

Conversion of Calcium Citrate to Citric Acid with Compressed CO₂

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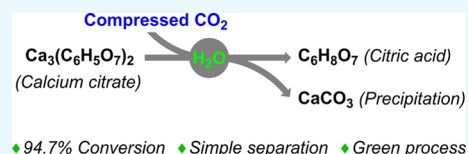


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ABSTRACT: Citric acid is mainly produced in the fermentation industry, which needs complex processes and produces a high amount of CaSO₄ as waste. In this study, CO₂ has been used to convert calcium citrate to citric acid and CaCO₃ by controlling the reaction parameters (reactants ratio, temperature, and pressure). The CaCO₃ produced in this conversion could further be used in the fermentation industry for citric acid production. The transformation condition has been optimized by controlling temperature, pressure, reaction time, and mass ratio of calcium citrate and water. The highest conversion could reach up to 94.7% under optimal experimental conditions of 18 MPa of pressure, 65 °C of reaction temperature, 4 h of reaction time, and 2 g/L of calcium citrate/water suspension solution. This method features simple process, easy separation of citric acid, and environmentally friendly process, which could be a potentially alternative route for downstream treatment in fermentation production of citric acid.



1. INTRODUCTION

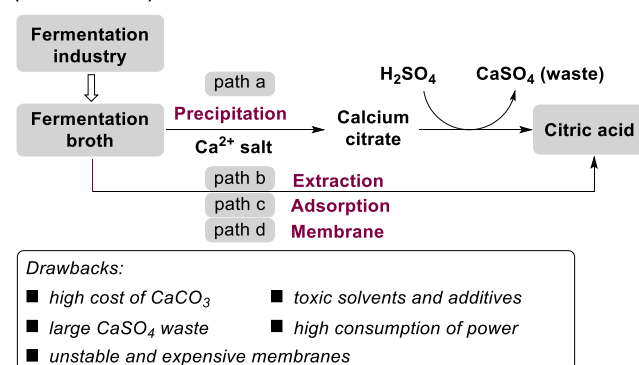
Citric acid is one of the most important organic acids mainly produced in fermentation using the microorganisms of filamentous fungus *Aspergillus niger*,^{1–5} possessing a wide range of applications in food additives, cosmetics, toiletries, buffering and chelating agents, pharmaceuticals, and other industries.^{6,7} Nowadays, it is the most in demand organic acid in the food industry in the world with an increased demand at a rapid rate of 5% per year. The fermentation industry contributes more than 90% of citric acid production, posing enormous challenges for conventional industrial recovery methods and processes.

There are several recovery technologies available, such as precipitation, extraction, adsorption, and membrane.^{8–10} The precipitation method is still dominantly used in large-scale production of citric acid, which converts crude acid in fermentation broth into calcium citrate tetrahydrate by using calcium carbonate, which after treating with sulfuric acid forms liquid citric acid and CaSO₄. After filtration, the free organic acid in the filtrate is purified using activated carbon and ion exchange and concentrated by evaporation (Scheme 1, path a).⁹ For this procedure, the downstream recovery process accounts for 30–40% of the production cost; a huge amount of CaSO₄ is produced as waste, and plenty of nonrenewable CaCO₃ resources are consumed.¹⁰ The high energy cost, complex process, and heavy use of reagents hazardous to the environment in the conventional industrial production and separation strongly call for technological innovation, which could improve the economic benefits and be environmentally benign and sustainable.

