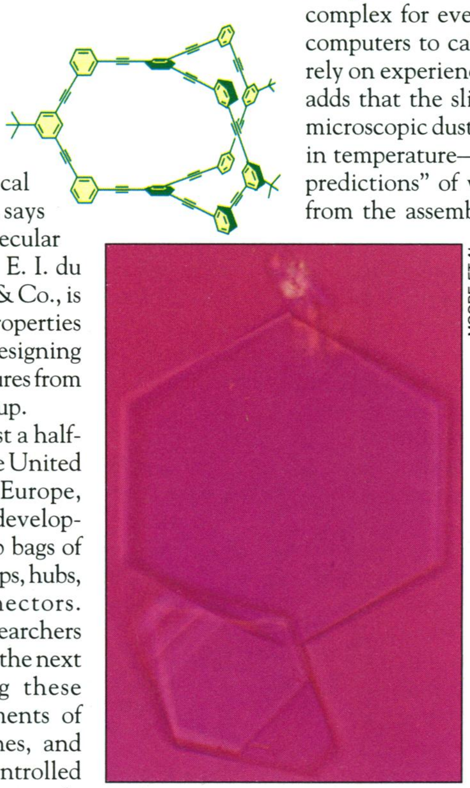
CHEMISTRY

Designer Solids: Haute Couture in Chemistry

It doesn't take long for children playing with a set of Lego blocks or Tinkertoys to go beyond assembling a few pieces into random shapes. Soon they adopt the role of structural engineer and start to put together magnificent grids, networks, and lattices. It's taken chemists a long time to make that transition, however. Until recently, they had mostly been relegated to making just the building blocks of the material world—the molecules. When these building blocks do coalesce into, say, a crystal or a glass, researchers have generally had little or no control over the process on the molecular level; they've had to let the pieces fall where they may.

Now chemists are following in their kids' footsteps, as groups around the world build molecular construction kits specifically designed to snap together into larger structures that have a predetermined architecture. "Our key goal is the deliberate synthesis of periodic matter [like crystals] on the nanometer scale," says New York University chemist Nadrian Seeman, who aims to build three-dimensional lattices from DNA. Some of Seeman's fellow tinkerers are pursuing what they call "designer solids"—molecular networks of indefinitely large sizes with tunable properties, such as the spacing of the lattice and the chemistry of the lattice members. Others seek smaller assemblages, composed of thousands of molecular pieces but no bigger, perhaps, than proteins or viruses, that could be studied and harnessed in solution.

Either way, these structures could open up whole new fields of chemistry and materials science, says J. Fraser Stoddart, a leading molecular constructionist at the University of Birmingham, in England. Chemists and solid-state scientists have long known that the chemical makeup of a substance doesn't explain all its properties. The way its molecules array themselves into a larger crystal structure also shapes key characteristics—whether the substance can serve as a window, a mirror, or a nonlinear optical crystal, for example; whether it is semiconducting or insulating; and whether its interstices will be hospitable to particular chemical reactions. One goal of the chemical constructionists, says Paul Fagan, a molecular crystal designer at E. I. du Pont de Nemours & Co., is to build specific properties into materials by designing their crystal structures from the molecules on up.


Crystal power. A tailor-made building block *(top)* self-assembles to form a microscopic crystal.

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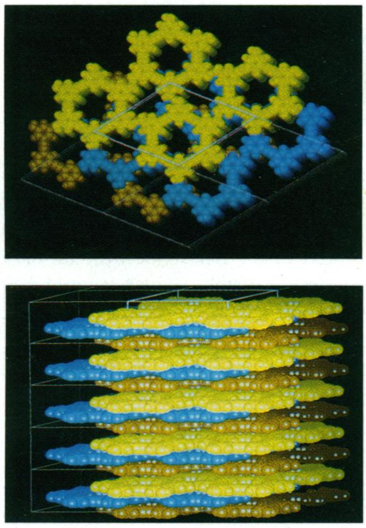
Stacking the deck. In a computer simulation, hexagonal phenylacetylene-based building blocks pack into a designer solid.

