Biotechnology Frontier
Volume 7, 2019, PP. 4-9

Application of Biocatalysis in Fine Chemical Industry

Mingze Wu[1], Tianci Zhou[2], Xianan Gao[3]

1.Kaiyuan senior high school, Liaoning, China

3.Shenyang Institute of Science and Technology, Liaoning, China

Abstract

The chemical industry has become one of the foundation of the national economy pillar industry, but at the same time, the environmental pollution problems caused by the chemical industry should not be ignored, so the sustainable development of chemical industry, constantly looking for new economic growing point, and the application of biocatalysis technology reform and gradually replace the traditional chemical products is one of the future development direction. Biocatalysis is characterized by mild conditions, energy saving, high conversion rate and selection rate, and environmental friendliness. It can also be used for the synthesis of chiral compounds and the synthesis of macromolecules and macromolecules with complex structures and biological activities.

Keywords: Biocatalysis; High Catalytic Efficiency; Specificity; Environment Friendly

1 INTRODUCTION TO BIOCATALYSIS

So far, the chemical industry has become one of the basic pillar industries of each country's economy, and continues to maintain a high-speed development momentum. The development direction of chemical industry in developed countries is to develop fine chemical industry, that is, to increase the proportion of fine chemical industry and develop special chemical industry. But at the same time, the development of the chemical industry is also facing great challenges. First of all, the oil resources are being exhausted. Second, the environmental pollution caused by the chemical industry cannot be ignored. The sustainable development of chemical industry needs to constantly look for new economic growth points, and the development and application of new technologies and processes in fine chemical industry has become the key, and the application of biological catalytic technology transformation and gradually replace the traditional chemical products is the promising development direction. Especially this year, the introduction of the biocatalysis technology for the development of fine chemical industry to bring a new bright spot, to become one of the keys to leap again in this field, biocatalysis is not only a mild conditions, energy saving, high conversion rate and selectivity, environment friendly, also can undertake the synthesis of chiral compounds and the complex structure, bioactive macromolecules and macromolecular synthesis. Therefore, biocatalysis has become the focus of development and investment of famous foreign pharmaceutical and chemical companies.

Biocatalysis refers to the use of a biological material (mainly enzymes or microorganisms) to catalyze a chemical reaction. Biocatalysis has been applied in China for a long time, such as fermentation in Xia and Shang dynasties. But large-scale industrial production began in the 1960s.

2 EXAMPLES OF INDUSTRIAL APPLICATION OF BIOCATALYSIS

In the industrial application of biocatalysis, enzyme as a biological catalyst has many advantages over chemical catalysts: (1) enzyme-catalyzed reactions are generally carried out in normal temperature, normal pressure and nearly neutral conditions, so the investment is small, energy consumption is low and the operation safety is high; (2) biocatalysts have extremely high catalytic efficiency and reaction speed, which is 107~1013 times higher than chemical catalytic reaction. (3) biocatalysis has high specificity, including substrate specificity and stereospecific specificity. Biocatalysis can only cause specific reactions to specific substrates, and has strict selectivity for product stereospecific configuration, structure and types of catalytic reactions. It can effectively catalyze chiral technologies that are difficult to carry out in general chemical reactions. (4) the biocatalyst itself is biodegradable protein, is the ideal green catalyst.

3 PRODUCTION OF D- PANTOTHENONE BY BIOCATALYSIS

Dl-pantothenolide was prepared by asymmetric hydrolysis reaction in the presence of d-d-pantothenolide hydrolytic enzyme. The product was stereotactic D type with optical purity up to 97.1%ee. After using the immobilized biocatalyst for 200 times, the optical purity of the product is still more than 90%ee.

In 1999, Fuji pharmaceutical produced d-pantothenone by biocatalytic method, and the production scale reached 3000t/a (measured by d-pantothenone). Compared with the chemical separation method, the energy consumption of biocatalytic method decreased by 30%, the use of organic solvents decreased by 49%, the use of salts decreased by 61%, the water consumption decreased by 49%, and the BOD in wastewater decreased by 62%. Using biocatalysts, azide amino racemic mixtures, amino alcohol racemic mixtures and amine racemic mixtures, etc. [1-3].

4 PRODUCTION OF ACRYLAMIDE BY MICROBIAL METHOD

Acrylamide is a kind of important organic chemical raw materials, widely used for large, more than 90% of the acrylamide production at home and abroad for the production of polyacrylamide and its derivatives, homopolymer and copolymer of polyacrylamide is widely used in oil drilling, water treatment, textile printing and dyeing, paper making, mineral processing, pharmaceutical, sugar, building materials, chemical industry, etc, have "all sectors additives", "universal product", so the corresponding demand of acrylamide is bigger.

