kyoto University, Uji, Kyoto 611

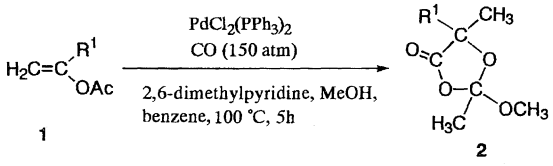
(Received November 22, 1995)

The palladium(II)-catalyzed carbonylation of various enol esters in the presence of methanol under pressurized carbon monoxide was investigated. As typical results, the carbonylation of isopropenyl acetate afforded a cyclocarbonylation product, 2-methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one, in 46% yield under carbon monoxide of 150 atm at 100 °C, whereas vinyl acetate selectively gave an α-hydroesterification product, methyl 2-acetoxypropionate, in 56% yield under 250 atm at 100 °C. On the contrary, the reaction of 3,3-dimethyl-1-buten-2-yl acetate gave exclusively a β-hydroesterification product, methyl 3-acetoxy-4,4-dimethylpentanoate, in 64% yield. The yields of these products show a maximum as a function of the base/palladium ratio and of the carbon monoxide pressure. The effects of the reaction variables, such as the MeOH/substrate ratio, the structure of the base, the base/Pd ratio, the CO pressure, and the reaction temperature, were examined for optimizing the process. The mechanisms for the unique cyclocarbonylation and highly regioselective hydrocarbonylation of enol esters involving hydridopalladium(II) intermediate are discussed.

The transition-metal-complex catalyzed reaction of carbon monoxide with olefins in the presence of acidic nucleophiles, like water or alcohols,affords carboxylic acids (hydrocarboxylation) or esters (hydrocarbonylation) respectively.[1,2] The major drawback of such reactions is that at least two isomeric products are usually formed. Consequently, a great deal of effort has been devoted to find ways to control the regioselectivity of the reaction.

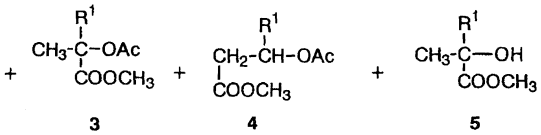
One of the most practical ways to synthesize an α- or β-functionalized carboxylic acid or esters is to regioselectively hydrocarboxylate or hydroesterify an olefin which bears the desired functional group on one of the olefinic carbons. Therefore, the hydrocarboxylation and hydrocarbonylation of such olefins has been extensively studied.[2] Recently, a few examples of the successful asymmetric hydroformylation of vinyl acetate by a chiral rhodium(I)-complex have been reported by Takaya et al.[3] However, no reports have been made for the regioselective hydrocarboxylation or hydrocarbonylation of enol acetates (Eq. 1). If the α-selective reaction is attained, it would give α-acetoxy acids or esters, which can be easily hydrolyzed into α-hydroxy acids, the potential synthetic intermediates of various natural products and biologically active compounds.[4].

We previously reported that a rhodium-phosphine complex is a very effective catalyst for the hydrocarbonylation of formaldehyde to afford hydroxyacetaldehyde.[5] Murai and co-workers have reported that a new catalytic reaction system of $HSiR_3/Co_2(CO)_8/CO$ can bring about incorporation of CO into aliphatic aldehyde[6] and cyclobutanones.[7] During our continued research to develop the method for carbonylation of the carbonyl carbon in aldehydes and ketones, we found a novel palladium(II)-catalyzed cyclocarbonylation of isopropenyl acetate (**1a**), which gives 2-methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one (**2a**) with high selectivity (Eq. 1, $R^1 = CH_3$).[8] This finding compelled us to examine the carbonylation of other enol esters in the presence of methanol. A marked difference in the product distribution and regioselectivity was observed depending on the structural factor. In this paper we report on the full details concerning the palladium-catalyzed carbonylation of the enolic olefins of various structures.



1 2

a: $R^1=CH_3$
b: $R^1=H$
f: $R^1=C(CH_3)_3$



3 4 5

(1)

Results

Cyclocarbonylation of Isopropenyl Acetate (1a). When isopropenyl acetate (**1a**) was carbonylated under 150 atm carbon monoxide at 100 °C in the presence of methanol and a catalytic amount of $PdCl_2(PPh_3)_2$ in benzene, a cyclocarbonylation product, 2-methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one (**2a**), was obtained as a main

product together with small amounts of methyl 2-acetoxyisobutyrate (**3a**) and methyl 3-acetoxybutyrate (**4a**) (see Eq. 1, $R^1=CH_3$). First, we examined the catalytic activities of other typical palladium complexes, such as $PdCl_2(PhCN)_2$, $PdCl_2(AsPh_3)_2$, $PdCl_2(PBu_3)_2$, $Pd(OAc)_2+2(PPh_3)$, $PdCl_2$(dppe), $PdCl_2$(dppb), and $Pd(PPh_3)_4$, for cyclocarbonylation at 100 °C and 200 atm of carbon monoxide; it was found that only $PdCl_2(PPh_3)_2$ showed a sufficient effective catalytic activity to promote the reaction. Alternatively, the addition of two molar amounts of triphenylphosphine to $PdCl_2$ catalyst exhibited nearly the same reactivity and regioselectivity as a reaction catalyzed by $PdCl_2(PPh_3)_2$. Other transition-metal complexes, such as $NiCl_2(PPh_3)_2$, $PtCl_2(PPh_3)_2$, and $RhCl(PPh_3)_3$, showed no catalytic activity. We thus decided to employ $PdCl_2(PPh_3)_2$ for the present study.

Next, in order to determine the optimum reaction conditions, the effects of the MeOH/**1a** ratio and the base/Pd ratio on the reactivity were examined. As Table 1 indicates, no reaction proceeded without methanol (Run 1), and the MeOH/**1a** ratio and base/Pd ratio significantly affected the yield and selectivity of **2a**. A nearly equimolar amount of methanol to **1a** (MeOH/**1a**=1.25) gave the highest yield of **2a** (Run 3), and a hydroxy ester **5a** was produced in place of **2a** as the MeOH/**1a** ratio became higher (Runs 4—6), presumably due to an in situ methanolysis of **2a**. The use of ethanol in place of methanol afforded the corresponding dioxolanone, 2-ethoxy-2,5,5-trimethyl-1,3-dioxolan-4-one, in 41.5% yield under the same conditions as in Run 3. One problem in this reaction is that the alcoholysis of the starting material **1a** to acetone and methyl acetate occurs in preference to the carbonylation, particularly in the presence of methanol in large excess, which causes a decrease in the selectivity of **2a**. This undesirable side reaction could be suppressed to some extent by using either a small amount of methanol (MeOH/**1a**<1) or adding a base; the selectivity of **2a** was improved at the cost of the conversion. However, the use of an excessive amount of base remarkably decreased the conversion, and the deposition of metallic palladium was observed (Run 9). Thus, when 2,6-dimethylpyridine was used as a base, a combination of 2,6-dimethylpyridine/Pd=1 and MeOH/**1a**=1.25 gave the highest selectivity in **2a** (Run 8). Other bases, such as pyridine, tributylamine, and sodium butyrate, were almost as effective as 2,6-dimethylpyridine (Runs 10, 11, and 12).

