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EDITORIAL

Industrial Biocatalysis

The field of catalysis of chemical reactions is contributing tremendously to the success of organic synthesis. Especially in the last decade or two, we have seen exceptional progress in the research of both biological as well as non-biological catalysis.

The belief among some chemists that enzymes, if at all available, are expensive catalysts which are exceedingly fragile to handle, is rapidly disappearing, with more and more impressive enzyme applications being realized in industrial processes. To a large extent, this is due to the impressive progress in molecular biology in recent years. Whereas in the past, the preparation of an enzyme for industrial application, in terms of quality, quantity and price, often posed an unsurmountable problem, this is not the case today. Molecular biological techniques such as gene shuffling have opened the way to tailoring enzymes with new substrate specificities, optimized selectivity, turnover, thermal stability, and solvent resistance. Efficient biological expression systems have been developed for the production of biocatalysts in quantities needed in the chemical industry. For the use in continuous biocatalytic processes, new membrane reactors were designed and new methods developed for the immobilization of whole cells and enzymes. Furthermore, methods are now at hand for the economical recycling of cofactors. Crystalline enzymes, highly stabilized by chemical means, are available to the industrial chemist for the catalysis of reactions in organic solvents, for instance.

The features of enzymes which make them so interesting for preparative organic chemistry are their, now tuneable, chemo- and regioselectivity and stereoselectivity. The conditions of enzyme-catalyzed reactions are usually mild with a relatively low energy consumption.

A broad range of reaction types are catalyzed by enzymes, including the *Diels-Alder* reaction, as recently reported. New enzymes are being discovered at an ever faster rate. Especially the microbial world is a cornucopia of new enzymes yet to be detected by means of intelligent screening systems.

This issue of CHIMIA is devoted to the application of biocatalysis in the chemical industry, in connection with studies of the structure-activity relationship of pharmacologically active compounds, metabolic studies, process development, screening for new enzymes, and strategies for the evolutionary optimization of enzyme biocatalysts.

The derivatization of complex natural products for the generation of structure-activity data is often a difficult task. *Chen et al.* (*Merck*) illustrate how they succeeded by microbial biotransformation. In the course of metabolism studies, the synthesis of drug metabolites is required for the elucidation of their pharmacological significance. Two successful biocatalytic approaches are described by *Pfaar et al.* and *Kittelmann et al.* (*Novartis*), whereby a membrane reactor was employed by the first authors for a continuous process.

How a biocatalytic production process is developed, is exemplified by *Orsat et al.* (*Roche*), who describe the industrial application of a fixed-bed reactor for the continuous production of a chiral vitamin intermediate, and by *Matcham et al.* (*Celgro*), who employ transaminases tailored for the efficient synthesis of a chiral herbicide intermediate. *Riethorst* and *Reichert* (*Biochemie*), on the other hand, take an industrial view on the optimum employment of enzymes for the production of key intermediates in the field of antibiotics.

In the production of chiral amino acids, biocatalytic processes combined with chemical methods have proven very successful. *Petersen* and *Sauter* (*Lonza*) show how cyclic (*R*)- and (*S*)-amino acids can be enantioselectively synthesized. In this context, *Bommarius* (*Degussa-Hüls*) will be reviewing and comparing the merits of different chemo-enzymatic processes to enantiomerically pure L- and D-amino acids (to appear in one of the next issues of this journal). *Hauer et al.* (*BASF*) summarize their experience in the screening for new enzymes for particular processes. They also give two examples of enzyme in the other.

Molecular breeding is a powerful tool to improve enzyme properties and will certainly lead to an increased use of biocatalysis in the chemical industry. *Crameri* (Univ. Basel) discusses the methods of gene shuffling, documenting their remarkable advantages over other, more traditional methods.

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