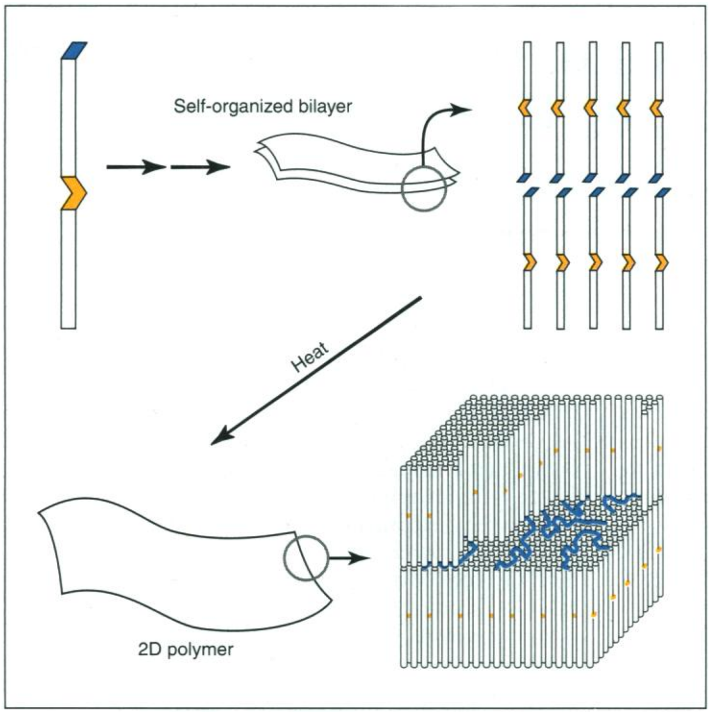
Gigamolecules in Flatland

Edwin L. Thomas

Scientists have long wanted to be able to construct polymer molecules of every possible architecture. They have succeeded in making many types: linear, branch, star, ladder, comb, ring, and network. But these are all basically one-dimensional objects. Now, as reported on page 59 of this issue, Stupp and his group at Illinois have produced a new two-dimensional sheet-like polymer object (*1*). Sheets afford many possibilities: ease of orientation, surface functionalization, tribological applications, and, as Stupp and coworkers have now demonstrated, second harmonic generation.

Polymers are usually defined to be long chains of thousands of small monomers linked together. Examples of polymer molecules are, of course, quite familiar. Among the largest are amylopectin (a multiply branched molecule and the principal component of starches) at 90 million daltons, or DNA (basically a ladder polymer of base pairs and backbone chains) at 6 million daltons. Many synthetic polymer molecules of commercial importance are simple linear chains, such as polyethylene, nylon, and polystyrene. These weigh between 5 × 10^4 daltons and 5 × 10^6 daltons; hence the name megamolecules (*2*). Apart from their high molar mass, polymer molecules are distinguished by the relative stiffness of their covalently bonded backbones.

There are two general backbone types: rigid rods and flexible coils. Rigid rod polymers are capable of forming lyotropic liquid crystalline phases and can be spun into high strength fibers. Flexible coil polymers are more common and comprise, for example, uncrosslinked rubbers and thermoplastics. Indeed, polymer chemists have developed an enormous variety of chain molecules, and these have provided a great variety of materials with quite diverse physical properties. The linear chain and its close cousins (branched chains, rings, networks, and so on) are all basically one dimensional in that they can be described by reference to the unit line (which represents location along a simple linear chain) with the appropriate added description of the branching nodes and their interconnections. Until now, experimental polymer science has virtually ignored two-dimensional polymers. Stupp's polymers must be described by a two-dimensional locus of points with reference to the unit disc. They are simply connected sheets with boundaries, and thus have two distinct surfaces as well as edges.



Weaving a two-dimensional polymer. The precursor molecule has a polymerizable group at one end (blue) and a chiral reaction center in the middle (yellow). In solution, the oligomers self-organize into a bilayer. At slightly higher temperature, the two types of reactive groups stitch the bilayer into a two-dimensional polymer (shown in cutaway).