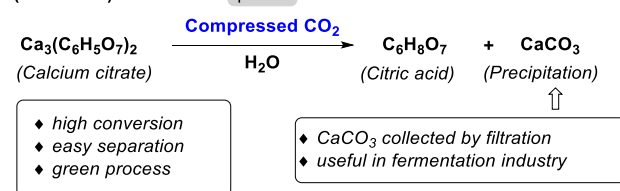
Various methods have been developed toward separation and purification of citric acid as alternatives. For instance, liquid–liquid extraction (alcohols and ketones)^{11–15} and reactive extraction (amines dissolved in various diluents)^{16–20}

Scheme 1. Production of Citric Acid

(Previous work)



(This work)



of citric acid from fermentation broth have been found to be a promising alternative to the conventional process, avoiding consumption of calcium carbonate and sulfuric acid (Scheme

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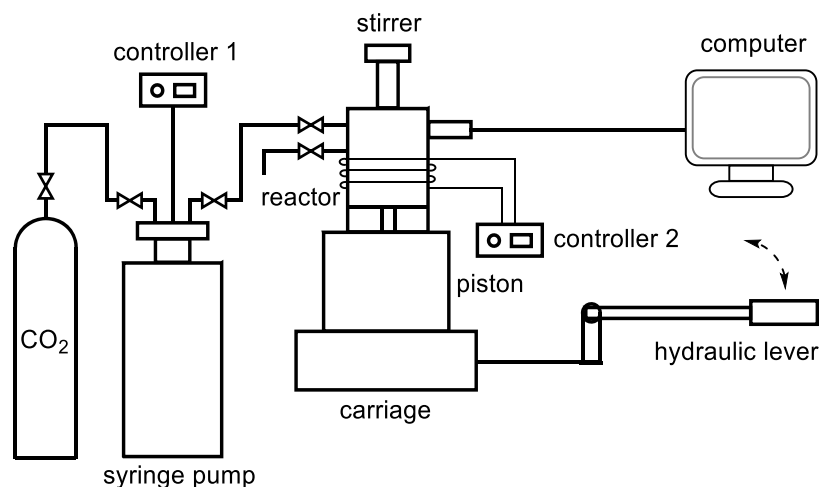


Figure 1. Apparatus for citric acid production using compressed CO₂.

1, path b). However, some of the solvents are toxic, volatile, and flammable, which limit their applicability in practice. Adsorption is the process established on the strong interaction of adsorbent materials with the target molecules. This technique can be employed at a large scale in the recovery and purification of biomolecules and has been used for citric acid recovery from fermentation broth by ion-exchange resins (Scheme 1, path c). Several resins are employed in this process such as macroporous resins Amberlite XAD-4 and XAD-16,²¹ commercial weakly basic resin Diaion WA30,²² Amberlite IRA-67,²³ and tailor-made tertiary PVP resin.²⁴ Although high selectivity and efficiency were achieved by the adsorption using ion-exchange resins, the resins need to be regenerated and replaced, producing a lot of solid and liquid waste. In addition, membrane separation techniques, such as ultrafiltration, electro dialysis and electrodeionization, and perstraction, have also been emerged as promising methods for the recovery of citric acid from fermentation broth (Scheme 1, path d).^{25–32} In this field, the electro dialysis process using bipolar membranes has predominated in citric acid recovery, which allows for impurity separation and organic acid concentration from an aqueous solution based on the electromigration of ions through ion exchange membranes. However, these methods still have drawbacks such as unstable and expensive membranes, toxic additives, and high consumption of power, limiting their applications for large-scale production.

The supercritical fluid technology has been carried out worldwide over the past several decades and successfully applied in some areas for scale-up production in extraction and separation processes.^{33–36} Meanwhile, due to the considerable influence on the kinetics and thermodynamics of chemical reactions, supercritical fluids, especially supercritical CO₂ as reaction media or even reactant, were widely used in chemical synthesis, which possess the advantages of the environmentally friendly process and high reactivity.^{37–43} Based on these research studies about supercritical CO₂, this green technology permits one to make products or operations by using supercritical CO₂ as the reaction solvent or reaction substrate. In this study, compressed CO₂, as both media and reactant, was employed for conversion of calcium citrate to citric acid and CaCO₃ (Scheme 1, path e). In this transformation, the reaction pressure, reaction temperature, reactant ratio, and reaction time were investigated for pushing the direction of reaction toward the desired product. Remarkably, the use of

CO₂ makes it convenient and efficient for separation of desired products, as CaCO₃ and calcium citrate are nearly insoluble in the reaction solvent (H₂O), which could be removed through a simple filtration. This method used green solvent water, avoiding the use of organic solvents and additives, which represents an environment-friendly technology and points to sustainable and green chemistry.

