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Methoxycarbonylation of propylene oxide: A new way to β-hydroxybutyrate

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Abstract

The methoxycarbonylation of propylene oxide (PO) to methyl β-hydroxybutyrate (MHB) catalyzed by dicobaltoctacarbonyl ($[Co_2(CO)_8]$) and 3-hydroxypyridine (3-OH-Py) in methanol system has been studied. The effects of different additives, the molar ratio of 3-OH-Py:$Co_2(CO)_8$, temperature, carbon monoxide (CO) pressure, reaction time on the conversion and selectivity have been investigated. The conversion of propylene oxide is 80.4%, and the yield of methyl β-hydroxybutyrate is 74.9% with selectivity 93.2% when the reaction is carried out for 16 h at 80 °C and 6.0 MPa of CO in methanol, with 0.125 mmol of $Co_2(CO)_8$, 0.25 mmol of 3-OH-Py. The mechanism of this catalytic reaction has also been proposed.

Keywords: Propylene oxide; Dicobaltoctacarbonyl; Methoxycarbonylation; Methyl β-hydroxybutyrate

1. Introduction

The introduction of a carbonyl moiety into organic substrates through transition metal-catalyzed reactions is of importance for numerous transformations in heterogeneous and homogeneous catalysis [1–3]. In addition, carbonylation chemistry using carbon monoxide as a "carbonyl source" is widely used in organic synthesis both in academia and in industry [4,5]. For example, the "Monsanto" process for the production of acetic acid from methanol [6–9] and the "Reppe carbonylation" to yield carboxylic acids from olefins and alkynes [10] are connected to the important industrial synthesis nowadays.

Among numerous carbonylation reactions, the direct insertion of CO into a carbon–heteroatom bond of a heterocyclic compound has attracted much attention of chemists, during the last three decades. By this very convenient and effective one-step procedure, lactams, lactones etc can be obtained with high yields [11]. In recent years, significant innovations have arisen successively in the area of the cobalt-catalyzed carbonylation of epoxides to synthesize β-lactones (Scheme 1) in aprotic mediums [12–16] since epoxides are readily available by epoxidation of olefins [17,18].

However, up to now, little attention has been paid to alkoxycarbonylation (hydroesterification) of epoxides. Eisenmann et al. [19] reported the carboxymethylation of epoxides (Scheme 2) using cobalt catalysts in the presence of CO and alcohols for the formation of difunctional β-hydroxyesters under high pressures of carbon monoxide as early as 1961. Recent efforts in this field derive from the milestone achievements reported by Drent and Kragtwijk [20] in their European patent (1994), involving the use of $Co_2(CO)_8$ and 3-hydroxypyridine to effect the carbonylation of ethene oxide to form β-lactone, polyester oligomers and 3-hydroxy methyl propionate. Hinterding and Jacobesn [21] have shown that enantiomerically pure β-hydroxy esters could be obtained through the carbomethoxylation of chiral epoxides in tetrahydrofuran (THF).

β-Hydroxyesters are highly attractive synthetic targets due to their versatility in organic and polymer chemistry. For example, hydrogenation on the ester moiety results in 1,3-alkanediols, the raw material for polyesters; dehydration and oxidation of hydroxyl group produce α, β-unsaturated esters and β-ketoesters, respectively; hompolymerization gives poly-β-

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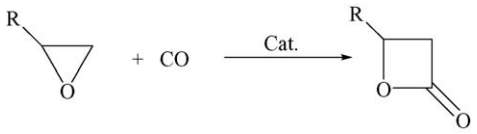


Scheme 1. Carbonylative ring expansion of epoxides to β-lactones.

hydroxyalkanoates, a class of biodegradable polyesters occurred in nature, sharing many of the physical and mechanical properties of poly(propylene). On the other hand, they are valuable intermediates in the production of pharmaceutical compounds.

A conventional route to produce synthetically valuable β-hydroxyesters is the Reformatsky reaction [22]. According to the reaction, the reactant, α-halogen ester, is not a readily available commercial chemical, a large of zinc powder is necessary and the yield of β-hydroxyesters is very low. Obviously, this method is not an environmentally benign process and does not have industrial application prospect. So it is urgent to find an efficient, effective and inexpensive process for the production of β-hydroxyesters.

Herein, we report a cobalt and base catalyst system for the efficient one-step procedure to implement the synthesis of β-hydroxyester from epoxide and carbon monoxide in an alcohol medium (both used as the reactant and solvent).