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Already, at least a half-dozen groups in the United States, Canada, Europe, and Australia are developing their own grab bags of molecular rods, loops, hubs, slabs, and connectors. Some of these researchers have begun taking the next step—assembling these pieces into rudiments of lattices, membranes, and other precisely controlled structures. The nanoscale engineers have one key advantage over children playing with Tinkertoys or Legos: They don't have to build their constructions one piece at a time. Instead, if the pieces are designed cunningly enough, they assemble themselves, says molecular engineer Jeffrey Moore of the University of Michigan.

The trick is to synthesize the building blocks, or "modular units," so that their physical and chemical properties dictate a "programmed assembly" protocol. Each unit's characteristics shape the weak intermolecular attractions—electrostatic, van der Waals, and hydrogen-bonding forces—between it and its neighbors so that they array themselves in a larger structure with the desired spacing and geometry. Ultimately, the strategy might enable chemists to combine well-chosen ingredients, wait a while, and then harvest, say, flat photovoltaic crystals that convert light into electricity, or soluble catalyst-adorned constructions in whose cavernous interiors sugar molecules get converted into fuels.

That's an untried vision, Moore admits, and there are obstacles galore. The pushes and pulls of the intermolecular forces are too complex for even the most powerful supercomputers to calculate, leaving chemists to rely on experience and intuition. And Fagan adds that the slightest perturbation—say, a microscopic dust particle or a slight variation in temperature—"can totally throw off your predictions" of what structures will emerge from the assembly process. Even when the assembly proceeds according to plan, the resulting molecular filigree may be too fragile to hold up, let alone be put to use. But Moore, Fagan, and their ilk are convinced that they are gradually learning the craft of molecular construction, and they're working toward the day when they can move from small-scale assembly to large-scale construction.

Nanoscaffolding

Assembling countless molecular components into a lattice can yield something that may sound mundane: a molecular scaffolding. But like the scaffolding around buildings, a nanoscaffolding would be valued not so much for what it is as for what it holds up. That's Moore's vision. At the spring meeting of the American Chemical Society in Denver, Moore talked up his "three-dimensional nanoscaffolding"—a molecular lattice that could serve as a framework for catalysts and photosynthetic molecules, which often function best when they are set in precisely shaped niches or arrayed in specific geometries.

Like full-sized scaffolding, Moore's lattice has simple components—just one basic unit, in fact. But by using a combination of strong covalent linkages and weaker hydrogen-bonding interactions, Moore can forge sequences of these units into a dizzying array of specifically shaped building blocks. Those, in turn, let him tailor-make molecular scaffolds that could be adorned with a series of different catalysts, creating a chemical factory in miniature, or light-sensitive appendages that could store and process laser-written information.

Moore and his colleagues are working toward that goal by linking chemical subunits called phenylacetylenes into sequences, or oligomers, of various lengths, which then bend and twist like wire sculptures, until their ends meet to form closed polyhedral molecules. That gives Moore and his colleagues the basic components of their scaffolds. "We have half a dozen shapes now," he says.

These building blocks in turn assemble into geometries at least partly controlled by hydrogen-bonding interactions designed into them, and the assembly process can continue indefinitely. "We have crystals you can hold in your hand," Moore says. Because the molecular polyhedra harbor several phenylene groups, which have chemical bonds to spare, he adds, "they have plenty of [chemical] handles" on which to hang other molecular groups.

Before the researchers start adorning their scaffolds with functional groups, though, they want to improve their construction skills. They are trying to make more polyhedra and modify them to gain additional control over the patterns of hydrogen bonding—and the resulting networks. But eventually, like any architect, they hope to put their scaffolds to work.

