New catalyst yields one-handed compounds

Like a pair of hands, molecules often come in mirror-image, or chiral, forms. Though this facet of nature has many virtues, it can be troublesome to chemists seeking to synthesize a particular drug, toxin, or insecticide.

Often during synthesis, the fabrication process yields both versions of a molecule, even though only one is desired. The two types appear nearly identical, yet display remarkably different properties. The chemist's craft lies in devising simple methods of separating such enantiomers — the left-handed or right-handed versions of a molecule — from one another.

In the Aug. 11 NATURE, Kam T. Wan and Mark E. Davis, both chemists at the California Institute of Technology in Pasadena, tell of a new way to achieve chiral separation. They describe the design and synthesis of a catalyst that favors enantiomers of only one type.

Their new catalyst, which they can tailor to speed up a wide range of reactions, has three critical features that distinguish it from similar catalysts, says Wan. It is heterogeneous, remaining a solid even when mixed into a liquid undergoing a reaction. This enables researchers to filter the catalyst out and reuse it easily once the chemical transformation is complete.

The catalyst is also asymmetric, says Wan: It facilitates the making of either a left-handed or a right-handed version of a specific molecule. "The catalyst itself is an enantiomer," says Wan, "so you can make it either way." Depending on the details of the reaction to be enhanced, a chemist can design the catalyst to speed up many kinds of chemical processes, creating the desired enantiomeric form.

A third noteworthy feature of this catalyst is its high selectivity, says Wan. The compound yields the correct form of a desired molecule at least 95 percent of the time, making it both practical and commercially viable. In one test, Wan and Davis designed the catalyst to reduce the compound 2-(6'methoxy-2'-naphthyl)-acrylic acid, yielding the anti-inflammatory agent naproxen. The catalyst achieved a selectivity above 96 percent, they report.

Only homogeneous catalysts have proved so highly selective. Yet these catalysts are difficult to separate from the final product once the reaction is finished.

"For this type of catalyst, this is unique," says Wan. "No one has reached that level of selectivity before with a heterogeneous asymmetric catalyst."

Indeed, high selectivity in a catalyst makes a great difference during drug synthesis. In the case of naproxen, for example, "the right-handed version relieves pain, while the left-handed form is a toxin," Wan observes.

One problem that has plagued previous attempts to make this type of catalyst is leaching, says Wan. During reactions, the catalytic agent will sometimes seep into the final product and contaminate it. Yet with this catalyst, leaching does not occur, he points out.

To prevent leaching, maximize the surface available for a reaction, and make it easy to recycle the catalyst, the chemists first dissolve the compound in ethylene glycol. They then soak tiny, porous glass beads in this solution. When added in this form to a chemical reaction, the catalyst promotes the making of one enantiomer, yet remains a solid, Wan says.

"This is a general type of catalyst," Wan adds. "It could be used to make many kinds of drugs or compounds — and almost any molecule that involves an asymmetric reaction. I don't really see any limitations." — *R. Lipkin*

Lake Apopka pollution hurts bass population

Lake Apopka near Orlando covers 38,000 acres and is one of Florida's largest freshwater lakes. It's also one of the state's most polluted. The reasons, says Tim Gross of the University of Florida in Gainesville, include a large chemical spill in 1980, pesticide pollution from the citrus industry, and chemical drainage from "muck farms," the marsh-rich farmland that is drained, farmed, and flooded two to four times a year.

The desire to understand this pollution's effects on lake animals steered Gross toward the largemouth bass. Earlier work by Gross and colleagues Franklin Percival and Louis Guillette suggested that pollution, particularly estrogenic pesticides, had caused Lake Apopka's alligator population to suffer reduced fertility and a surprising feminization of males (SN: 1/8/94, p.145).

The bass research, carried out by Gross, Percival, and William Johnson of the Florida Game and Freshwater Commission, began this April and ended in August. They collected 60 fish from each of three comparably sized lakes — Lake Woodruff, pristine; Lake Griffin, mildly polluted; and Lake Apopka, heavily polluted. "The numbers of bass [in Apopka] are a tenth of what they'd be on most lakes," says Gross. In 2 to 4 hours, the team collected 30 bass from Lakes Woodruff and Griffin; it took 8 to 16 hours to collect the same number of fish from Lake Apopka.

The researchers report that though the female bass appeared fertile, there were far fewer juvenile and adult bass in Lake Apopka than in the other two lakes. Gross notes that they found no fingerlings. "This suggests," he says, "that [the Apopka bass] are not producing as well." In addition, the team observed that 90 percent of the Lake Apopka bass contained high numbers of parasites, cysts, and liver tumors, whereas only 5 percent of the fish from the other lakes did. Next year, the team will further investigate these abnormalities, says Gross. "This [work] may indicate that the immune system is affected." — *G. Marino*

AIDS research: From vaccines to safer sex

This week, researchers from around the world met at the Tenth International AIDS Conference in Yokohama, Japan, to report scientific findings on topics ranging from vaccine development to long-term survivors of HIV infection. At the same time, several major journals published updates on this devastating disease.

• At the AIDS meeting, National Institute of Allergy and Infectious Diseases (NIAID) Director Anthony S. Fauci and his colleagues reported preliminary results from a study of people who had remained healthy despite being infected with HIV for about a decade. Their study suggests that such people may show a more aggressive immune response to HIV, the virus that causes AIDS. Compared to HIV-infected people who progressed to AIDS, those who did not had very high concentrations of HIV-destroying antibodies.

• In the Aug. 10 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Robert B. Belshe of the St. Louis University School of Medicine and his colleagues demonstrated that a genetically engineered vaccine triggers the production of antibodies that attack several strains of HIV.

The study involved 57 volunteers who were not infected with the AIDS virus. Forty-eight of them received varying amounts of vaccine, a product genetically engineered to look like the gp 120 protein that sits on the surface of the AIDS virus. The remaining nine recruits got an inactive placebo.

"We were delighted to learn that two shots of the vaccine stimulated antibodies that could attack and kill a strain of HIV in the laboratory," Belshe says. After giving three or four doses of vaccine, the researchers documented antibodies that neutralize additional strains of HIV. An effective vaccine must recognize and kill many different types of HIV, Belshe points out.

The vaccine, made by Genentech of South San Francisco, seemed to spur the production of an antibody that attacks