Earlier this year, Shea demonstrated that the idea works, at least in a simple system: He reported that he has developed an imprinted polymer that can catalyze the removal of a hydrogen fluoride group from a complex molecule. If Shea can extend this success, he thinks his artificial enzymes should have a decided advantage over natural enzymes and the catalytic antibodies that biochemists have recently been developing. Explains Shea: "Because the [imprinted polymer] materials are hardy, they can be used at high temperature in organic solvents, unlike protein catalysts [enzymes and antibodies] that have to be in water and are rather sensitive."

While Shea and his colleagues say they are looking mainly at applications in chemistry, Mosbach says he and his group in Sweden are concentrating on opportunities in biomedicine. Last year in *Nature*, he and his colleagues described an imprinted polymer that can monitor levels of drugs such as Valium in the bloodstream—a task that now falls to immunoassays based on antibodies, he says. "Now, you don't need biological antibodies—you can use plastic antibodies. That makes life much easier," he says, explaining that polymer imprints should be cheaper to make than antibodies, which usually come from laboratory animals.

Antibodies and enzymes still have the upper hand in one key area, however: They can recognize proteins, the complex molecules that are the key actors in most of biology. Molecular imprinting, in contrast, hasn't been able to produce binding sites for proteins, because bulky protein templates can't slip in and out of the polymer network.

Now Mosbach is trying to erase that distinction with a variation of the molecular imprinting technique called surface imprinting. Instead of creating three-dimensional imprints within a mass of polymer, he forms shallow, two-dimensional molecular impressions in a thin polymer coating on the surface of a bead. Mosbach hasn't published his surface imprinting technique formally, though he described it briefly in the January *Trends in Biochemical Sciences*. But already he has some competition. Arnold says she, too, has developed a version of surface imprinting and has tested it on several different proteins.

To Oklahoma's Ford, surface imprinting sounds like the only promising way around the problem of getting proteins in and out of a polymer scaffolding. If it lives up to expectations, the technique may open the way to polymer-based biosensors and catalysts for proteins—and present enzymes and antibodies with their first serious rivals as biomedical tools. Evolution may have passed over the template-and-cast system for the immune system, but human beings, facing an equally daunting job of molecular recognition, may find it the method of choice.

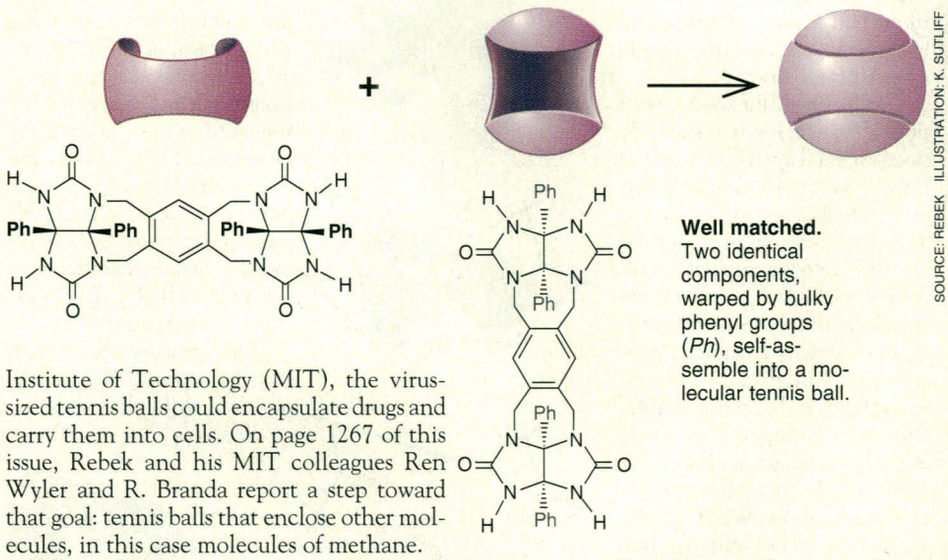
**–Faye Flam**

CHEMISTRY

# A Game of Molecular Tennis, Anyone?

The spherical geometry of buckminsterfullerene may have forged an unbreakable link between chemistry and soccer, but a group of chemists has now come up with another contender for the chemico-athletic crown: the molecular tennis ball. Like their athletic counterparts, these two molecular constructions have little in common other than their shape. While fullerenes form when many simple carbon units link up in the flame of an electric arc, the tennis balls take shape in solution, at room temperature, when two complex molecular components meet and stitch themselves together.