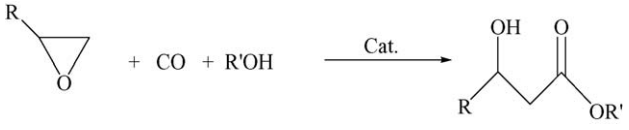
2. Experimental

2.1. Reagents

Dicobaltoctacarbonyl ($[Co_2(CO)_8]$) was synthesized according to literature [23], 3-hydroxypyridine and 2-hydroxypyridine were purchased from Fluka. Epoxide and methanol were freshly degassed and used. Carbon monoxide with a purity of 99.99% was commercially available. All other reagents were of analytical grade and were used as received.

2.2. General procedure of alkoxycarbonylation experiments

$Co_2(CO)_8$ (0.125 mmol), base (0.25 mmol), propylene oxide (1 mL,14.3 mmol) and alcohol (4 mL) were successively placed in a 35-mL stainless steel autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with a desired pressure of CO and then placed in a preheated oil bath for periods of 2–16 h. At the end of the reaction, the reactor was cooled to room temperature and ventilated to terminate the carbonylation reaction. Qualitative analyses were conducted with a HP 6890/5973 GC CMS and quantitative analyses were carried out over a TM 7890 GC equipped with a FID detector.



Scheme 2. Alkoxycarbonylation of epoxides to β-hydroxyesters.

3. Results and discussion

3.1. Effect of additives

P-donating and N-donating chelates are good ligands for metals. They have broad use in the field of homogeneous catalysis [10]. A series of N-containing and P-containing compounds have been investigated in the methoxycarbonylation of propylene oxide (Table 1). The catalytic activity of $Co_2(CO)_8$ without any additive is examined and poor selectivity (72.7%) is obtained (Table 1, entry 1).The main byproducts are diethers (2,2-dimethoxypropane, 1,2-dimethoxypropane) and ethers (2-hydroxymethylpropylether and 2-methoxy propanol). In order to further improve both the catalytic activity of $Co_2(CO)_8$ and selectivity of methyl β-hydroxybutyrate, different N-containing and P-containing compounds are added to the reaction system. The best results are achieved over $Co_2(CO)_8$/3-OH-Py catalyst system, in which the conversion reaches 73.9% with a 94.0% selectivity for methyl β-hydroxybutyrate (Table 1, entry 3). To investigate the influence of the amount of the additive 3-hydroxypyridine, the ratio of 3-hydroxypyridine:dicobaltoctacarbonyl (3-OH-Py:$Co_2(CO)_8$) varies in the range of 1–5 (Table 1, entries 2–6). Clearly, The highest yield of methyl β-hydroxybutyrate is obtained when the ratio of 3-OH-Py:$Co_2(CO)_8$ is about 2.0. The molar ratio of 3-OH-Py:$Co_2(CO)_8$ is less than 2.0, the quantities of byproducts increase. However, to raise higher ratios of 3-OH-Py to $Co_2(CO)_8$ does not increase the yield of methyl β-hydroxybutyrate. Pyridine or 2-hydroxypyridine has little influence on the results of the reaction. On the contrary, the relative distribution of byproducts changes when amino group modified pyridine is added to the reaction system, the opportunity of etherification reaction between one molecule of propylene oxide and one molecule of methanol is more than that of between one molecule of propylene oxide and two molecules of methanol (Table 1, entries 9–11). 1,10-Phenanthroline, 2,2-bipyridine and 4,4-bipyridine having expanded conjugated ring system leads to a rather low yield of methyl β-hydroxybutyrate (Table 1, entries 12–14). May be it because that their larger steric blocking is unfavourable to the interruption of the Co–Co bond in $Co_2(CO)_8$ in forming the previous active catalyst species $Co(CO)_4^-$ anion. Imidazole and 1-methylimidazole also show poor results. When phenol replaces N-containing ligands in the carbonylation reaction, it also displays poorer activity (Table 1, entry 17). Conventional ligands such as triphenylphosphine (TPP) and triethylamine give poorer results (Table 1, entries 18 and 19). Unfortunately, when we used 3-hydroxypyridine with acid or salt as the combinational co-catalyst, the results are also unsatisfactory (Table 1, entries 20 and 21).