The effect of the carbon monoxide pressure on the conversion and yield of **2a** at 100 °C is shown in Fig. 1 (marked △ and ▲). With an increase of the carbon monoxide pressure both the conversion and yield increased, passed through a maximum, and then gradually decreased. The maximum yield of **2a** (48%) was obtained at 160 atm. At higher pres-

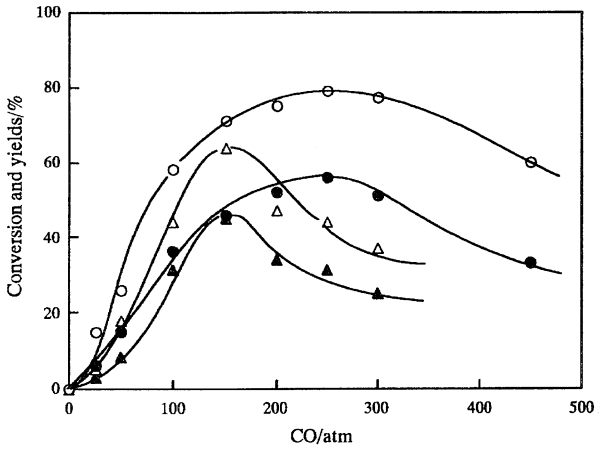


Fig. 1. Effects of CO pressure on the cyclocarbonylation of **1a** and hydrocarbonylation of **1b**. Reaction conditions: **1a** and **1b** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), MeOH (2.5 mmol), 2,6-dimethylpyridine (0.1 mmol), and benzene (10 ml), 100 °C. △: conversion of **1a**, ▲: yield of **2a**, ○: conversion of **1b**, ●: yield of **3b**.

Table 1. $PdCl_2(PPh_3)_2$-Catalyzed Cyclocarbonylation of **1a**[a)]

Run	Base/Pd	MeOH/**1a**	Conversion and yields/%[b)]					Select. of
			Conv.	**2a**	**3a**	**4a**	**5a**	**2a**/%[c)]
1	0	0	6	0	0	0	0	—
2	0	0.5	11	6.7	0.5	0.2	0	61
3	0	1.25	71	46	0.8	1.6	0	66
4	0	2.4	83	33	1.1	1.7	1.1	40
5	0	3.7	81	13	1.2	1.3	5.7	16
6	0	9.9	81	2.8	0.9	1.3	12	3.5
7	0.5[d)]	1.25	38	26	4.8	1.4	0	68
8	1.0[d)]	1.25	42	34	3.2	2.3	0	81
9	2.5[d)]	1.25	5.5	2.9	0.3	0	0	53
10	1.0[e)]	1.25	51	38	4.7	1.7	0	75
11	1.0[f)]	1.25	54	44	3.2	1.4	0	81
12	1.0[g)]	1.25	46	40	1.2	1.5	0	87

a) Conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), benzene (5 ml), CO (150 atm), 100 °C, 5 h. b) Determined by GLC and based on **1a** employed. c) Yield of **2a**/conversion in %. d) 2,6-dimethylpyridine. e) Pyridine. f) Tributylamine. g) Sodium butyrate.

sures, saturation of the active palladium(II) species with carbon monoxide may prevent the coordination of olefin to the metal center; this can account for the decrease in the yield.

The effect of the reaction temperature on the yield and products distribution under 200 atm of carbon monoxide is shown in Fig. 2. The best result with respect to the yield and selectivity of the desired product **2a** was achieved at 100 °C. Decreasing the temperatures to 70 °C greatly retarded the reaction, and higher temperatures (>120 °C) did not offer any advantages. Deactivation of the catalyst seems to occur significantly at temperatures higher than 120 °C, and a considerable amount of metallic palladium covered the inside of the reaction vessel as a mirror at 140 °C. Although the yield of hydrocarbonylation products (**3a** and **4a**) slightly increased with an increase in the reaction temperature at a very low level, the type and regioselectivity of products did not depend largely on the temperature.

A yield-time profile of the products in the reaction of **1a** is shown in Fig. 3, where an induction period of ca. 1 h was observed under the standard conditions. At an early stage (2—5 h), the yield of **2a** sharply increased; the reaction rate then gradually decreased at a later stage. Even after a prolonged reaction, the yields of the hydrocarbonylation products, **3a** and **4a**, were low. This catalytic reaction was complete within about 15 h, and afforded **2a** in 67% yield. However, the material balance of the starting material **1a** was not very good (80%) as the result of an inevitable decomposition (or alcoholysis) of the substrate. As discussed later, the presence of an induction period is of interest in connection with an activation step of the catalyst precursor.

Hydrocarbonylation of Vinyl Acetate (1b). In contrast to the case of isopropenyl acetate (**1a**), the most simple enol ester **1b** did not give any cyclization product, the major product being methyl 2-acetoxypropionate (**3b**) with high α-regioselectivity (Eq. 1, R^1=H). The reason for this marked difference in the reaction pathway is discussed later. The effects of several factors in the reaction conditions on the hydrocarbonylation of **1b** are summarized in Tables 2 and 3. As Table 2 shows, the type of phosphine ligands also exerts a marked influence upon both the yield and conversion for hydrocarbonylation as well as for cyclocarbonylation; the use of $PdCl_2(PPh_3)_2$ was most effective for the hydrocarbonylation of **1b** (Run 2). It should be noted that the halogen present as a ligand on the palladium(II)-phosphine complex has noticeable effects on the reactivity and regiochemistry. When a palladium(II) bromide complex, $PdBr_2(PPh_3)_2$, was used as a catalyst precursor, small amounts of a cyclocarbonylation product **2b** and a β-functionalized product **4b** were observed in addition to α-functionalized **3b** (Run 5), whereas $PdI_2(PPh_3)_2$ showed less catalytic activity and very poor regioselectivity (Run 6). The results that chloride (as a ligand on palladium) is more effective than bromide and iodide in the reactivity and regioselectivity correlate with the order of the bond strength of Pd(II)–X; X=I>Br>Cl. This correlation means that an electron-deficient, poorly coordinated Pd(II) center favors α-esterification, whereas a strongly coordinated palladium retards the reaction and causes a loss of regioselectivity.

