An enzyme that can switch scents

From Gasoline to Hyacinth

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For more than two centuries, scientists and technologists have been seeking better and cheaper methods of chemical synthesis using catalysts - molecules that can accelerate and boost the efficiency of certain chemical processes. But over millions of years of evolution, Nature itself has developed extremely specialized catalysts, called enzymes. Chemists are nowadays looking more and more to such extant bio-catalysts found in living organisms

Chemical synthesis constitutes the largest sector of industry in Europe. According to the CEFIC 2006 report, as much as 80% of all industrial processes nowadays involve catalysts, which assist in the manufacture of better and cheaper fuels, various types of plastic, cleaning products and medications. Catalysts are also used in environmental protection, e.g. reducing fume emissions in every car.

How do catalysts work?

How might a catalyst lower production costs? Firstly, it may speed up a chemical reaction. In the manufacturing process, we would like to be able to produce large quantities of a given compound relatively quickly. One way of accelerating such a reaction is to carry it out at a higher temperature. However, when a catalyst is applied, it is possible to lower the reaction temperature, thereby saving energy. Secondly, a catalyst can cause a certain "reaction path" to become more privileged. This means that only a single, desired compound is produced, avoiding synthesis of chemical wastes. A catalyzed production process can be significantly cheaper, as well as significantly more ecological in view of the energy savings and minimal waste production.

An ideal catalyst should operate at room temperature, in a non-toxic environment, and stimulate the production of only a single, desired product. However, such a catalyst is very difficult to obtain by chemical methods. Fortunately, Nature has done quite a bit of that work for us - having created enzymes, which meet all these conditions and catalyze millions of chemical reactions that occur inside living organisms.

These biocatalysts are extraordinary complex biological polymers. Most of them are protein enzymes (consisting of combined amino acids), although there are also known biocatalysts which have nucleic acids as their main component (such as ribozymes). The biopolymer thread of an enzyme, folding into a complex pattern, forms a stable skeleton which encircles an active center, where the catalytic reaction occurs. Enzymes are very productive and selective catalysts - they operate at room temperature, in a water environment, and usually synthesize only a single product. We are unfortunately still unable to synthesize enzymes out of individual amino acids. Instead we use microorganisms to do the whole job for us. First, a DNA segment encoding the synthesis of a given enzyme is first implanted into bacteria. Then, after the bacteria colony is grown, its biosynthesis is stimulated. This causes the bacteria to produce a complete enzyme, which can then be purified and used for carrying out the desired reaction.

From the Weser bottom to the lab

At the Institute of Catalysis and Surface Chemistry, Polish Academy of Sciences, we study a fairly atypical enzyme called ethylbenzene dehydrogenase. It comes

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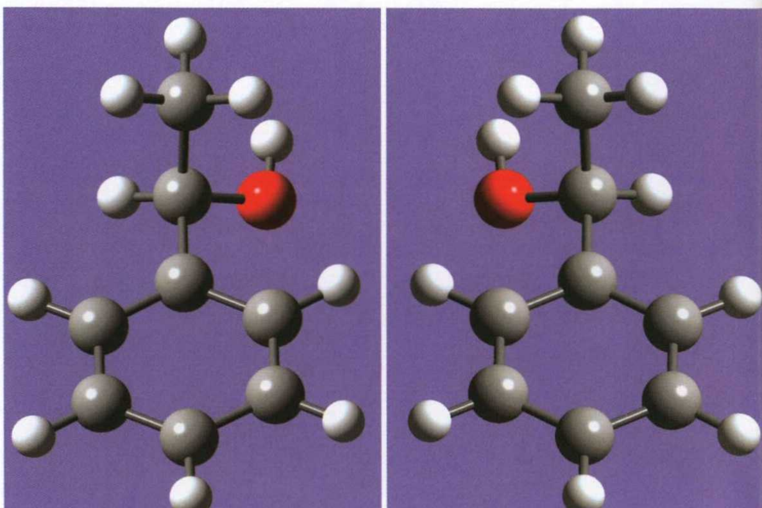

Enantiomers - molecules which are identical except being mirror images of one another - can sometimes demonstrate surprisingly different properties

Tomasz Wiech, Agencja Gazeta

A properly-selected catalyst can minimize the volatile pollutants emitted by industrial processes, or even transform them into harmless carbon dioxide and steam

from the bacterium *Aromatoleum aromaticum* (EbN1 *Azoarcus* sp.), discovered in the bottom sediments of the Weser River near Bremen in Germany. This bacterium lives in an anaerobic environment, feeding upon substances that are poisonous to most living organisms: toluene, ethylbenzene, and propylbenzene. Ethylbenzene dehydrogenase catalyzes a reaction whereby ethylbenzene is oxidized into S-1-phenylethanol. Why is this reaction unusual? Firstly, because under anaerobic conditions the enzyme is unable to utilize molecular oxygen in the oxidizing reaction, as happens in most organisms capable of oxidizing hydrocarbons. Instead, it uses a special molybdenum cofactor present in its active center, which obtains oxygen from water. Secondly, the reaction produces only a single optical isomer, with an S configuration.

Optical isomers are compounds which have identical physiochemical properties, aside from the fact that they alter the polarization of light passing through them in opposite directions. A small difference? Well, as far as biological action is concerned, such optical isomerism is in fact extremely important. All the amino acids which comprise living organisms are built solely from one type of optical isomer (called "enantiomers"), and no terrestrial organisms are able to utilize amino acids of the other configuration in biosynthesis. Our senses of smell and taste can also distinguish between enantiomers very well: S-1-phenylethanol, used in the food industry as an scent additive, smells delicately of hyacinth with a detectable note of gardenia and strawberries, while its mirror image, called R-1-phenylethanol, exudes a honey-floral smell and is reminiscent of unripe fruit in taste.

Different optical isomers can have different effects not only on our senses, but also on our health. Frequently, one optical isomer has therapeutic properties while the other may cause undesirable side effects. That is why the pharmaceutical industry is interested in compounds with high optical purity, which can be used in the synthesis of new drugs.

We have discovered ethylbenzene dehydrogenase to be a highly versatile enzyme, able to catalyze the oxidation reaction of as many as 21 different compounds structurally similar to ethylbenzene. In each case, an alcohol is produced - most likely in an way analogous to the synthesis of 1-phenylethanol.

Via this discovery, Nature has given us a tool able to produce 21 new alcohols which could prove useful not only as scents for perfumes and creams, but above all as building blocks for new drugs design. We expect the enzyme to demonstrate a high selectivity for only a single optical isomer, both in ethylbenzene oxidation and for the other substrates.

How does ethylbenzene dehydrogenase perform these extraordinary reactions? In order to solve that intriguing riddle, we are also studying the possible reaction mechanisms by theoretical methods. Our hope is that one day we will not only be able to utilize ethylbenzene dehydrogenase in synthesizing optically pure alcohols, but also grasp precisely what makes this enzyme such an extraordinarily effective catalyst. Such knowledge could someday prove much more valuable than the ability to transform the odor of a gas station into a delicate whiff of hyacinths... ■

Further reading:

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