Clean carbonylations in supercritical carbon dioxide. Part 1: Palladium-catalyzed alkoxycarbonylation of allyl bromide

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Palladium-catalyzed alkoxycarbonylation of allyl bromide to unsaturated esters in supercritical carbon dioxide (sc-CO_2) was performed and compared with alkoxycarbonylation in organic solvents in this paper. Effects of the catalytic precursor, triphenyl phosphine ligand, base, pressure, and reaction temperature on the reaction yield and selectivity were mainly discussed. The results showed that sc-CO_2 was a favorable reaction medium for the reaction under lower CO pressure. Small changes, both in the CO_2 pressure as well as the amount of cosolvent ethanol, can cause drastic changes in both the reaction yield and selectivity. Moreover, $FeCl_2$ was found to have a promoting effect as cocatalyst on the reaction. The synergic effect of cosolvent ethanol with $FeCl_2$ can lead to an even better result than that in organic solvents.

KEY WORDS: alkoxycarbonylation; supercritical fluids; carbon dioxide; palladium; allyl bromide; cosolvent; cocatalysis.

1. Introduction

There has been increasing interest in using supercritical fluids as reaction media during the past decade, firstly as powerful tools for probing solvent effects, and more recently for the environmental consideration of replacing organic solvents in a wide variety of conventional chemical systems [1–3]. There are several examples of transition-metal-catalyzed reactions, most of which employ supercritical carbon dioxide (sc-CO_2) as the reaction medium for several reasons [2].

CO_2 is environmentally benign, nontoxic, nonflammable, and inexpensive. Its low critical temperature and moderate critical pressure make the supercritical state of CO_2 easily reached and it provides an important advantage for practical application [1–3]. Further reasons that make the sc-CO_2 medium attractive in transition-metal-catalyzed reactions include effective mass transfer, lower cage effects, higher concentrations of reactant gases, and strongly temperature- and pressure-dependent tunability [2,4]. All the properties can afford an easily controlled ratio of the reaction products, higher conversion, and higher yield.

Unsaturated esters (USEs) are one kind of versatile chemical which can be used as plasticity agents, intermediates, and solvents. Palladium-catalyzed alkoxycarbonylation reactions of allylic halides in organic solvents provide a useful route to synthesize USEs [5,6]. But use of such conventional processes is associated with a number of problems. A major drawback is that severe reaction conditions, such as high reaction temperature and CO pressure, are generally involved. Besides, large amounts of organic solvents which need to be removed by distillation after reactions are used in the processes, such as alcohol and benzene. All these disadvantages badly restrict the sustainability of conventional processes. At present, most investigations focus on the exploration of mild reaction conditions. Although the conditions can be improved by use of the solid–liquid two-phase technique, a large amount of solid base is required [7]. Disposal of the corrosive waste base also leads to other environmental problems. Thus, a new and clean technique is still required to improve the reaction.

With all the advantages of performing transition-metal-catalyzed reactions in sc-CO_2, alkoxycarbonylation of allyl bromide with palladium catalyst in sc-CO_2 was carried out in our laboratory. We hoped, therefore, to understand the behavior of sc-CO_2 as a reaction medium in the reaction on the fundamental level and overcome drawbacks of conventional processes. Effects of catalytic systems, the catalyst/substrate ratio, bases, pressure, reaction temperature, and cosolvents were investigated in the present work. The results obtained in sc-CO_2 were compared with those obtained in organic solvents. The effect of the palladium-based bimetallic catalysts was also examined.

2. Experimental

2.1. Materials

CO_2 (food grade) and CO (99.95%) were supplied by Guangzhou Gas Plant. Ethanol (99.8%) was purchased