And while fullerenes are prized for the unique chemical and electronic properties of their carbon cages, the creators of these molecular tennis balls think they will be most valuable as containers for other compounds. Just as viruses slip into cells and release their DNA, says Julius Rebek of the Massachusetts Institute of Technology (MIT), the virus-sized tennis balls could encapsulate drugs and carry them into cells. On page 1267 of this issue, Rebek and his MIT colleagues Ren Wyler and R. Branda report a step toward that goal: tennis balls that enclose other molecules, in this case molecules of methane.




**Well matched.** Two identical components, warped by bulky phenyl groups (*Ph*), self-assemble into a molecular tennis ball.

SOURCE: REBEK ILLUSTRATION: K. SUTLIFF

The achievement is attracting high marks from other chemists, not so much because of the promise of "artificial viruses" as because of the elegant molecular assembly technique adopted by the MIT group, who worked with Javier de Mendoza of Spain's Universidad Autónoma de Madrid. Instead of relying on extreme conditions or complicated chemical syntheses to form their cages, Rebek and his colleagues created components that would recognize each other and "self-assemble" in solution. That's the same approach the body uses to create complicated biomolecules, says Fraser Stoddart, an organic chemist at the University of Birmingham in the U.K., and the Rebek group's use of it, he says, "gets 5.9 from me for technical merit and 6.0 for artistic impression."

The trick to making the tennis balls self-assemble was to design identical pieces that, like the two segments of a tennis ball, can fit together in only one possible way: as a sphere. That meant shaping each piece so that its ends would be complementary to the middle of another piece, and curving it so that it can meet another piece in the proper embrace (see diagram). To create each curved component, the team reacted two molecules of diphenyl glycouril with one of durene tetrabromide. This resulted in a molecule with four bulky phenyl groups ($C_2H_5$) sticking out from one face. Phenyl groups prefer to stay apart, and the strain generated by the adjacent phenyl groups bends the molecule into the required half-tennis-ball shape.

Each of the resulting components is edged with alternating N-H and C=O groups. The researchers knew that when these groups are brought close together, weak hydrogen bonds form between the oxygen and hydrogen atoms. The shape of the molecules is such that when any two of them meet, each N-H group comes face to face with a C=O group. The result is eight bonds—the stitches that hold the tennis ball together. In work reported last year in *Angewandte Chemie*, the team used spectroscopy to confirm that their components had indeed assembled into supramolecular spheres. Since then, Carolyn Knobler of the University of California, Los Angeles, and William Davis of MIT have confirmed the structure by x-ray crystallography. "We really do [now] have proof of the shape," says Rebek.

They also know that the tennis balls can capture other substances. In this issue he and his colleagues report evidence from nuclear magnetic resonance spectroscopy showing that if they assemble the tennis balls in the presence of small molecules such as meth-

ane, the molecules can become trapped inside. Most of the molecules that researchers would like to ferry into cells are larger than methane, however, and so the team is working on larger capsules—already dubbed "molecular softballs"—that have the same simple structure.

Rebek admits that harnessing the new structures to carry drugs is something of a dream, but the researchers are taking steps toward realizing it. In one line of research, they are looking for ways to trigger the release of the spheres' contents at the required time. One scheme entails attaching carboxylic acid groups to the outside of the spheres. If a sphere's surroundings become more alkaline, the acid groups are converted to negative ions; the charges repel each other, bursting the sphere open and releasing the contents.

Rebek isn't stopping there, however. He thinks that, for maximum effect, an artificial virus should, like a real virus, carry a self-replicating molecule, something that Rebek has worked on extensively in the past (*Science*, 22 May 1992, p. 1179). Such a molecule, once released inside the cell, could use the cell's raw materials to copy itself. If the self-replicating molecule were also a drug, the result would be a much higher dosage than could be achieved by simply trying to smuggle the drug through the cell membrane.

Stoddart isn't sure the analogy between viruses and molecular tennis balls can be pushed that far. But he applauds the spirit: "Chemists are beginning to see how the concepts of biology, such as self-assembly and self-replication, can be transposed to chemistry."

