

Thermoregulated phase-transfer ligands and catalysis VIII. Two-phase hydroformylation of 4-isobutylstyrene catalyzed by thermoregulated phase-transfer catalyst OPGPP/Rh

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Abstract

Aqueous/organic biphasic hydroformylation of 4-isobutylstyrene (IBS) catalyzed by OPGPP/Rh catalyst which possesses the function of 'thermoregulated phase-transfer catalysis' (TRPTC) was investigated. A high IBS conversion of 99.5% and an aldehyde yield of 99.0% were obtained under the condition of 80°C and 4.0 Mpa. The molar ratio of branched/normal (b/n) aldehyde in the product reaches 2.5. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: IBS; Biphasic hydroformylation; OPGPP/Rh; TRPTC

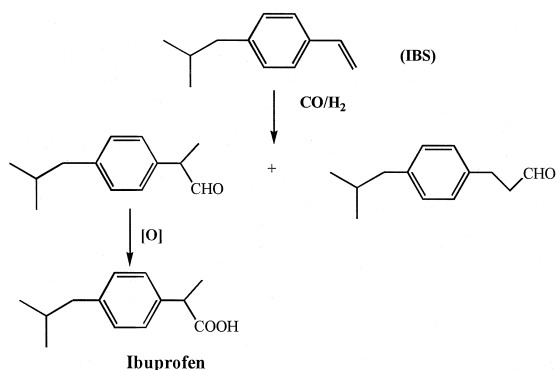
1. Introduction

The potential for use of ibuprofen, 2-(4-isobutyl-phenyl)propionic acid, currently known as one of best nonsteroidal anti-inflammatory agents, has promoted much interest in improving the methods of its synthesis [1,2]. The hydroformylation of 4-isobutylstyrene (IBS) [3–5] is significant since subsequent oxidation of the resulting aldehyde [6] affords ibuprofen (Scheme 1). However, few reports, as to our knowledge, on the use of water-soluble catalyst for the

hydroformylation of IBS were found in the literature.

It is known that polyether-substituted non-ionic surface-active phosphines exhibit inverse temperature-dependent solubility in water [7], i.e., they can be precipitated from water when heating the solution to above a critical temperature called cloud point (T_p) and become water-soluble again on cooling to a temperature lower than T_p . This property enables them to act as thermoregulated ligands (TRLs) in the process of 'thermoregulated phase-transfer catalysis' (TRPTC) [8] in the aqueous/organic two-phase hydroformylation. In such a process, the catalyst modified by TRL can transfer into the organic phase to catalyze the reaction at a temperature higher than T_p and return to the aqueous phase

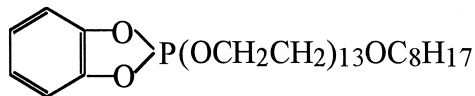
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Scheme 1. Production of ibuprofen from hydroformylation of IBS.

to be separated from the reaction product at a temperature lower than T_p . The concept of TRPTC has been applied successfully to the biphasic hydroformylation of substrates having poor water solubility [9].

In a previous paper [10], we reported the synthesis of a novel TRL named octylpolyglycol-phenylene-phosphite (OPGPP), the investigation of ‘TRPTC’



function of OPGPP/Rh catalyst and its use as a thermoregulated phase-transfer catalyst in the biphasic hydroformylation reaction of styrene.

In the present work, we have investigated the two-phase hydroformylation of IBS by applying OPGPP/Rh catalyst. The effects of reaction time, P/Rh mol ratio, reaction temperature, total pressure, organic solvents, $V_{\text{water}}/V_{\text{IBS}}$ (v/v) as well as different water-soluble phosphines on the IBS hydroformylation were fully studied. Moreover, the catalytic activity of recycled OPGPP/Rh catalyst was also examined.

2. Experimental section

2.1. Starting materials

All solvents were distilled prior to use. Distilled deionized water was used. $\text{Rh}(\text{acac})(\text{CO})_2$

was purchased from the Beijing Research Institute of Chemical Industry. OPGPP was synthesized as previously described [10], and the catalyst $\text{OPGPP}/\text{Rh}(\text{acac})(\text{CO})_2$ was generated in situ. IBS is prepared according to the published procedure [11].

2.2. Hydroformylation experiment

Hydroformylation of IBS was carried out in a 75 ml stainless steel autoclave, which was placed in a thermostatted oil bath. $\text{Rh}(\text{acac})(\text{CO})_2$, OPGPP, water, organic solvent, IBS and internal standard decane were charged into the autoclave being flushed four times with 2.0 MPa of CO. The reactor was pressurized with synthesis gas ($\text{CO}/\text{H}_2 = 1/1$) up to the reaction pressure and held at a predetermined temperature with magnetic stirring for a fixed time. After cooling, the reactor was discharged and the reaction solution was siphoned into a separatory funnel. After phase separation, the organic layer was washed with distilled water, dried over anhydrous magnesium sulfate and subjected to GC analysis.