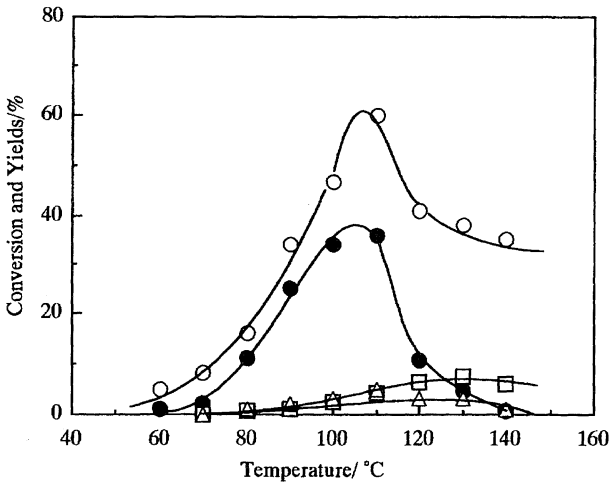


Fig. 2. Effect of reaction temperature on the cyclocarbonylation of **1a**. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), 2, 6- dimethylpyridine (0.1 mmol), MeOH (2.5 mmol), and benzene (5 ml) for 5 h under 200 atm of CO. ○: conversion of **1a**, ●: yield of **2a**, △: yield of **3a**, □: yield of **4a**.

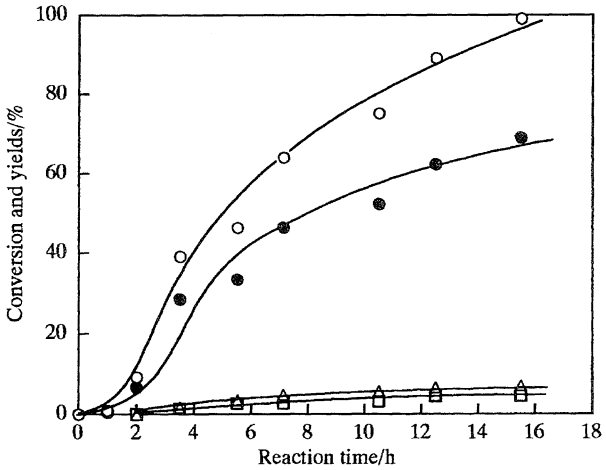


Fig. 3. Time-yield profile of cyclocarbonylation of **1a**. Reaction conditions: **1a** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), MeOH (2.5 mmol), 2,6-dimethylpyridine (0.1 mmol), and benzene (5 ml) at 100 °C under 200 atm of CO. ○: conversion of **1a**, ●: yield of **2a**, △: yield of **3a**, □: yield of **4a**.

Although the effect of the reaction temperature indicated a general trend analogous to that of **1a** (Runs 1, 2, 3, and 4), the influence was rather mild compared to that for **1a**. The optimum temperature was around 100 °C, and the decomposition of **1b** into acetaldehyde and methyl acetate became more apparent at higher temperatures. It is noteworthy that, at least over a time range of 2—10 h, and a temperature range of 80—150 °C, the regioselectivity of the catalytic reaction remains unchanged as long as $PdCl_2(PPh_3)_2$ is used as a catalyst.

The effect of the base is summarized in Table 3. Although

Table 2. Pd Complex-Catalyzed Hydrocarbonylation of **1b**[a)]

Run	Catalyst	Temperature/°C	Conversion and yields/%[b)]				
			Conversion	**2b**	**3b**	**4b**	AcOMe[c)]
1	$PdCl_2(PPh_3)_2$	80	27	0	13	0	1.7
2	$PdCl_2(PPh_3)_2$	100	71	Trace	46	Trace	5.4
3	$PdCl_2(PPh_3)_2$	120	85	0	48	Trace	25
4	$PdCl_2(PPh_3)_2$	150	96	0	40	0	39
5	$PdBr_2(PPh_3)_2$	100	66	7.3	30	3.0	13
6	$PdI_2(PPh_3)_2$	100	51	2.6	2.9	1.3	3.3
7	$PdCl_2$+P(*p*-tolyl)$_3$[d)]	100	73	Trace	36	Trace	4.6
8	$PdCl_2(P(OPh)_3)_2$	100	53	0	Trace	0	1.5
9	$PdCl_2$	100	27	0	0	0	4
10	$PdCl_2(PBu_3)_2$	100	23	0	0	0	0
11	$PdCl_2$(dppe)[e)]	100	21	0	0	0	0
12	$PdCl_2$(dppb)[f)]	100	19	0	0	0	0
13	$Pd(PPh_3)_4$	100	30	0	0	0	0
14	$PtCl_2(PPh_3)_2$	100	5	0	0	0	0

a) Conditions: **1b** (2.0 mmol), catalyst (0.1 mmol), CH_3OH (2.5 mmol), 2,6-dimethylpyridine (0.1 mmol), benzene (10 ml), CO (150 atm), time 5 h. b) Determined by GLC and based on **1b** employed. c) Attributed to methanolysis of **1b**. d) $PdCl_2$ 0.1 mmol, P(*p*-tolyl)$_3$ 0.2 mmol. e) dppe=1,2-bis(diphenylphosphino)ethane. f) dppb=1,4-bis(diphenylphosphino)butane.

Table 3. Effect of Bases and Methanol on the Hydrocarbonylation of **1b**[a)]

Run	Base	Base/Pd	MeOH/**1b**	Conversion and yields/%[b)]			
				Conv.	**3b**	**5b**	Select. of **3b**[c)]
1	None	—	1.25	56	15	0	27
2	Et_3N	1.0	1.25	72	44	0	61
3	*n*-Bu_3N	1.0	1.25	67	45	0	67
4	Pyridine	1.0	1.25	82	62	0	76
5	2,4,6-Trimethylpyridine	1.0	1.25	77	49	0	64
6	DBU[d)]	1.0	1.25	82	60	0	73
7	2,6-Dimethylpyridine	0.5	1.25	64	33	0	52
8	2,6-Dimethylpyridine	1.0	1.25	71	46	0	62
9	2,6-Dimethylpyridine	2.0	1.25	59	39	Trace	66
10	2,6-Dimethylpyridine	4.0	1.25	36	27	Trace	75
11	2,6-Dimethylpyridine	1.0	0.25	30	14	0	46
12	2,6-Dimethylpyridine	1.0	2.6	78	49	9.5	63
13	2,6-Dimethylpyridine	1.0	5.0	83	47	21	57
14	2,6-Dimethylpyridine	1.0	12.5	86	44	29	51

a) Conditions: **1b** (2.0 mmol), $PdCl_2(PPh_3)_2$ (0.10 mmol), MeOH (2.5 mmol), base (0.10 mmol), benzene (10 ml), CO (150 atm), 100 °C, 5 h. b) Determined by GLC and based on **1b** employed. c) yield of **3b**/conversion in %. d) 1,8-Diazabicyclo[5.4.0]undec-7-ene.