3.2. Effect of different cobalt sources

In order to understand the role of cobalt precursors played in the formation of active catalytic species, various cobalt precursors are screened under the same condition and the results are given in Table 2. Obviously, cobalt sources have a strong

Table 1
Effects of different base additives on activity

Entry	Base	Conversion of PO (%)	Selectivity (%)			Yield of ester[d] (%)
			Diethers[a]	Ethers[b]	Ester[c]	
1	None	76.0	20.5	6.8	72.7	55.3
2	3-OH-Py:$Co_2(CO)_8$ (1:1)[e]	74.9	10.4	3.6	85.8	64.3
3	3-OH-Py:$Co_2(CO)_8$ (2:1)[e]	73.9	1.9	4.1	94.0	69.5
4	3-OH-Py:$Co_2(CO)_8$ (3:1)[e]	68.3	0.9	5.1	94.0	64.2
5	3-OH-Py:$Co_2(CO)_8$ (4:1)[e]	66.3	1.0	5.7	93.2	61.8
6	3-OH-Py:$Co_2(CO)_8$ (5:1)[e]	64.3	0.9	7.7	91.3	58.7
7	Pyridine	45.4	4.5	1.6	93.5	42.4
8	2-Hydroxypyridine	72.2	15.2	6.4	77.7	56.5
9	4-Aminopyridine	48.7	1.4	9.1	89.5	43.6
10	2-Aminopyridine	45.4	1.5	9.8	88.8	40.3
11	4-Dimethylaminopyridine	46.0	1.3	10.0	88.7	40.8
12	2,2-Bipyridine	42.5	2.9	5.8	89.9	38.2
13	4,4-Bipyridine	35.5	8.3	4.3	87.1	30.9
14	1,10-Phenanthroline	34.6	2.3	10.1	87.5	30.3
15	Imidazole	57.8	1.0	6.5	92.5	53.4
16	1-Methylimidazole	46.5	1.5	9.7	88.7	41.2
17	Phenol	76.0	17.2	6.9	74.6	56.7
18	Triphenylphosphine	15.7	20.9	9.1	69.8	10.9
19	Triethylamine	34.7	8.3	4.1	87.3	30.3
20	3-Hydroxypyridine + sodium acetate[f]	56.9	0.9	5.9	93.2	53.0
21	3-Hydroxypyridine + *p*-toluenesulfonic acid[g]	77.9	5.5	14.1	80.4	62.6

Reaction conditions: 0.125 mmol $Co_2(CO)_8$; 5 mmol base; 1.0 mL propylene oxide; 4.0 mL methanol; reaction temperature: 80 °C; $P(CO) = 6.0$ MPa; reaction time: 10 h.

[a] Diethers: 2,2-dimethoxypropane + 1,2-dimethoxypropane.
[b] Ethers: 2-hydroxymethylpropylether + 2-methoxy propanol.
[c] Ester: methyl β-hydroxybutyrate (β-hydroxybutanoic acid methyl ester).
[d] Yield = conversion × selectivity.
[e] The data in brackets are molar ratio of 3-hydroxypyridine:dicobaltoctacarbonyl.
[f] 0.25 mmol sodium acetate was added additionally.
[g] 0.25 mmol *p*-toluenesulfonic acid was added additionally.

impact on the reaction and the following sequence is observed, $Co_2(CO)_8 > CH_3Co_3(CO)_{12} > Co(OAc)_2{\cdot}4H_2O > Co(acac)_3 \approx Co(NO_3)_2{\cdot}6H_2O$. $Co_2(CO)_8$ has the highest catalytic activity with 3-hydroxypyridine (Table 2, entry 1). $CH_3Co_3(CO)_{12}$ which decomposes to form $Co(CO)_4^-$ under the presence of base [24], such as, 3-hydroxypyridine shows a better catalytic activity than other cobalt precursors (Table 2, entries 2–5). These results maybe suggest that $Co(OAc)_2{\cdot}4H_2O$, $Co(acac)_3$ or $Co(NO_3)_2{\cdot}6H_2O$ do not produce active catalytic intermediate under the reaction conditions.