3. Results and discussion

Results of the hydroformylation of IBS over $\text{OPGPP}/[\text{Rh}(\text{acac})(\text{CO})_2]$ catalytic system at different reaction times were summarized in Table 1. The results show that IBS hydroformylation reaction can be completed in 5 h. Moreover, the mol ratio of branched to normal (i.e.,

Table 1
Effect of reaction time on aqueous/organic two-phase hydroformylation of IBS

Time (h)	Conversion (%)	Yield of aldehyde (%)	b/n
1.0	23.6	22.1	2.5
2.0	45.4	44.3	2.4
3.0	72.1	70.2	2.4
4.0	89.5	87.3	2.5
5.0	99.5	99.0	2.5

Reaction conditions: $T = 80^\circ\text{C}$, $P = 4.0$ MPa ($\text{CO}/\text{H}_2 = 1$), $\text{P}/\text{Rh} = 13$, $\text{IBS} = 1.0$ ml, $\text{IBS}/\text{Rh} = 1000$ (mol ratio), n -heptane = 2.0 ml, $\text{H}_2\text{O} = 2.0$ ml.

Table 2
Effect of P/Rh mol ratio on the (aqueous/organic) two-phase hydroformylation of IBS

P/Rh (mol ratio)	Conversion (%)	Yield of aldehyde (%)	b/n
2	61.4	60.3	2.7
8	90.3	88.9	2.6
13	99.5	99.0	2.5
20	97.5	96.4	2.3

Reaction conditions: $T = 80^{\circ}\text{C}$, $P = 4.0$ MPa ($\text{CO}/\text{H}_2 = 1$), $t = 5$ h, other conditions are the same as those given in Table 1.

b/n) aldehyde does not change with reaction time.

The effect of OPGPP/Rh molar ratio on the catalyst activity was presented in Table 2. The conversion of IBS and yield of aldehydes increase as OPGPP/Rh ratio increases from 2 to 13. The yield of aldehydes reaches its maximum value when P/Rh (mol ratio) is 13 and drops slightly when P/Rh mol ratio exceeds 13. While the b/n ratio of aldehyde decreases slightly with an increase of the P/Rh mol ratio.

Under the experimental conditions, the conversion of IBS and yield of aldehyde increase with the increase of temperature (Table 3). The water-soluble phosphine ligand OPGPP has a 'cloud point' (T_p) of 56.5°C . At 40°C , lower than its T_p , OPGPP/Rh catalyst remains in the aqueous phase where the solubility of the substrate IBS is very poor, so the conversion of IBS is very low. When reaction temperature is raised to 60°C , which is higher than its T_p , the catalyst OPGPP/Rh transfers into the organic phase, where IBS solved, to catalyze the hydroformylation of IBS resulting in high IBS con-

Table 3
Effect of reaction temperature on aqueous/organic two-phase hydroformylation of IBS

T ($^{\circ}\text{C}$)	Conversion (%)	Yield of aldehyde (%)	b/n
40	10.8	9.8	13.0
60	76.3	75.7	7.6
80	99.5	99.0	2.5
100	99.9	98.0	1.2

Reaction conditions: $P = 4.0$ MPa ($\text{CO}/\text{H}_2 = 1$), P/Rh = 13, $t = 5$ h, the other conditions are the same as in Table 1.

Table 4
Effect of pressure on the (aqueous/organic) two-phase hydroformylation of IBS

p (MPa)	Conversion (%)	Yield of aldehyde (%)	b/n
2.0	35.3	34.8	0.9
3.0	76.6	75.6	1.7
4.0	99.5	99.0	2.5
5.0	99.6	98.3	2.8

Reaction conditions: $T = 80^{\circ}\text{C}$, P/Rh = 13, $t = 5$ h, other conditions are the same as those given in Table 1.

version. In addition, b/n aldehyde ratio depends largely on temperature. It decreases remarkably as temperature raised. The optimum temperature for the most favorable production of the branched aldehyde is 80°C .

Data in Table 4 indicated that the IBS conversion increases with the total pressure ($\text{CO}/\text{H}_2 = 1/1$) while aldehyde b/n ratio remained the same. Little changes of the values of IBS conversion and aldehydes yield with pressure was observed when the total pressure was above 4.0 MPa. Therefore, a reaction pressure of 4.0 MPa was chosen for this hydroformylation.

Table 5 showed the results of IBS hydroformylation in various organic solvents. Little effect on the catalytic results was observed with different non-polar solvents. However, at the end of hydroformylation, the color of organic layer, which indicated the loss of Rh, varied with different solvent. Using toluene as solvent, the organic layer was pale yellow ash; while it was almost colorless when *n*-heptane was used as solvent. Thus, *n*-heptane is a better selection in order to reduce the Rh loss.

Table 5
Effect of organic solvent on aqueous/organic two-phase hydroformylation of IBS

Organic solvent	Conversion (%)	Yield of aldehyde (%)	b/n
Toluene	99.2	98.1	2.4
<i>n</i> -heptane	99.5	99.0	2.5
<i>n</i> -hexane	98.4	97.3	2.3
cyclohexane	98.6	97.3	2.1

Reaction conditions: $t = 5$ h, other conditions are the same as those given in Table 1.