2. MATERIALS AND METHODS

2.1. Materials. Citric acid (99.0%) used for the standard curve of high-performance liquid chromatography (HPLC), calcium citrate (99.0%), methanol (>99.9%), acetonitrile (>99.9%), potassium phosphate monobasic (>99.0%), and phosphoric acid (85.0 wt % in H₂O) were purchased from Sigma-Aldrich. CO₂ (99.99%) was supplied by Shanghai Wujing Chemical Co. Ltd. (China).

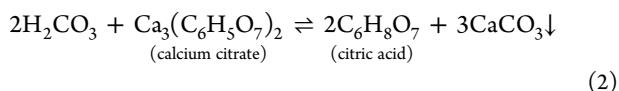
2.2. Apparatus. Super Phase Monitor SPM20 (Thar Technologies, Inc.) is applied in the transformation of calcium citrate to citric acid using compressed CO₂. The schematic diagram of the apparatus is presented in Figure 1. A dip tube is used in the CO₂ cylinder to ensure that CO₂ is supplied from the bottom of the bottle in a liquid state. The syringe pump is used for the delivery and pre-pressurization of CO₂ according to the parameter setup by controller 1. The reactor has an internal reaction chamber equipped with a sapphire window and pressure and temperature sensors. The volume of the reaction chamber is variable (maximum: 20 mL) and could be adjusted by a piston. Temperature in the chamber is controlled by the controller 2 using four electrical heaters, and pressure is controlled by the hydraulic lever connecting with the piston. Phase behavior can be monitored via a video camera adapted with the sapphire window. The motor-driven stirrer is installed at the top of the reactor.

2.3. Procedure for Synthesis of Citric Acid. The weighed calcium citrate (5–50 mg) in a nylon bag was put in the reactor, and the required amount of solvent water (5 mL) was added. Then, the outlet valve of the syringe pump and the valves of the reactor were closed before the syringe pump was cooled to 0–5 °C with the closed circuit cooling water pump. Then, the valve of the CO₂ cylinder was opened and CO₂ was charged into the syringe pump according to the set volume by controller 1. Then, the valve of the CO₂ cylinder and the inlet valve of the syringe pump were closed, and the syringe pump was run to compress CO₂ to set pressure (8–20

MPa). After the pressure was stable, the outlet valve of the syringe pump and the inlet valve of the reactor were opened to let the compressed CO₂ into the reactor. Next, the inlet of the reactor was closed, and the reactor was heated by controller 2 according to set temperature (35–75 °C) and regulated the pressure in the reactor by a hydraulic lever to the corresponding pressure (8–20 MPa). The reaction was stirred by a stirrer for a specific time (0.5–5.5 h), and then, the outlet valve of the reactor was opened to release the gas very slowly until the pressure reached the standard atmospheric level. The reaction mixture was placed at room temperature for 30 min. After filtration through a sand core funnel, 1 mL of the filtrate was extracted using an injector and diluted it into 10 mL with water, and then, the citric acid conversion was detected with HPLC. Considering that CaCO₃ and calcium citrate are nearly insoluble in water and only trace of Ca²⁺ in the reaction mixture was detected by inductive coupled plasma (ICP) emission spectrometry, the interference of calcium citrate in water could be ruled out, and thus, the product citric acid in the reaction mixture could be used for calculation of conversion directly.

