Journal of Natural Gas Chemistry 14(2005)40–46

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Study on the Synthesis of Phenylacetic Acid by Carbonylation of Benzyl Chloride under Normal Pressure

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[Manuscript received November 15, 2004; revised January 27, 2005]

Abstract: The influences of some factors on the yield of phenylacetic acid in the carbonylation of benzyl chloride were studied in this paper. These factors included the variety and content of catalyst, and that of solvent, way of material feeding, reaction temperature, sodium hydrate concentration, triphenylphosphine content, presence of surfactant, the ratio of organic phase volume to aqueous phase volume *etc.* The optimum reaction conditions were found to be: with a one-time pour of 0.15 g $Pd(PPh_3)_2Cl_2$, 0.24 g PPh_3, 75 ml NaOH of 3.5 mol/L, 20 ml benzyl chloride and 55 ml *n*-butyl alcohol, and the reaction was carried out at 50 ℃ for about 3 hours. The as-obtained yield of phenylacetic acid was as high as 97.6%. In addition, the influences of the presence of phenylacetic acid and air in the reaction system were also studied. The results showed that the presence of air in the system and the entrainment of phenylacetic acid in the circulating organic phase had great influence on the reaction rate, the stability and performance of catalyst and the yield of phenylacetic acid.

Key words: synthesis, phenylacetic acid, carbonylation, phenyl chloride, dichloro-bistriphenylphosphine palladium

1. Introduction

Phenylacetic acid is one of important organic chemical materials, which is widely used in the field of medicine, pesticide, aromatizer and so on. There exist several routes to synthesize phenylacetic acid, such as cyanobenzyl hydrolysis [1–5], phenylacetamide hydrolysis [6–8], electrochemical process [9–11], carbonyl process [12–20], *etc.* At present, cyanobenzyl hydrolysis is mainly used in China, but it belongs to an out-of-date technology, as it causes serious pollution and the quality of the product is not so good. In comparison, the synthesis of phenylacetic acid in the carbonylation reaction described in this paper has the advantage of offering a milder condition, better product quality and less polluting emissions. Especially when dichloro-bistriphenylphosphine palladiums were used as the catalyst in the carbonylation of benzyl chloride or benzalcohol to synthesize phenylacetic acid, they could exhibit high activity at normal pressure and temperature. Furthermore the preparation was simple and they were non-toxic. Meanwhile they were easy to recover, and the carbon oxide produced in chemical fertilizer plants could be used as the raw material effectively, which not only made full use of wastes and protected environment, but also provided a good chance for chemical fertilizer plants to improve the structure of their products and lead to a combined way of making fertilizer as well as chemicals. Thus this method has a bright perspective. The influences

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Project supported by the foundation of Scientific and Technological from the Ministry of Education (03071), of Natural Science Foundation of Jiangxi Province (0320013) and of the Youth Foundation of Nanchang University.

of some factors on the yield of phenylacetic acid in the carbonylation of benzyl chloride were mainly studied in this paper. Furthermore perfect solvent and effect of various factors were obtained. These haven't been reported in previous literature.

2. Experimental

2.1. Preparation of catalyst

The catalyst $Pd(PPh_3)_2Cl_2$ was mainly prepared according to a method given in reference[21]. The newly made $Pd(PPh_3)_2Cl_2$ was mixed with the oxides or chlorides of some rare earth elements, such as Ce, La, *etc*, in the weight ratio of 10:1. A modified composite catalyst of $Pd(PPh_3)_2Cl_2$ can be prepared by stirring.