Table 6
Effect of $V_{\text{water}}/V_{\text{IBS}}$ on the aqueous/organic two-phase hydroformylation of IBS

$V_{\text{water}}/V_{\text{IBS}}$	Conversion (%)	Yield of aldehyde (%)	b/n
0	99.4	99.0	2.5
1.0	99.6	99.1	2.4
2.0	99.5	99.0	2.5
4.0	99.6	99.1	2.4

Reaction conditions: $t = 5$ h, other conditions are the same as those given in Table 1.

Table 6 showed that the $V_{\text{water}}/V_{\text{IBS}}$ ratio had no effect on IBS conversion and yield of aldehydes. It should be emphasized that common aqueous/organic two-phase hydroformylation occurred in the aqueous phase or at the aqueous/organic interface [12,13], obviously $V_{\text{water}}/V_{\text{IBS}}$ ratio had some effect on the reaction results. However, the biphasic hydroformylation catalyzed by OPGPP/Rh at a temperature higher than T_p occurred in the organic phase, so the $V_{\text{water}}/V_{\text{IBS}}$ ratio has no influence on the reaction results.

Table 7 summarized the results of biphasic IBS hydroformylation catalyzed by the [Rh(acac)(CO)₂] modified by various water-soluble ligands such as TPPTS [trisodium salt of trisulfonated triphenylphosphine], TPPMS [sodium salt of mono-sulfonated triphenylphosphine], PETPPs [$\text{Ph}_n\text{P}[p\text{-C}_6\text{H}_4(\text{OCH}_2\text{CH}_2)_m\text{OH}]_{3-n}$, $n = 0,1,2$] and OPGPP. The catalytic activity was low with rhodium catalyst modified by

Table 7
Comparison of the catalytic activity of different water-soluble phosphine modified Rh catalysts in biphasic hydroformylation of IBS

Phosphine ligand	Conversion (%)	RCHO (%)	b/n
$\text{P}[p\text{-C}_6\text{H}_4(\text{OCH}_2\text{CH}_2)_{16}\text{OH}]_3$	96.2	95.0	0.9
$\text{PhP}[p\text{-C}_6\text{H}_4(\text{OCH}_2\text{CH}_2)_{16}\text{OH}]_2$	94.8	93.2	0.8
$\text{Ph}_2\text{P}[p\text{-C}_6\text{H}_4(\text{OCH}_2\text{CH}_2)_{16}\text{OH}]$	95.3	93.7	0.8
OPGPP	99.9	98.0	1.2
TPPMS	78.4	76.2	0.8
TPPTS	33.3	31.2	1.0

Reaction conditions: IBS = 1 ml, IBS/Rh = 1000 (mol ratio), P/Rh = 13 (mol ratio), IBS/Rh = 1000, heptane = 2.0 ml, H₂O = 2.0 ml, decane = 0.1 ml, $P = 4.0$ MPa ($\text{CO}/\text{H}_2 = 1/1$), $T = 100^\circ\text{C}$, for 3.0 h.

Table 8
Catalytic activity of recycled OPGPP/Rh catalyst in aqueous/organic two-phase hydroformylation of IBS

Cycles	Conversion (%)	Yield of aldehyde (%)	b/n
0	99.6	98.3	2.5
1	95.1	93.2	2.5
2	72.6	70.6	2.4
3	52.8	50.1	2.4

Reaction conditions: $t = 5$ h, other conditions are the same as those given in Table 1, except the catalyst is recycled.

anionic water-soluble ligand TPPTS, and the same effect was observed with the catalyst containing TPPMS. This can be attributed to the fact that Rh catalyst modified by these two ligands, which do not possess TRPTC function, remained in aqueous phase where IBS is severely insoluble [14]. Rhodium catalyst modified with TRL OPGPP or PETPPs exhibited significant high catalytic activity resulting in high conversion of IBS. Such a special high catalyst activity relies on its function of thermoregulated phase-transfer. That is, under the reaction conditions, the thermoregulated phase-transfer catalyst PETPPs/Rh or OPGPP/Rh transfers from the aqueous phase into the organic phase where IBS is located. Therefore, catalytic hydroformylation takes place in a homogeneous, organic phase with a concomitantly high conversion.

Results of experiments using recycled OPGPP/Rh catalyst under the conditions of 80°C , 4.0 MPa ($\text{CO}/\text{H}_2 = 1/1$) and IBS/Rh = 1000 were listed in Table 8. Conversion and yield decreased remarkably after three cycles. The probable reason is that the P–O bond OPGPP could be hydrolyzed, leading to the destruction of the thermoregulated phase transfer function of the catalyst. Therefore, the recycling uses of OPGPP/Rh catalyst are not so satisfactory.

4. Conclusions

Thermoregulated-phase transfer catalyst OPGPP/Rh exhibits excellent catalytic activity

for the hydroformylation of IBS in aqueous/organic two-phase system. High IBS conversion and aldehydes yield (99.5 and 99.0%, respectively) can be obtained under mild reaction conditions.

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