Ordered structure in materials is highly dependent on the character of the basic building blocks. As one departs from simple spherical shape and spherically symmetric interaction potentials, the candidate structures for an assembly of the building blocks become an extremely rich realm. One problem with complex, one-dimensional chains is that with such a large number of degrees of freedom in the basic building block, such systems form structures that contain many defects or that are amorphous. These defects create an isotropically averaged macrostructure that exhibits scalar physical properties.

The synthesis of two-dimensional objects has been previously accomplished, for example, with Langmuir-Blodgett film processing and bilayer self assembly of amphiphiles (such as vesicles). The major problem inherent in these previous approaches is the poor stability of the structure: the relatively weak interactions between the component low molecular weight molecules permit large thermal fluctuations which eventually destroy the structure. Chemists sought to overcome this limitation via polymerization of the self-assembled layers. However, for the materials thus far investigated, the polymerization reactions are correlated along special directions within the layers so that the structure is not sufficiently stabilized.

Stupp and his students have succeeded in making a two-dimensional polymerized bilayer that is both robust and flexible. The thin sheet is produced by employing oligomers containing two different reactive sites: one site at one end of the oligomer and the other in the middle. The oligomers spontaneously self-organize into bilayers in solution. This locates one set of the reactive sites at the mid-plane thickness. Two independent, low-temperature reactions are then initiated and "stitch" the bilayer together via covalent coupling at the three bilayer levels. Even though the conversion of reaction sites is not 100%, there is sufficient redundancy created by the three layers of stitching that the bilayer is robust. The approximately 10-nm-thick sheets are very uniform in thickness, while their areal size is a function of the polymerization efficiency and the size of the preassembled oligomeric state. Many of the objects have areas of several square micrometers, corresponding to molecular weights of over 10^9 daltons. The electron diffraction evidence convincingly demonstrates the crystalline perfection of assembly within a single sheet and between several stacked sheets. Hot stage optical microscopy demonstrates the melting into a smectic phase and then, at higher temperatures, transformation into an isotropic phase.

These objects are likely to contain holes because the stitching reactions are not 100% efficient. The reactive nitrile group stitching at the 1/4 and 3/4 layer height reaches only about 30 to 50% conversion; the mid-plane reactive acrylate group stitching is about 90%. This looseness in the structure is likely important for sample solubility and flexibility necessary to exhibit an isotropic phase at high temperature. Upon solvent evaporation or cooling, sheets are reformed. Statistical

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mechanical models suggest that, unlike linear chains, a two-dimensional polymer network can undergo a low-temperature transition to a flat phase (3). The transformation from smectic layers into the isotropic state may be an experimental manifestation of the so-called "crumpling transition" of a two-dimensional polymer network. Further experimental work will be needed to examine how the bilayer structure actually changes so as to produce an isotropic liquid.

Scale up in materials processing is always a concern because one often finds that the required human assistance to realize ordered materials requires prohibitive cost. High molecular weight in polymers normally limits solubility and processibility. But these sheet-like gigamolecules are ideal smectogens, forming a relatively low viscosity liquid which can be readily processed into oriented films. Self-assembly of the two-dimensional sheets in bulk followed by thermal- or radiation-induced polymerization-stabilization of the objects appears to avoid such problems. Further processing of the individual sheets into ordered films for a variety of applications is promising, but will require more detailed understanding of the nature of this new structure. Properties that will need characterization include surface and edge energies, mean thickness, roughness, number and type of holes and other defects, curvature, modulus, the nature of the stitching networks, and oligomer conformation. The influence of the stitching temperature and inter-sheet interactions on molecular mobility will be of prime interest concerning the crystal to smectic to isotropic phase transitions and the physical properties that assemblies of such sheets will exhibit.

