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Synthesis of phenylacetic acid by carbonylation

Jiarong Duan, Jing Jiang, Junfang Gong, Qinghua Fan, Dazhi Jiang [*]

Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, People's Republic of China

Abstract

The carbonylation of benzyl alcohol to phenylacetic acid and its derivatives in the presence of rhodium catalysts is reported in this work. The influence of different reaction conditions, such as total reaction pressure, hydrogen partial pressure, catalyst, promoter and reactant concentrations, as well as reaction temperature on the catalytic activity and selectivity has been investigated. The activation parameters of the carbonylation have been measured and a possible mechanism of the reaction has been proposed. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Benzyl alcohol; Phenylacetic acid; Carbonylation; Rhodium catalyst

1. Introduction

Phenylacetic acid and its derivatives are valuable intermediates in the manufacture of pharmaceuticals, cosmetics, and fragrances. The current industrial production of phenylacetic acid starts with the corresponding benzyl chloride. The latter at first is converted by chloride/cyanide exchange to benzyl cyanide [1–7]. Subsequent hydrolysis with sulfuric acid yields the phenylacetic acid. This two-step process has considerable drawbacks such as formation of a stoichiometric amount of salt, for example, sodium chloride (exchange reaction) and ammonium sulfate (hydrolysis). Additionally, the introduction of a carbon atom by a cyanide molecule is fairly expensive compared to the much cheaper monoxide (1.4 vs. 0.2 US$/kg, respectively).

The transition-metal-catalyzed carbonylation of benzyl halides to yield phenylacetic acid was extensively studied in the past several decades. However, a disadvantage of the process using the organic halides to prepare carboxylic acids and their derivatives are that the halide employed has to be eventually removed as a salt with a base. This is not environmentally favorable, nor preferable from the economic viewpoint. So a process without using an organic halide is desirable [8,9].

In the present communication, we report the successful direct carbonylation of benzyl alcohol to phenylacetic acid catalyzed by rhodium complexes. The process uses benzyl alcohol and carbon monoxide (CO) as the starting materials, benzyl chloride and KI as promoters, and a hydrated rhodium chloride as the catalyst precursor.

[*] Corresponding author. Tel.: +86-10-6255-4472; fax: +86-10-6255-9373.

E-mail address: jiangdz@infoc3.icas.ac.cn (D. Jiang).

2. Experimental

2.1. Materials

Benzyl chloride, benzyl alcohol, the catalyst precursor $RhCl_3 \cdot 3H_2O$, all the other solid and liquid materials were commercial products (of chemical or analytical purity) and used without further purification.

Carbon monoxide and hydrogen with 99.9% purity were used directly from the cylinders.

2.2. Carbonylation procedure

The carbonylation experiments were carried out in a 250-ml zirconium autoclave, equipped with electric heating jacket, thermocouple and sealed mechanical stirrer driven by electromagnet. In a typical experiment, this autoclave was charged with calculated quantities of benzyl alcohol, catalyst precursor, promoters and other additives (if used). Then it was sealed and flushed with CO two to three times. Hydrogen (if used) was introduced to a desired value and the reaction system was heated. After the desired reaction temperature was reached, the reactor was filled with CO up to the required pressure and a liquid sample was withdrawn for gas chromatography (GC). The total pressure was maintained constant by continuously introducing CO during the process. At the end of the reaction, the product mixture was cooled and analyzed by GC.

2.3. Analysis of GC

The analysis of liquid reaction mixture was carried out using a temperature-programmed HP 5890I capillary gas chromatograph with a FID detector. An FFAP column ($\varnothing$ 0.25 mm $\times$ 38 m) was used. The column temperature was from 150°C to 240°C at a heating rate of 5°C/min. The temperatures of vaporization chamber and detector, respectively, were 250°C and 300°C. Front pressures of nitrogen column and hydrogen column were 20 and 150 kPa, respectively.