In the industrial production of acrylamide after catalysis, copper sulfate catalyst catalysis, enzyme catalysis three generations of technology, the core of the biological method is with microbes produce nitrile hydratase is nitrile compounds directly into a kind of enzyme, amide is widespread in plants and microorganisms, microbial synthesis Galzy etc was first reported in 1973, acrylamide, they found a catalyze nitrile BrevbacteriumR312 hydrolysis of microorganisms. In 1985, Rhodococcus sp n-774 strain was used to build an industrial unit of 4,000 tons per year in yokohama. In 1991, Rhodococcusrhodoccoccus j-1, the third generation strain with higher enzyme activity, was adopted to increase the production scale to 20,000 tons per year. At present, the global production of acrylamide by microbial method exceeds 300,000 tons/year.

$$H_2C-CH-CN \rightarrow H_2C=CH-CONH_2$$

Compared with the chemical method, the microbial method saves acrylamide recovery section and copper separation section, and the reaction is carried out at normal temperature and pressure, which reduces energy consumption and improves production safety. The conversion rate of acrylonitrile can be large, up to 99.0%, and the product purity is high, without causing environmental pollution, and the production economy is high. The cost of a new biological industrial installation is about one-third that of a chemical one.

Of Shanghai pesticide research institute since 1984 for microbiological method of acrylamide production research, through the ">", "five-year", many researches of the ninth five-year plan, and succeeded, screening and breeding of the strains, and built 2000 ton/year of production equipment, after years of efforts, the scale of production and technology have reached a higher level, is the national key scientific research project of the ninth five-year plan and the national key promotion project of scientific and technological achievements, won the second prize of national scientific and technological progress in 1998, at present, the cumulative has to accept the transfer of the enterprise more than a dozen, total unit size of more than 150000 tons/year.

5 PRODUCTION OF NICOTINAMIDE BY MICROBIAL PROCESS

Nicotinamide coenzyme Ⅰ and coenzyme Ⅱ composition, nicotinic acid and nicotinamide are always become vitamin B_3, nicotinic acid in animals can be converted into niacinamide and play a role. Animals lacking nicotinic acid or nicotinamide will develop skin diseases, digestive tract diseases, such as psoriasis, keratitis and so on. Therefore, niacinamide and niacinic acid have important applications in the fields of medicine, food and feed. At present, the global annual demand reaches 40,000 tons, and the existing domestic production cannot meet the market demand, partly relying on imports. The traditional production methods of niacinamide are niacinic acid ammoniation and niacinitrile alkaline water hydrolysis. Most domestic manufacturers adopt the second method, which is backward in production process, small in scale, high in cost and less than 0.15 million tons/year in output. In recent years, the conversion of CO_2 into high value-added chemicals has attracted wide attention. Among them, the three-component reaction of CO_2, propargyl alcohol and nucleophile can be used to prepare carbonyl compounds with a wide range of USES. This method has the advantages of step economy and atomic economy. Due to the thermodynamic stability and kinetic inertia of CO_2 molecules, most chemical reactions involved in CO_2 are not supported by thermodynamics. However, the three-component reaction of CO_2, propargyl alcohol and parental nuclear reagent is a thermodynamic favorable CO_2 conversion reaction, which achieves the efficient conversion of o-diol or amino-alcohol and CO_2 to cyclic carbonate and 2-oxazolinone. This review aims to summarize and discuss the main progress in the preparation of carbonyl chemicals by the reaction of CO_2, propargyl and nucleophile in recent years. Hydrogen peroxide (H_2O_2) is an important green fine chemical product, with an annual output of about 12.5 million tons (27.5%) in China. It is widely used as a green catalyst, oxidant and disinfectant in many fields such as petrochemical industry, fine chemical industry and environmental protection. At present, the anthraquinone method is the only method to produce hydrogen peroxide on a large scale at home and abroad. However, the current domestic 2 - EAQ mainly adopts fuming sulfuric acid catalytic Friedel - Crafts craft production, every year hundreds of thousands of tons of rich in organic compounds waste sulfuric acid to produce 30-50 wt %, serious corrosion of equipment, environmental pollution and increase the product cost, thereby seriously affecting 2 - EAQ product market competition and the hydrogen peroxide industry healthy and rapid development, therefore, to conduct 2 - ethyl anthraquinone efficient green catalytic technology research is of great significance and practical application value. In Friedel - Crafts process, 2 - (4 '- ethyl benzene formyl) benzoic acid (BE) n-cyclohexylmaleimide is the key step, often require catalyzed carboxylic acid species dehydration of hydroxyl groups on the closed loop, therefore, to replace fuming sulfuric acid catalyst, are looking for super acid such as heteropoly acid and perfluorinated sulfonic acid resin (such as Nafion - H) green catalyst, the other one is based on the reaction mechanism, modification reaction activity, so as to realize no new green catalytic technology of fuming sulfuric acid. Based on the above ideas, this paper firstly systematically investigated the closed-loop reaction of BE acid catalyzed by heteropoly acid and perfluorosulfonic acid resin catalysts with different acid strengths, and discussed the technological conditions and industrial application feasibility of super acid green catalysis. Then the closed loop route is systematically analyzed, and a new green catalytic process of two-step acyl halogenation followed by dehalogenation of hydrogen to form 2-eaq is studied in detail.