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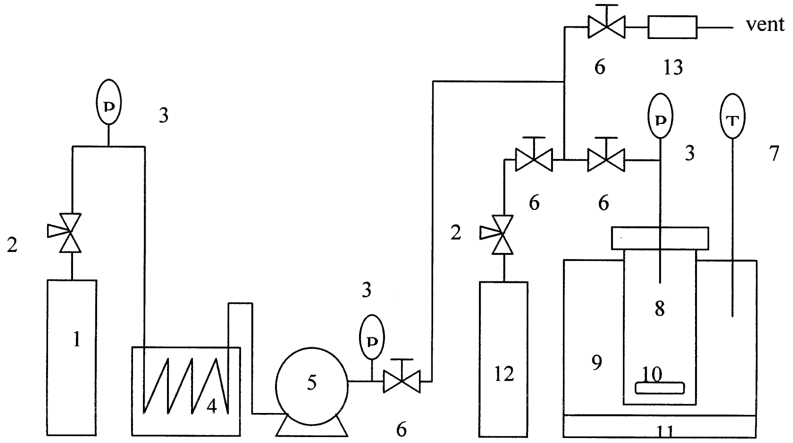


Figure 1. Apparatus flow scheme. 1. CO_2 cylinder; 2. regulator; 3. pressure gauge; 4. ice bath; 5. liquid pump; 6. valve; 7. thermocouple thermometer; 8. 30 ml autoclave; 9. autoclave heating system; 10. magnetic stir bar; 11. magnetic stirrer; 12. CO cylinder; 13. carbon bed.

from Shantou Haoda Fine Chemicals Co. Palladium chloride ($PdCl_2$), triphenyl phosphine (PPh_3), allyl bromide (97%), triethyl amine (Et_3N) (98%), diethyl amine (Et_2NH) (98%) and *n*-hexane (98%) were obtained from Shanghai Dongling Metallic Material Co., Shanghai Medical Co., Beijing Chemical Reagent Plant, Guangdong Shiqi Chemical Plant, and Tianjin Chemical Reagent Co., respectively. Pd/C catalyst was provided by Tokyo University. A phosphine complex of palladium chloride was prepared *in situ* by mixing $PdCl_2$ and PPh_3 together [8]. All the other transition metallic compound were provided by the Department of Chemistry of Jinan University.

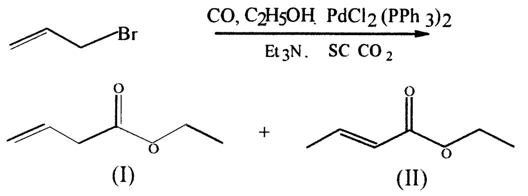
HP 6890-5937 GC-MS was used to identify the reaction products. Gas chromatograph analyses were performed on a Shimadzu GC-9A, with flame ionization detector using a SE-54 (30 m × 0.25 mm i.d.) capillary column.

2.2. General procedure

Allyl bromide, Et_3N, ethanol and catalyst were added into a 30 ml stainless steel autoclave. After the atmosphere was replaced with CO_2, CO was introduced. Then CO_2 was pumped in through a cooler and a liquid pump. The mixture was stirred at the required reaction temperature. After the reaction, the autoclave was cooled and depressurized slowly. The residue mixture was washed with *n*-hexane and analyzed by GC using an internal standard method. A schematic diagram of the apparatus flow is shown in figure 1.

3. Results and discussion

The main products of the alkoxycarbonylation of allyl bromide in sc-CO_2 were 3-butenoic acid ethyl ester (I) and 2-butenoic acid ethyl ester (II). Allyl ethyl ether and ethyl isobutyrate as by-products were trace. The reaction can be demonstrated as follows:



3.1. Effect of catalytic systems

Table 1 lists the effect of palladium-based catalytic systems on the total yield of I and II and their ratio in different reaction media. Better catalytic activity of $PdCl_2$ was obtained in sc-CO_2 than that in ethanol or in the absence of any media. The Pd/C system exhibited lower activity in sc-CO_2, compared with that of $PdCl_2$. The addition of PPh_3 gave rise to further higher total yield of I and II both in sc-CO_2 and in ethanol, possibly due to the protection of PPh_3 on the active transition intermediate. Moreover, the effect of the molar ratio of PPh_3 to $PdCl_2$ on the reaction in sc-CO_2 was also investigated. The best result was given when the molar

Table 1
Effects of catalytic precursors and PPh_3

Catalyst	Y (I + II) (%)	I : II
$PdCl_2$ [a]	2.6	16.6
$PdCl_2$ [b]	3.4	7.1
$PdCl_2$	7.3	20.6
Pd/C (Pd 5%, powder)	1.0	1.0
$PdCl_2 + 2PPh_3$ [a]	39.2	20.6
$PdCl_2 + 2PPh_3$	12.0	7.5
$PdCl_2 + 4PPh_3$	5.1	16.2
$PdCl_2 + 8PPh_3$	Trace	–

Conditions: 0.125 mmol $PdCl_2$; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO 1.0 MPa, CO_2 7.5 MPa, 50 °C, 4 h.
[a] Using 5 ml ethanol as the reaction medium.
[b] With no media.

