Fullerene Formation and Annealing

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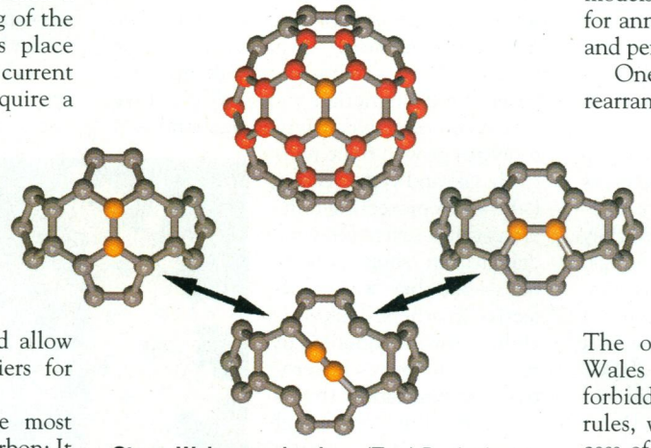
Why does the highly symmetric carbon cluster C_{60} form in such profusion under the right conditions? This question was first asked in 1985, when Kroto *et al.* (*1*) suggested that the predominance of the C_{60} carbon clusters observed in the molecular beam experiments could be explained by the truncated icosahedral (or soccer ball) form (see figure). The name given to this cluster, buckminsterfullerene, led to the use of the term fullerenes for the family of hollow-cage carbon clusters made up of even numbers of triply coordinated carbons arranged with 12 pentagonal rings and an almost arbitrary number of hexagonal rings. More than a decade later, we still lack a completely satisfying understanding of the fundamental chemistry that takes place during fullerene formation. Most current models for fullerene formation require a facile mechanism for ring rearrangement in the fullerene structure, but the simplest proposed mechanisms are believed to have unrealistically high activation barriers. In this issue, Eggen *et al.* (*2*) report calculations suggesting that atomic carbon in the reaction mixture could act as a catalyst and allow substantially lower activation barriers for fullerene annealing.

Buckminsterfullerene is not the most thermodynamically stable form of carbon: It has a smaller binding energy per carbon than graphite or any of the larger fullerenes (*3*). Under proper conditions, however, the Krätschmer-Huffman (*4*) process, which vaporizes graphite or other carbon sources in the presence of an inert buffer gas, can produce yields of buckminsterfullerene in excess of 20%. An efficient kinetic mechanism must exist that directs carbon clusters down the road to buckminsterfullerene before they have an opportunity to grow to a larger size. At the same time, although buckminsterfullerene is only one of 1812 possible C_{60} fullerene isomers (*5*), the highly symmetric buckminsterfullerene structure shown in the figure is essentially the only C_{60} fullerene isomer experimentally observed in macroscopic samples (*6*). This uniqueness has been ascribed to the fact that the icosahedral form is the only one that does not have pentagons sharing a common edge. This tendency to avoid adjacent pentagons in the fullerene structure, known as the isolated pentagon rule (IPR), arises from the increased steric strains imposed by adjacent pentagons (*7*). Carbons in a hexagonal bonding structure remain planar; pentagons are required for curvature of the fullerene, with 12 required for closure. Deforming a graphitic sheet from planarity exacts a cost in terms of a strain energy; adjacent pentagons cost more than the sum of isolated pentagons. Buckminsterfullerene thus represents the smallest fullerene for which the IPR is satisfied; the second-most common fullerene, C_{70}, is the next largest fullerene for which the IPR is satisfied. Theoretical calculations estimate that the strain energy of the buckminsterfullerene structure is at least 2 eV lower than that of any other C_{60} fullerene isomer with adjacent pentagons (*8*).