**–David Bradley**

*David Bradley is a science writer based in Cambridge, England.*

OCEANOGRAPHY

# Dialing Up Undersea Data—Long Distance

In the deep waters off the California coast, around the submerged faults that make up Monterey Canyon, oceanographers this winter deployed a trailblazing underwater research system. At first glance, it includes just a few ocean bottom seismometers, current meters, temperature and pressure sensors—nothing out of the ordinary. But each of these traditional research instruments also contains a state-of-the-art underwater "acoustic modem," which can detect and bark out digital information, sending it surfing along sound waves that slice through the ocean. And by doing so, these modems could very well bring about a sea change in the way oceanographers work.

Those sound waves can carry data from the instruments to a surface buoy, which then relays it via radio waves to onshore computers. As a result, instead of sending ships out to recover instruments—a time-consuming, expensive effort that may yield nothing if the instrument has broken down—land-based scientists can continuously eavesdrop on their bottom-dwelling instruments, retrieving data at near real-time speeds. Investigators can even interact with their experiments, increasing data collection if events such as an underwater eruption occur. These are options researchers never had before. "The acoustic modems are a great idea. We see the whole oceanographic community needing them," says Steve Etchemendy of Monterey Bay Research Aquarium Institute (MBARI), which operates the Canyon network.

Ultimately, the modems may help ocean scientists address what some call one of the most fundamental problems of the field: the "ocean sampling problem," which is an inability to monitor the world's waters comprehensively over large distance and periods of time. Until now, scientists have been limited to relatively brief glimpses of the ocean from research vessels and short-lived instruments. But one day, in the words of engineer Josko Catipovic of Woods Hole Oceanographic Institution (WHOI), acoustic modems will provide a "global underwater cellular network." This novel idea will allow oceanographers to give early warning of deadly tsunamis, watch video images of marine animals and mid-ocean ridges, do long-term environmental monitoring of dumpsites and sunken nuclear subs, and control autonomous research vehicles—all from dry land.

That optimistic vision has already attracted generous developmental funding from a host of federal entities like the Advanced Research Projects Agency (ARPA), the Office of Naval Research (ONR), and the National Science Foundation (NSF), which is sponsoring Monterey's prototype network. Other projects garnering government interest are proposed arrays of modem-equipped instruments around the Juan de Fuca Ridge off Seattle and in the Labrador Sea, the latter to study Arctic water flowing into the Atlantic. There are, of course, still a few waterbugs in the systems,-chief among them the reluctance of many oceanographers to trust their experiments to new technology whose long-term reliability has not yet been proven. The allure of the technology, however, is very powerful, because researchers have long coveted this type of remote communication.

Chatting across large stretches of water is a formidable task. The ocean effectively scatters electromagnetic radiation, making communication with most radio waves or lasers feasible only for short distances. That leaves sound waves, which can punch through water for miles. Acoustic modems generate these waves by converting digital data into electrical signals that vibrate a metal plate, like a stereo's tweeter. These devices also have receivers that capture acoustic waves and reverse the process.

Underwater acoustic communication dates back at least to the 1950s, but until recently it has been hampered by a phenomenon called multipath, which is particularly troublesome in shallow coastal water, undersea canyons, and other places of great research interest. Multipath is caused by acoustic waves bouncing off the sea floor, the ocean surface, and even layers of water at different temperatures, which produces confusing echoes that arrive seconds apart. "The reverberation is so bad. It's a very nasty problem," says Northeastern University electrical engineer David Brady. Primarily because of that, sea acoustic links were limited to low data rates—"speaking" slowly to avoid confusion from the echoes—and even then useful only in low-echo conditions, such as in the deep ocean.

That limitation left oceanographers stuck with their two traditional research methods, neither of which made them very happy. Scientists could adopt what might be called a dump and pray strategy, where experiments that record data internally are dropped off a ship and picked up days, weeks, or months later. This approach is restricted by the amount of data each device can store, as well as by all-too-frequent equipment failures. "There's been more than one experiment that when you fetched it, there had been a malfunction and you lost a year of data," laments Massachusetts Institute of Technology (MIT) ocean engineer Arthur Baggeroer. Alternatively, ship-based oceanographers can study the ocean with submersibles or towed instrument arrays. Not only is this expensive—an oceanographic research vessel might cost $15,000 a day to operate—but the data only describe the ocean when and where the ship was.

In the late 1980s, thanks largely to low-cost digital signal processing hardware, modem technology—and their data rates—sped forward. Engineers could construct, with just a few integrated circuits, acoustic modems that filtered out signals from noise and even took advantage of the multipath nuisance, using the late-arriving echoes to check the accuracy of the original signal. Investigators