

Hydrocarboxylation of 1-(4-isobutylphenyl) ethanol catalyzed by heterogeneous palladium catalysts

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Abstract

Heterogeneous palladium catalysts were employed for the synthesis of 2-(4-isobutylphenyl) propionic acid (ibuprofen) by carbonylating 1-(4-isobutylphenyl) ethanol (IBPE) with carbon monoxide and water. Among the supported palladium catalysts tested, palladium anchored on montmorillonite showed good activity for the carbonylation and good selectivity to ibuprofen. For the palladium/montmorillonite catalyst, the presence of triphenylphosphine and hydrogen chloride in the reaction solution was essential for its catalytic activity even if triphenylphosphine and chloride ion had already been coordinated to the palladium precursor. The effects of reaction variables on the heterogeneous carbonylation have been investigated for the regiospecific synthesis of ibuprofen, and it was revealed that the palladium/montmorillonite showed better selectivity to ibuprofen than the homogeneous counterpart. This heterogeneous catalyst recovered by filtration after a batch of the reaction showed activity similar to that of the fresh catalyst for a new batch of reaction. Furthermore, the filtrate without the solid catalyst did not show any carbonylation activity. These implied that dissolution of palladium component from the solid catalyst had not been serious. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Synthesis of ibuprofen; Heterogeneous palladium catalyst; Montmorillonite; Hydrocarboxylation; Regioselectivity

1. Introduction

Hydrocarboxylation of 1-(4-isobutylphenyl) ethanol (IBPE) is the last step in the new three-step process developed by Hoechst-Celanese to synthesize 2-(4-isobutylphenyl) propionic acid (ibuprofen) from isobutylbenzene. Ibuprofen is an important nonsteroidal anti-inflammatory drug with a substantial size of market [1]. Us-

ally homogeneous palladium complex catalysts such as $\text{PdCl}_2(\text{PPh}_3)_2$ has been used for the regioselective carbonylation of alcohol or olefin substrates to produce propionic acids or their esters [2–5]. We also recently reported carbonylation of IBPE for the regiospecific synthesis of ibuprofen catalyzed by homogeneous palladium complexes [6].

In order to make the recovery of catalysts more facile, heterogeneous or heterogenized catalysts have attracted much interest. Frequently used supports such as activated carbon, alumina, silica, and inert polymers could be em-

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ployed for the immobilization of homogeneous catalysts, and palladium on suitable supports could form an active complex with phosphine ligands [7]. Recently, a swelling-type layered silicate clay, montmorillonite has been reported as an excellent support for immobilization of cationic transition metal complexes to conduct solution-like reactions in the solid state [8–12]. These heterogenized catalysts involving anchored palladium showed enhanced activity in many reactions including carbonylation [13–15]. Encouraged by these previous reports, our investigation was extended to the heterogeneous carbonylation of IBPE with supported palladium catalysts.

Heterogeneous palladium catalysts supported on activated carbon, alumina, and silica showed different activities and selectivities, which indicated that the nature of support and the state of the palladium on the support were important to determine the catalytic performance. Palladium immobilized in montmorillonite showed excellent catalytic activity and selectivity, and it was very stable under this reaction condition. Employing palladium catalysts anchored in montmorillonite, effects of reaction variables such as CO pressure, nature of phosphine ligand, ratio of phosphine to palladium, and presence of hydrogen halide were studied and compared to those observed for the homogeneous catalysts.

2. Experimental

The hydrocarboxylation of IBPE was performed in 100 ml or 300 ml Hastelloy C autoclave reactor (Autoclave Engineers) according to a procedure described elsewhere [6]. Typically, into a reaction mixture of IBPE (2.5–5 g), triphenylphosphine and aqueous hydrochloric acid dissolved in 3-pentanone, palladium catalyst (Pd content 0.1–0.5 mmol) was added. The reactor was purged three times with CO (10 bar) and pressurized to 40 bar at room temperature. Then it was heated to 398 K and kept at the temperature for desired reaction time with vig-

orous stirring. During the reaction, the reaction mixture was sampled and analyzed by a gas chromatograph (GC, HP 5890 series II) with a 50 m DB-5 capillary column, and a flame ionization detector.