2.2. Experimental installation and flow

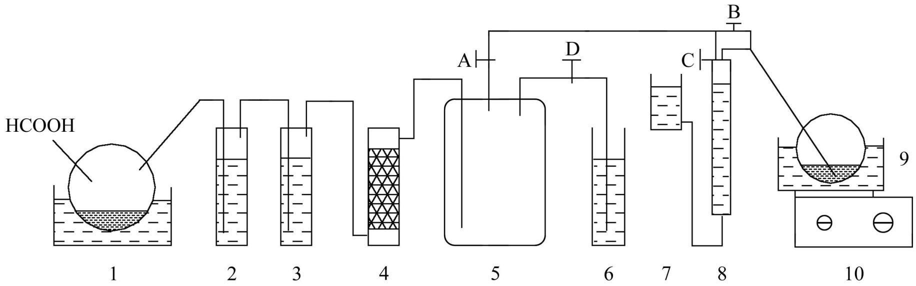
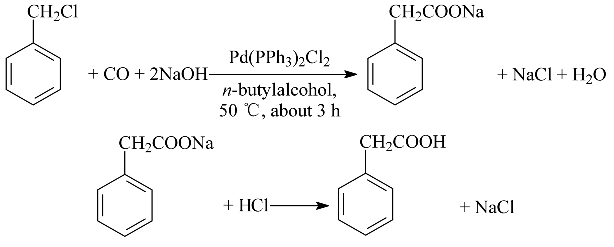


Figure 1. Experimental installation

1—Producing installation of CO, 2—Bottle filled with NaOH, 3—Bottle filled with concentrated H_2SO_4, 4—Desiccator filled with anhydrous $CaCl_2$, 5—Container, 6—Hydraulic packing, 7—Elevated trough, 8—Eudiometer, 9—Reactor, 10—Magnetic heater

As can be seen in Figure 1, the CO produced in the process of sulfuric acid-methanoic acid was deposited in a container after scrubbing and drying. After exchanging the air in the reactor, the CO was measured by eudiometer, and then flowed into a constant temperature reactor under magnetic stirring, where a gas-liquid-liquid-solid heterogeneous catalytic reaction between CO, benzyl chloride, alkali liquor, organic solvent and $Pd(PPh_3)_2Cl_2$ took place. After the reaction, the mixed phase was cooled to room temperature and settled still to demix. The aqueous phase was taken out and the small amount of organic solvent dissolved in it was extracted out with anhydrous ethyl ether, and then the aqueous phase was acidified to pH=2–3 with concentrated hydrochloric acid. After crystallizing, filtrating, scrubbing, and drying, the product (phenylacetic acid) could thus be obtained. The main reactions were:



3. Results and discussion

The result of the reaction could be characterized by the yield of phenylacetic acid. The calculating equation was:

$$\text{Product yield (\%)} = \frac{n_{C_6H_5CH_2CO_2H-\text{actual}}}{n_{C_6H_5CH_2CO_2H-\text{theoretical}}} \times 100\%$$

In the above equation, $n_{C_6H_5CH_2CO_2H-\text{actual}}$ means the actual amount of phenylacetic acid obtained; $n_{C_6H_5CH_2CO_2H-\text{theoretical}}$ means the theoretical amount of phenylacetic acid obtained if all phenyl chloride reacted.

In addition, the rate and extent of reaction could be reflected by the relation curve between the absorbed amount of CO and reaction time.

3.1. Effect of catalysts

As shown in Table 1, $Pd(PPh_3)_2Cl_2$ exhibited high activity, but the addition of some rare earth compounds, such as CeO_2, $CeCl_6$, La_2O_3, *etc*, had little influence. Probably because the intermediate product formed by $Pd(PPh_3)_2Cl_2$ and reagents failed to provide the rare earth ions or compounds with lone electron pair, the correlation between the catalyst and rare earth elements was lacking. The catalysts $PdCl_2$, Pd, and $(Pd+PPh_3)$, failed to show any catalytic activity, and the catalytic activity of $(PdCl_2+PPh_3)$ was not so good, which might result from the formation of only a little $Pd(PPh_3)_2Cl_2$ in the process.

So $Pd(PPh_3)_2Cl_2$ was chosen as the catalyst.