2.4. FT-IR study

The infrared spectra were recorded on a Bruker IFS-25 FT-IR spectrometer after 32 scans with 2 cm^{-1} resolution.

3. Results and discussion

In all the experiments the conversion (%) of benzyl alcohol ($PhCH_2OH$, or BzOH), the selectivity (%) of carbonylation, the average reaction rate (expressed as space-time yield, STY) and the catalytic activity (expressed as turn over number, TON) were defined as:

$$BzOH \, conversion \, (\%)$$
$$= \frac{BzOH \, consumed \, (mol)}{BzOH \, charged \, (mol)} \times 100$$

$$Selectivity \, (\%)$$
$$= \frac{Increment \, of \, PAA \, and \, BPA \, (mol)}{Benzyl \, alcohol \, consumed \, (mol)} \times 100$$

$$STY \, (mol/lh)$$
$$= \frac{Increment \, of \, PAA \, and \, BPA \, (mol)}{Reaction \, volume \, (l) \times Reaction \, time \, (h)}$$

$$TON \, (mol/mol_{Rh} \, h)$$
$$= \frac{Increment \, of \, PAA \, and \, BPA \, (mol)}{Catalyst \, amount \, (mol \, Rh) \times Reaction \, time \, (h)}$$

In addition, the selective conversion of all possible products from benzyl alcohol (mol%), such as phenylacetic acid (PAA), benzyl phenylacetate (BPA), dibenzyl ether (DBE) and toluene (TOL) etc., were described, respectively by their individual increment molar ratio to the consumed benzyl alcohol in the reaction system, i.e., their individual yield (mol%). Accordingly, the carbonylation selectivity would be the sum of both PAA and BPA yields. If the catalyst concentration is kept constant, the changing tendencies of both TON and STY will be identical.

That is, in this case one of them can be easily calculated from another one.

3.1. Influence of rhodium catalyst concentration

The effect of the rhodium catalyst concentration on the synthesis of phenylacetic acid was investigated. Except the added premier materials such as benzyl alcohol, benzyl chloride, potassium iodide and water etc., there were the following new compounds to be detected in the liquid reaction system: phenylacetic acid, benzyl phenylacetate, dibenzyl ether and toluene etc. The results detailed in Table 1 indicate that the conversion of benzyl alcohol, the carbonylation selectivity and STY increase with increment of the rhodium concentration. Total tendency of the toluene yield also slightly increases with the rise in rhodium catalyst concentration, while the yield of dibenzyl ether as another by-product decreases with the increase of catalyst concentration.

As might be anticipated, it was observed that TON increased linearly with the catalyst concentration at first, while it came down after the rhodium catalyst concentration passed over 1 mmol/l. STY essentially had a linear relationship with the catalyst concentration in the range up to 1.5 mmol/l. The carbonylation activity or the reaction rate was examined to be first-order dependent on the concentration of rhodium catalyst at least in the range of 0–1.0 mmol Rh/l.
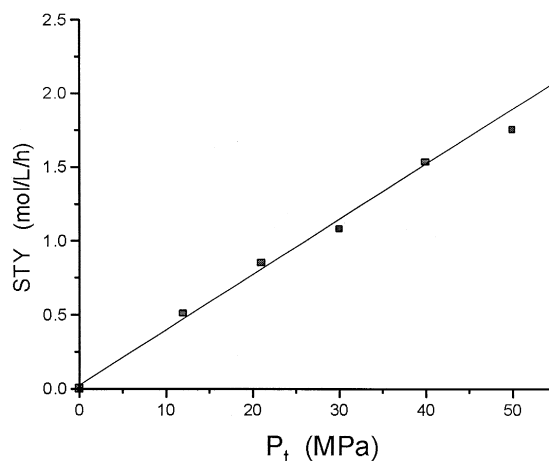

Fig. 1. Effect of total reaction pressure on carbonylation rate of benzyl alcohol. Reaction conditions: $T = 413$ K, $t = 1$ h, [BzOH] $= 7.61$ mol/l, [BzCL] $= 0.68$ mol/l, [KI] $= 0.76$ mol/l, [H_2O] $= 7.31$ mol/l, [Rh] $= 1.59$ mmol/l, stirring speed: 400 rpm.