Palladium catalysts supported on carbon, alumina, and silica were typically prepared by a precipitation method with a support material and an aqueous solution containing desired amount of palladium. The prepared samples were dried at 393 K for 24 h and reduced in hydrogen flow (purity > 99.995%) of 20 $\mu\text{mol/s}$ at 423 K for 3 h. In most cases, palladium chloride (Aldrich 95%) was used as the catalyst precursor.

The preparation of functionalized montmorillonite palladium catalysts was reported by Choudary et al. [10]. Commercially available Na–montmorillonite was treated with a HCl solution to afford H–montmorillonite and then was refluxed with 3-aminopropylethoxysilane solution for about 48 h. The silane-exchanged montmorillonite was complexed with palladium ion during the reflux with a palladium-containing solution and then was subjected to Soxhlet extraction for about 24 h.

3. Results and discussion

As in our previous study [6], the substrate (IBPE) was prepared by Friedel–Craft acylation of 4-isobutylbenzene and subsequent hydrogenation. No impurity was detected in the substrate. The main product obtained in the hydrocarboxylation of IBPE was 2-(4-isobutylphenyl) propionic acid (IBPA(B)), i.e., ibuprofen. Other products include 3-(4-isobutylphenyl) propionic acid (IBPA(L)) which is the linear isomer of ibuprofen, 4-isobutylstyrene (IBS), 1-(4-isobutylphenyl)ethyl chloride (IBPCl), 4-isobutylphenylethane (IBE) and trace of a heavy component that was found to be a dimer of IBS. As described below, some of these by-products were detected only under certain reaction conditions. This spectrum of products is the same as

observed in our earlier study of the homogeneous palladium-catalyzed reaction [6]. This fact together with similar concentration–time curves for each species in homogeneous and heterogeneous systems (*vide infra*) also suggests that the same reaction schemes could be applied for both systems, namely, acid-catalyzed dehydration of IBPE to form the key intermediate, IBS, followed by palladium-catalyzed carbonylation to IBPA or hydrogenation to IBE.

Heterogeneous palladium catalysts on several supports were tested for their carbonylation reactivity (Table 1). Palladium on activated carbon prepared by precipitation at a slightly acidic condition (pH 4.0) catalyzed the formation of hydrogenation product, IBE, as well as the carbonylation product, IBPA (Run 1 and 2). Over 1% Pd/C, more hydrogenated by-product was produced than over 5% Pd/C. The particle sizes of palladium calculated from CO chemisorption were 4.2 nm for 1% Pd and 9.2 nm for 5% Pd assuming spherical Pd particles and an adsorption stoichiometry (CO/Pd) of 1.0. Since the fraction of surface atoms and the coordination number of surface atoms are sensitive to particle size of the metal in the range below 10 nm, one might suspect that smaller particles of 1% Pd/C with more low-coordination atoms could have catalyzed the hydrogenation prefer-

entially, because only the fraction of surface atoms were important, the difference between 1% Pd/C and 5% Pd/C should have been in their rates of the reaction only. However, the preferred hydrogenation over carbon-supported Pd is believed to be due to the contribution of activated carbon support. Since the palladium content was maintained constant for all data in Table 1, 1% Pd/C contained carbon support five times as much as 5% Pd/C. When only activated carbon was used without any palladium (Run 3), the hydrogenation product was still formed, but the carbonylation did not take place. Based on the results, it was concluded that activated carbon catalyzed the hydrogenation and that palladium catalyzed the competing carbonylation reaction. Thus, the difference between 1% Pd/C and 5% Pd/C can be understood in terms of different contributions of these hydrogenation function of the support and carbonylating function of Pd. There is a concern that palladium supported on activated carbon could be leached out in the form of ion and a homogeneous catalytic complex formed *in situ* could catalyze the carbonylation reaction. In this case, 1% Pd/C which had smaller particle sizes and a larger fraction of surface atoms would lose more easily its metallic palladium into the acidic reaction medium than 5% Pd/C