the addition of one equivalent base to the catalyst led to a significant increase in the yield and selectivity of **3b**, no systematic correlation was observed between the basicity or bulkiness of the tertiary amines and the reactivity for the hydrocarbonylation. The use of pyridine gave a preferable result (Run 4), though other bases, such as triethylamine, tributylamine, 2,4,6-trimethylpyridine, and 2,6-dimethylpyridine, were also effective (Runs 2, 3, 5, and 7). As the 2,6-dimethylpyridine/Pd ratio increased, an ascending tendency in the selectivity was observed, although both the conversion and yield tended to be suppressed (Runs 7, 8, 9, and 10). This sensitivity to the base/Pd ratio was much smaller than that observed for **1a**. The yield of **3b** also depended on the MeOH/**1b** ratio. Although this dependence of the reactivity on the MeOH/**1b** ratio is in the same direction as that observed for **1a**, the influence of the MeOH/**1b** ratio was much smaller than that for **1a**. When the MeOH/**1b** ratio was raised to over 2.6, methyl 2-hydroxypropionate (**5b**), which is the methanolysis product of **3b**, began to be produced, and its yield gradually increased (Runs 7, 10, 11, 12, and 13). The use of excess amounts of methanol (MeOH/**1b**$>$20) only accelerated the methanolysis of the substrate. When *t*-butyl alcohol was used in place of methanol, only *t*-butyl alkanoate corresponding to **3b** was obtained in 34% yield.

As shown in Fig. 1 (marked ○ and ●) the pressure-dependent hydrocarbonylation of **1b** was similar to, but less pronounced than, the cyclocarbonylation of **1a**. The maximum yield of **3b** was 55% with 79% conversion at 250 atm

of carbon monoxide.

Hydrocarbonylation of Other Enol Acetates. Several enol esters were studied in order to determine the scope of the hydrocarbonylation reaction; the results are summarized in Table 4. The structure of the acyloxy group in vinyl esters (**1c**, **1d**, and **1e**) did not cause any significant change in either the product yield or the regioselectivity (Runs 1, 2, and 3). Apparently, α-esterification is the preferred course, due to the electronic of an acyloxy group upon hydropalladation (vide infra). Of particular interest is the steric effect of an α-substituent R^1 upon the regioselectivity. A remarkable result was obtained for the hydrocarbonylation of 3,3-dimethyl-1-buten-2-yl acetate (**1f**). The regioselectivity was completely reversed from α- to β-esterification, and β-acetoxy ester **4f** was obtained exclusively in 64% yield (Run 4). When the substituent R^1 was a phenyl group (**1g**, R^1=Ph), no appreciable reaction took place, presumably because of the substrate's low stability under the given conditions, since the starting material was only recovered as acetophenone (Run 5).

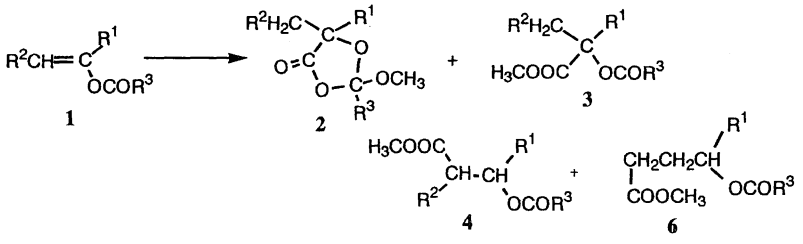
The reaction of enol esters of internal olefins was sluggish and did not show any selectivity (Runs 6 and 7). When the α-carbon carried a methyl group (**1i**) a small amount (3%) of the cyclic compound **2i** was obtained. Apparently, in these sluggish reactions a double-bond migration occurred competitively, which led to the formation of compounds **6**. A cyclic enol ester was even less reactive, probably due to a rearrangement of the intermediate into the π-allyl complex, which is known to be much less reactive in catalytic carbonylation.[9]

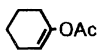
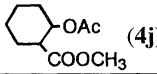
From the above results, it is disclosed that the nature of the substituent group on the α-carbon plays a decisive role in determining the regioselectivity of the reaction, and that the methyl group on the α-carbon is essential for the occurrence of cyclocarbonylation. Moreover, the dependency of the regioselectivity upon the substituent R^1 in the present reaction is quite remarkable compared with that of other ordinary olefins.[10] This highly regiospecific hydroesterification should be under electronic control due to the strongly polarized olefinic bond, and should differ from the reaction of less polarized olefins for which the regiochemistry appears to be determined by steric factors.[11] In the present study, a steric-controlled reaction was observed in the case of **1f**, in which the incorporation of carbon monoxide occurred exclusively at the less hindered β-olefinic carbon.

Mechanistic Study. The time-yield profiles of the products in the hydroesterification of **1b** under various MeOH/**1b** ratios and under various pressures of carbon monoxide are shown in Figs. 4 and 5, respectively. In an early stage of the reaction, there is an induction period which depends on the MeOH/**1b** ratio and carbon monoxide pressure. The induction period becomes shorter with an increase in the MeOH/**1b** ratio or with an increase in the carbon monoxide pressure, along with an enhancement of the reaction rate. These findings indicate that both methanol and carbon monoxide play an essential role not only on the catalytic cycle of the reaction, but also on the activation of the catalyst precursor prior to the catalytic cycle.

In order to verify such an activation process, an examination of the spectral change occurring during the course of the reaction is most interesting and should have significant mechanistic implications. The infrared spectral change of $PdCl_2(PPh_3)_2$ as a catalyst precursor was followed under the reaction conditions without or with substrate **1a**, i.e., under

Table 4. $PdCl_2(PPh_3)_2$-Catalyzed Hydrocarbonylation of Various Enol Esters[a]



Run	Enol ester				Time	Conv. [b]	Products and Yields/%[b]			
		R^1	R^2	R^3	h	%	**2**	**3**	**4**	**6**
1	**1c**	H	H	CH_2Cl	5	79	0	64	0	—
2	**1d**	H	H	C_3H_7	5	68	0	54	0	—
3	**1e**	H	H	C_6H_5	5	58	0	54	0	—
4	**1f**	$C(CH_3)_3$	H	CH_3	5	74	0	0	64	—
5	**1g**	C_6H_5	H	CH_3	5	34	0	0	0	—
6	**1h**	C_2H_5	CH_3	CH_3	24	51	Trace	0	19[c]	3
7	**1i**	CH_3	CH_3	CH_3	24	36	3	1	7[c]	2
8	**1j**				24	38	 (**4j**)			5

a) All reactions were carried out with enol ester (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), MeOH (2.5 mmol), and 2,6-dimethylpyridine (0.1 mmol) in benzene (10 ml) under CO (150 atm) at 100 °C. b) GLC yield based on enol ester employed. c) A mixture of diastereomers.