Table 1. Effects of different catalysts

Catalyst	Product yield (%)
$Pd(PPh_3)_2Cl_2$	97.6
$Pd(PPh_3)_2Cl_2+CeO_2$	98.0
$Pd(PPh_3)_2Cl_2+CeCl_6$	97.4
$Pd(PPh_3)_2Cl_2+La_2O_3$	97.2
$PdCl_2+PPh_3$	54.0
$PdCl_2$	0.0
Pd	0.0
$Pd+PPh_3$	0.0

Reaction conditions: with a one-time pour of 20 ml benzyl chloride, 75 ml NaOH of 3.5 mol/L, 55 ml *n*-butyl alcohol, 0.15 g catalyst, 0.24 g PPh_3, the mixture was held at 50 ℃ for 3 h, under normal pressure. Conditions in the following text were the same unless stated otherwise.

3.2. Effects of solvents

The solvent had a remarkable influence on the carbonylation. The influences of alcohols, alcamines, arenas, alkanes, *etc*, were mainly investigated in this section. The results are shown in Table 2.

The results in Table 2 demonstrated the fact that *n*-butyl alcohol and *tert*-butyl alcohol exhibited excellent performance in the reaction. When they were used as the solvent during the synthesis of phenylacetic acid in the carbonylation reaction, a faster rate and a higher yield could be obtained, and the stability of catalyst could also be assured. The reason might be that they were partly or completely water soluble, which greatly enlarged the contact surface area between the reaction phases, then accelerated the reaction. But *tert*-butyl alcohol was compatible with water, which was against the separation of phenylacetic acid and the recovery of catalyst, so *n*-butyl alcohol was selected as the solvent. The small amount of *n*-butyl alcohol dissolved in the aqueous phase could be extracted out with anhydrous ethyl ether, and pure products could be obtained after acidification, with only a little loss of the solvent. Furthermore the recovery of catalyst was also very easy.

Table 2. Effects of different solvents

Solvent	Product yield (%)
n-Butyl alcohol	97.6
tert-Butyl alcohol	96.8
Propanetriol	5.1
Cyclohexanol	23.5
Phemethylol	5.0
Phenol	0.0
Ethanolamine	0.0
Diethanolamine	0.0
Triethanolamine	4.9
N, *N*-Dimethylaniline	26.9
Benzopyridine	22.3
Phenylamine	5.1
Benzene	16.4
Methylbenzene	6.9
Dimethylbenzene	16.4
Bromobenzene	26.2
n-Heptane	0.0
n-Hexane	7.1
Hexane	9.9
Diphenyl ether	0.0
Trichloromethane	0.0
Butylene oxide	20.1

3.3. Effects of material feeding

As shown in Table 3, the first two ways of material feeding, *i.e.* pouring all the materials at one time and dripping NaOH and phenyl chloride at a certain ratio simultaneously, were favorable for a higher yield and higher stability of the catalyst. But in comparison, the former was more convenient, so it was used as the way of material feeding. While the effects of the latter two ways were not so good, the reason for which will be discussed in another article.

Table 3. Effects of material feeding

Material feeding	Product yield (%)	Color of catalyst
Pouring at one time	97.6	yellow
Dripping NaOH, benzyl chloride	97.2	yellow
Pouring benzyl chloride, then dripping NaOH	20	black
Pouring NaOH, then dripping benzyl chloride	9	black

In addition, the color of catalyst could also qualitatively reflect its catalytic activity. When showing yellow, it exhibited highest activity; when changed between yellow and black, it exhibited part deactivation; but when showing black, it exhibited no activity at all.

3.4. Effects of reaction temperature

From Table 4, it can be concluded that temperature affected the reaction remarkably. The rate was very slow at 20–30 ℃. The rate increased quickly along with the increase of temperature, reaching the maximum rate at 50 ℃, and the catalyst had high stability at that temperature. But if the temperature kept on increasing, the fractional pressure of solvent would increase and the fractional pressure of CO would decrease in the system, which went against the absorption of CO, and the stability of catalyst would also decrease with the increase of temperature. The coactions led to the downtrend of the yield.