Table 1

The carbonylation of IBPE with heterogeneous palladium catalysts on various supports^a

Run	Catalyst	Conv. of IBPE (%)	Selectivity (%)					
			IBE	IBS	IBPCl	IBPA (B)	IBPA (L)	dimer
1	1% Pd/C	96.3	57.6	17.5	1.2	23.7	0	0
2	5% Pd/C	99.9	25.6	1.0	0.1	77.0	3.8	0
3	Activated carbon ^b	97.8	40.1	59.2	0.7	0	0	0
4	1% Pd/alumina	20.2	0	60.1	1.8	0	0	34.6
5	5% Pd/alumina	34.6	0	68.6	0.4	0	0	31.1
6	PdCl ₂ and alumina ^c	14.2	0	92.5	7.5	0	0	0
7	1% Pd/silica ^d	89.1	0	70.2	3.5	25.1	0	1.2
8	5% Pd/silica	77.6	0	94.5	4.8	0.8	0	0
9	Pd/montmorillonite	94.4	0	34.6	5.4	58.7	0.2	1.1

^aThe following reaction conditions were used unless otherwise stated: IBPE = 5.0 g, P/Pd = 2.2, PPh₃ = 0.13 g, 5% HCl = 10.0 g, 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h. Pd content was the same for all runs.

^bThe amount of carbon support was the same as that of 1% Pd/C.

^cThe amount of alumina was the same as that of 1% Pd/alumina.

^dThe catalyst was prepared by an ion-exchange method.

would do. Nevertheless, the rate of carbonylation over 5% Pd/C exceeded that of 1% Pd/C. Therefore, the hypothesis that active palladium catalytic species is a homogeneous Pd complex dissolved into the solution from the support is not substantiated.

Both 1% Pd/alumina and 5% Pd/alumina did not show any activity for the carbonylation (Run 4 and 5). Even the dehydration step of IBPE, which was catalyzed by the acid catalyst HCl, was apparently inhibited by the alumina support. Probably, alumina scavenges HCl and inhibits dehydration and following reaction steps. Since 1% Pd/alumina contained greater amount of alumina support than 5% Pd/alumina, the inhibition of dehydration was more effective and resulted in a lower conversion of IBPE and production of less *p*-isobutylstyrene. X-ray diffraction pattern (Fig. 1) shows that used catalysts have lost a significant part of XRD intensity due to alumina phase, which reveals that alumina is reactive in the reaction medium. The interference of alumina was confirmed by introducing a homogeneous catalyst PdCl₂ and alumina into the reaction mixture (Run 6). Severe inhibition of dehydration of IBPE was observed. Thus, the reaction between alumina and HCl seemed to be responsible for the inhibition of dehydration reaction by alumina. Pd/silica (1%) was provided by G. V. Smith [15], and the catalyst was prepared by

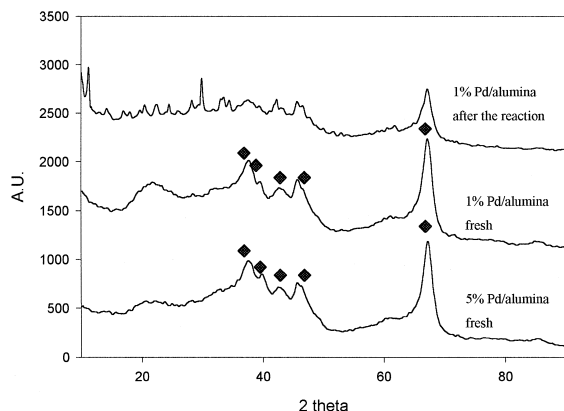


Fig. 1. X-ray diffraction pattern of palladium catalysts supported on alumina.