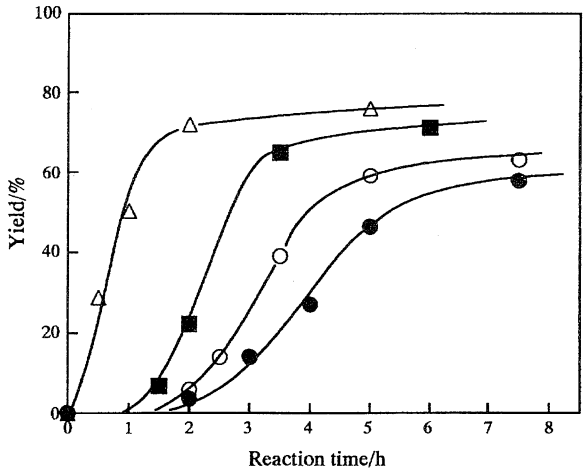


Fig. 4. Dependence of MeOH/**1b** ratio on the time-course of hydrocarbonylation of **1b**. Reaction conditions: **1b** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), 2,6-dimethylpyridine (0.1 mmol), and benzene (10 ml) at 100 °C under 150 atm of CO. △: MeOH/**1b**=6.5, ■: MeOH/**1b**=4.0, ○: MeOH/**1b**=2.5, ●: MeOH/**1b**=1.25.

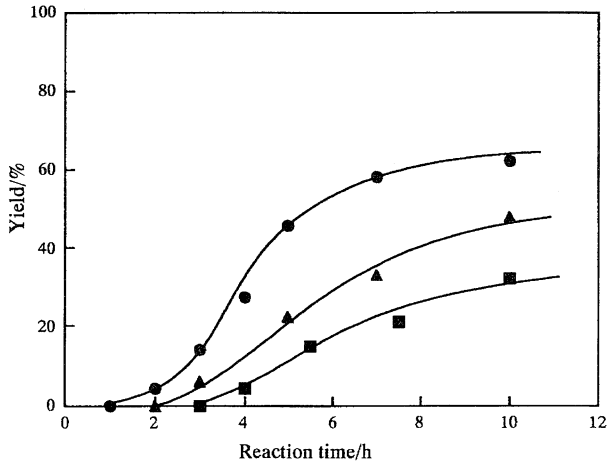


Fig. 5. Dependence of pressure on the time-course of hydrocarbonylation of **1b**. Reaction conditions: **1b** (2 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), MeOH (2.5 mmol), 2,6-dimethylpyridine (0.1 mmol), and benzene (10 ml) and 100 °C. ●: 150 atm, ▲: 100 atm, ■: 50 atm.

100 atm of carbon monoxide at temperature of 25—100 °C, by in situ IR spectroscopic techniques.[12] Since benzene has misleading absorption bands in the 1900—2000 cm^{-1} region, we chose chloroform as the solvent so as to avoid complications. The result is shown in Fig. 6. As the temperature was raised to around 100 °C, the characteristic absorption of $HPdCl(PPh_3)_2$ (**9**)[13] was observed at 2050 cm^{-1} (marked ● in Fig. 6) with added methanol (chloroform : methanol=10 : 1 by volume). This formation of a hydridopalladium complex at 100 °C is consistent with the temperature-dependence of both the hydrocarbonylation and the cyclocarbonylation reaction, as shown in Fig. 2. This absorption did not diminish after cooling down to room temperature and by reducing the pressure of carbon monoxide to 1 atm, unless exposed to air.

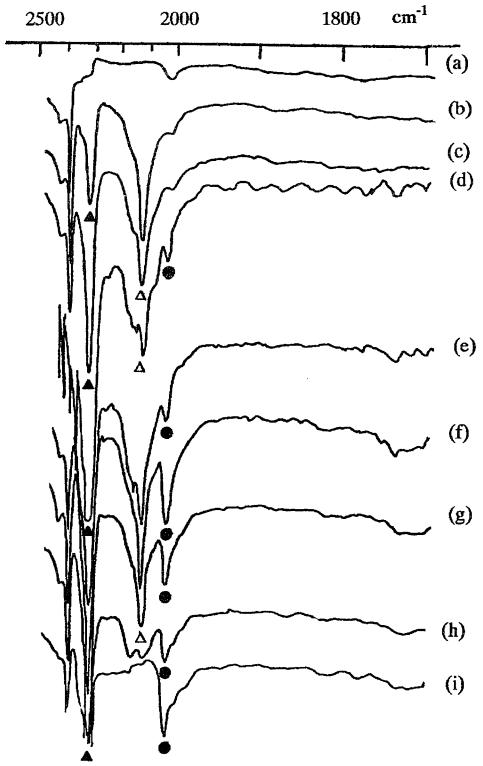
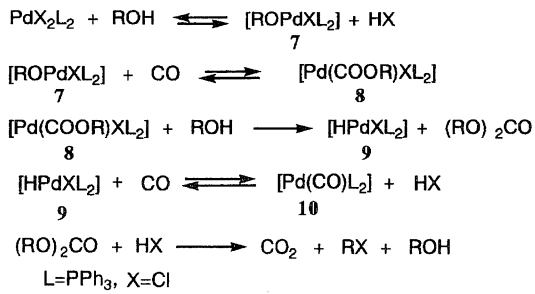


Fig. 6. In situ IR spectra of $PdCl_2(PPh_3)_2$ in methanol–chloroform mixed solvent (1 : 10 by vol.): (a) under 1 atm of CO at 18 °C, (b) under 100 atm of CO at 18 °C, (c) under 100 atm of CO at 60 °C, (d) after 1 h under 100 atm of CO at 100 °C, (e) cooled to 80 °C under 100 atm of CO, (f) cooled to 18 °C under 100 atm of CO, (g) CO pressure released to 35 atm at 18 °C, (h) pressure released to 8 atm at 18 °C, (i) pressure released to 1 atm at 18 °C. ●: $HPdCl(PPh_3)_2$, △: dissolved CO, ▲:dissolved CO_2.