3. RESULTS AND DISCUSSION

In a reversible reaction, the reactant ratio would not be ignored as it is essential for adjusting reactions' chemical equilibria. Thus, the ratio of calcium citrate/water should be taken into consideration. Furthermore, as the reaction is achieved by the activation of calcium citrate by carbonic acid, the first step of dissolution of CO₂ in water was essential for the transformation (eqs 1 and 2). The temperature and pressure not only directly affect the chemical equilibrium of the reaction but also influence the solubility of CO₂ in water, which leads to the formation of carbonic acid. In addition, solubility of calcium citrate in water would be also the important factor in a reversible transformation. For these reasons, the effect of the calcium citrate/water ratio, reaction temperature, and pressure was investigated for transformation of calcium citrate to citric acid under compressed CO₂.



As the critical temperature and pressure of CO₂ are 31.1 °C and 7.38 MPa, the screening of temperature and pressure for this transformation started from 35 °C and 8 MPa, respectively. As the reactant ratio and temperature are important factors in chemical reactions, we first investigated the effect of ratio of calcium citrate/water suspension solution within 4 h of reaction time at the temperature of 35–75 °C under the pressure of 15 MPa. Under the pressure of 8–14 MPa, the reaction generally afforded <40% conversion at different temperatures, which will probably be attributed to the low solubility of CO₂ in water under these conditions, as the increase in pressure has a linearly positive effect on solubility of CO₂ in water experiments.⁴⁴ In all the screening experiments, the volume of water is 5 mL, and 5–50 mg of calcium citrate was used for investigation of the conditions. As shown in Figure 2, the amount of calcium citrate clearly impacted the conversion; a 2 g/L ratio of calcium citrate/water gave the highest conversion (slightly higher than ratio of 1 g/L) at a temperature of 35–75 °C, while decreased conversion was

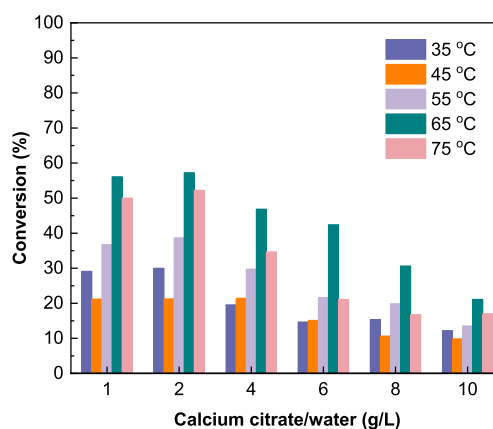


Figure 2. Effect of reactant ratio under different temperatures at a pressure of 15 MPa.

observed when larger ratios of calcium citrate/water were used. This indicates that the 2 g/L ratio of calcium citrate/water probably reached the limitation of this reversible reaction. Increasing the temperature in this transformation could dramatically promote the conversion of calcium citrate, and 57.27% conversion could be obtained at a temperature of 65 °C with a 2 g/L ratio of calcium citrate/water. The conversion decreased when a higher temperature of 75 °C was used. This result could be attributed to the parabolic effect of calcium citrate solubility in water and the decreased solubility of CO₂ at higher temperature.^{44,45} With the optimized ratio and temperature in hand, we pay our attention to the reaction pressure, which is the important factor in supercritical reactions due to its dominated impact on CO₂ solubility.

Le Châtelier's principle states that if we increase the pressure, the equilibrium will change to reduce the pressure, which can be done by favoring the side of the reaction with fewer gas molecules. This could help the consumption of H₂CO₃ by reacting with calcium citrate, resulting in the formation of citric acid. By this hypothesis, the increasing of pressure might be beneficial to this reversible reaction. The reaction was then conducted under a pressure of 15–20 MPa and temperature of 35–65 °C with a 2 g/L ratio of calcium citrate/water. As shown in Table 1, high pressure has a positive

