visit a signal processing center set up at NRL to study IUSS data. Eventually, some data might be made available on tape, according to Navy officials—although they rule out distributing raw IUSS data. (Reliable submarine surveillance remains the primary mission of the IUSS.)

Even before more scientists get their hands on this data windfall, they are getting an early taste of what it may yield. At the briefing, Commander John Liechty, the Navy's project manager for Whales '93, flashed a striking view graph showing that an artificial sound source near Puerto Rico that had an intensity and frequency mimicking a finback whale vocalization could be detected 1000 miles away. Such data support a 20-year-old hypothesis that whales communicate over large stretches of ocean. Later, Clark added that data on finback whales near Iceland support the idea, first suggested by Watkins, that only some members of a migratory whale species take part in a particular migration.

To learn more, Clark and his Navy colleagues are honing their acoustic skills. Since last November, Clark and Readiness Officer Lieutenant George Gagnon, who has been tracking submarines for more than 20 years, have learned to distinguish five whale species, and, Gagnon says, even follow individual whales around the Atlantic. Blue whale calls look like "commas" amidst the TV static of the spectrograms, says Gagnon, who claims that he can pick out individual whales based on the precise shape and timing of their rumbling calls. Relying on that kind of signature, Gagnon says he tracked a whale, affectionately named Old Blue, for 43 days as it circled Bermuda, covering a total of 1450 miles.

Could that be a whaling yarn? Watkins is not convinced that individual discrimination is possible, though he admits that being able to follow individuals for weeks, without having to tag them, would be "a big thing" for marine mammal specialists. He is more optimistic about IUSS's ability to track whale populations over large areas. And that's exactly what Clark and his Navy collaborators are trying to do with data collected mostly between November 1992 and last May. At press time, Clark was slated to present early results at a meeting of the Animal Behavior Society, held this week at the University of California, Davis.

Among his early findings: Evidence that whales, like dolphins, use their vocalizations as sonar to form acoustic images of their ocean environment for navigation and feeding. Presumably, whales have had 35 million years of evolution to optimize that skill. If people could learn enough about how the whales manage their acoustic feats, perhaps they could pull off technological impersonations that would do more than just please audiences.

–Ivan Amato

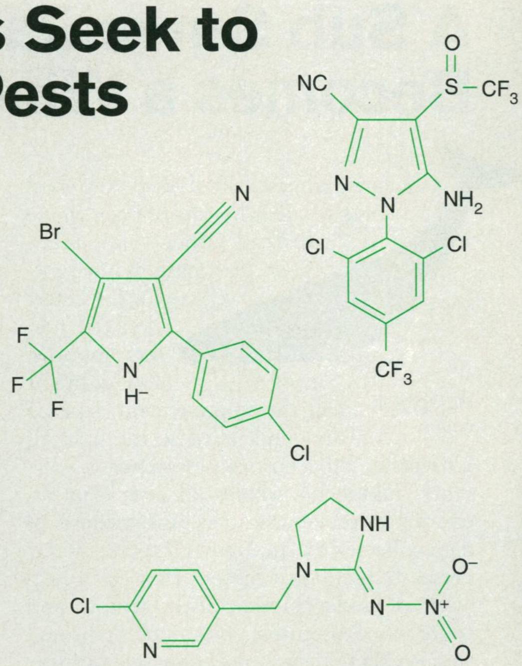
AGRICULTURE

New Chemicals Seek to Outwit Insect Pests

When it comes to insect pest control, most of the headlines these days go to research aimed at developing biological controls. Driven by the desire to protect the environment, there are many efforts afoot to use genetic engineering to create new plant strains with their own built-in insecticides, or to find bacteria, viruses, and other parasites that can keep a pestiferous insect in check with fewer of the problems that have been linked to chemical insecticides. But while these innovative forms of pest control have been grabbing all the attention, traditional chemical pesticides still dominate the world pesticide market: Their annual sales of more than $7 billion account for about 95% of the total. And those chemicals aren't standing still, since the chemical industry has been mounting its own efforts to develop new, more environmentally friendly insecticides.

