Natural biopolymer-supported bimetallic catalyst system for the carbonylation to esters of Naproxen

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Abstract

A silica-supported chitosan (CS)–palladium complex $CS–PdCl_2/SiO_2$ shows good conversion and higher regioselectivity in carbonylation of 6-methoxy-2-vinylnaphthalene. The high selectivity of the catalyst was achieved by the synergic effect of Pd–Ni bimetallic system and by polymer protection. Effects of reaction variables have been studied to optimize the reaction conditions. The hydroesterification of various substrates were also investigated. XPS and TEM showed that the catalytically active species were composed of particles of nanometric size and then the polymer would serve as a ligand. Finally, the reuse of the catalyst was studied and the mechanism was discussed.
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1. Introduction

Recently, homogenous or polymer-supported bimetallic catalysts have been attracting considerable attention because of their high activity and selectivity in various reactions [1,2]. The enhanced activity and selectivity are due to the synergic effect of two metals. The transition metal complex catalyzed hydroesterification of olefins in the presence of CO and alcohol is of great interest for the synthesis of industrially valuable carboxylic esters. α-Arylpropionic acids are a class of non-steroidal anti-inflammatory drugs with a substantial market size. Ibuprofen and Naproxen are the important members of this family. Since carbonylation catalyzed by transition metal complexes

would provide an environmentally benign process for their synthesis, there have been numerous patents and publications related to the carbonylation of alcohols and alkenes to produce α-arylpropionic acids or their esters [2–9].

In order to increase the selectivity and to make the catalyst recovery more facile, some natural biopolymers such as chitosan (CS) have recently attracted a great interest as supports for "heterogenized" homogeneous catalytic reactions [10,11]. Chitin is the most abundant natural amino polysaccharide and estimated to be produced annually almost as much as cellulose. Chitin is widely dispersed in living organisms, such as crustaceans of crab, lobster, etc. Chitin becomes of great interest not only as an underutilized resource, but also as a new function material of high potential in various fields. Chitosan is the N-deacetylated derivative of chitin. Chitin and chitosan have excellent properties such as biocompatibility, biodegradability,

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non-toxicity, adsorption properties, etc. Chitosan has a high nitrogen content, which makes it useful for chelating agent. Chitosan is a highly insoluble material resembling cellulose in its solubility and low chemical reactivity [12,13]. So chitosan is a good support to chelate metal ions as catalyst and to recycle the catalyst.

We now first report the efficient hydroesterification of 6-methoxy-2-vinylnaphthalene using the silica-supported natural biopolymer–palladium complex (CS–PdCl$_2$/SiO$_2$) and the reuse of the catalyst. It achieved higher regioselectivity of esters of Naproxen than other results in preceding literature.

2. Experimental

2.1. Materials and analysis

Tryphenylphosphine (PPh$_3$) was purchased from Fluka. 4-Chlorostyrene, 4-bromostyrene, 4-methoxystyrene and 4-methystyrene were purchased from Acros. Carbon monoxide with a purity of 99.95% was commercially available. Chitosan finely purified to a de-acetyl degree of 91.4% and with viscosity molecular weight (M_v) of 6.54×10^5 was used. Other reagents were of analytical grade and were used as received. 6-Methoxy-2-acetonaphthone was purchased from the factory of zhe jiang heng dian, and was rectystallized with absolute ethanol before used. 6-Methoxy-2-vinylnaphthalene was prepared from 6-methoxy-2-acetonaphthone as described in [15].

The identification of gas chromatography (GC) peaks was done by GC/MS (HP 6890/5973) analysis. The conversion of 6-methoxy-2-vinylnaphthalene and the yield of products calculated by gas chromatography on a GC (HP 5890 II) with a SE-54 capillary column using biphenyl as the internal standard. X-ray photoelectron spectroscopy (XPS) measurements were carried out on an ESCALAB 210 photoelectron spectrometer (VG Scientific Co.). Transmission electron micrograph (TEM) was taken on a Philips CM 120 analytical electron microscope.