Table 4. Effects of reaction temperature

Temperature (℃)	Product yield (%)	Color of catalyst
20	3.0	milk white
30	4.5	milk white
40	80.0	yellow
50	97.6	yellow
60	82.6	black
70	78.8	black
80	67.4	black
90	51.6	black

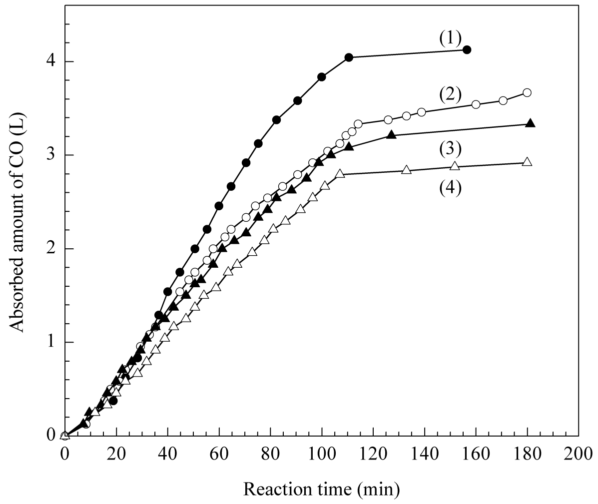


Figure 2. Relation between the reaction time and the absorbed amount of CO at different temperatures

(1) 50 ℃, (2) 60 ℃, (3) 70 ℃, (4) 80 ℃

Figure 2 showed the relation between reaction time and the absorbed amount of CO at different temperatures. It can be concluded that the yield of phenylacetic acid reached the highest at 50 ℃, and the reaction rate was also the maximum. So the optimum temperature should be 50 ℃.

3.5. Effects of the concentration of alkali liquor

Table 5 shows that the concentration of the alkali liquor poured to the reaction system not only influenced the yield, but also influenced the stability of catalyst. The optimum concentration of alkali liquor should be 3.5 mol/L. Too low concentration led to slower rate, and excessive alkali accelerated the initial rate but it could also accelerate the deactivation of catalyst, both of which would lead to the decrease of total catalytic effect and the yield.

Table 5. Effects of alkali liquor concentration

Concentration of NaOH (mol/L)	Product yield (%)	Color of catalyst
2.0*	95.5	yellow
3.5	97.6	yellow
5.0	90.0	deep yellow
7.5	80.0	snuff color
10.0	75.0	brown

* Reaction conditions: 10 ml benzyl chlorides, 65 ml NaOH, 0.075 g catalyst, 55 ml n-butyl alcohol.

3.6. Effects of catalyst content

Figure 3 showed the relation between the absorbed amount of CO and reaction time with different catalyst contents.

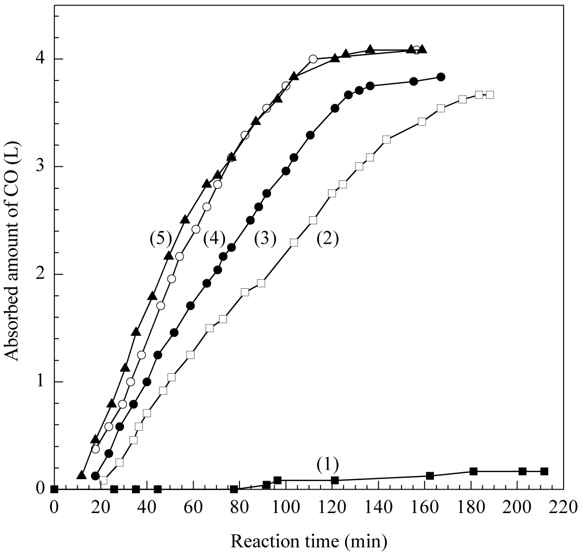


Figure 3. The relation curve between the absorbed amount of CO and reaction time with different catalyst contents

(1) 0.00 g, (2) 0.05 g, (3) 0.10 g, (4) 0.15 g, (5) 0.30 g

It can be seen that the more catalyst used, the higher the reaction rate. But when the amount of catalyst was more than 0.15 g, there was little change on the relation curve of reaction time and the absorbed amount of CO after 80 min's reaction. So from the economic point of view, the content of catalyst should be 0.15 g.