3.2. Influence of the total reaction pressure

The effect of the total reaction pressure on the carbonylation rate of benzyl alcohol is illustrated in Fig. 1. Here the total reaction pressure (P_t) is, in fact, the pressure of carbon monoxide in the reaction system (P_{co}), because we did not add any other gas in the system.

It can be found that the space-time yield and the catalytic activity all increase linearly with the increase of total reaction pressure up to 5.0 MPa, demonstrating the considerable important influence of CO pressure on the carbonylation of benzyl alcohol. Unfortunately, we did not continue the experiments at higher pressures

Table 1
Effect of rhodium concentration on synthesis of phenylacetic acid
Reaction conditions: $p_t = 4.0$ MPa, $T = 413$ K, reaction time $= 1$ h, [BzOH] $= 6.40$ mol/l, [BzCL] $= 0.77$ mol/l, [KI] $= 1.55$ mol/l, [H_2O] $= 13.75$ mol/l, stirring speed $= 400$ rpm.

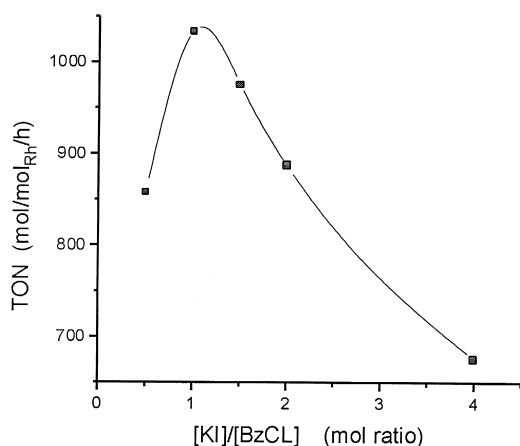| [Rh] (mmol/l)	BzOH conversion (%)	Selectivity (%)	STY (mol/l/h)	TON (mol/mol/h)	Toluene yield (%)	DBE yield (%)
0	0	0	0	0	–	–
0.52	67.8	11.9	0.51	988.5	3.9	38.1
1.02	76.7	22.6	1.11	1084.1	3.8	30.1
1.30	80.2	24.1	1.24	953.2	3.4	27.6
1.67	84.8	27.4	1.48	887.0	3.6	25.0
2.99	90.9	35.2	2.05	685.1	6.6	19.7
5.94	91.8	40.5	2.38	400.2	7.5	15.9

Fig. 2. Effect of the ratio of KI and $PhCH_2Cl$ on the $PhCH_2OH$ carbonylation. Reaction conditions: $T = 413$ K, $t = 1$ h, $P_{CO} = 4$ MPa, [Rh] $= 1.68 \pm 0.02$ mmol/l, [BzCL] $= 0.77$ mol/l, [BzOH] $= 6.40$ mol/l, [H_2O] $= 13.75$ mol/l (24.8 vol.%), stirring speed $= 400$ rpm.

because of a limited installation in our laboratory.

3.3. Influence of the promoters benzyl chloride and potassium iodide

The influence of the promoters benzyl chloride and potassium iodide on the rate of phenylacetic acid synthesis was examined. The results are shown in Fig. 2 and Table 2.