2.2. Preparation of CS-PdCl$_2$/SiO$_2$ catalyst [10]

To a mixture of 4 mmol/ml HCl 1.0 ml and 368.2 mg (2 mmol) PdCl$_2$, 19.0 ml of absolute ethanol was

added. After the mixture was stirred at room temperature for 24 h, a red–brown solution (0.1 mmol/ml PdCl$_2$–EtOH solution) was obtained. One gram of chitosan and 60.0 ml 1.5% acetic aqueous solution were placed in a 100 ml three-necked flask equipped with a mechanical stirrer, a thermometer and a dropping funnel. After dissolving chitosan by stirring at 50 °C, 2.0 g of silica (184 m^2/g) was added to the solution. The mixture was stirred for 3 h then 4 mmol/ml sodium hydroxide aqueous solution was added dropwise to cause chitosan to completely deposit on the surface of silica by adjusting the pH value of the mixture to 13. The product was filtered and washed with water until the pH value of the filtrate become 8, and then dried by infra-red ray to obtain fine white particles—CS/SiO$_2$. CS/SiO$_2$ (1.0 g), 0.1 M PdCl$_2$–EtOH solution (4.0 ml) and ethanol (10 ml) were placed in a flask equipped with magnetic stirrer and a reflux condenser. The mixture was stirred and refluxed for 10 h to cause solid particles to become dark gray, and the solution to become colorless and transparent. The product was filtered, washed with ethanol and dried to obtain dark gray powder (CS–PdCl$_2$/SiO$_2$). The filtrate was collected and titrated with EDTA, indicating that the lost Pd was less than 1%.

2.3. Hydroesterification reaction

The hydroesterification reaction was performed in a 30 ml autoclave. In a typical reaction, known quantities of catalyst, PPh$_3$, the second metal MCl$_n$, 6-methoxy-2-vinylnaphthalene, HCl, MeOH, dioxane and biphenyl were charged into the reactor. The reactor was flushed three times with CO, pressurized to the desired pressure, heated to the desired temperature and kept at this temperature for the desired reaction time with stirring. After the reaction, the reactor was cooled to room temperature and slowly depressurized.

2.4. Recycling of catalyst

After the reaction, the mixture was filtrated to recover the catalyst, which was dried up at 80 °C, and then added to the reactor as catalyst to perform the same hydroesterification reaction.
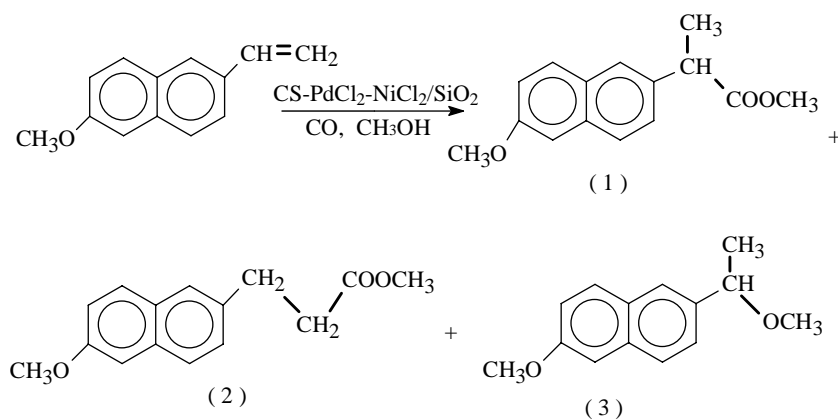
3. Results and discussion

3.1. Hydroesterification of 6-methoxy-2-vinylnaphthalene

The hydroesterification of 6-methoxy-2-vinylnaph-thalene with CO and methanol is shown in Scheme 1. The major products were methyl ester of Naproxen (1) and its linear isomer, methyl 3-(6′-methoxy-2′-naphthyl) propanoate (2). Besides those, a few of products (3) of etherification reaction of MeOH and α-(6′-methoxy-2′-naphthyl) ethanol were detected.

The results of hydroesterification of 6-methoxy-2-vinylnaphthalene to methyl ester of Naproxen with different catalyst systems are listed in Table 1. It could be seen that the silica-supported chitosan–palladium–nickel complex CS–PdCl$_2$–NiCl$_2$/SiO$_2$ showed better conversion and regioselectivity to the branched ester (entry 3).

In order to obtain optimum reaction conditions, we studied the various reaction variables in hydroesteri-fication of 6-methoxy-2-vinylnaphthalene in the pres-ence of CS-PdCl$_2$/SiO$_2$ catalyst. The reaction was strongly influenced by temperature, CO pressure, re-action time and the acid promoter.