Table 2
Effect of the ratio of catalyst : substrate

Catalyst : substrate (molar ratio)	Y (I + II) (%)	I : II
1 : 2	4.4	2.7
1 : 1	12.1	7.5
2 : 1	9.4	28.5
4 : 1	2.7	0.8

Conditions: allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO 1.0 MPa, CO_2 7.5 MPa, 50 °C, 4 h.

ratio was 1. For too high a ratio, almost no activity was observed.

3.2. *Effect of the catalyst : substrate ratio*

Table 2 shows the effect of the ratio of catalyst to substrate on the catalytic alkoxycarbonylation in sc-CO_2. An increase of the molar ratio led first to an increase of total yield of I and II, but too high ratios caused a decrease. The optimum molar ratio of catalyst to substrate was 1 : 1.

3.3. *Effect of bases*

The results obtained by varying the amount of Et_3N are summarized in table 3. It shows that the reaction can be badly suppressed and no product II was formed when no base was used, suggesting that I undergoes isomerization reaction to II in the presence of strong base, which can meanwhile neutralize hydrogen bromide formed in the alkoxycarbonylation to initiate the reaction. The optimum result was given when Et_3N was added at 1.25 ml. Table 3 shows also that no USEs can be obtained when diethyl amine was used instead of Et_3N. Two interpretations of this result were taken into account: (1) Et_2NH competed strongly with alkoxy for attacking the coordinated carbonyl on the palladium center to give a carbamoyl palladium complex or (2) the strong adsorption of Et_2NH on the catalyst surface due to its lower solubility than that of Et_3N in sc-CO_2 prevented adsorption of other reaction reagents. The fact that the total yield of I and II was 1.2% even in the absence of bases reinforced the interpretations.

Table 3
Effect of bases

Base	Yield (%)		
	I + II	I	II
Without	1.2	1.2	0.0
1.75 ml Et_3N	10.9	9.1	1.8
1.25 ml Et_3N	12.1	10.6	1.5
1.0 ml Et_3N	7.5	6.9	0.6
1.25 ml Et_2NH	0.0	0.0	0.0

Conditions: 0.125 mmol $PdCl_2$; 0.25 mmol PPh_3; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; CO 1.0 MPa, CO_2 7.5 MPa, 50 °C, 4 h.

Table 4
Effect of CO pressure

CO (MPa)	Y (I + II) (%)	I : II
1.0	12.1	7.5
2.0	9.0	9.5
3.0	17.3	6.4
4.0	36.6	3.3
5.0	12.8	4.5
6.0	14.8	1.8

Conditions: 0.125 mmol $PdCl_2$; 0.25 mmol PPh_3; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO_2 7.5 MPa, 50 °C, 4 h.

3.4. *Effect of the CO pressure*

Table 4 shows the effect of the CO pressure. The total yield of I and II was increased with the CO pressure until a maximum yield was attained at 4.0 MPa CO, accompanied by a rapid decrease in the I : II ratio. However, further increasing the CO pressure over 4.0 MPa, both the yield and the ratio declined. This result is different from that in ethanol reported by Tsuji *et al.* [5,6], which required the CO pressure no lower than 9–10 MPa to maintain the best yield. A possible explanation of this difference is that sc-CO_2 can improve the contact between different phases for its good mass-transfer property, leading to a higher CO concentration at the catalyst. When the CO pressure is no higher than 4.0 MPa, the adsorption and coordination of CO on the palladium center to form the active transition intermediate is admitted to be the rate-controlling step. So increasing CO pressure below 4.0 MPa CO resulted in higher reaction yields. But at higher CO pressure over 4.0 MPa, the adsorption of CO may be so extensive that CO competes effectively with allyl bromide for adsorption and coordination on the palladium center, thereby depressing the adsorption and coordination of allyl bromide.