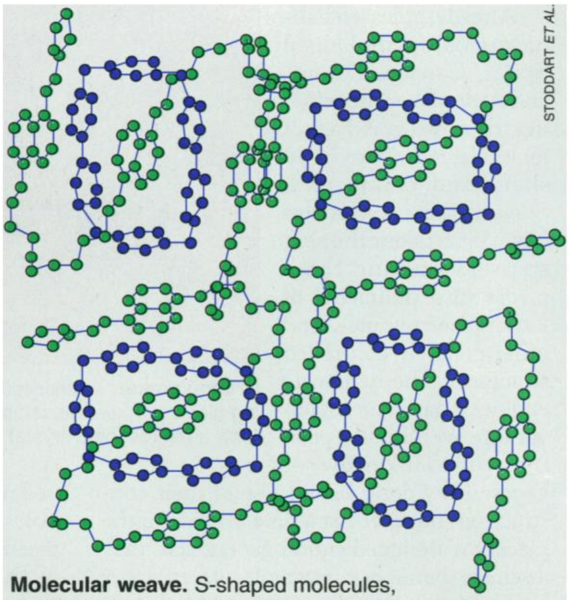
Tinkertoys

Josef Michl loves to tell a story about the day around Christmas 1986 when his former graduate student, Piotr Kaszynski, came into his office at the University of Texas to tell him about his latest research. Michl, who is now at the University of Colorado in Boulder, credits his son's fanatic devotion to Tinkertoys for the thought that crossed his mind when Kaszynski reported that the propeller-shaped hydrocarbon molecules he was studying, known as propellanes, had linked to form knobby rod-like structures, much like propellers attached to a shaft. "Here is an approach to molecular Tinkertoys," Michl recalls thinking.

Thus began a project that now is well into its seventh year. So far, Michl and colleagues have designed a toolbox of molecular rods and linkers, which sport positively and negatively charged regions that cause the pieces to gravitate toward each other in specific geometries. Under the right conditions, Michl and his colleagues are finding, these then react to form sturdier, covalently bonded "supramolecular" structures—a first step, Michl believes, toward networks that could serve as molecular fishnets, catalytic particles, and other designer solids.

Soon after Kaszynski's first glimpse of molecular rods, Michl and his colleagues were fashioning the rods in a range of lengths. Next came linkers. In one strategy for making them, Michl and postdoctoral associate Mohamed A. Ibrahim combine pairs of rhodium atoms with other ingredients, forming spool-shaped complexes each carrying four positive charges. Each charge later becomes an attachment point for a negatively charged carboxylate group on one end of a rod. The result: small constructions that resemble "planar crosses," consisting of four rods covalently linked to a central spool. Next Michl hopes to assemble such components into two-dimensional grids of arbitrary size, with mesh openings of prechosen dimensions—something that could be valuable, he suggests, for industrial chemical separation processes.

So far Michl's efforts to build these networks have been hampered by the tendency of the rods and spools to bend and twist out of a single plane as they assemble. In search of more controllable parts, Michl and his colleagues have developed a variety of new rods based, for example, on carboranes—cage-like molecules made of carbon and boron, which link "like a bunch of spheres on an abacus," Michl says.



Molecular weave. S-shaped molecules, each sporting a movable loop, pack into a regular array.

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Ultimately, this expanded tool kit may enable Michl to go from two dimensions to three. Having mastered what he calls "the first floor," he says, "we could build up from there," using each layer as a template for the next one. The result would be an orderly three-dimensional structure in which the chemists could, by judicious choices of self-assembling components, control the composition of each story. Therein lies the route to more exotic constructions—including, Michl hesitantly suggests, a compact particle accelerator. A crystal designed to host a layer cake of alternating electric fields, he proposes, could deliver a long series of tiny pushes to an electron traversing it, creating, in effect, an accelerator in a crystal. Coming from a box of Tinkertoys, that would be heady stuff.