The effect of temperature is shown in Table 2. A large product (entry 3) of etherification reaction of MeOH and α-(6′-methoxy-2′-naphthyl) ethanol were found, when the temperature was under 80 °C (entries 1 and 2). As the temperature was raised from 100 to 120 °C, the conversion increased, but the selectivity to the branched ester over the linear isomer decreased (entries 3 and 4). So the most suitable reaction tem-perature was 100 °C. The effect of CO pressure could be seen from Table 2 too. The trend was similar to that of the effect of temperature (entries 3 and 5–7). The highest conversion and selectivity were achieved when the CO pressure was 4.0 MPa. The reaction time

Scheme 1. The reaction of hydroesterification.

Table 1

Hydroesterification of 6-methoxy-2-vinylnaphthalene to methyl ester of Naproxen with different catalyst systems

Entry	Catalyst	Conversion (%)	Selectivity (%)			i/n
			1	2	3	
1[a]	PdCl$_2$-NiCl$_2$	91.2	47.6	6.8	45.6	7.1
2[b]	PVP-PdCl$_2$-NiCl$_2$	94.4	71.4	3.8	24.8	18.7
3[c]	CS-PdCl$_2$-NiCl$_2$/SiO$_2$	96.1	95.3	4.7	0	20.2

Reaction conditions: 6-methoxy-2-vinylnaphthalene 1.0 g; 5 M HCl 0.8 ml; NiCl$_2$·6H$_2$O 38.0 mg; CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.24 mmol; temperature 100 °C; CO pressure 4.0 MPa; time 10 h.

[a] Homogenous reaction: PdCl$_2$ 0.1 mmol.

[b] PVP–PdCl$_2$–MeOH 0.8 ml (0.1 mmol Pd/ml).

[c] Catalyst 0.20 g (0.4 mmol Pd/g).

Table 2
Effect of various reaction condition on the hydroesterification of 6-methoxy-2-vinylnaphthalene

Entry	Temperature (°C)	Pressure (MPa)	Time (h)	Conversion (%)	Selectivity (%)			i/n
					1	2	3	
1	70	4.0	10	96.6	9.76	0.5	89.8	20.6
2	80	4.0	10	96.3	17.4	0.9	81.7	19.3
3	100	4.0	10	96.1	95.3	4.7	0	20.2
4	120	4.0	10	97.2	90.1	8.8	1.1	10.3
5	100	2.0	10	89.4	50.3	8.1	41.6	6.2
6	100	3.0	10	92.3	79.7	10.4	9.9	7.7
7	100	5.0	10	97.1	88.8	9.8	1.4	9.0
8	100	4.0	2	88.8	67.6	7.5	24.9	9.0
9	100	4.0	6	94.7	88.1	8.9	3.0	9.9

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); NiCl$_2$·6H$_2$O 38.0 mg; CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.24 mmol; 5 M HCl 0.8 ml; 6-methoxy-2-vinylnaphthalene 1.0 g.

also had a profound effect on the selectivity (Table 2). These results suggested that, when the time increased, both the conversion and the selectivity to the branched ester increased (entries 8, 9 and 3). The best result was obtained when the reaction time was about 10 h.

The presence of an acid promoter was essential for significant catalytic activity (Table 3). In the absence of HCl (entry 1), etherification occurred selectively. As the amount of HCl increased, the selectivity of hydroesterification reaction increased and the selectivity to the branched ester also increased (entries 2–5). As an acid promoter, HCl was more effective than *p*-toluenesulfonic acid (entry 6).

Thiphenylphosphine played an important role in the reaction to stabilize molecular Pd species and to prevent the formation of inactive bulk Pd particles [14]

(Table 4). In the absence of PPh$_3$, the conversion was only 39.0% (entry 1). It could be seen that the increase in the P/Pd mole ratio improved the conversion but reduced the i/n ratio (entries 2–4). The best result in terms of conversion and selectivity was obtained when the P/Pd mole ratio is 3/1.

The results of hydroesterification of 6-methoxy-2-vinylnaphthalene, when methanol was replaced by others alcohols, are presented in Table 5. It showed that the activity of the catalyst was always high; the sterical hindrance of *i*-propanol did not produce an adverse effect.