3.7. Effects of triphenylphosphine content

As shown in Table 6, when the content of triphenylphosphine increased from 0.00 g to 0.24 g, the yield of phenylacetic acid increased from 25% to 97.6%, and the stability of catalyst also enhanced. But if kept on increasing, the yield started to decrease, although the stability of catalyst was still good. The reason might be that the addition of a bit triphenylphosphine could effectively slow down the hydrolysis of $Pd(PPh_3)_2Cl_2$, but excessive triphenylphosphine might also form oxinium salt with phenyl chloride or combine with the active intermediate complex compound, which would bind the catalyst, decrease reagent concentration and the catalytic efficiency, and would finally lead to the decrease of yield.

Table 6. Effects of triphenylphosphine content

Triphenylphosphine content (g)	Product yield (%)	Color of catalyst
0.00	25.0	black
0.06	51.1	black
0.12	57.1	brown
0.24	97.6	yellow
0.38	85.6	yellow
0.48	85.6	yellow
0.96	80.0	yellow
1.92	66.6	yellow

3.8. Effects of surfactant

It had little influence on the yield of phenylacetic acid whether to add the surfactants listed in Table 7 or not, which was mainly because *n*-butyl alcohol, the solvent in the reaction system, had excellent hydrophilic performance. This heterogeneous catalytic reaction system approximated to the homogeneous reaction system under severe stirring. So it had little influence whether to add surfactants or not, which was different from the results of previous investigations [22,23].

Table 7. Effects of different surfactants

Surfactant	Amount (g)	Product yield (%)
No surfactant	0.00	97.6
Sodium dodecyl benzene sulfonate	0.16	97.0
Benzyl triethyl ammonia chloride	0.10	97.2
Tetrabutyl ammonia bromide	0.10	97.3
Tetrabutyl ammonia chloride	0.10	97.5
PEG-400	0.12	97.6
PEG-600	0.50	97.8
PEG-2000	1.00	97.2

3.9. Effects of the ratio of organic phase volume to aqueous phase volume

If the ratio of organic phase volume to aqueous phase volume (V_o:V_w) was too large, aqueous phase cannot disperse effectively in the continuous organic phase, then alkali liquor could not react effectively, and some local concentration of alkali might be too high, which would accelerate the deactivation of catalyst. But, if the ratio was too small, organic phase couldn't disperse completely in the aqueous phase, which would restrain the reaction and lead to the deactivation of catalyst. So the ideal ratio appeared to be 1:1.

Table 8. Effects of the ratio of organic phase volume to aqueous phase volume

V_o:V_w	Product yield (%)	Color of catalyst
7:3	4.5	black
2:1	63.8	black
6:4	70.7	yellow
1:1	97.6	yellow
4:6	69.8	yellow
1:2	58.4	yellow
3:7	2.7	brown

Note: with the same total volume of reaction system and the same content of benzyl chloride, V_o:V_w was adjusted by changing the content of alkali and solvent. Other conditions are shown in Table 1.

3.10. Effects of air

As shown in Table 9, the yield decreased greatly in the presence of air, as the fractional pressure of CO decreased and the oxygen in the air accelerated the deactivation of catalyst and affected its stability.

Table 9. Effects of air on the reaction

Reaction surrounding	Product yield (%)	Color of catalyst
Excluding air	97.6	yellow
Not excluding air before reaction	46.0	black
Feeding N_2 after excluding air	65.0	yellow

3.11. The cyclical use of catalyst

The reaction was carried out repeatedly with the cyclical use of the organic phase and the mesophase (the solid phase of catalyst) left in the reaction just completely in which the same amount of phenyl chloride and sodium hydrate liquor were added, but no more catalyst and solvent. The result is shown in Figure 4.