The main research contents are as follows :(1) using phosphotungstic acid, silicotungstic acid, phosphomolybdate acid and nafion-h as catalysts, respectively catalyze the intracolecular friedel-crafts acylation of BE acid to obtain 2-eaq. The catalytic activity and optimum process conditions of heteropoly acids were investigated. The results showed that the catalytic activity was consistent with the acid strength sequence, and the phosphotungstic acid catalyst had the best catalytic activity. For example, when chlorobenzene was used as solvent and reflux for 3h at 135℃, the BE acid conversion rate was 97.8%, and the 2-eaq yield was 75.4%, which was lower than that of the current fuming sulfuric acid process (80-85%). The conversion rate of BE acid and the yield of 2-eaq were 98.5% and 73.8%, respectively. The catalytic activity of nafion-h was slightly lower than that of phosphotungstic acid, but the recycling performance was good. Overall, the two green catalytic processes have significantly improved environmental protection, but the yield is low, which is not conducive to the current industrial implementation. (2) considering that the hydroxyl group on acyl halide is more easily removed than that on carboxyl group, the two-step process of first acyl halide and then hydrogen halogenation was designed and optimized to overcome the strong acid catalysis process.

The new process parameters, such as solvent, the regulation of each intermediate key step and amplification effect, were systematically studied, and the 2-eaq green catalytic synthesis was achieved. The results showed that CH_2C_{12} was used as solvent and the BE acid conversion rate was 99.7% and the 2-eaq yield was as high as 97.9% under optimal reaction conditions. The BE acid conversion rate was 99.5% and the 2-eaq yield was 95.1% after 20 times amplification (2 L reactor) of the reaction system. The purity of crude 2-eaq products was 98.6% and 99.6% respectively in the new amplification process. In general, the yield of 2-eaq is higher than that of raw sulfuric acid, the quality of 2-eaq products is better, and the production cost is equal to that of fuming sulfuric acid.

6 SOME PROBLEMS IN DEVELOPING FINE CHEMICAL INDUSTRY

As most fine chemicals have different special requirements in terms of purity and intrinsic quality, the traditional fine chemical production process is of high complexity, which is mainly reflected in the following aspects: the production of fine chemicals is mostly carried out in heterogeneous phase, and the reaction efficiency is limited; There are many steps of synthesis and large amount of by-products [4-6]. The reaction products are complex, unstable, high boiling point and difficult to separate. Some materials are corrosive, toxic, flammable and explosive, etc. The range of synthetic processes is wide, such as thermochemistry, photochemistry, electrochemistry, and acoustic chemical reactions, so the special equipment involved in chemical engineering is much more complex than common chemicals. At present, there are mature production routes for the production of vinyl chloride in industry, but people pay more and more attention to the energy and environmental problems and the defects of the current production route still urge us to further explore new production routes for vinyl chloride. In view of the high cost of ethylene process equipment and low energy efficiency of dichloroethane cracking unit mercury catalyst used in acetylene process harms the environment and hydrogen chloride transport and storage inconvenience. In this study, a new reaction path was reported for the production of vinyl chloride by direct catalytic reforming of acetylene and dichloroethane. This reaction route can realize the energy distribution in China by diversifying the raw materials.

Therefore, the development of fine chemical industry will face the following problems: (1) environmental pollution can not be ignored, fine chemical production on the impact of the ecological environment is very prominent, the fact also proves that the destruction of the environment at the cost of economic development is not a long-term plan, must take chemical production green and sustainable development road; (2) energy shortage. Energy conservation in chemical industry is an important subject. Oil, natural gas and coal are non-renewable energy resources, and their depletion will cause a worldwide energy crisis. (3) must pay attention to reduce the consumption of raw materials. Modernization is largely based on petroleum as the initial raw material, and petroleum is a non-renewable resource, and increasingly scarce, so in the development of fine chemical synthesis process to improve product yield and reduce raw material consumption is one of the very important tasks.