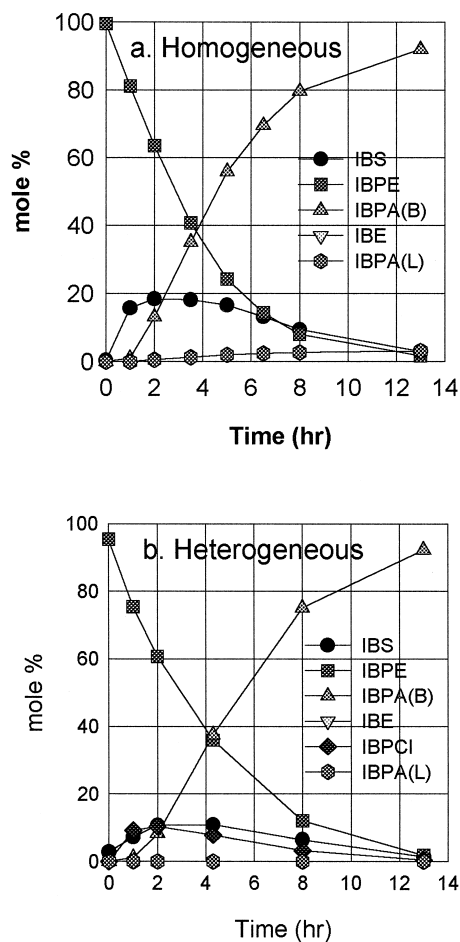


Fig. 2. Carbonylation of IBPE with homogeneous PdCl₂ catalyst (a) and heterogeneous palladium-montmorillonite catalyst (palladium precursor: (C₆H₅)₂PdCl₂, silane ligand: (C₂H₅O)₃-Si(CH₂)₃NH₂) (b). The following reaction conditions were applied for both cases: IBPE = 5.0 g, PPh₃ = 0.13 g, 5% HCl = 10.0 g, 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h, P/Pd (mol/mol) = 2.2.

ion-exchange between Pd(NH₃)₄Cl₂ and amorphous silica. As the amount of employed catalyst (Run 7) was half of other catalysts, the rate of carbonylation was slow but the selectivity for IBPA(B) was good with no formation of the linear isomer. The 5% Pd/silica that was made by a usual precipitation method at pH 4.0 was not active for the carbonylation. Therefore, the catalysts showed different activities depending on the preparation method even if palladium was supported on the same material.

Palladium-exchanged montmorillonite catalyst showed good activity and selectivity. Its palladium content analyzed by atomic absorption spectroscopy was around 3% to 4% of the total catalyst mass. The concentration–time curve of carbonylation with heterogenized palladium in montmorillonite (Fig. 2b) was compared to that of homogeneous PdCl_2 catalyst (Fig. 2a). Surprisingly, the rate of reaction and selectivity to branched acid with heterogenized catalyst was almost the same as those with homogeneous PdCl_2 catalyst. However, the concentration of IBS during the reaction was lower and that of 1-(4-isobutylphenyl) ethyl chloride was higher for the heterogeneous catalyst. This indicates that the rate of carbonylation of olefin intermediate was faster in heterogeneous catalyst system and that IBPCl as well as IBS appeared to serve as intermediates to IBPA. In addition, the similar rates for two systems suggested that there is no mass-transfer limitation of reactants between liquid phase and the catalytic component in the clay.

The active palladium/montmorillonite catalyst was thus selected in order to study further effects of different silane ligands and palladium

precursors for its optimum catalytic performance (Table 2). Montmorillonite is a swelling-type clay whose interlayer spaces are expected to be different according to the size of used silane ligand. However, activity and selectivity were not much related to the size of the ligand and $(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NH}_2$ was the most effective ligand (Run 6). Among the tested palladium precursors, diphenyl palladium chloride was more active than acetate-complexed palladium precursors (Run 9). Probably, the acetate originally coordinated to the palladium prevented the chloride ion or other necessary ligands from complexing with palladium in montmorillonite. In a homogeneous reaction, palladium acetate also showed a low activity under the same carbonylation conditions. This fact suggests the possibility of acetate ion's strong coordination to palladium metal that inhibits formation of an active catalytic complex. Lee and Alper [14] reported that palladium-anchored montmorillonite catalyst could be applied to the carbonylation of aryl compounds. In their study, a silylphosphine type ligand was used to immobilize the palladium ion since the coordinated phosphine was expected to give a beneficial