3.2. Hydroesterification of various substrates

The hydroesterification of various substrates could be catalyzed by CS-PdCl$_2$/SiO$_2$ catalyst (Table 6). But

Table 3
Effect of [H$^+$] on the hydroesterification of 6-methoxy-2-vinylnaphthalene

Entry	HCl	Conversion (%)	Selectivity (%)			i/n
			1	2	3	
1	0	94.2	1.2	0.5	93.5	7.6
2	0.2	92.8	21.9	1.5	76.6	14.9
3	0.4	95.4	62.9	7.4	29.8	8.6
4	0.6	96.8	85.8	6.4	7.7	13.3
5	0.8	96.1	95.3	4.7	0	20.2
6	*p*-TsOH	89.4	46.8	1.6	51.6	29.4

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.24 mmol; 6-methoxy-2-vinylnaphthalene 1.0 g; NiCl$_2$·6H$_2$O 38.0 mg; temperature 100 °C; CO pressure 4.0 MPa; time 10 h.

Table 4
Effect of P/Pd on the hydroesterification of 6-methoxy-2-vinylnaphthalene

Entry	P/Pd	Conversion (%)	Selectivity (%)			i/n
			1	2	3	
1	0	39.0	6.0	0	94.0	–
2	1/1	91.6	87.0	3.4	9.6	25.7
3	3/1	96.1	95.3	4.7	0	20.2
4	4/1	95.7	91.3	8.8	0	10.5

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); NiCl$_2$·6H$_2$O 38.0 mg; CH$_3$OH 0.8 ml; dioxane 5 ml; 5 M HCl 0.8 ml; 6-methoxy-2-vinylnaphthalene 1.0 g; temperature 100 °C; CO pressure 4.0 MPa; time 10 h.

Table 5
Effect of different alcohols on the hydroesterification of 6-methoxy-2-vinylnaphthalene

Entry	Solution	Conversion (%)	Selectivity (%)			i/n
			1	2	3	
1	MeOH	96.1	95.3	4.7	0	20.2
2	EtOH	96.1	92.5	7.5	0	12.5
3	n-PrOH	95.3	91.7	8.3	0	11.0
4	i-PrOH	94.0	85.6	14.4	0	6.0

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); NiCl$_2$·6H$_2$O 38.0 mg; dioxane 5 ml; PPh$_3$ 0.24 mmol; 5 M HCl 0.8 ml; 6-methoxy-2-vinylnaphthalene 1.0 g; temperature 100 °C; CO pressure 4.0 MPa; time 10 h; alcohols 0.8 ml.

the conversion and selectivity of styrene derivatives were worse than those of styrene.

3.3. Effect of the second metal on the hydroesterification of 6-methoxy-2-vinylnaphthalene

It was noteworthy that when other metals were used as the second metal component (Table 7), they all led to higher activity than when no second metal was added (entry 11), but NiCl$_2$ gave the highest activity. It can be seen that the Ni/Pd mole ratio had a profound effect on the reaction (entries 8–10). The best result in terms of conversion and selectivity was obtained when the Ni/Pd mole ratio was 2 (entry 9). When NiAc$_2$ replaced NiCl$_2$ as the second metal component, the conversion and selectivity remarkably decreased (entry 7). It suggested that Cl$^-$ would serve as a ligand to protect palladium particles against aggregation.

Table 7
Effect of the second metal on the hydroesterification of 6-methoxy-2-vinylnaphthalene

Entry	M	M/Pd	Conversion (%)	Selectivity (%)			i/n
				1	2	3	
1	CoCl$_2$	2	91.3	84.9	10.9	4.2	7.8
2	FeCl$_3$	2	95.6	89.7	6.7	3.6	13.4
3	FeCl$_2$	2	96.7	92.0	8.0	0	11.5
4	CrCl$_3$	2	97.0	93.3	6.7	0	14.0
5	MnCl$_2$	2	96.0	90.6	8.4	1.0	10.8
6	CuCl$_2$	2	88.8	80.4	7.6	12.0	10.6
7	NiAc$_2$	2	90.9	77.3	9.6	13.1	8.0
8	NiCl$_2$	1	95.6	92.9	7.1	0	13.1
9	NiCl$_2$	2	96.1	95.3	4.72	0	20.2
10	NiCl$_2$	3	94.8	94.1	5.93	0	15.9
11	–	0	86.8	80.7	10.2	9.0	7.9

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.24 mmol; 5 M HCl 0.8 ml; 6-methoxy-2-vinylnaphthalene 1.0 g; temperature 100 °C; CO pressure 4.0 MPa; time 10 h.

3.4. Characterization of catalysts

Transmission electron micrograph was taken for the CS-PdCl$_2$/SiO$_2$ catalyst (Fig. 1). The TEM showed that the catalytically active species were composed of particles of nanometric size (5–15 nm) and even by dispersed on surface of the carrier.