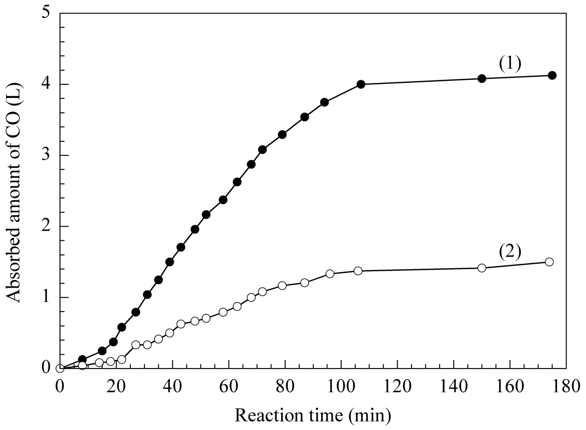


Figure 4. The relation between absorbed amount of CO and reaction time

(1) Fresh catalyst, (2) Circulating catalyst

As can be seen from Figure 4, the catalytic activity of the cyclically used catalyst was apparently not so good as the catalyst newly made. The activity of the former was only about one third of the latter, which might result from the deactivation of some catalyst and that the catalyst bled into aqueous phase in the form of some soluble substance during the separation process. In addition, the absorption curve of CO also indicated that the induction period was longer under the catalysis of the cyclically used catalyst, which might result from the strong inhibition of product in the organic phase that had not been separated completely.

A supplementary experiment was carried out to illuminate this problem. The effects of the presence of phenylacetic acid in stock solution was investigated in this experiment.

3.12. Effects of the product

Figure 5 presented the effects of addition of product (phenylacetic acid) to the stock solution. As shown in the Figure, adding 1.4 g phenylacetic acid before reaction led to apparent decrease in the absorbing rate of CO compared with adding no product. And the yield of phenylacetic acid also declined from 97.6% to 41.2% (having subtracted the phenylacetic acid added).

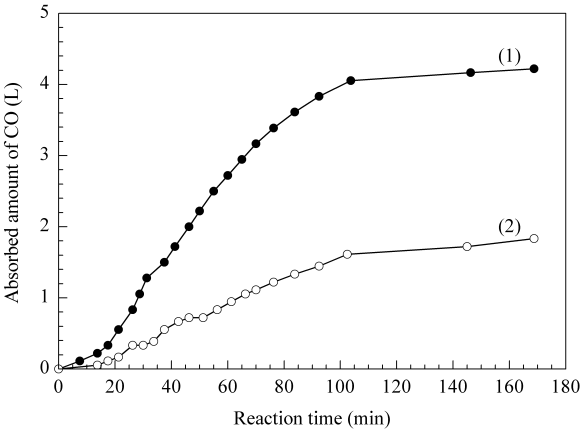


Figure 5. Effects of product on the relation between the absorbed amount of CO and reaction time

(1) 0.0 g, (2) 1.4 g

There were some products in the circulating organic phase and catalyst, while the product had strong inhibition on the reaction, so it had a great influence on the reaction whether the product could be separated completely or not.

4. Conclusions

The factors that would affect the yield of phenylacetic acid in the carbonylation of benzyl chloride included the variety and content of catalyst, and that of solvent, material feeding, reaction temperature, the concentration of sodium hydrate liquor, triphenylphosphine content, presence of surfactant, the ratio of organic phase volume to aqueous phase volume *etc*, the influences of which were investigated in this paper. And the optimum reaction conditions have been obtained: with a one-time pour of 0.15 g $Pd(PPh_3)_2Cl_2$, 0.24 g PPh_3,75 ml NaOH of 3.5 mol/L, 20 ml benzyl chloride and 55 ml n-butyl alcohol, the reaction was carried out at 50 ℃ for about 3 h. In addition, the presence of air in the system and the entrainment of phenylacetic acid in the circulating organic phase were found to have sever unfavorable effects on the reaction rate, the stability and performance of catalyst and the yield of phenylacetic acid.

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