

## Chemicals get tied up in complex knots

Even the most dexterous Scout would have trouble making a knot in an organic molecule. Drawing on years of experience, however, three chemists in France have done just that, synthesizing a chemical knot that's more complex than earlier ones.

They made a composite knot, a combination of two simple knots, each shaped like a trefoil. Knots provide a basis for studying how a molecule's shape and structure influence its physical and chemical properties.

What's more, mathematical models of knots can help scientists understand and describe those properties (SN: 3/21/92, p. 186). For example, both knots and molecules can exhibit chirality, meaning that like a person's left and right hands, they are mirror images of each other. Proving mathematically that a difference exists is not a trivial problem, says Kenneth C. Millett of the University of California, Santa Barbara.

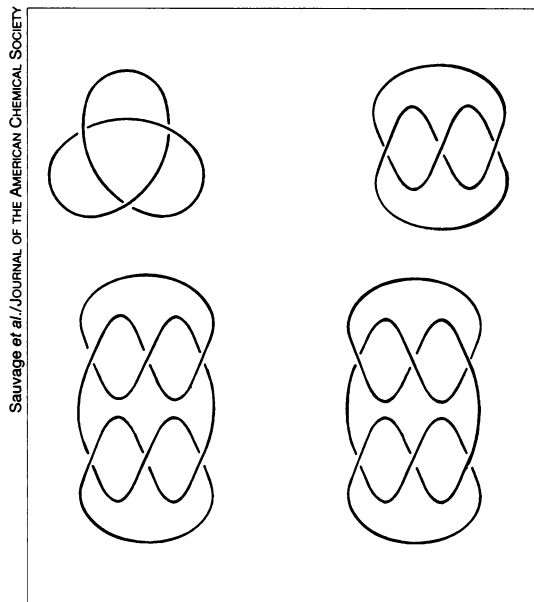
Riccardo F. Carina, Christiane Dietrich-Buchecker, and Jean-Pierre Sauvage of Louis Pasteur University in Strasbourg, France, report their findings in the Sept. 25 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY. Dietrich-Buchecker and Sauvage first synthesized the simple trefoil knot in 1989 (SN: 9/8/90, p. 149).

The new composite knot required more

than just twisting a molecule and securing the ends. The researchers' approach was first to make the two halves and then to connect them. They took simple, linear organic molecules and bent them around two copper atoms—like wrapping a piece of string around each of two fingers—leaving the ends free. They then attached the ends of two twists together, completing the composite knot. The knots came in three different conformations: two chiral knots that are mirror images of each other and one that is achiral, or the same as its reflection. An equilateral triangle, for example, is achiral.

Other scientists have tied different complicated knots using DNA, a much longer molecule than the one used in the current study. However, "to synthesize a specific knot with a small molecular weight is a real achievement," says Millett, who has created models that relate the length of a molecule to the different ways it can be knotted. "Being able to move from a simple knot to a composite is—from a mathematical point of view—a real step."

It's also a significant step from a chemical point of view, he adds. The researchers got a good yield of knotted molecules, despite using a multistep synthesis that loses a little bit of product after each reaction. "They got more than



The simple trefoil knot (top left) can twist into another conformation (top right) that forms one-half of a composite knot. One composite knot (bottom left) differs from its mirror image (not shown), while the other (bottom right) looks the same as its mirror image.

just the mathematical or statistical analysis would have suggested," he says, which implies that some unknown process is boosting the level of output.

— C. Wu

## Smokers risk vision loss in twilight years

"Smoke Gets in Your Eyes" used to be just an old nightclub lament. Now, with the publication of two reports that strongly link cigarette smoking to vision loss, the phrase seems prophetic.

The studies show that long-term, heavy smokers have more than twice the normal risk of age-related macular degeneration (AMD), a disorder in which the region of the retina that captures images in the center of the visual field breaks down. The leading cause of vision loss and newly diagnosed blindness in people age 65 and older, AMD afflicts 1.7 million people in the United States.

"It can make it very difficult to perform the activities of daily living—including driving, reading, and watching TV," says William G. Christen of Harvard Medical School in Boston. Christen is coauthor of a report on AMD and smoking in 21,157 men in the Physicians' Health Study. That article, along with a comparable report on AMD among women in the Nurses' Health Study, appears in the Oct. 9 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

Doctors have yet to determine why AMD occurs. Previous research has implicated low concentrations of zinc,

vitamin E, and beta carotene in the blood; these antioxidants sop up harmful molecules called free radicals. Poor blood flow to the retina may also be a cause. Smoking ranks as a risk factor because it reduces concentrations of these antioxidants and impairs circulation, Christen says.

Once AMD begins, the pinhead-size macula develops yellow spots and lumps called drusen. Drusen apparently accumulate because garbage disposal cells, called phagocytes, fail to clear away cellular debris. In the worst cases, leaky blood vessels worm their way into the retina and flood the macula. The eye's efforts to repair itself lead to scarring, which only makes matters worse.

Doctors lack an effective means of halting this process. Although laser surgery can seal off wayward blood vessels, it only delays the inevitable, studies have shown. Peripheral vision may survive, but faces blur into featureless ovals. The central words in any sentence disappear.

In such a situation, prevention becomes a person's best defense—hence the rising interest in the link between AMD and smoking.

Christen and his coworkers probed

for such a link in the huge study of male physicians, age 40 to 84 when the study began in 1982. Relying on medical records and questionnaires with detailed questions on smoking, they identified 268 cases of AMD. The study found that two-pack-a-day smokers had 2.5 times the disease risk of men who had never smoked—and the longer the men smoked, the higher their risk.

Johanna M. Seddon, also of Harvard Medical School, and her coauthors focused on the 31,843 women in the Nurses' Health Study, who were 50 to 59 at the outset in 1980. Their results were virtually identical. Women who smoked two packs a day had a 2.4 times greater risk of AMD than women who never smoked. The study also found that much of the excess risk persisted, even in women who had quit smoking 15 years ago. "Women who choose not to smoke can reduce their risk of developing this disease by more than half," Seddon asserts.

Saying no to cigarettes "may reduce the loss of vision and may ensure a brighter view of the world for years to come," conclude Ronald Klein and Barbara E. K. Klein of the University of Wisconsin Medical School in Madison in an accompanying editorial aptly titled, "Smoke gets in your eyes, too." — S. Sternberg