Table 8 shows the XPS data for CS/SiO$_2$, PdCl$_2$, catalyst and the reused catalyst (re-catalyst). The binding energy of N$_{1s}$ in the catalyst is 399.50 eV, which is 0.52 eV higher than that in support CS/SiO$_2$, but the binding energy of O$_{1s}$ has no obvious variations. The Pd$_{3d_{5/2}}$ and Cl$_{2p}$ binding energies in the catalyst are 0.87 and 1.18 eV lower than that in PdCl$_2$,
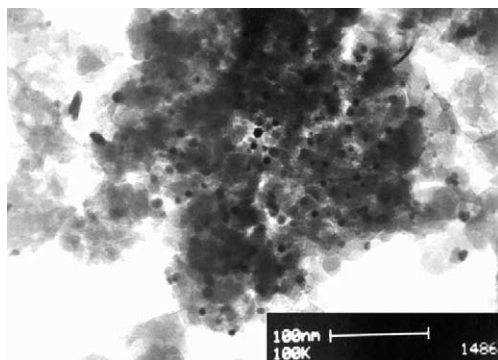
Table 6
Effect of different substrates

Substrate	Conversion (%)	Selectivity (%)			i/n
		1	2	3	
Styrene	98.4	97.9	1.2	0.9	80.3
4-Chlorostyrene	49.5	97.8	1.9	0.3	52.0
4-Bromostyrene	72.9	96.6	1.8	1.6	54.6
4-Methylstyrene	82.3	90.2	3.2	7.5	30.2
4-Methoxystyrene	85.6	76.2	4.0	20.1	19.3
6-Methoxy-2-vinylnaphthalene[a]	96.1	95.3	4.7	0	20.2

Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); styrene or styrene derivative 0.2 ml; NiCl$_2$·6H$_2$O 38.0 mg; CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.1 mmol; 5 M HCl 0.2 ml; temperature 80 °C; CO pressure 2.5 MPa; time 10 h.

[a] 6-Methoxy-2-vinylnaphthalene 1.0 g; temperature 100 °C; CO pressure 4.0 MPa; time 10 h; alcohols 0.8 ml.

Fig. 1. TEM photograph of CS-PdCl$_2$/SiO$_2$ catalyst.

Table 8
X-ray photoelectron spectroscopy (XPS) data

XPS peak	Binding energy (eV)			
	PdCl$_2$	CS/SiO$_2$	Catalyst	Re-catalyst
N$_{1S}$	–	398.98	399.50	400.08
O$_{1S}$	–	532.54	532.58	532.58
Pd$_{3d_{5/2}}$	338.18	–	337.31	335.08
Cl$_{2p}$	199.14	–	197.96	198.06
Si$_{2p}$	–	103.4	103.4	103.4

respectively. These results imply that coordination bonds are formed between N and metal atoms, suggesting that Pd(II) are immobilized on the polymer (Scheme 2).

It can be seen that the binding energies of Pd$_{3d_{5/2}}$ in the re-catalyst are 2.23 eV lower than that in the fresh catalyst, suggesting that molecular Pd species formed inactive bulk Pd particles.
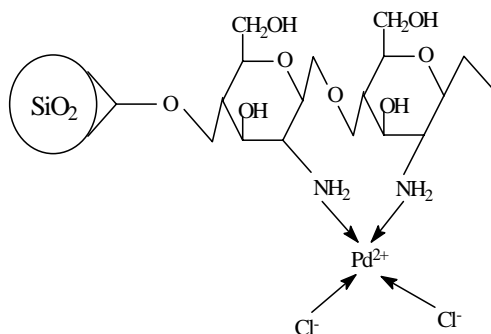
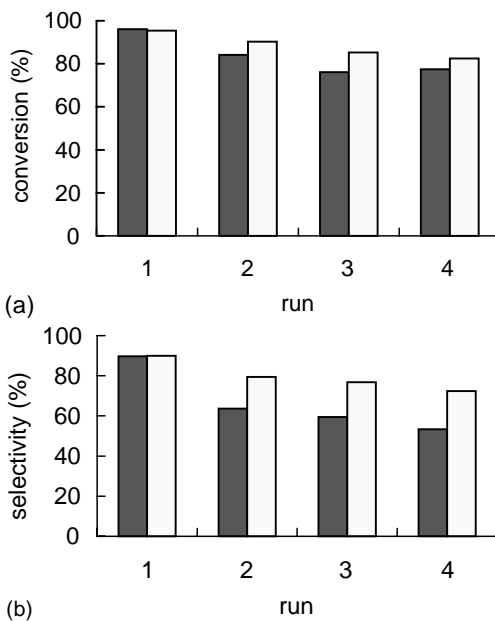Scheme 2. The structure of CS-PdCl$_2$/SiO$_2$ catalyst.