3.3. Effect of temperature

To find the reaction temperature at which the consecutive processes of etherification and carbonylation take place with both an optimum conversion of propylene oxide and an acceptable yield for methyl β-hydroxybutyrate, the temperature range from 50 to 120 °C was investigated. The results of the conversion of propylene oxide and the yield of methyl β-hydroxybutyrate are showed in Table 3. Clearly, temperature strongly affects the yield of methyl β-hydroxybutyrate in the reaction. At moderate

Table 2
Effect of different cobalt resources on reaction

Entry	Co source	Conversion of PO (%)	Selectivity (%)			Yield of ester (%)
			Diethers	Ethers	Ester	
1	$Co_2(CO)_8$	73.9	1.9	4.1	94.0	69.5
2	$CH_3Co_3(CO)_{12}$	44.2	1.3	9.7	84.5	37.3
3	$Co(acac)_3$	35.3	6.9	93.0	0	0
4	$Co(NO_3)_2{\cdot}6H_2O$	10.6	22.5	77.5	0	0
5	$Co(OAc)_2{\cdot}4H_2O$	12.1	16.6	80.7	2.7	3.3

Reaction conditions: 0.125 mmol Co; 0.25 mmol 3-hydroxypyridine; 1.0 mL propylene oxide; 4.0 mL methanol; reaction temperature: 80 °C; $P(CO) = 6.0$ MPa; reaction time: 10 h. Others are the same as in Table 1.

Table 3
Effect of temperature on reaction

Entry	T (°C)	Conversion of PO (%)	Selectivity (%)			Yield of ester (%)
			Diethers	Ethers	Ester	
1	50	20.7	0	1.3	98.7	20.4
2	60	45.3	4.3	1.0	94.7	42.9
3	70	59.3	1.3	2.8	95.8	56.8
4	80	73.9	1.9	4.1	94.0	69.5
5	90	61.7	9.9	5.5	84.5	52.1
6	100	57.8	18.0	4.3	77.7	44.9
7	120	34.7	33.7	5.3	60.9	21.1

Reaction conditions: 0.125 mmol $Co_2(CO)_8$; 0.25 mmol 3-hydroxypyridine; 1.0 mL propylene oxide; 4.0 mL methanol; $P(CO) = 6.0$ MPa; reaction time: 10 h. Others are the same as in Table 1.

Table 4
Effect of CO pressure on reaction

Entry	P (MPa)	Conversion of PO (%)	Selectivity (%)			Yield of ester (%)
			Diethers	Ethers	Ester	
1	4.0	59.2	3.8	3.5	92.8	54.9
2	5.0	71.3	3.2	3.4	93.5	66.0
3	6.0	73.9	1.9	4.1	94.0	69.5
4	7.0	74.8	1.9	4.6	93.6	70.0
5	8.0	60.4	0.1	2.4	97.4	58.8
6	9.0	54.7	0.2	2.8	97.1	53.1

Reaction conditions: 0.125 mmol $Co_2(CO)_8$; 0.25 mmol 3-hydroxypyridine; 1.0 mL propylene oxide; 4.0 mL methanol; reaction temperature: 80 °C; reaction time: 10 h. Others are the same as in Table 1.

temperatures between 50 and 70 °C, the conversion of propylene oxide and the yield of methyl β-hydroxybutyrate are relatively low (Table 3, entries 1–3). But at temperatures higher than 80 °C, both the conversion of propylene oxide and the selectivity of methyl β-hydroxybutyrate decrease (Table 3, entries 5–7). When the reaction temperature is too low, propylene oxide may not be activated. And since this is an exothermic reaction too high a temperature is disadvantageous. Hence, the optimum reaction temperature is 80 °C.

3.4. Effect of CO pressure

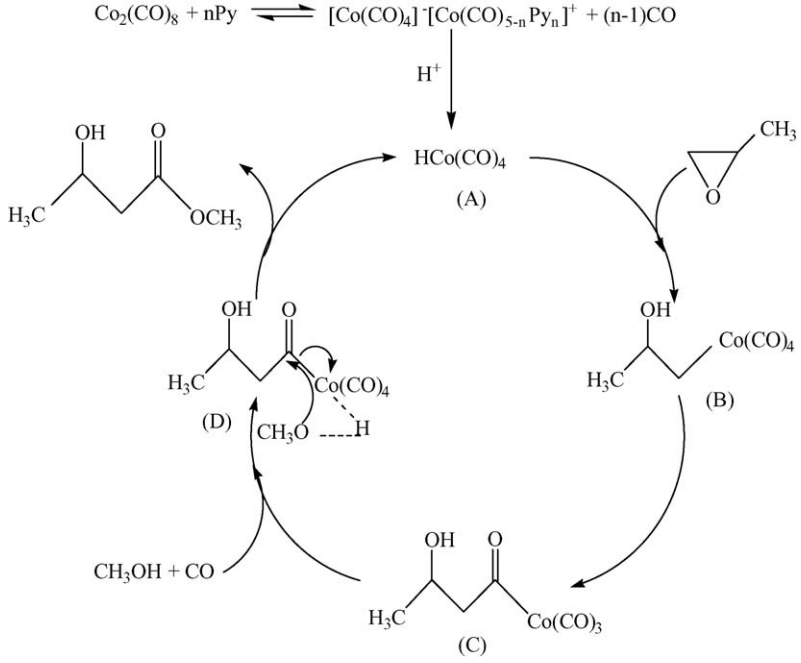
The effect of carbon monoxide pressure on the yield of methyl β-hydroxybutyrate is shown in Table 4. As expected, for methoxycarbonylation of propylene oxide, a higher CO pressure (not above 7.0 MPa) enhances both the conversion of propylene oxide and selectivity of methyl β-hydroxybutyrate. But the increase in conversion of propylene oxide is much greater than that of the yield of methyl β-hydroxybutyrate. However, a too high increase in the CO pressure cannot increase the yield of methyl β-hydroxybutyrate (Table 4, entries 5 and 6).