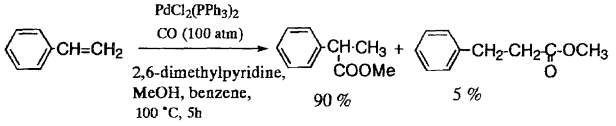
If either methanol or carbon monoxide was not present in the system, this band at 2050 cm^{-1} did not appear. In addition, when a large excess of substrate (MeOH/**1a**=0.5) was added into this system, this absorption disappeared. It should be noted that the conspicuous absorption at 2330 cm^{-1}, attributable to the generation of carbon dioxide (marked ▲ in Fig. 6), increases at a higher temperature. These results suggest that the hydridopalladium complex **9** is formed by the reaction of its precursor, $PdCl_2(PPh_3)_2$, with methanol and carbon monoxide, as shown in Scheme 1, and that **9** is the active species for the present reaction, as previously



Scheme 1.

reported.[14]

Furthermore, in order to confirm the active catalytic species in the present reaction, the hydrocarbonylation of styrene was performed in the present catalytic system, and was found to afford methyl 2-phenylpropionate as the main product in 90% yield together with a small amount of methyl 3-phenylpropionate (5%); no methyl cinnamate was detected (Eq. 2). These results also support a mechanism involving a hydridopalladium(II) complex **9** as catalytic species, because if alkoxycarbonyl-palladium(II) complex **8** is present as the main catalytic species, the production of methyl cinnamate and/or dimethyl phenylsuccinate would be preferred.[10b]



(2)

It is known that $PdCl_2(PPh_3)_2$ can abstract hydrogen from alcohol to form a hydrido complex **9** under these conditions.[14,15] Complex **9** is also known to undergo a reductive transformation into a carbonyl complex **10** under higher pressure of carbon monoxide,[15,16] which is consistent with the inactivation of the present system at higher pressure of carbon monoxide (Fig. 1).

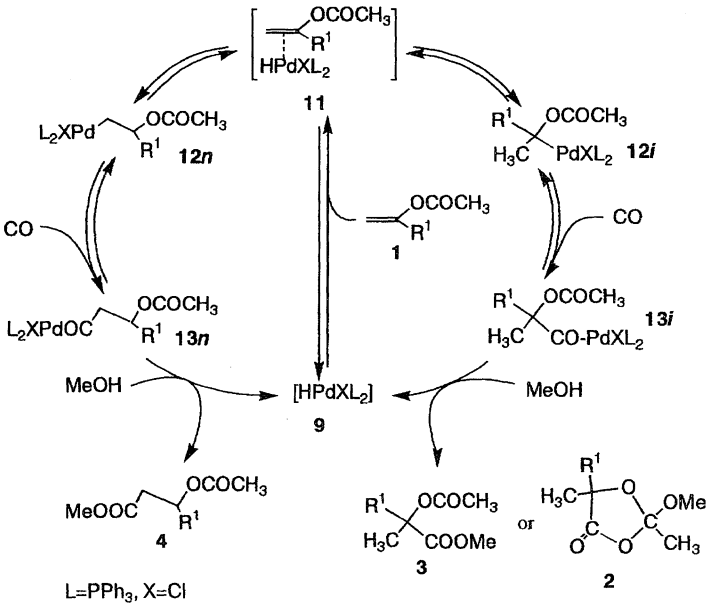
Discussion

The mechanisms of hydrocarbonylation catalyzed by transition-metal complexes have been extensively studied,[1,2] and two kinds of mechanism have been proposed: One mechanism involves hydridometal and acylmetal intermediates followed by alcoholysis; the other one involves (alkoxycarbonyl)metal and [β-(alkoxycarbonyl)alkyl]metal intermediates followed by an acid cleavage of the metal-alkyl bond.[11] One of the characteristic features of the present reactions is that the high regioselectivity is almost insensitive to the change of reaction variables, such as the temperature, reaction time, and pressure of carbon monoxide, although the regioselectivity and pattern of the reaction can dramatically change due to the bulkiness of a substituent at α-olefinic carbon (R^1).

We propose here a possible mechanism for the present reaction, which involves hydridopalladium(II) complex **9** as an active catalyst (Scheme 2). This scheme, similar to those for related catalyses,[10a,11,14] except for the case of **1a**, which undergoes a novel cyclocarbonylation, is consistent with prior studies with respect to each of the key steps of carbonylation, i.e., the formation of labile alkylpalladium intermediate (**12**) via olefin migration[11c,17] and acylpalladium species (**13**) via carbon monoxide insertion.[18]

The regioselectivity of the reactions would be determined by the relative stability of the two alkylpalladium(II) intermediates, **12*i*** and **12*n***. Since a partial negative charge develops on the α-carbon of the alkylpalladium intermediate, which should be stabilized by the electron-withdrawing group on the α-carbon, **12*i*** should be more favorable than **12*n***, and thus the α-acetoxy ester **3** should be produced selectivity. The results of the reactions of **1a** and **1b** are in accord with this interpretation, taking into account the inductive electron-withdrawing effect of the acetoxy group. In sharp contrast with this, when a bulky substituent is attached to the α-carbon, as in **1f**, the influence of a steric hindrance becomes predominant, and the less sterically demanding *n*-alkylpalladium complex **12*n*** is much more favorable, and thus gives the corresponding β-ester **4** exclusively.

The difference in reaction products **2** and **3** can apparently be attributed to the substituents R^1. In the cyclocarbonylation of **1a**, the methyl group attached to the α-carbon appears to be responsible for the cyclization. The restricted conformational flexibility of **13*i*** (R^1=CH_3) may result in an intramolecular interaction of an acylpalladium group with an



Scheme 2.

acetoxy group. Thus, the acetoxy carbonyl oxygen would undergo cyclic acylpalladation, i.e., an external attack by methanol on the acetoxy carbonyl carbon and simultaneous cyclization to give a five-membered ring (Scheme 3).

In the reaction of **1b**, the competitive methanolysis of the acylpalladium intermediate **13*i*** (R^1=H) to give **3b** proceeds in preference to cyclization, since that is a less conformational restriction. However, although there is no direct evidence, the other possible pathway from **13*i*** (R^1=H) into **3b**, via ketene intermediate formed by β-hydride elimination, is worth mentioning as one reason for the unfavorable cyclocarbonylation of **1b**.[19]

Experimental

Measurements. Analytical gas–liquid chromatography (GLC) was carried out with a Shimadzu GC-8A or Yanaco GC-3800 chromatograph using a column packed with PEG-1000 (2 m×3 mm) or a capillary column (OV-1701, 50 m×0.25 mm). The peak areas were determined by using an SIC 7000AS integrator with toluene as an internal standard. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-200 or Varian XL-300 spectrometer in deuteriochloroform using TMS as an internal standard. A GC-MS analysis was conducted on a Nichiden-Varian NEVA-TE600 spectrometer.

Materials. Solvents, alcohols, tertiary amines, and enol esters were dried by standard methods and distilled under nitrogen before use. 3,3-Dimethyl-1-buten-2-yl acetate (**1f**), 1-acetoxy styrene (**1g**), 2-penten-3-yl acetate (**1h**), 2-buten-2-yl acetate (**1i**) and 1-cyclohexenyl acetate (**1j**) were prepared following the literature methods.[20,21] Vinyl acetate (**1a**) and isopropenyl acetate (**1b**) were purchased from Nacalai Tesque Co. and used as received. Palladium-phosphine complexes such as $PdCl_2(PPh_3)_2$, $PdBr_2(PPh_3)_2$, $PdI_2(PPh_3)_2$, $PdCl_2(PBu_3)_2$, $PdCl_2$(dppe), $PdCl_2$(dppb), and $Pd(PPh_3)_4$ were prepared following the literature methods.[22,23] Other palladium complexes and platinum complex were purchased from Strem Chemicals, Inc., and used as received.