In the experiments, we found that there was an important influence of the benzyl chloride and potassium iodide on each other's concentration ratio on the carbonylation rate and activity. It is illustrated in Fig. 2 that TON, the same for

STY, varied with the molar ratio of potassium iodide to benzyl chloride, and reached up to the maximum value, so long as the KI/PhCH$_2$CL or PhCH$_2$CL/KI molar ratio was equal to one or nearly one. This means that the real promoter of the benzyl alcohol carbonylation in our experiments was the reaction product of benzyl chloride with potassium iodide, benzyl iodide. That is, the following reaction existed:

$$PhCH_2CL + KI \rightarrow PhCH_2I + KCL$$
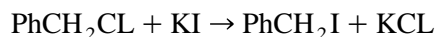
The analysis of the reaction solution confirmed the presence of benzyl iodide in it; however, due to its instability, its quantitative analysis by column chromatography did not carry out correctly.

In Table 2, the second example (No. 2) is in fact an exception because of its higher rhodium concentration than others; we list it here only for reference. Totally Table 2 exhibits that, as the concentration of benzyl chloride increases, the conversion of benzyl alcohol grows, and the rate of carbonylation, its activity and selectivity change. It can be found that the latter parameters have the best values in the range of benzyl chloride concentration between 0.7 and 1.1 mol/l, of which STY and TON increase linearly with the benzyl chloride concentration nearly before 0.75 mol/l. That is, the carbonylation activity and the reaction rate have been detected to be first-order dependent on the benzyl chloride, or exactly say, on its derivative benzyl iodide concentration in the range of 0–0.75 mol/l.

Table 2
Effect of the benzyl chloride concentration on the carbonylation

No.	[BzCL] (mmol/l)	[Rh] (mmol/l)	[BzOH] (mmol/l)	BzOH conversion (%)	Selectivity (%)	STY (mol/l/h)	TON (mol/mol/h)	Toluene yield (%)
1	0.30	1.41	8.09	42.2	15.6	0.53	378.6	2.7
2[a]	0.89	1.93	7.36	81.8	25.9	1.56	807.9	4.7
3	1.00	1.40	7.32	74.3	23.2	1.32	941.6	3.6
4	1.49	1.38	6.79	74.5	12.4	0.63	456.2	4.7
5	1.98	1.36	6.26	97.7	6.7	0.41	301.2	5.5

Reaction conditions: $T = 413$ K, t $= 1$ h, $P_{CO} = 4$ MPa, [KI]/[BzCL] $= 2.0$ (molar ratio), stirring speed $= 550$ rpm.
  [a][H_2O] $= 7.36$ mol/l (13.2 vol.%) for this experiment and [H_2O] $= 6.94$ mol/l (12.5 vol.%) for others.

Table 3
Effect of the added water concentration on the carbonylation
Reaction conditions: $T = 413$ K, $t = 1$ h, $P_t = 4$ MPa, initially added BzOH 0.646 mol, BzCL 0.078 mol, KI 0.156 mol, stirring speed = 400 rpm.

[H$_2$O] (vol.%)	[Rh] (mmol/l)	BzOH conversion (%)	Selectivity (%)	STY (mol/l/h)	TON (mol/mol/h)	PAA yield (%)	DBE yield (%)	Toluene yield (%)
3.7	2.13	76.6	5.4	0.34	157.7	1.1	42.2	6.1
7.1	1.99	78.8	6.1	0.38	189.4	1.5	41.5	6.5
13.2	1.93	81.8	25.9	1.56	807.9	7.3	25.4	4.7
24.8	1.67	84.8	27.4	1.48	887.0	8.3	25.0	3.6

On the other hand, Table 2 also indicates that the yield of toluene occurring in the carbonylation process likely increases considerably with the concentration of benzyl chloride.

3.4. Influence of the added water on the carbonylation

In the experiments it was observed that the catalytic activity varied obviously with the water concentration in the reaction solution (Table 3).

Table 3 shows that the conversion of benzyl alcohol, the carbonylation selectivity, STY, TON and the yield of phenylacetic acid all increase clearly with the added water concentration. In particular, these increments have a jump at the water concentration being nearly 10 vol.%. In addition, with the increase of the added water quantity in the system, the yields of both dibenzyl ether and toluene as by-products decrease. However, it is worth noting that too much water would bring the problem of phase separation.