Stone-Wales mechanism. (**Top**) Buckminsterfullerene, with the two most mobile carbon atoms of the Stone-Wales transformation depicted in yellow. Red atoms outline the active region of the fullerene ring structure changed by the Stone-Wales transformation, with the inclusion of two peripheral pentagons. (**Bottom**) Changes in bonding by the Stone-Wales transformation, with active regions of icosahedral buckminsterfullerene (left), C_{2v}-symmetry C_{60} isomer (right), and (bottom) an intermediate transition state (bottom). Note that two pairs of adjacent pentagons are formed by the Stone-Wales transformation in a C_{2v}-symmetry C_{60} isomer.

Any reasonable reaction mechanism must therefore include a kinetics-driven process that goes directly to fullerene rather than other carbon allotropes (*9*). At the same time, it must produce buckminsterfullerene in profusion at the expense of isomers of C_{60} not satisfying the IPR as well as other fullerenes, a neat trick in the chaotic mix of vaporized carbon and inert gas. Most current models for buckminsterfullerene formation thus assume growth from smaller carbon clusters to fullerene size with constant annealing so that high-energy adjacent pentagons are minimized. The pentagon road model proposed by Smalley (*7*) assumes the growth of open graphitic sheets of 30 to 60 carbons containing both pentagons and hexagons, where annealing would help minimize adjacent pentagons. Closure of the sheets to form buckminsterfullerene or larger fullerenes would terminate growth. The fullerene road model and alternatives propose the initial formation of smaller fullerenes with 30 to 58 carbons that would continue to incorporate smaller carbon fragments (*10*). Buckminsterfullerene in both of these models represents a relatively inert fullerene that is resistant to further growth or reaction. All of these possible models imply some facile, low-energy mode for annealing the arrangement of hexagons and pentagons.

One of the most basic mechanisms for rearranging the hexagons and pentagons in a fullerene is the Stone-Wales transformation (*11*). As can be seen in the figure, this mechanism is a concerted rearrangement of the bonds involving four carbons, leading to the transposition of hexagons and pentagons around a bond between two hexagons. The only drawback is that the Stone-Wales mechanism as shown is thermally forbidden under the Woodward-Hoffmann rules, with large activation barriers in excess of 5 eV predicted by electronic structure calculations (*12, 13*). Murry *et al.* (*13*) have proposed an alternative path for the Stone-Wales transformation with an activation barrier predicted to be about 2 eV lower than the concerted rearrangement, but requiring two sequential bond rearrangements. Eggen *et al.* (*2*) examine how a carbon atom attached to buckminsterfullerene effects the energetics of the Stone-Wales transformation. They found that the attached carbon acts as a catalyst to reduce the activation barrier by about 2 eV. This might also apply to possible catalytic activity of C_2 and C_3 clusters attached to C_{60}; these larger clusters should be more common than atomic carbon in the high-temperature reaction environment.

As Curl has pointed out (*9*), any model that accounts for the observed formation of buckminsterfullerene and C_{70} must be a kinetic one with at least one major pathway leading directly to buckminsterfullerene. All of the proposed models for fullerene formation require a facile mecha-

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nism for fullerene ring rearrangement at high temperatures, and the lack of a plausible mechanism represents a major roadblock in our understanding of the formation of these materials. On the other hand, just a decade ago no one expected the relative ease with which this family of carbon-based nanostructures would form. The next decade should see the evolution and maturation of this exciting new branch of organic chemistry and materials science along with the answers to some of these fundamental questions.

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New Lessons for Rotavirus Vaccines