Table 1. Effect of Reaction Pressure at Different Temperatures in a Ratio of 2 g/L of Calcium Citrate/Water

pressure (MPa)	conversion (%)			
	35 °C	45 °C	55 °C	65 °C
15	30.01	21.28	38.68	57.27
16	42.32	43.07	36.13	57.86
17	27.37	28.59	37.52	69.80
18	50.18	29.60	52.86	94.70
19	36.54	39.80	39.85	74.28
20	43.76	40.02	49.61	86.40

effect on the conversion of calcium citrate to citric acid. For the reaction temperature of 35 and 55 °C, best conversion could be obtained at a pressure of 18 MPa. 43.07% conversion was observed at a pressure of 16 MPa when the reaction temperature was 45 °C. To our delight, under a temperature of 65 °C, the conversion exhibited a dramatic increase, and the good to high conversion was achieved at all levels of pressure, and the condition with reaction temperature of 65 °C and

pressure of 18 MPa delivered the best conversion (94.70%). The changes in temperature and pressure strongly affect the chemical equilibrium and solubility of carbon dioxide, which further influences the formation of carbonic acid. Increasing the reaction temperature and pressure could be beneficial to promote the reaction toward citric acid. However, the conversion smoothly decreased when the pressure was further increased to 19 and 20 MPa. This might be explained by calcium carbonate solubility increase with the pH decrease, which could promote the reverse reaction toward calcium citrate, as increasing the reaction pressure results in an increase in the solubility of CO₂ in water, which could increase the concentration of carbonic acid, leading to a pH decrease.⁴⁶

To provide insights into this compressed CO₂-involved process, we monitored the reaction for a specified time. As shown in Figure 3, the conversion increased smoothly from 0.5

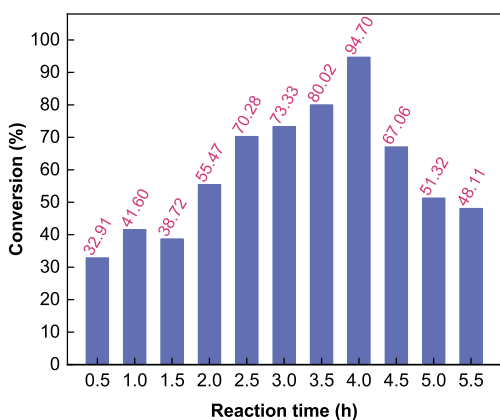


Figure 3. Time courses of reaction under optimal conditions.

h and reached the highest conversion (94.70%) at 4 h. Notably, the conversion had a sharp decrease after 4 h. Only 67.06% conversion could be obtained at 4.5 h reaction time and less of that would be obtained with further extension of time. From the point of view of thermodynamics of reaction, the reaction reached the chemical equilibrium at 4 h, and further increase in the concentration of citric acid and the decrease in the concentration of calcium citrate could lead the reaction to proceed in a reverse direction, finally leading to a decreased conversion. Thus, the time effect should be taken into consideration on compressed CO₂-involved reactions especially on those of the reversible process.

As the scale-up reaction is of great importance and it is a challenge to implement it in practical applications especially in industrial processes, we also explored the large scale of this compressed CO₂-involved transformation. Unfortunately, the reaction in the 0.5 L volume of the reactor with 0.1–20 g calcium citrate and 50–200 mL water only afforded <10% conversion, which was probably limited to the low stability of the apparatus for scale-up experiments and the complex phase behavior under compressed conditions. Thus, more stable apparatus meeting the compressed conditions in large-scale reaction should be developed and more efficient methodologies need to be designed.

4. CONCLUSIONS

In summary, we have developed a novel and efficient route for production of citric acid from calcium citrate in the solvent of water under compressed CO₂. Reactant ratio, reaction

temperature, pressure, and time have an essential effect on this reversible reaction. This transformation features high conversion (94.7%) under optimal conditions, simple reaction operation, and easy separation of the product, providing an innovative and promising route for citric acid production and separation, as it could shorten the downstream operations and lower the cost by using clean and economic solvent and reactants under simple operations.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.1c05316>.

Procedure for conversion detection on HPLC; image of apparatus; and data for screening of temperature, pressure, reactant ratio, and reaction time (PDF)

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Notes

The authors declare no competing financial interest.

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