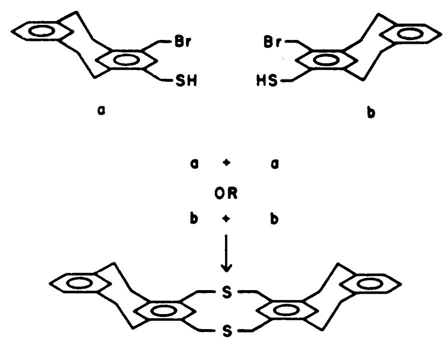
Merging molecules of the one 'hand'

At the end of a dinner with chemistry colleagues several years ago, Kurt Mislow asked the waiter to bring him an apple and a knife. He proceeded to cut the apple in a rather curious fashion that resulted in two oddly shaped but identical halves. The scientist then noted that there was no molecule known to have a structure that could illustrate one of the specific geometrical concepts of chirality, or handedness, embodied by the apple halves. Now, Mislow and colleagues of Princeton University in New Jersey, along with Frank A. L. Anet and colleagues of the University of California at Los Angeles, report they have found such a molecule.

What they have found is a molecular counterpart to apple halves formed by *la coupe du roi* ("the cut of the king"), a parlor stunt known among some families in France. To achieve this curious cut, two vertical half-slices are made through the apple: one from the top to the equator and the other, perpendicular to the first, from the bottom to the equator. Then, two nonadjacent horizontal quarter-slices are made along the equator of the apple to connect the vertical cuts, and the apple separates into two identical halves.

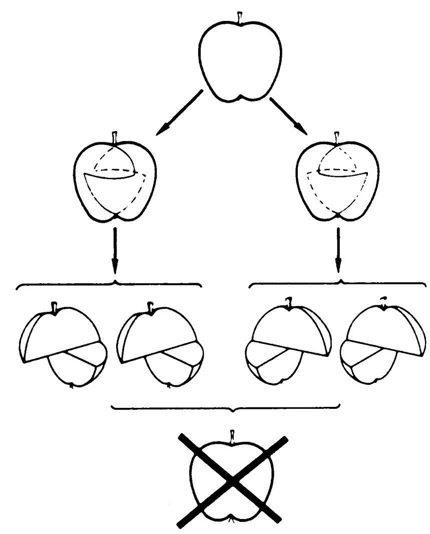
An apple is an object with no chirality (*chiros* is Greek for "hand"). In other words, an apple's mirror image is "identical" to and can be superimposed on the real object. On the other hand, the halves formed by the "cut of the king" are chiral — they have nonsuperimposable mirror images. In fact, each cut of the king results in a pair of homochiral (same-handed) halves — objects that have the same relationship to each other as do, for example, two right hands. But, unlike two right hands, these homochiral halves can be reassembled into an object without chirality — that is, the original whole apple. (Two merged right hands would constitute an object *with* chirality.)

The night Mislow performed the apple-cutting stunt, he and dinner companion Anet found it intriguing that despite the vast number of known chiral molecules — including biologically important ones such as amino acids and enzymes — there was no known example of a handed molecule that could be self-coupled to form a new molecule without handedness. Their piqued curiosities eventually led to their synthesis of just such a molecule: 4-(bromomethyl)-6-(mercaptomethyl) [2.2] metacyclophane, shown in the diagram above in its nonsuperimposable mirror images, "a" and "b." Two same-handed versions of this molecule (a+a or b+b), Mislow and cohorts discovered, can be combined to form an achiral molecule — one that previously had been reported in unrelated research by S. Misumi of Osaka University in Japan. Note that the structural framework of a and b keeps the Br and SH on the same molecule far enough



apart to prevent them from reacting with each other, as is their tendency.

This discovery of the molecular counterparts to the cut-of-the-king apple halves "is pure research," Anet told SCIENCE NEWS. The work, described in the March 23 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, "is not something that has immediate or even far-reaching applications," he says. But, "In our view, it fills in something that has been missing from the area of stereochemistry [the study of the spatial arrangements of molecules]," Anet says; "it sort of tidies up our knowledge of stereochemistry." And, he adds, "I think most chemists would be surprised that it could be done. —*L. Garmon*



Mislow et al./JACS

Each of the two apples, sliced in half by la coupe du roi, *can be reassembled to form a whole apple with no chirality, or handedness. (However, one half from each apple cannot be merged into a whole because the apples were sliced in opposite directions and each pair of halves is opposite-handed.) Similarly (diagram at left), two homochiral (same-handed) versions of 4-(bromomethyl)-6-(mercaptomethyl) [2.2] metacyclophane, either a+a or b+b, can be assembled to form a molecule with no chirality.*

New route found to fish 'hot spots'

Pheromones are chemicals that, when secreted by one animal or insect, will attract another. Many types of pheromones play a role in sexual attraction. Researchers presumed for years that these chemical attractants were sensed by the olfactory (smell) system and that the olfactory nerve transmitted this chemical message to the brain. Now, however, biologists Leo S. Demski of the University of Kentucky in Lexington and R. Glenn Northcutt of the University of Michigan in Ann Arbor have proposed that the terminal nerve (TN), which runs alongside the olfactory nerve, may be the key to understanding pheromone-induced behavior in fish and other vertebrates.

Demski and Northcutt describe their experiments in the April 22 SCIENCE. They draw on the work of other researchers, who have demonstrated that the TN contains luteinizing hormone releasing hormone (LHRH), a chemical that aids in the development of sex organs and is implicated in other sexual responses. They found that the TN fibers run from the epithelial cells lining the nasal passages of goldfish to the anterior commissure — an area in the brain that Demski terms a "hot spot" for controlling sexual behavior. The olfactory nerves do not contain LHRH and go to other areas of the brain as well.

Demski hypothesizes that fish sense pheromones in the nasal epithelium, but the message is sent to the brain via the TN instead of, or perhaps in addition to, the olfactory nerve. The chemical messenger of the TN is LHRH, which Demski calls a "neuromodulator," as opposed to a neurotransmitter. A neuromodulator, he says, "is squirted out of the nerve endings and helps different systems to work better." For example, when cells near the anterior commissure of a male goldfish are stimulated, the fish will release sperm, but if the fish is treated first with LHRH and then stimulated, sperm release is even greater.

Because the TN and the olfactory nerve are so closely associated, many previous experiments that cut the olfactory nerve also cut the TN. So any effects attributed to the olfactory nerve could have been due solely to the action of the TN. "What we're doing is questioning the older work," Demski told SCIENCE NEWS. "We're asking: Is it possible that [the TN] is controlling this input from pheromones rather than the olfactory system? It makes a lot of sense because there is some evidence that LHRH enhances sexual behavior in fish and other vertebrates."

Demski believes that this knowledge doesn't just apply to fish. "This may be a system that triggers sexual behavior using this hormone, LHRH, as a connecting link, squirting it out from these nerve endings and enhancing different systems in the brain of many different animals," he said. "It could be going on in humans as well." —*P. Taulbee*