Fig. 2. (a) Conversion and (b) selectivity for recycle experiments of catalyst. (■) Reaction conditions: catalyst 0.20 g (0.4 mmol Pd/g); CH$_3$OH 0.8 ml; dioxane 5 ml; PPh$_3$ 0.24 mmol; 5 M HCl 0.8 ml; 6-methoxy-2-vinylnaphthalene 1.0 g; NiCl$_2$·6H$_2$O 38.0 mg (Ni/Pd = 2/1); temperature 100 °C; CO pressure 4.0 MPa; time 10 h. (□) *p*-Benzoquinone 5.4 mg (0.04 ml); other reaction conditions with the above homology.

3.5. Recycling of catalyst

Fig. 2 showed the results of the reuse of the catalyst. It can be seen that the catalyst could not be reused without appreciable change in the catalytic activity. In order to protect palladium particles against aggregation, *p*-benzoquinone was added as a co-catalyst [15]. By addition of *p*-benzoquinone, the conversion and selectivity for the recycled catalyst increased obviously.

3.6. The mechanism of reaction of 6-methoxy-2-vinylnaphthalene

The effect of various reaction conditions on hydroesterification in the presence of CS-PdCl$_2$/SiO$_2$ catalyst permitted us to postulate a mechanism for the hydroesterification of 6-methoxy-2-vinylnaphthalene with CO and methanol (Scheme 3). In the process of hydroesterification, etherification proceeded at the
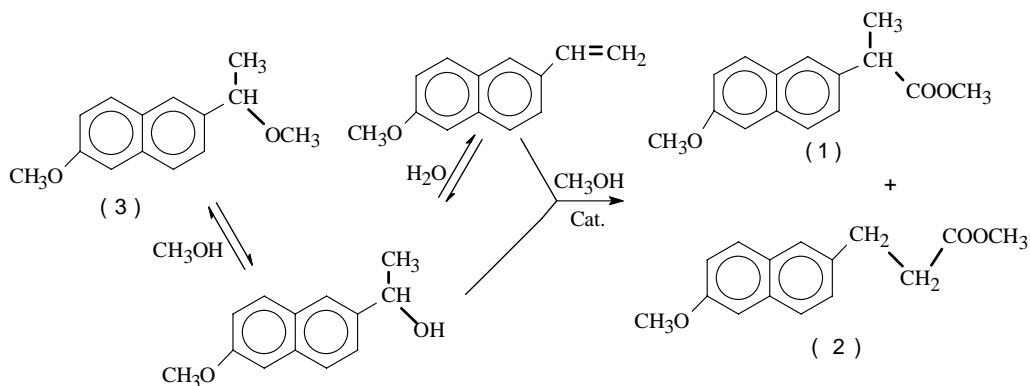
Scheme 3. Mechanism of reaction of 6-methoxy-2-vinylnaphthalene.

same time: 6-methoxy-2-vinylnaphthalene formed α-(6′-methoxy-2′-naphthyl) ethanol with a little amount of water, then α-(6′-methoxy-2′-naphthyl) ethanol reacts with MeOH to form ether (entry 3). So the focus was how to increase the selectivity of hydroesterification by varying reaction conditions. We found that raising temperature, pressure of CO, reaction time, and combining HCl, PPh$_3$, and NiCl$_2$ could increase the selectivity to hydroesterification remarkably.

4. Conclusions

The natural biopolymer-supported bimetallic catalyst system CS-PdCl$_2$-NiCl$_2$/SiO$_2$ shows good conversion and high regioselectivity in the carbonylation to esters of Naproxen. The optimum reaction conditions were: temperature 100 °C; CO pressure 4.0 MPa; time 10 h; P/Pd 3/1; 5 M HCl 0.8 ml; NiCl$_2$ as the second metal component and Ni/Pd 2/1. XPS and TEM showed that Pd(II) were immobilized on the polymer and composed of particles of nanometric size; the polymer serving as a ligand. After addition of *p*-benzoquinone as a co-catalyst to protect palladium particles against aggregation, and thus the conversion for the recycling of catalyst increased obviously.

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