General Procedure for the Hydrocarbonylation. The typical procedure is as follows. A stainless-steel autoclave with a 40 ml glass liner was charged with enol ester **1** (2 mmol), methanol (2.5 mmol), 2,6-dimethylpyridine (0.1 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol), and benzene (5 ml), and pressurized with carbon monoxide to 150 atm (initial pressure at room temperature). The mixture was then stirred magnetically at 100 °C for a given period of time. After the autoclave was rapidly cooled by air-blowing, the reaction mixture was taken out from the autoclave and submitted to a quantitative GLC analysis for determining the product distribution and yield by using the internal-standard method. The products were isolated by column chromatography on silica gel and identified by a comparison of the ^{1}H and ^{13}C NMR and GC-MS fragmentation pattern with those of authentic compounds prepared in accordance with the literature methods.

In situ IR Spectra. A 10 ml autoclave directly equipped to a high-pressure IR cell block was charged with $PdCl_2(PPh_3)_2$ (0.05 mmol), methanol (0.5 ml), and chloroform (5 ml); the autoclave was then pressurized with carbon monoxide at room temperature. The IR cell block consisted of a stainless-steel body and polycrystalline CaF_2 optical flats (10 mm^t×20 mm$^\phi$), and had an optical pathlength of ca. 0.1 mm.[12] The mixture was stirred by a magnetically driven vertically moving mixer; the system was electrically heated. IR spectra were recorded with a Hitachi EPI-G3 IR spectrometer. The pressure of carbon monoxide was maintained at 100 atm, and the temperature of the systems was gradually increased to 100 °C and a variable period was allowed for the spectra changes.

2-Methoxy-2,5,5-trimethyl-1,3-dioxolan-4-one (2a): An authentic compound was prepared by a literature method.[24] ^{1}H NMR δ=3.26 (s, 3H), 1.64 (s, 3H), 1.48 (s, 3H), and 1.43 (s, 3H); ^{13}C NMR δ=174.7, 120.5, 78.6, 49.4, 25.3, 24.8, and 24.4. GC-MS *m/z* 129 (M^+-OCH_3) 101 and 59.

Methyl 2-Acetoxypropionate (3b): An authentic compound was prepared by the acetylation of methyl 2-hydroxypropionate using acetic anhydride in the presence of *p*-toluenesulfonic acid monohydride (2%) by a literature method.[25] ^{1}H NMR δ=5.05 (q, *J*=7.1 Hz, 1H), 3.71 (s, 3H), 2.10 (s, 3H), and 1.45 (d, *J*=7.0 Hz, 3H).

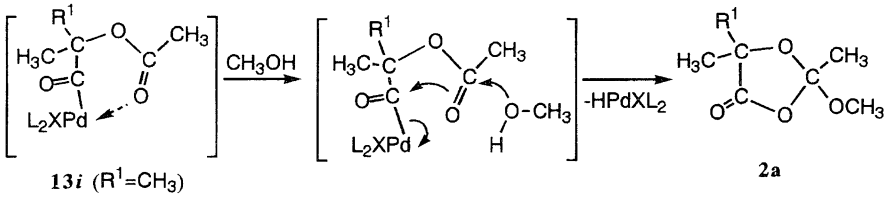
Methyl 2-Chloroacetoxypropionate (3c): An authentic compound was prepared by the acylation of methyl 2-hydroxypropionate using chloroacetyl chloride by a literature method.[26] ^{1}H NMR δ=5.19 (q, *J*=7.1 Hz, 1H), 4.16 (s, 3H), 3.77 (s, 3H), and 1.54 (d, *J*=7.1 Hz, 3H); ^{13}C NMR δ=171.2, 167.5, 70.8, 53.3, 41.3, and 17.6.

Methyl 2-Butyroxypropionate (3d): An authentic compound was prepared by the acylation of methyl 2-hydroxypropionate using butyryl chloride by a similar method to that of **3c**. ^{1}H NMR δ=5.09 (q, *J*=7.1 Hz, 1H), 3.74 (s, 3H), 2.33—2.40 (m, 2H), 1.63—1.73 (m, 2H), 1.48 (d, *J*=7.1 Hz, 3H), and 0.97 (t, *J*=7.4 Hz, 3H); ^{13}C NMR δ=173.0, 171.44, 68.4, 52.3, 35.9, 18.4, 17.0, and 13.6.

Methyl 3-Acetoxy-4,4-dimethylpentanoate (4f): An authentic compound was prepared from methyl 3-hydroxy-4,4-dimethylpentanoate[27] by a similar method to that of **3b**. ^{1}H NMR δ=5.14 (dd, *J*=9.8, 3.1 Hz, 1H), 3.68 (s, 3H), 2.60 (dd, *J*=15.0, 3.1 Hz, 1H), 2.46 (dd, and *J*=15.0, 9.8 Hz, 1H), 2.06 (s, 3H), and 0.94 (s, 9H); ^{13}C NMR δ=171.8, 170.4, 76.7, 51.9, 35.6, 34.5, 25.7, and 20.9.

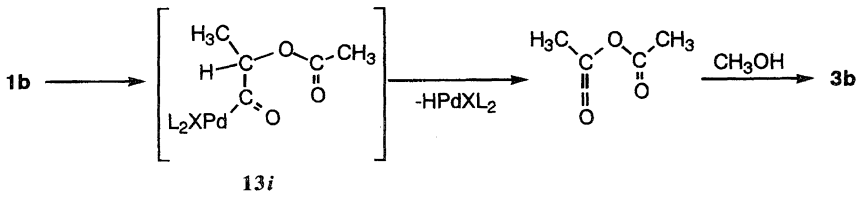
Methyl 3-Acetoxy-2-methylpentanoate (4h): An authentic compound was prepared from methyl 3-hydroxy-2-methylpentanoate[28] by a similar method to that of **3b**. ^{1}H NMR δ=5.07 (td, *J*=7.5, 4.2 Hz, 1H), 3.69 (s, 3H), 2.26—2.72 (m, 1H), 2.06 (s, 3H), 1.56—1.66 (m, 2H), 1.17 (d, *J*=7.1 Hz, 3H), and 0.91 (t, *J*=7.5 Hz, 3H); ^{13}C NMR δ=174.4, 170.6, 75.4, 51.8, 42.7, 25.0, 20.9, 11.8, and 9.9.

