ring compound to the reaction vessel and let the chain of broken rings grow to a certain length, then add a second compound and let the chain incorporate a string of the new monomers, and so on.

Finally, there is perhaps the most intriguing potential application of the ROMP catalysts, says Parshall: the synthesis of polyacetylene and other conductive polymers. As it happens, ROMP is particularly well suited to making these compounds because it produces a chain in which the opened ring fragments are joined by double bonds. And a polymer rich in double bonds seems to be precisely what is needed for conductivity: when the bonds are spaced closely enough, an electron in one can easily jump to the next and thus carry a flow of current down the chain.

In Ginsburg and Gorman's work with polyacetylene, for example, the foul-smelling yellow liquid they start with is cyclooctatetraene, or COT: essentially just four acetylene molecules, each with two carbons, linked into an eight-sided ring. When the catalyst is added—in this case, one based on tungsten—the broken rings link up to directly give the alternating string of double and single bonds characteristics of polyacetylene. "When you make it this way," says Ginsburg, "it doesn't involve polymerizing acetylene gas," which is dangerously explosive and which requires a catalyst that is extremely sensitive to air and water. COT has a high boiling point and is not nearly as difficult or as dangerous to handle.

"Also," Ginsburg says, "you can extend the chemistry [of the polyacetylene] by hanging substituent groups off the side of the COT." If these side groups are chosen carefully, they will force the resulting chains to twist a bit. "That means they're floppy and don't stack together quite as well," says Ginsburg, "and you do lose a bit of conductivity—but now the stuff is soluble."

■ M. MITCHELL WALDROP

"Hairy Enzymes" Stay in the Blood

For the first 3 years of her life, Laura Boren was in the hospital almost all the time. A genetic defect kept her body from making the enzyme adenosine deaminase (ADA), which in turn stymied the development of her immune system. Vulnerable to almost any type of infection, the little girl from Kentucky could look forward to little but a short life of almost constant illness.

That has changed now, thanks to a drug called PEG-ADA, a modified enzyme that remains active in the blood much longer than normal enzymes. In the past 3 years, Laura has steadily gained weight and has been free of infection for long periods. Almost 8, she can even attend school. Last month the U.S. Food and Drug Administration approved the drug for treating the one child in every million who suffers from severe combined immunodeficiency disease (SCID) caused by ADA deficiency. Moreover, the method that makes the drug effective against ADA-SCID may have a broad range of other applications, from treating some leukemias and lymphomas to making artificial blood.

Children with ADA-deficient SCID now have few treatment options. Bone marrow transplants cure the disease, but less than 20% of the victims have compatible donors. And even when such donors are found, the transplants fail more often than they succeed because of infection or graft-versus-host disease. The National Institutes of Health are now considering a proposal to do gene therapy on ADA-SCID kids (*Science*, 16 March, p. 1287), but the success of that untested technique is not assured. And efforts to inject ADA—which can be obtained from calf intestines—directly into the bloodstream have failed because the liver filters ADA molecules out of the blood within minutes, preventing the enzyme from restoring the immune system.

This is exactly where the strategy taken with the new drug, developed by Enzon Inc. of South Plainfield, New Jersey, comes in.

PEG-treated enzymes are nearly invisible to the immune system.

To disguise the enzyme from the liver, dozens of long polyethylene glycol (PEG) molecules are attached to each ADA, says Abraham Abuchowski, Enzon's president and a developer of the PEG technique. "It's a hairy enzyme when it's done," he says.

The modified enzyme, PEG-ADA, stays in the blood for 1 to 2 weeks. Surprisingly, the addition of PEG to the enzyme does not kill its activity. The activity is reduced by about 40%, Abuchowski says, but that is more than made up for by its increased lifespan in the bloodstream.

The PEG-ADA treatments strengthen a child's immune system considerably, but they are not a complete cure, notes immunologist Michael Blaese of the NIH, who is part of the team that wants to try gene therapy on ADA-SCID. Some immune responses, such as the production of antibodies, show little improvement, he says, but overall "it's a wonderful advance."

Researchers have tried enzyme masking in the past using other molecules, but PEG has been the most successful, Abuchowski says. One reason is that it has a simple linear structure that is constantly in motion. This makes it virtually invisible to various receptors in the body, which respond to specific three-dimensional structures. That's why it's not recognized and taken out of action by the liver, for example. And PEG by itself is inert, so injecting it into the body is safe.

One disadvantage of PEG-ADA is that it is very expensive—a year's treatment costs about $60,000. This is unlikely to go down much because the market is so small—ADA-deficient SCID is diagnosed in only about 40 children worldwide each year.

Enzyme masking with PEG has one other characteristic that makes little difference in treating ADA-deficient patients but could be a major advantage with other diseases. The "hairy enzymes" are nearly invisible to the immune system, again because PEG hides the sites that normally trigger immune responses, and this may open up a number of enzyme treatments. For instance, the enzyme L-asparaginase has been used since the early 1970s to treat acute lymphoblastic leukemia. But the treatment with the enzyme, which does not occur naturally in humans, runs a risk of triggering potentially fatal allergic reactions. PEG–L-asparaginase is now in clinical trials. Besides avoiding the immune response, PEG–L-asparaginase, with a half-life of 2 weeks, stays in the bloodstream much longer than unmodified L-asparaginase, which has a half-life of only about 18 hours. PEG–L-asparaginase has also induced remissions in patients with non-Hodgkin's lymphoma, Abuchowski says.

Perhaps the most promising use of PEG is in making artificial blood. The protein hemoglobin is the part of blood that carries oxygen. But hemoglobin molecules that are not encased in red blood cells are quickly removed from the blood by the body. Given PEG technology, the solution is obvious. "We have a PEG hemoglobin that works exceedingly well right now," Abuchowski says. It stays in the blood system for about 3 days and could be used as a temporary replacement for blood. PEG-hemoglobin stays good for up to a year at 4°C, and unlike whole blood, PEG-hemoglobin can be warmed up to body temperature in a few seconds in a microwave oven. These qualities should make it valuable for emergency uses, for the military, and for ambulances and emergency rooms. ■ ROBERT POOL