3.5. *Effect of the CO_2 pressure*

For reactions in sc-CO_2, the CO_2 pressure usually has a great influence on the reaction [1,2]. From table 5, we can see that the total yield of I and II obtained in sc-CO_2 was much higher than those in lower pressure CO_2. The possible reason is the high local concentration of the reaction reagents due to the higher diffusivity and lower cage effects around the active transition intermediate in sc-CO_2, which is beneficial to the alkoxycarbonylation reaction because it is diffusion-controlled. In addition, the CO_2 pressure can also directly increase the CO concentrations through the compressibility of gases. It is noteworthy that the I : II ratio decreased

Table 5
Effect of the CO_2 pressure

CO_2 (MPa)	Y (I + II) (%)	I : II
5.0	17.9	4.3
6.0	29.3	5.6
7.5	36.6	3.3
10.0	36.8	2.4
12.0	39.5	1.6

Conditions: 0.125 mmol $PdCl_2$; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO 4.0 MPa, 50 °C, 4 h.

with increasing CO_2 pressure. This could be attributed to the possibly weaker interaction between sc-CO_2 and I than that between sc-CO_2 and II, which makes the isomerization reaction activated volume changed in sc-CO_2.

3.6. *Effect of the reaction temperature*

Table 6 shows the results obtained at different reaction temperatures. A strong enhancement in the total yield of I and II was observed when the reaction temperature was increased from 50 to 70 °C. However, further increases of the temperature caused a decline in the total yield due to the formation of considerable amounts of palladium black. Moreover, the I : II ratio rose steadily upon increasing the reaction temperature.

3.7. *Effect of cosolvents*

Inspired by the good improving effect of cosolvents such as ethanol on the solubility of varieties of solutes, which has been widely used in sc-CO_2 extractions [2,3], we investigated the effects of several cosolvents on the palladium-catalyzed alkoxycarbonylation of allyl bromide in sc-CO_2. From table 7, we can see that both the total yield of I and II and their ratio in sc-CO_2 was improved dramatically by increasing the amount of cosolvent ethanol. When the molar percentage of cosolvent ethanol reached 16.9%, the total yield of I and II can be tuned to nearly four times over that in the pure sc-CO_2 solvent. Next, in comparison of the effect of several cosolvents listed in table 7, cosolvent ethanol gave the most significant rise in the total yield of I and II, while cyclohexane raised the total yield of I and II in a modest way, and toluene gave an almost identical result with that in pure sc-CO_2. Although CH_2Cl_2 has a slightly weaker cosolvent effect on the total yield of I and II than that of cosolvent ethanol, it decreased the selectivity of I and there is a large disadvantage for CH_2Cl_2 concerning clean chemistry.

Table 6
Effect of the reaction temperature

T (°C)	CO (MPa)	Y (I + II) (%)	I : II
50	1.0	12.1	7.5
60	1.0	20.1	10.4
70	1.0	26.5	9.6
80	1.0	13.4	9.7
90	1.0	13.8	10.6
50	4.0	36.6	3.3
60	4.0	35.0	2.5
70	4.0	47.1	4.9
80	4.0	42.0	5.1
90	4.0	36.9	6.7

The other conditions were same as those in table 4.

Table 7
Effect of cosolvents

Media	Cosolvent/ cosolvent + CO_2 (mol %)	Y (I + II) (%)	I : II
CO_2	0.0	12.1	7.9
CO_2 + ethanol	5.5	15.1	12.6
CO_2 + ethanol	10.4	34.2	14.1
CO_2 + ethanol	16.9	45.9	12.2
CO_2 + cyclohexane	16.9	19.8	10.0
CO_2 + toluene	16.9	12.4	13.9
CO_2 + CH_2Cl_2	16.9	42.3	4.7
5 ml ethanol	0.0	39.2	20.6
5 ml *n*-hexane	0.0	13.1	8.6
5 ml CH_2Cl_2	0.0	30.2	34.0
5 ml benzene	0.0	40.1	24.5

Conditions: 0.125 mmol $PdCl_2$; 0.25 mmol PPh_3; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO 1.0 MPa, CO_2 7.5 MPa, 50 °C, 4 h.