Table 2

The carbonylation of IBPE with various palladium/montmorillonite catalysts^a

Run	Silane ligand	Conversion of IBPE (%)	Selectivity (%)					Pd content (wt.%) ^b
			IBS	IBPCI	IBPA (B)	IBPA (L)	dimer	
1	$(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{CN}^c$	93.4	35.4	1.8	61.7	1.1	0	4.66
2	$(\text{CH}_3\text{O})_3\text{Si}(\text{CH}_2)_3\text{C}_6\text{H}_9\text{O}^c$	96.8	16.6	1.6	80.4	1.4	0	4.56
3	$(\text{CH}_3\text{O})_3\text{Si}(\text{CH}_2)_3\text{CO}-(\text{CH}_2)_3\text{HC}=\text{CH}_2$	99.7	3.0	0.7	93.1	3.2	0	3.74
4	$(\text{C}_2\text{H}_5\text{O})_3\text{SiHC}=\text{CH}_2$	99.7	1.1	0.4	95.7	2.9	0	2.37
5	$(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NCO}^c$	94.2	11.6	1.0	86.9	0	0.3	3.02
6	$(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NH}_2^c$	98.5	1.9	0.5	97.6	0	0	3.3
7	$(\text{Ph}_3\text{P})_2\text{Pd}(\text{O}_2\text{CCH}_3)_2^d$	92.1	54.9	5.8	41.9	0.5	0	— ^e
8	$(\text{Ph}_3\text{P})_2\text{Pd}(\text{O}_2\text{CCH}_3)_2^f$	90.5	94.2	5.8	0	0	0	—
9	$\text{Pd}(\text{O}_2\text{CCH}_3)_2^g$	84.0	23.5	2.9	56.9	1.3	5.4	0.87

^aThe following reaction conditions were used unless otherwise stated: IBPE = 5.0 g, PPh_3 = 0.13 g, 5% HCl = 10.0 g, 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h, P/Pd = 2.2.

^bPalladium content characterized by atomic absorption spectroscopy.

^cPalladium precursor = $(\text{C}_6\text{H}_5\text{CN})_2\text{PdCl}_2$.

^dSilane ligand: $(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NH}_2$.

^eSamples not analyzed. The content of palladium was assumed to be 3.0% of the total mass.

^fWithout PPh_3 .

^gBalance product was IBE (10.0%).

effect on the carbonylation. But in our preparation, a silane compound was applied to exchange the palladium ion because the presence of additional phosphine in the reaction solution was absolutely necessary even when palladium complex containing phosphine ligand was employed as palladium precursor (Run 8).

When hydrogen chloride was not supplied, the carbonylation did not proceed at all although the dehydration of IBPE occurred to some extent (Table 3, Run 1). This means that hydrogen chloride as a source of additional chloride ion was essential for the catalysts to work even though the palladium precursor already contained chloride ion. As the content of water was decreased for the same amount of hydrogen chloride (Run 3), chlorinated compound, 1-(4-isobutylphenyl) ethyl chloride (IBPCI), became a dominant product. Apparently, the next carbonylation step was slow because of the shortage of water, a reactant needed for carbonylation. Furthermore, the olefin (IBS) was dimerized to produce another by-product. Actually the stoichiometric amount of water for the carbonylation is about 0.5 g, but the use of sufficient water is important to increase the rate of carbonylation by saturating organic phase with water. CuCl_2 known for its beneficial effect on selectivity to the branched acid [16] was added in order to identify the effect of copper ion over palladium/montmorillonite catalyst (Run 6). Additional copper ion did not improve