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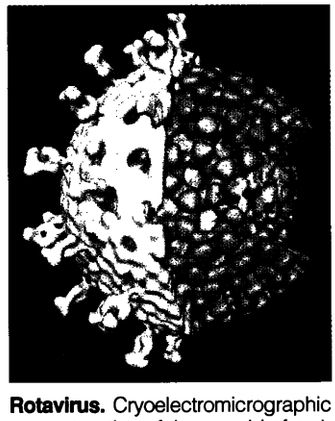
Two decades ago, Bishop discovered human rotaviruses, the most common cause of severe dehydrating diarrhea in children worldwide (*1*). Although most rotavirus infections are mild, field studies from more than 50 countries document tremendous morbidity and mortality. Rotaviruses are detected in 20 to 70% of fecal specimens from children hospitalized with acute diarrhea, and in developing countries they cause about 870,000 deaths each year (*2*). Even in the United States, rotavirus is associated with 3% of all hospitalizations of children younger than 5 years old, which translates to a staggering 55,000 to 70,000 hospitalizations per year, with medical and indirect costs in excess of $1 billion (*3*). Efforts to prevent disease by improving water or sanitation seem unlikely to succeed, because all children in developed and developing countries become infected with rotavirus in the first 3 to 5 years of life. A high priority has therefore been placed on the generation of a safe and effective vaccine.

Development of a vaccine for rotavirus has progressed rapidly, aided by several key breakthroughs. Most important was the recognition that the primary infection induces natural immunity to rotavirus and protects a child from subsequent episodes of severe disease (*4*). Once the virus could be propagated by cell culture, vaccine seeds could be prepared (*5*). Finally, cross protection is induced between human and animal strains, so that animal strains hypothesized to be naturally attenuated for humans could be tested as first-generation candidates for heterotypic "Jennerian vaccines" (*6*). Live oral vaccines derived from animal strains of rotavirus proved to be relatively safe and very effective (>80%) in protecting children against severe rotavirus diarrhea in some populations—but they were ineffective in others. This variability was attributed in part to differences in serotypes of circulating strains and the failure of animal strains to elicit heterotypic protection in some studies.



Rotavirus. Cryoelectromicrographic reconstruction of the capsid of a virus particle. Outer capsid (yellow); inner capsid (blue). [Photo courtesy of B. V. V. Prasad]

To increase the efficacy of the Jennerian vaccine, researchers developed second-generation polyvalent reassortant vaccines. These contained neutralization antigens that could provide homotypic (serotype-specific) immunity against all four predominant human rotavirus serotypes. Of the 11 segments of double-stranded RNA in the rotavirus core, two encode the proteins of the outer capsid—the VP4 hemagglutinin spike and the VP7 glycoprotein—that are key targets for virus neutralization. Coinfection of cells under selective pressure leads to the reassortment of these gene segments, and vaccine candidates can be selected from these reassorted rotaviruses. The candidate strains contained 10 segments from the original animal rotavirus strain and a single gene encoding one of the outer capsid proteins from each of the four major human strains. Mixtures of these reassortants have been combined to form tetravalent vaccines that can be given orally to children, and they protect in the field against severe rotavirus diarrhea. These vaccines have an efficacy of >80% against severe rotavirus diarrhea (similar to the protection conferred by natural infection) and could be licensed for use within a year or two (*7*). Although these modified Jennerian vaccines were engineered to produce serotype-specific immunity, community studies and vaccine trials have not yet convincingly demonstrated that homotypic (serotype-specific) immunity is more protective than heterotypic immunity. If it is not, some basic assumptions underlying the development of this vaccine are called into question.

The progress toward an effective rotavirus vaccine is way ahead of our understanding of how rotaviruses cause disease and how immunity is generated. Studies in animals indicate that damage occurs in epithelial tissue in the proximal small intestine (*8*). The villi become shortened and slough, mitochondria swell, the cisternae of the endoplasmic reticulum become distended, and mononuclear cells infiltrate the lamina propria. This cellular damage, associated with a loss of the ability to control fluids and electrolytes, has been postulated to cause severe diarrhea. However, limited studies in humans are less clear-cut. Among 40 ill German infants biopsied by intestinal suction, only 5% had damage by histologic analysis, whereas in another small study intestinal damage was observed (*9*). Therefore, diarrhea may occur in the absence of substantial cellular damage, suggesting that the conclusions of the animal studies do not apply to humans (or that subtle epithelial damage in humans was overlooked).

Of the 11 rotavirus proteins, no single gene product has yet been clearly associated with virulence. Such an association could be

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