Molecular Meccano

While Michl, living on this side of the Atlantic, casts his dreams in terms of Tinkertoys, a U.S. plaything, Stoddart, of the University of Birmingham, draws his inspiration from Meccano, the European version of the Erector set. The difference is more than a matter of cultural reference point, however. Both groups are aiming at molecular construction, but Stoddart and his colleagues are following a distinctly different blueprint.

Like others developing molecular construction sets, Stoddart starts by synthesizing a variety of molecular building blocks using standard covalent chemistry. Then, noncovalent interactions such as hydrogen bonds and electrostatic repulsions and attractions coerce these blocks to "self-assemble" into larger molecular arrangements, which Stoddart then welds together with "finishing" reactions that forge a new set of strong covalent bonds. But unlike the elegant but rigid molecular gridworks Michl and others are building, the constructions Stoddart envisions—in keeping with the Meccano image—have movable parts, such as interlocking rings and movable molecular beads.

"We are just now constructing the hardware" for the molecular Meccano set, Stoddart says. So far, he and his colleagues have built it out of chemical components such as crown ethers, which serve as rings, and benzene and a benzene-like molecule, pyridinium, for rods and blocks. From these simple parts, Stoddart and various collaborators have assembled more complex components such as molecular shuttles, in which a loop of crown ethers threaded on a molecular rod is free to hop between two different sites (*Science*, 12 February, p. 890). More recently, the chemists have replaced the rod with an S-shaped thread. And in the next step, they hope to weave those sinuous shuttles into larger gridworks riddled with movable parts. So far, Stoddart and colleagues have succeeded in loosely packing these units into crystals, but they have yet to actually pull off the intricate interweaving they have in mind.

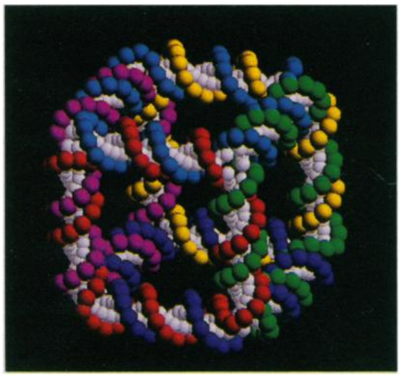
Stoddart's ultimate goal? Nothing less than molecular computers in which an array of nanoscale switches—each one, perhaps, a molecular shuttle—might behave like the integrated circuitry of semiconductor chips.

Networking with DNA

Molecular architecture can take on added drama when you use the world's most celebrated molecule. Seeman of New York University and his colleagues have been doing exactly that—developing a molecular scaffold using DNA as the girders. And they're finding that DNA is an appealing building material.

For one thing, it can be made in many lengths and in several branching shapes. Moreover, its sequences of building blocks—called nucleotides—can be exploited as a tool for self-assembly, because "complementary" sequences on different DNA strands recognize and bind to each other. By engineering matching sequences into the pieces of the construction kit, Seeman and his colleagues can specify a particular assembly pattern. It's like having an unlimited number of specific glues that connect only those parts you want to link.

Seeman drew his inspiration from naturally branched DNA structures called Holliday junctions, which form during genetic recombination, when two chromosomes swap parts. "I realized that these provided us with [corners]," he says. "When linked with straight segments [of DNA, the corners] would open a route to making two- and perhaps three-dimensional molecular networks made entirely of DNA."


SEEMAN

DNA does double duty. The double helix as molecular scaffolding.

He and colleagues were quick to act on the realization by making a DNA square in the mid-1980s. They followed that achievement 2 years ago with their most intricate DNA construction to date: a bona fide cube fashioned from intricately twined segments of DNA. To make the cube, the scientists relied on DNA's sequence specificity—the specific glue trick—to interlace six DNA components, each forming one face of the cube. Next, Seeman hopes to join multiple cubes into a lattice, a task that will require the development of more complex building blocks resembling jacks, with six, eight, or even 12 arms.