To solve these problems, the key is to rely on scientific and technological innovation, on the one hand to develop clean production technology to reduce environmental factors; On the other hand, the application of energy-saving devices and more efficient catalysts and reaction energy utilization measures; On the other hand, improve reaction selectivity and develop comprehensive utilization of by-products. Therefore, the application of biocatalytic technology with mild conditions, high selectivity and environmental friendliness in the production of fine.

7 CHEMICAL PRODUCTS HAS BECOME A DEVELOPMENT TREND

Some problems and Suggestions on the application of biocatalysis in fine chemical industry Despite the prospects are very broad, biocatalysis is applied in industrial production is also facing some problems: (1) enzyme usually don't have enough stability, easy to inactivation, applicability is too narrow, can effect the substrate is limited, to adapt to the substrate concentration and low product concentration, the temperature difference of applicability, resistance to pH range is too narrow, sometimes need to the existence of the cofactor, low to the natural substrate and catalytic activity of the environment, so in most industrial systems are difficult to use this fragile catalyst. (2) the existence level of various enzymes in nature is low, and there is a lack of applicable species. Therefore, there are limited enzymes that can be obtained in large quantities through commercial channels, and it is difficult to guarantee the production of various high-quality and inexpensive biocatalysts on an industrial scale. Although there are biocatalysts for many reactions, the vast majority of known enzymes are either not fully identified, patented or commercially available. Currently, there are about 200 kinds of commercial enzymes, while there are only more than 50 kinds of enzymes in industrial application, and only 10 kinds of enzymes in mass industrial production. (3) the application and development cycle of new enzymes is too long. Some of today's iconic biocatalytic processes have gone through 10-20 years of development[7-8]. the spatio-temporal yield of the enzyme reaction is low, although the enzyme has a satisfactory cycle specific number, that is, the unit activity point can catalyze the production of a large number of products in a unit time. However, most enzymes have large molecular weight, only a single active site, and are usually used in low concentrations. As a result, the yield per unit time and space of biocatalytic reactions is sometimes very low. Therefore, the above problems must be considered when applying biocatalysis to fine chemical production.

China's biocatalysis technology has been used in the field of fine chemicals for more than 10 years, and some research and development projects have made great progress and accumulated some experience. Based on the above reasons, the industrial application of biocatalysis, especially its application in fine chemical industry, some Suggestions are put forward: (1) we must strengthen basic research in the field of biotechnology, including biological diversity, biological catalyst selection and transformation, the catalytic mechanism, reaction rules, genetic engineering and directed evolution, catalytic antibodies and ribozymes, because industrial application of biocatalysis can rapid development, thanks to many innovative technology to promote basic research, such as gene cloning technology can be used to express a variety of enzyme genes, to a great extent, can get rid of the limitation on the natural enzyme source, using genetic modification technology can get a new enzyme, etc. (2) in the development of emphasis, in the product focus on the development of chiral fine chemical products, in the biocatalysts to develop heat resistance, acid and alkali, salt and organic solvent resistance extremophiles or enzymes, in the reaction to pay attention to the non-natural environment enzyme reactions[9-10]. (3) attach importance to the downstream development and the combination of upstream and downstream, biological catalysis industrialization support technology and equipment development and research, including the preparation of biological catalyst technology and equipment and bioreactor manufacturing technology, new biological separation technology and equipment. (4) must pay attention to the protection of intellectual property rights, for new biocatalysts and preparation technology, new biocatalytic process should be applied for patent protection in time. Actively carry out scientific and technological cooperation and exchanges with other countries, keep abreast of hot spots and new technologies in the industry, develop through cooperation, and introduce advanced technologies and equipment as appropriate.

CONCLUSION

In summary, ionic liquids are studied in the laboratory because of their unique properties. At the same time, because of the use of ionic liquids, the products can be easily separated, the catalyst can be recycled, the pollution is greatly reduced, and the "green catalysis" is really realized. In addition, the anionic and cationic adjustability of ionic liquids provides a wide space for designing and preparing task-specific ionic liquids. People can design and prepare special ionic liquids according to their needs. For example, in recent years, the proposition of functionalized acidic ionic liquids is based on the research idea of getting rid of the use of ready-made ionic liquids, improving some reactions, and encouraging the production of ionic liquids tailored to specific application purposes or actual needs. It can both start. To promote the reaction, it also plays a dual role of solvent/catalyst, replacing traditional acid catalytic materials which do not meet the requirements of green chemistry and are uneconomical, and ultimately achieving the goal of environmentally friendly green catalysis. However, many mechanisms of ionic liquids have not been solved, and general ionic liquids reagents suitable for various types of reactions need to be studied.

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