As a matter of fact, the total yield of I and II obtained in sc-CO_2 modified by 16.9% cosolvent ethanol was even higher than that obtained in organic solvents such as ethanol, *n*-hexane, CH_2Cl_2, and benzene, as shown in table 7.

3.8. *Effect of the palladium-based bimetallic catalysts*

In order to improve the catalytic activity of the monometallic catalyst further, more recent work has been focused on the palladium-based bimetallic catalysts. Several transition metal compounds which exhibit no catalytic activity if used alone were added as the second component to $PdCl_2 + 2PPh_3$, such as $FeCl_2$, $FeCl_3$, $CoCl_2$, $NiSO_4$, $CuBr_2$ and $ZnCl_2$. As shown in table 8, the effect of the second transition metal components on the alkoxycarbonylation of allyl bromide in sc-CO_2 differs largely. Only $FeCl_2$ can obviously promote the catalytic activity, while the other transition metal components caused a decrease. In addition, the Fe(II) : Pd ratio also affected the activity. The optimum yield appeared when the Fe(II) : Pd ratio was 1, while the result decreased sharply when the Fe(II) : Pd ratio was too high.

Finally, the synergic effect of cosolvent ethanol with $FeCl_2$ cocatalyst on the reaction was investigated at 70 °C. As shown in table 8, increasing the amount of

Table 8
Effect of bimetallic catalysts

Catalyst	Y (I + II) (%)	I : II
$PdCl_2 + 2PPh_3$	12.1	7.5
$PdCl_2 + 2PPh_3 + FeCl_3$	1.1	98.0
$PdCl_2 + 2PPh_3 + CoCl_2$	11.1	18.3
$PdCl_2 + 2PPh_3 + NiSO_4$	10.4	18.0
$PdCl_2 + 2PPh_3 + CuBr_2$	7.4	19.7
$PdCl_2 + 2PPh_3 + ZnCl_2$	1.0	99.0
$PdCl_2 + FeCl_2 + 2PPh_3$	23.6	10.4
$PdCl_2 + 2PPh_3 + 0.5FeCl_2$	22.0	9.6
$PdCl_2 + 2PPh_3 + 2FeCl_2$	20.2	11.3
$PdCl_2 + 2PPh_3 + 3FeCl_2$	19.4	12.5
$PdCl_2 + 2PPh_3 + 4FeCl_2$	10.0	19.3
$PdCl_2 + 2PPh_3$ [a]	26.5	9.6
$PdCl_2 + FeCl_2 + 2PPh_3$ [a]	30.8	10.9
$PdCl_2 + FeCl_2 + 2PPh_3$ [a,b]	34.0	11.0
$PdCl_2 + FeCl_2 + 2PPh_3$ [a,c]	49.0	12.2

Conditions: 0.125 mmol $PdCl_2$; 0.25 mmol PPh_3; allyl bromide, 1.25 mmol; ethanol, 0.5 ml; Et_3N, 1.25 ml; CO 1.0 MPa, CO_2 7.5 MPa, 50 °C, 4 h.

[a] 70 °C.

[b] Cosolvent ethanol/CO_2 + cosolvent ethanol = 10.4 (mol%).

[c] Cosolvent ethanol/CO_2 + cosolvent ethanol = 16.9 (mol%).

cosolvent ethanol led to higher total yield and higher selectivity of I in the presence of $FeCl_2$.

4. Conclusions

1. Clean catalytic alkoxycarbonylation of allyl bromide has been achieved by using sc-CO_2 as the reaction medium, with easier separation and no hazardous organic solvents used.
2. The CO pressure which is needed for the optimum result has been largely reduced in sc-CO_2, compared with that in organic solvents.
3. The sensitivity of the total yield of USEs and their ratio to the CO_2 pressure and the concentration of cosolvent ethanol suggests that tuning the reaction by controlling the CO_2 pressure as well as cosolvent ethanol is possible, with even better results than those obtained in organic solvents.
4. In combination with $FeCl_2$ cocatalyst, cosolvent ethanol can promote the result to an even better level.

Acknowledgments

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