One goal of the work is to develop materials that will trick noncrystallizable molecules such as membrane proteins into an orderly, crystalline array. That way, crystallographers (and crystallography is Seeman's original specialty) might be able to determine their structures. The key here, Seeman notes, is to build three-dimensional beehives of DNA, each cell able to host one copy of a noncrystallizable molecule. The result would be a regular array of the molecules—an arrangement that would open the way to x-ray analysis. Or, Seeman suggests, the DNA structures could serve as frameworks for the assembly of other molecules into intricate architectures, after which the DNA scaffolding could be dismantled. In this case, the DNA would serve as a template for some other structure—a distant echo of its original role in biology.

A growth industry

Tinkertoys, Meccano, and the various molecular scaffolds aren't all that can be found in the molecular toy store. Many other researchers have created their own construction kits, each with its own principles of assembly and potential technological niches. James Wuest of the University of Montreal and his colleagues, for example, have been developing what they call "molecular tectonics" (from a Greek word meaning builder). In work that parallels Moore's, they concoct building blocks of various shapes from simple chemical ingredients and then rely on hydrogen bonding to gather the building blocks into airy crystals. Fagan and Michael Ward, who recently moved from du Pont to the University of Wisconsin, are rekindling a molecular construction project that they had started in the late 1980s. Their goal is to design artificial crystals in which both electrostatic interactions and hydrogen bonds conspire to assemble the crystals' components into pillars that could, say, conduct electricity like minuscule molecular wires, or align to form novel magnetic materials. Even the buckyball crowd has jumped into the nanoscaffolding fray with speculations about latticeworks of buckytubes—tubular relatives of the all-carbon soccerball molecules that now are all the rage.

For the moment, the competition among all these approaches is muted. Things may get dead serious in the future, say researchers, but for now, their field has a playful quality because it's far too early to know which approaches to molecular construction will test out. Indeed, the spirit of play is so strong that some of these gridwork chemists admit to playing with construction toys. Says Michl, "It helps me think about what I'm doing in my nanoscopic world."

–Ivan Amato

Additional Reading

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MATERIALS SCIENCE

Finally, a Hotter Superconductor

To the community of researchers fashioning new high-temperature superconductors (HTSs), 127 degrees Kelvin was starting to look like a permanent barrier. Since 1988, when researchers reported a thallium-based material with the composition $Tl_2Ca_2Ba_2Cu_3O_{10}$ that loses its electrical resistance if chilled to 127 K or lower, no new superconductor—and there have been dozens of them—has worked at a higher temperature. Now that barrier has gone the way of the 4-minute mile.

This work "shows that things are still out there to be found."

—David Larbalestier

A quartet of researchers led by Hans Ott at the Eidgenossische Technische Hochschule (ETH) in Zurich reports in the 6 May *Nature* that they have broken the 127 K barrier with a new material, made of two distinct compounds, that starts to become a superconductor at about 133 K. The material, which is difficult to make and has toxic ingredients, isn't likely to find practical uses, says Andreas Schilling, one of the ETH scientists. But he thinks the finding "will have a high psychological value" to the HTS research community as it searches for commercially viable superconductors. "This work is absolutely fantastic for the field," agrees David Larbalestier of the University of Wisconsin's Applied Superconductivity Center. "It shows that things are still out there to be found."

The key to this discovery was a new ingredient, mercury. Just 7 weeks earlier, in the 18 March *Nature*, another group led by S. N. Putilin of Moscow State University had dropped a hint that mercury was worth some serious attention. They reported that a new compound composed of mercury, barium, copper, and oxygen becomes a superconductor at 94 K. Although that's lower than the 127 K of the thallium-based compound, the new material's molecular structure hinted that it might be just the first and simplest member of an ever improving new family of superconductors.

One clue lay in its multilayered crystal structure, each unit of which includes only one copper oxide layer. Experience with analogous copper oxide compounds based on thallium or bismuth atoms had shown that