selectivity to branched acid. For the carbonylation of 4-methylstyrene [3,16], copper ion was quite effective to promote the selective synthesis of the branched acid. The difference in the effect of copper on carbonylations of two substrates could be explained by the difference in the rate of reaction. Without copper ion, 4-methylstyrene was carbonylated in 2–3 h. In the presence of copper chloride under otherwise the same conditions, the carbonylation of 4-methylstyrene was slowed down and selectivity to the branched acid or its ester was increased. In the reaction of IBPE, dehydration to form IBS was found to be a slow step [6]. Therefore, the carbonylation of the olefin intermediate proceeds slowly according to the rate of dehydration, and copper chloride is not useful in our homogeneous and heterogeneous catalytic system to slow down the reaction and to enhance the selectivity to the branched acid. The effect of halide ion that played an important role in the homogeneous carbonylation was also examined in the Pd–montmorillonite system. When HBr was used instead of HCl in Run 4, the rate of carbonylation and selectivity to branched acid were improved slightly. With HI in Run 5, dehydration occurred most rapidly, but carbonylation barely proceeded. The hydrogenation, which was the characteristic feature of homogeneous reaction in the presence of HI, did not proceed much in heterogeneous reaction. Although the rate of dehydration increased as HI

Table 3

The effects of halide additives on the carbonylation of IBPE^a

Run	Hydrogen halide	Conversion of IBPE (%)	Selectivity (%)				
			IBE	IBS	IBPCI	IBPA(B)	IBPA(L)
1	None	0	0	0	0	0	0
2	5% HCl	95.3	0	48.2	13.2	38.0	0
3	35% HCl	93.6	17.1	19.9	30.3	10.0	0
4	5% HBr	91.0	0	32.6	0	64.6	2.8
5	5% HI	91.0	17.9	74.5	0	4.6	3.0
6	5% HCl and CuCl_2	98.0	0	6.3	0.5	89.0	4.2

IBPE = 5.0 g, PPh_3 = 0.13 g, Pd/montmorillonite = 0.32 g ($(\text{C}_6\text{H}_5\text{CN})_2\text{PdCl}_2$, $(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NH}_2$), 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h. The dimer of IBS was the main balance product.

Table 4
The effect of CO pressure

CO pressure (bar)	Conversion of IBPE (%)	Product distribution (%)		
		IBS	IBPA(B)	IBPA(L)
10	71.1	80.0	3.5	0
25	88.7	67.8	19.2	0
30	91.5	57.5	32.7	0
50	98.1	1.4	92.3	0

IBPE = 5.0 g, PPh_3 = 0.13 g, 3-pentanone = 81 ml, temperature = 398 K, time = 13 h, Pd/montmorillonite = 0.65 g, palladium precursor = $(\text{C}_6\text{H}_5\text{CN})_2\text{PdCl}_2$, silane ligand: $(\text{C}_2\text{H}_5\text{O})_3\text{-Si}(\text{CH}_2)_3\text{NH}_2$.

and HBr were used instead of HCl, the effects of hydrogen halides were not consistent with those observed for the homogeneous application regarding the selectivity to branched acid and production of by-products.

Generally, the pressure of carbon monoxide was known to be a very important reaction variable for regioselective carbonylation [17]; a pressure higher than 100 bar was usually required to obtain a good selectivity to branched acid. Table 4 shows the effect of CO pressure on the carbonylation over palladium/montmorillonite. At increasing CO pressures, both the rate of dehydration of IBPE and the rate of carbonylation of IBS were increased. Apparently, the rate of the carbon-addition step was dependent on the concentration of carbon monoxide dissolved in the reaction solution. Although the dehydration of IBPE catalyzed by HCl was not related with dissolved CO, the rate of dehydration and overall conversion of IBPE was increased. This may reflect the reversibility

of the dehydration step under this reaction condition and that the rate of dehydration is increased because the increase in the rate of carbonylation would decrease the concentration of IBS. It was quite interesting to observe that the selectivity to branched acid was perfect even at low pressure without formation of any detectable amount of the linear acid. In homogeneous system, the ratio of branched/linear acid was increased linearly as the CO pressure was increased. This might imply that the wall of clay where palladium complex anchored could form selective surroundings for the pathway to branched acid. However, mechanism by which dissolved CO affects the selectivity to branched acid in homogeneous and heterogeneous reaction is not clearly identified yet.