The comparison of the data in Table 3 demonstrates that the concentration of added water preferably is in the range of 13–20 vol.%.

3.5. Influence of the hydrogen concentration on the carbonylation

The effect of the hydrogen partial pressure on the carbonylation was also studied. The results are summarized in Table 4.

Table 4 indicates that the carbonylation rate and its activity, as well as the reaction selectivity in the presence of hydrogen gas are double or even more than those obtained in the case without hydrogen gas in the fed carbon monoxide. The experiments revealed that the use of hydrogen gas was favorable to increase the yield of phenylacetic acid from 7% to more than 21% and to decrease the production of dibenzyl ether, the yield of which fell gradually from 27.6% down to 16.4% or less. However at the same time, there was more toluene formed in the reaction system. With the further rise of

Table 4
Effect of the hydrogen concentration on the carbonylation
Reaction conditions: $T = 413$ K, $t = 1$ h, $P_t = 4.0$ MPa, [BzOH] = 6.40 mol/l, [BzCL] = 0.77 mol/l, [KI] = 1.55 mol/l, stirring speed = 400 rpm.

[H$_2$] (vol.%)	[Rh] (mmol/l)	BzOH conversion (%)	Selectivity (%)	STY (mol/l/h)	TON (mol/mol/h)	PAA yield (%)	DBE yield (%)	Toluene yield (%)
0	1.30	80.2	24.1	1.24	953.2	7.0	27.6	3.4
5.9	1.33	95.4	41.9	2.56	1919.6	23.8	16.4	7.3
9.1	1.44	95.3	46.0	2.66	1847.1	27.5	14.1	7.1
11.4	1.67	94.7	45.8	2.77	1655.8	27.8	13.9	8.3
14.3	1.30	95.7	46.0	2.66	2046.2	28.8	14.6	7.8
17.6	1.39	93.6	41.6	2.49	1785.3	24.3	16.4	8.4

hydrogen partial pressure in the fed material gas, its effectiveness became weaker. Thus, the preferred H_2 concentration likely would be in the range of 5–15 vol.% in the fed material gas.

In the carbonylation reaction of benzyl alcohol, the added hydrogen gas probably acted as a reducing agent accelerating the higher-valence rhodium catalyst intermediate appeared in the oxidative addition process to be converted to zero-valence rhodium active species $[Rh(CO)_2I_2]^-$ and rapidly completing the catalytic cycle.

3.6. Influence of reaction temperature on the carbonylation

The effect of the reaction temperature on the carbonylation was investigated in the temperature range from 373 to 453 K. The results presented in Table 5 show that the benzyl alcohol conversion, the carbonylation selectivity, the reaction rate and its activity all increase with the reaction temperature. The reaction temperature, in particular, likely favored the rising of phenylacetic acid yield and reduced the formation of dibenzyl ether. However, at 160°C or higher, more toluene appeared in the reaction solution.

3.7. Side reactions in the carbonylation of benzyl alcohol catalyzed by Rh / BzCL-KI

For almost all the carbonylation of benzyl alcohol catalyzed by rhodium metal compounds and benzyl chloride/potassium iodide (Rh/

BzCL-KI), there were always noticeable toluene and dibenzyl ether present as by-products in the reaction solution. The condensation of benzyl alcohol molecules leads to form dibenzyl ether and water; this is an indisputable fact. So we discuss here only the question: where did toluene come from? As described above, the experiments revealed that the yield of toluene obviously increased with the rise of the benzyl chloride concentration and when hydrogen was used in the fed material gas. Besides, it was found that the augmentation of the water quantity in the reaction system reduced the formation of toluene. Based on these observations, we guess the following reactions probably took place in the carbonylation process:

$$PhCH_2I + H_2 \rightarrow PhCH_3 + HI \qquad (1)$$

$$PhCH_2OH + HI \rightleftharpoons PhCH_2I + H_2O \qquad (2)$$
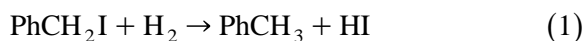
The total reaction is:

$$PhCH_2OH + H_2 \rightarrow PhCH_3 + H_2O \qquad (3)$$

Because of the above reaction (2) being reversible, the fed water increment in the system would be favorable to prevent the generation of more toluene in the reaction (Table 3). But why was there a certain amount of toluene that appeared in the case without the addition of hydrogen in the fed material gas? There were two other factors that perhaps provoked the formation of toluene. Firstly, the transformation of water and CO to H_2 and CO_2 could take place at higher temperature, while the produced hydrogen promoted the formation of toluene in the

Table 5
Effect of reaction temperature on the carbonylation
Reaction conditions are the same as in Table 1, except that the reaction temperature varied.

T (°C)	BzOH conversion (%)	Selectivity (%)	STY (mol/l/h)	TON (mol/mol/h)	PAA yield (%)	DBE yield (%)	Toluene yield (%)
100	37.1	18.8	0.45	248.2	3.8	32.9	0.7
120	56.5	25.5	0.92	511.5	7.4	27.4	1.6
140	87.3	30.5	1.70	944.4	17.9	26.6	3.7
160	98.5	52.0	3.28	1822.2	49.8	19.0	7.9
180	65.0[a]	75.5	6.28	3488.8	75.5	4.3	16.0

[a] The reaction time was half an hour.
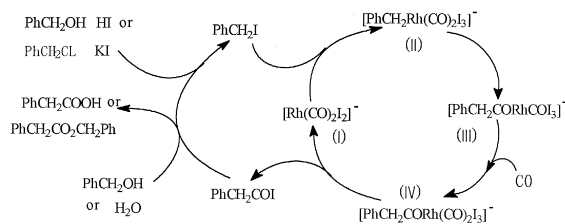
Scheme 1. Proposed mechanism for the carbonylation of benzyl alcohol catalyzed by rhodium and $PhCH_2CL/KI$.

carbonylation reaction. On the other hand, there possibly existed the oxidation of benzyl halide, especially since its iodide was known to be easily oxidized under the actions of heating, light and air. Moreover, benzyl iodide could easily react with HI to produce toluene and iodine. As the reaction temperature and/or the rhodium catalyst concentration were raised, leading to acceleration of the carbonylation process, the above side reactions would be initiated in parallel, resulting in the formation of more toluene. It is just the case we have observed in Tables 1 and 5.

3.8. Mechanism for the carbonylation of benzyl alcohol catalyzed by Rh / BzCL-KI

The infrared spectra of the reaction solution exhibited two typical absorption bands appearing at 1878 and 1953 cm^{-1}. These two bands were considered to belong to the C–O stretching vibrations in the rhodium complex $K^+[Rh(CO)_2I_2]^-$. It is reminiscent of the rhodium-catalyzed carbonylation of methanol to acetic acid. So we thought that the catalytic active species still was $[Rh(CO)_2I_2]^-$. As we discussed above and as reported in the literature [10], we proposed the mechanism of the carbonylation reaction would have the following catalytic cycle (Scheme 1).

As reported in the literature [11], in the first step $RhCl_3 \cdot nH_2O$ was transformed to the initial complex $[Rh(CO)_2I_2]^-$(I); in the next step, oxidative addition of $PhCH_2I$ yielded the complex (II), and due to the CO migration on rhodium and external supplement, the complex

(II) became successively the complex (III) and then the complex (IV). The complex (IV) easily released $PhCH_2COI$ and returned to the complex (I). Finally, $PhCH_2COI$ suffered from the reaction with water or benzyl alcohol to give the phenylacetic acid or benzyl phenylacetate. Based on the analysis of experimental results, it was believed that the oxidative addition of benzyl iodide to $[Rh(CO)_2I_2]^-$ was the rate-determining step in this catalytic cycle.