3.5. Effect of reaction time

The effect of reaction time on yield of methyl β-hydroxybutyrate is shown in Fig. 1. As expected, for the reaction of propylene oxide in methanol under CO pressure, long reaction time enhances both the conversion of propylene oxide and yield of methyl β-hydroxybutyrate, but has little effect on the selectivity of methyl β-hydroxybutyrate.

3.6. Proposed catalytic mechanism

Elucidation of mechanism of this reaction is still an intriguing field especially with respect to the roles of 3-hydroxypyridine. More recently, Rieger and co-workers [25–28] have reported analogous copolymerization and (or) carbonylative ring



Scheme 3. Proposed catalytic mechanism for formation of methyl β-hydroxybutyrate.

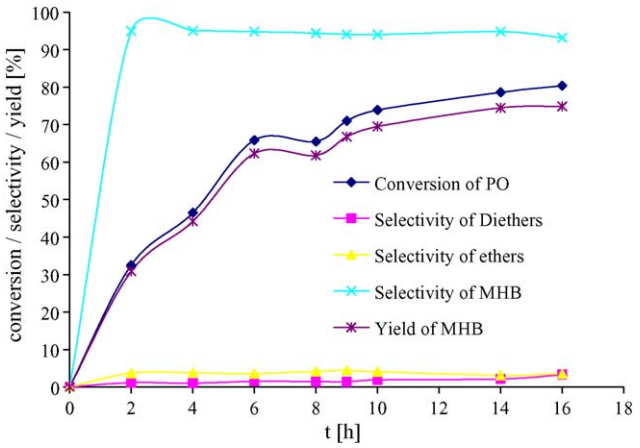


Fig. 1. Influence of reaction time on conversion and yield. Reaction conditions: 0.125 mmol $Co_2(CO)_8$; 0.25 mmol 3-hydroxypyridine; 1.0 mL propylene oxide; 4.0 mL methanol; reaction temperature: 80 °C; $P(CO) = 6.0$ MPa.

expanding of ethylene oxide or propylene oxide with carbon monoxide. We proposed a mechanism of the formation of methyl β-hydroxybutyrate (Scheme 3). N-donors, such as pyridine compounds, either looked as a proton or a Lewis acid, are known to cleave the Co–Co bond in carbonyl clusters leading to the formation of $Co(CO)_4^-$ anion [29]. $HCo(CO)_4$ (**A**), which results probably from protonation of $Co(CO)_4^-$ by the acidic OH group of 3-hydroxypyridine, reacts smoothly with epoxide (facilitating ring opening through backside attack) to give compound **B**; intramolecular migratory insertion of CO into the $Co–C_{alkyl}$ bond occurs in compound **B** may be form the complex **C**; this reactive species undergoes a facile carbonylation in the presence of carbon monoxide to form the acyl complex **D**; acyl complex **D** affords methyl 3-hydroxybutyrate after treatment with methanol [30].

4. Conclusion

The cobalt-catalyzed methoxycarbonylation of propylene oxide to methyl β-hydroxybutyrate in the presence of methanol (both used as the reactant and solvent) has been successfully demonstrated. Interestingly, this one-step reaction could take place under mild condition and the $Co_2(CO)_8$/3-OH-Py catalyst system is very easy to handle and has a good industrial application prospect. Under the optimized reaction conditions, the yield of methyl β-hydroxybutyrate is reasonable high. The mechanism of methyl β-hydroxybutyrate formation has been proposed. Further work will be focus on the development of new and high activity catalysts and the understanding of the mechanism operable in this catalyst system.

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