Triphenylphosphine was the essential ligand to form active catalytic Pd complex because the carbonylation did not occur unless the phosphine ligand was present (Table 5, Run 1). As the amount of triphenylphosphine was increased, the rate of carbonylation was increased but the selectivity to branched acid was decreased. It has been known to be advantageous to use the ligand in excess rather than in stoichiometric amount in several respects especially in preventing palladium complex from being reduced to inactive palladium metal [18]. Therefore, the excess amount of phosphine ligand could be needed to activate decomposed palladium back to an active catalytic complex. The decrease in selectivity to branched acid resulted from the fast rate of reaction in the presence of abundant catalytic species.

Table 5
The effects of phosphine ligands

Run	Amount of PPh_3 (mmol)	Conversion of IBPE (%)	Selectivity (%)			
			IBS	IBPCL	IBPA(B)	IBPA(L)
1	0	88.1	96.5	3.5	0	0
2	0.44	98.1	1.5	0.5	98.0	0
3	0.88	99.0	1.3	0.1	94.4	3.9
4	1.76	97.2	2.1	0.6	91.7	5.6

IBPE = 5.0 g, 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h, Pd/montmorillonite = 0.645 g, palladium precursor = $(\text{C}_6\text{H}_5\text{CN})_2\text{PdCl}_2$, silane ligand: $(\text{C}_2\text{H}_5\text{O})_3\text{Si}(\text{CH}_2)_3\text{NH}_2$.

The effect of bulky phosphine ligand was investigated in Table 6. Sterically hindered bidentate phosphine ligand (*R*)-(+) -1,2-bis(diphenylphosphino) propane (dppp or PROPHOS) did not show much activity in this system even though it was an active ligand in the homogeneous condition (Run 1 and 2). But, this reduction of activity should not have resulted from the limited interlayer spacing of the swelling montmorillonite [19]. Bidentate ligand (–)-2,3-isopropylidene-2, 3-dihydroxy-1, 4-bis(diphenylphosphino) butane (DIOP) is bulkier than dppp, yet is active both in homogeneous and heterogeneous system. DIOP ligand with Pd/montmorillonite gave an excellent selectivity to branched acid unlike DIOP with PdCl₂ in homogeneous reaction [20]. An important chiral ligand (*R*)-(–)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate (BNPPA) which was known for its high enantioselectivity to (*S*)-ibuprofen [21] was employed in our homogeneous and heterogeneous reactions, but it gave no carbonylated product. Hence, the activity of phosphine ligand seems to be independent of the size of the ligand. Phosphorous ligands with different substituents have various electronic effects on binding of phosphorous [22]. Oxygen complexed phosphorous ligand has weaker electron-donating ability than PPh₃ [22], and DIOP showed good carbonylating effect. Alkylated phospho-

rous ligands such as PPh₂R (R = Et, Me) could donate electrons better than PPh₃; however, (PPh₂)₂(CH₂)₂R (dppp and dppb) were not good ligands for the carbonylation of IBPE. Phosphorous ligand containing binaphthyl functional group expected to have similar electronic effect to PPh₃ showed no activity for the carbonylation. Therefore, electronic configuration of phosphorous ligand did not correlate with the result of carbonylation of IBPE.

Fig. 3a shows the results of a blank experiment carried out without palladium–montmorillonite catalyst. After several hours of the reaction, the solid catalyst was filtered out and the substrate was added again, then the reaction was resumed maintaining the same CO pressure and the same temperature. Initially, there were IBPE (substrate), IBS (dominant intermediate), IBPA (carbonylated product), and traces of other components that were left behind from the previous reaction. During the reaction, carbonylation of substrate hardly took place after removing the solid Pd catalyst. HCl catalyzed dehydration of IBPE and chlorination of the substrate to produce more IBS and IBPCL were the only reactions observed. This suggests that most palladium complex did not depart from the support during the reaction and that the active catalytic component was fixed to the clay when it catalyzed the carbonylation. Furthermore, the re-