To sum up it seems that the carbonylation of benzyl alcohol catalyzed by rhodium and $PhCH_2CL/KI$ is very similar to the carbonylation of methanol to acetic acid by rhodium/iodide catalyst system. It was detected to be first-order dependent on the concentration of rhodium catalyst and benzyl iodide formed in the process, respectively, i.e., $r = k[Rh][Iodo-promoter]$, provided that some relative reaction conditions, such as the ratio of $PhCH_2CL/KI$, the composition and pressure of the fed material gas, and the content of water, were maintained to be identical, and the concentrations of rhodium catalyst precursor, $PhCH_2CL$ and KI were not in excess. In this case, that is totally a second-order reaction. According to the results listed in Table 5, the apparent activation energy (E_a) and the preexponential factor (k_o) of the
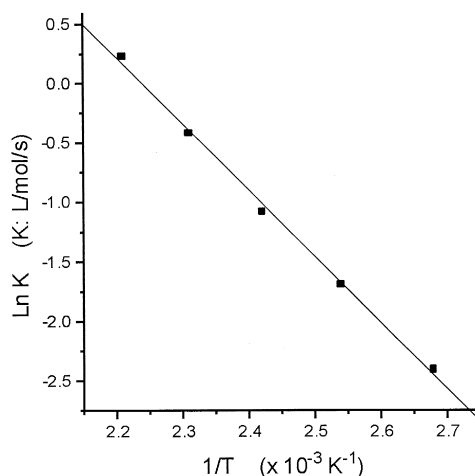

Fig. 3. Arrhenius plot of the carbonylation of benzyl alcohol catalyzed by rhodium and $PhCH_2CL/KI$.

reaction derived from the Arrhenius plot (Fig. 3), respectively are $E_a = 46.4$ kJ $\cdot$ mol^{-1} and $k_o = 2.67 \times 10^5$ 1 $\cdot$ mol^{-1} $\cdot$ sec^{-1}. The activation enthalpy ($\Delta H^{\neq}$) and the activation entropy ($\Delta S^{\neq}$) of the reaction derived from the Eyring equation are $\Delta H^{\neq} = 42.9$ kJ $\cdot$ mol^{-1} and $\Delta S^{\neq} = -152.3$ J $\cdot$ mol^{-1} $\cdot$ K^{-1}, respectively.

4. Conclusions

The carbonylation of benzyl alcohol to phenylacetic acid and its derivatives in the presence of rhodium trichloride trihydrate and benzyl chloride/potassium iodide were studied. This reaction was detected to be very similar to the carbonylation of methanol in the homogeneous rhodium/iodide catalytic system. The experiments revealed that the above rhodium catalyst precursor was at first transformed to be the more stable active species, $[Rh(CO)_2I_2]^-$, and the real promoter was benzyl iodide which was provided by the exchanging reaction between two promoter precursors, benzyl chloride and potassium iodide added in the reaction system. The rate-controlled step of carbonylation was the oxidative addition of benzyl iodide to the rhodium active species. So, totally it is still a second-order reaction in a certain range of rhodium and benzyl iodide concentrations.

The optimum carbonylation conditions have been confirmed to be as follows. Carbon monoxide pressure is preferred up to more than 4–5 MPa. Hydrogen gas concentration in the fed material gas is better between 5 and 15 vol.%. Optimum reaction temperature is set at 140–160°C. The promoter precursors, benzyl chloride and potassium iodide, should be in equivalent weight, and benzyl chloride concentration of which is better between 0.7–1.1 mol/l in the reaction solution. A certain quantity of water is needed in the reaction system, so as to favor the formation of final product phenylacetic acid; the added water concentration is better between 13 and 20 vol.%.

The activation parameters of the carbonylation have been measured and a reasonable mechanism of the reaction has been proposed.

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