Methyl 3-Acetoxy-2-methylbutyrate (4i): An authentic compound was prepared from methyl 3-hydroxy-2-methylbutanoate[29] by a similar method to that of **3b**. ^{1}H NMR δ=5.04 (qd, *J*=6.3, 7.3 Hz, 2H), 3.58 (s, 3H), 2.54 (qd, *J*=7.1, 6.1 Hz, 2H), 1.93 (s, 2H),



13*i* (R^1=CH_3) **2a**

Scheme 3.



Scheme 4.

1.14 (d, J=6.4 Hz, 3H, and 1.08 (d, J=7.0 Hz, 3H).

Methyl 4-Acetoxypentanoate (6i): An authentic compound was prepared from methyl 4-hydroxypentanoate[30] by a similar method to that of **3b**. ^{1}H NMR δ=4.79—4.95 (m, 1H), 3.63 (s, 3H), 2.27—2.35 (m, 3H), 1.98 (s, 3H), 1.78—1.89 (m, 2H), and 1.18 (d, J=6.2 Hz, 3H).

Methyl 2-Acetoxycyclohexanecarboxylate (4j): An authentic compound was prepared from methyl 2-hydroxycyclohexanecarboxylate[31] by a similar method to that of **3b**. ^{1}H NMR δ=5.24 (td, J=10.3, 4.3 Hz, 1H), 2.72—2.81 (m, 1H), 2.28 (s, 3H), 2.24—2.40 (m, 2H), 1.97—2.09 (m, 2H), and 1.45—1.88 (m, 4H); ^{13}C NMR δ=174.7, 170.9, 73.8, 52.6, 49.3, 31.6, 29.2, 25.2, 24.6, and 21.9.

The authors wish to thank Mr. M. Yasumoto for manufacturing the in situ high-pressure IR cell and assembling the high-pressure experimental equipment.

References

1) I. Wender and P. Pino, "Organic Synthesis via Metal Carbonyls," Wiley-Interscience, New York (1977).

2) J. Falbe, "New Syntheses with Carbon Monoxide," Springer-Verlag, West Berlin (1980).

3) a) N. Sakai, K. Nozaki, K. Mashima, and H. Takaya, *Tetrahedron: Asymmetry*, **3**, 583 (1992); b) N. Sakai, S. Mano, K. Nozaki, and H. Takaya, *J. Am. Chem. Soc.*, **115**, 7033 (1993).

4) For example, see: J. A. M. Bont, *Tetrahedron: Asymmetry*, **4**, 1331 (1993).

5) T. Suzuki, K. Kudo, and N. Sugita, *Nippon Kagaku Kaishi*, **1982**, 1357.

6) a) Y. Seki, S. Murai, and N. Sonoda, *Angew. Chem., Int. Ed. Engl.*, **17**, 119 (1978); b) S. Murai, T. Kato, N. Sonoda, Y. Seki, and K. Kawamoto, *Angew. Chem., Int. Ed. Engl.*, **18**, 393 (1979).

7) N. Chatani, H. Furukawa, T. Kato, S. Murai, and N. Sonoda, *J. Am. Chem. Soc.*, **106**, 430 (1984).

8) For the preliminary report of this work, see: K. Kudo, K. Mitsuhashi, S. Mori, K. Komatsu, and N. Sugita, *Chem. Lett.*, **1993**, 1615.

9) a) R. F. Heck and D. S. Breslow, *J. Am. Chem. Soc.*, **83**, 1097 (1961); b) J. Powell and B. L. Shaw, *J. Chem. Soc. A*, **1967**, 1830; c) V. P. Barllargen and J. K. Stills, *J. Am. Chem. Soc.*, **108**, 45 (1986).

10) a) J. F. Knifton, *J. Org. Chem.*, **41**, 792 (1976); b) D. E. Jame and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 1810 (1976).

11) a) R. F. Heck and D. S. Breslow, *J. Am. Chem. Soc.*, **85**, 2779 (1963); b) R. F. Heck, *J. Am. Chem. Soc.*, **85**, 2013 (1963); c) J. Tsuji, *Acc. Chem. Res.*, **2**, 144 (1969).

12) K. Watanabe, K. Kudo, and N. Sugita, *Bull. Chem. Soc. Jpn.*, **58**, 2029 (1985).

13) K. Kudo, M. Hidai, T. Murayama, and Y. Uchida, *J. Chem. Soc., Chem. Commun.*, **1970**, 1701.

14) T. Fuchikami, K. Ohishi, and I. Ojima, *J. Org. Chem.*, **48**, 3803 (1983).

15) P. E. Garrou and R. F. Heck, *J. Am. Chem. Soc.*, **98**, 4115 (1976), and reference cited therein.

16) H. C. Clark, K. R. Dixon, and W. J. Jacobs, *J. Am. Chem. Soc.*, **91**, 1346 (1969).

17) D. M. Fenton, *J. Org. Chem.*, **38**, 3192 (1973).

18) a) G. Booth and J. Chatt, *J. Chem. Soc. A*, **1966**, 634; b) L. S. Hegedus and K. Siirala-Hansen, *J. Am.Chem. Soc.*, **97**, 1184 (1975).

19) We acknowledge the contributions of referee to this paper. One referee suggested that the methanolysis proceeds through a ketene intermediate formed by β-hydride elimination as one reason for the unfavorable cyclocarbonylation of **1b** (Scheme 4). We have adopted this suggestion in the revision of this paper as one possible pathway.

20) H. O. House and V. Kramar, *J. Org. Chem.*, **28**, 3362 (1963).

21) H. J. Hagemeyer and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949).

22) J. Chatt and F. G. Mann, *J. Chem. Soc. A*, **1966**, 770.

23) Y. Sugi and K. Bando, *Chem. Lett.*, **1976**, 727.

24) N. Cohen, B. L. Banner, A. J. Laurenzano, and L. Carozza, *Org. Synth.*, Coll. Vol. VII, 297 (1990).

25) R. H. Baker and F. G. Bordwell, *Org. Synth.*, Coll. Vol. III, 141 (1955).

26) C. R. Hauser, B. E. Hudson, B. Abramovitch, and J. C. Shivers, *Org. Synth.*, Coll. Vol. III, 142 (1955).

27) E. Wahlberg, *Ber. Dtsch. Chem. Ges.*, **65**, 1863 (1932).

28) G. A. Snow, *J. Chem. Soc.*, **1954**, 4080.

29) A. Michael and J. Rose, *J. Am. Chem. Soc.*, **55**, 3684 (1933).

30) E. Y. Spencer and G. F. Wright, *J. Am. Chem. Soc.*, **63**, 1281 (1941).

31) E. R. Marshall, J. A. Kuck, and R. C. Elderfield, *J. Org. Chem.*, **7**, 444 (1942).