Table 6
The effects of bulky chiral phosphine ligands^a

Phosphine	Conversion of IBPE (%)	Product distribution (%)			
		IBS	IBPCL	IBPA(B)	IBPA(L)
dppp ^b (hetero)	63.7	95.3	3.5	3.1	0
dppp ^c (homo)	96.2	33.4	4.1	55.3	0
DIOP ^d (hetero)	90.8	60.1	3.5	36.5	0
DIOP ^c (homo)	90.5	22.1	4.6	60.6	12.2
BNPPA ^e (hetero)	91.2	97.3	2.7	0	0
BNPPA ^c (homo)	94.9	5.4	4.2	0	0

^aThe following reaction conditions were used unless otherwise stated: IBPE = 2.5 g, 3-pentanone = 40 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h, Pd/montmorillonite = 0.323 g, P/Pd = 2, palladium precursor = (C₆H₅CN)₂PdCl₂, silane ligand: (C₂H₅O)₃Si(CH₂)₃NH₂.

^bdppp: (*R*)-(+) -bis(diphenylphosphino)propane.

^c(homo): homogeneous condition, PdCl₂ was used instead of Pd–montmorillonite catalyst, Pd = 0.1 mmol.

^dDIOP: (–)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino) butane.

^eBNPPA: (*R*)-(–)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate.

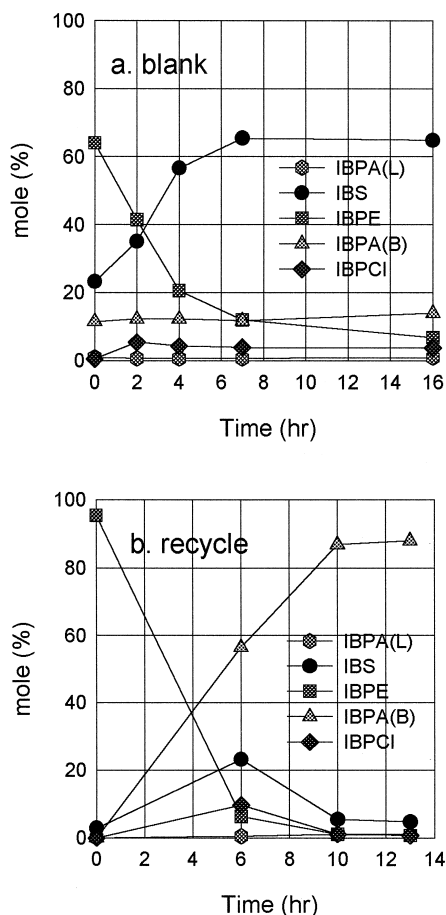


Fig. 3. The blank and the catalyst recycle experiment with filtrate, without palladium catalyst recovered palladium–montmorillonite (palladium precursor: $(C_6H_5)_2PdCl_2$, silane ligand: $(C_2H_5O)_3Si(CH_2)_3NH_2 = 0.5$ g, IBPE = 5.0 g, $PPh_3 = 0.13$ g, 5% HCl = 10.0 g, 3-pentanone = 81 ml, temperature = 398 K, CO pressure = 40 bar, time = 13 h.

covered catalyst by filtration could be recycled. The recovered catalyst was employed again (Fig. 3b). The activity and the selectivity of the used catalyst were as good as those of the fresh one.

4. Conclusion

Several palladium catalysts immobilized on solid supports were employed for the carbonylation of IBPE to synthesize ibuprofen. Activated carbon and alumina inhibited carbonylation by

promoting side-reaction or consuming necessary additive HCl. For palladium on silica, catalytic activity was different according to the preparation method. Palladium-exchanged montmorillonite had good activity and selectivity. Especially palladium/montmorillonite showed better selectivity to branched propionic acid even at low CO pressures than homogeneous palladium catalysts under the same reaction condition. Among tested silane ligands and palladium precursors that were used for immobilizing palladium in montmorillonite, $(C_2H_5O)_3Si(CH_2)_3NH_2$ and $Pd(C_6H_5CN)_2Cl_2$ were most effective. Triphenylphosphine and hydrogen chloride were essential and had to be added in the reaction mixture regardless silane ligand or palladium precursor already contained those ligands. Palladium/montmorillonite was easily recovered after the reaction and it was stable enough to be recycled.

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