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Organic Synthesis of Prostaglandins: Advancing Biology

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Prostaglandins (PGs), a family of C_{20}-unsaturated polyoxygenated fatty acids, regulate diverse functions of the circulatory and respiratory systems and digestive organs and are also crucial for such vital defense processes as inflammation, tissue repair, and immune responses. In addition, PGs are showing new potential as therapeutic agents with the recent demonstrations of their antineoplastic and sleep-inducing activities. Thus, this intriguing family of substances has attracted broad attention in fields ranging from chemistry and biochemistry to pharmacology and medicine (1). Organic synthesis is pivotal in developing such an interdisciplinary scientific endeavor and, in this context, the Corey PG synthesis is a triumph of synthetic organic chemistry (2). This pioneering accomplishment not only allowed the commercial production of PGs of great therapeutic value but also contributed enormously to the progress of fundamental life science.

Now this field is shifting to a new phase for which new PGs must be synthesized. Several ongoing projects that reflect these new directions are described below.

Synthesis of Isocarbacyclin

The three-component synthesis developed in our laboratories consists of a one-step construction of the PG framework by combining the C_8 and C_7 side chains with the cyclopentenone unit (Fig. 1). Various new selective reagents containing main-group and transition metal elements as well as asymmetric reactions (3) were essential in realizing the long-sought synthesis (4, 5). Use of a C_8 organometallic reagent and a C_7 acetylenic halide as the lower and upper side-chain units, respectively, leads to the 5,6-didehydro-PGE_2 derivative 1, which serves as the common intermediate for the synthesis of most natural PGs. This direct method also allows preparation of a wide array of artificial analogs. Particularly significant is the synthesis of isocarbacyclin (2), a promising therapeutic agent for various thrombotic diseases (6). Combination of a controlled radical reaction, photochemical process, and organometallic and organosilicon chemistry allowed the selective synthesis of 2 from the acetylenic intermediate 1 or related compounds (7). Although natural prostacyclin (PGI_2) (3) possesses remarkable physiological activities including antihypertensive and platelet-aggregation inhibiting effects, the high sensitivity of the 2-alkylidenetetrahydrofuran structure to hydrolysis has prevented its use as a therapeutic agent. The carbocyclic analog 2 overcomes this stability problem yet maintains sufficient physiological activities. A clinical trial is now in progress for the use of this compound in the treatment of cerebral ischemic disease and of peripheral vascular diseases.

A Probe for PG Receptors

PGI_2 activates adenylate cyclase in platelets, vascular smooth muscle, NCB-20 cells, and mastocytoma P-815 cells, but its low stability, the low concentration of a receptor in the cell membranes, and the lack of a suitable agonist or antagonist to facilitate purification of a receptor protein have prevented a

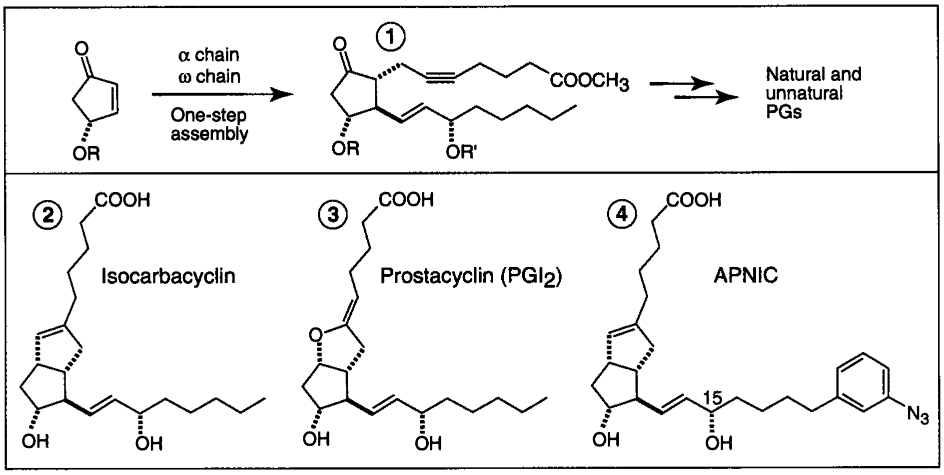

Fig. 1. Three-component synthesis for prostacyclins.

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