Now, that work may be beginning to pay off. Three companies, two in Europe and one in the United States, that are in the vanguard of the research effort have either brought new insecticides to market or soon will. "There's some excitement at the moment because a number of companies have products different from the existing chemistries," says Allan Woodburn, an independent agrichemical consultant based in Edinburgh, Scotland. "If successfully commercialized, they would give a welcome boost to the chemical control of insects." They would also be the first chemical insecticides with novel modes of action to be introduced in nearly a decade, and those novel mechanisms are raising expectations that these chemical newcomers can alleviate a problem that has plagued the insecticide industry almost from its inception.

The problem is simply stated: Chemical insecticides frequently lose their effectiveness, because insects, among the most adaptable of creatures, develop resistance if repeatedly exposed. One classic example is DDT. When that much-maligned pesticide was introduced in the late 1940s, it virtually wiped out infestations of malaria-causing mosquitoes. But a few insects survived each exposure, eventually breeding resistant populations. And that's what makes it so attractive to have many different pesticides at hand, with varying mechanisms of action. Rotating pesticides with different modes of actions can limit the development of resistance, since the pest population can be fought with a second or third chemical before it builds up resistance to the first.



Benign control? From the top, Rhône-Poulenc's fipronil, American Cyanamid's pyrrole (active form), and Bayer's imidacloprid.

In addition, although chemical pesticides are a bugaboo of the environmental movement, the new insecticides may be safer for the environment than the older ones. "These new chemistries have greater specificity to a particular pest, [and therefore] less toxicity to nontarget species," says Phil Calderoni, an agrichemical specialist at SRI International, a research and consulting institute in Menlo Park, California.

The first of the new insecticides to reach market is imidacloprid, developed by the German chemical giant Bayer AG. The company has already introduced the chemical in France, Spain, Japan, and South Africa and expects that the Environmental Protection Agency (EPA) will give the go-ahead to begin selling it in the United States within a few weeks.

Bayer's development of imidacloprid illustrates the emerging trend in the pesticide industry away from trial and error and toward rational design of products based on a knowledge of insect biology. In this instance, the design process began with the knowledge that nicotine can kill insects. It's lethal because of its ability to bind to one type of receptor for the neurotransmitter acetylcholine, causing the insect's nerves to fire uncontrollably and leading to muscle paralysis. But nicotine itself cannot be used for insect control in the field because work done before 1950 showed that sunlight breaks it down very rapidly.

Two decades ago, researchers at Shell

tried to get around this problem, attempting to improve the stability of nicotine by making nitromethylene derivatives. But while the derivatives were better, they were still not stable enough for field use. Then in the mid-1980s, chemists S. Kayabu, K. Moriya, K. Shiokawa, and S. Tsuboi at Nihon Bayer Agrochem, a Japanese subsidiary of the German company, synthesized imidacloprid, a chlorinated derivative of nicotine that persists long enough in the field to control insects but is not so stable that it will accumulate and cause environmental problems. Walt Mullins, an entomologist at Miles Inc. of Kansas City, Missouri, also a Bayer subsidiary, says imidacloprid has been called a "Goldilocks compound. It's not too hard, not too soft, but just right" in its stability.

The Goldilocks quality made imidacloprid promising enough that Bayer put it through an intensive series of tests, starting 8 years ago, to assess its effectiveness and safety for humans and the environment. In field tests, it has done "very well," says Mullins. It controls most sucking insects, including aphids and whiteflies—even the silverleaf whitefly, the "pest of the decade" that devastated crops in California, Arizona, Florida, and South Texas and is resistant to most other insecticides. It's less effective against chewing insects, however. While it works against some, such as the Colorado potato beetle, ants, and termites, it does not control the voracious "worms" (caterpillar larvae of moths and butterflies) that feed on many crops.

The agent also looks promising in safety and toxicity tests, Mullins says. Assays for long-term effects, such as carcinogenicity or the ability to cause birth defects, came up negative, and its short-term toxicity is relatively low. For example, its LD50 (the dose required to kill half the animals on which it was tested) was in most tests greater than 2000 milligrams per kilogram of body weight. In contrast, many currently used chemical insecticides have LD50s of less than 50 milligrams per kilogram.

This apparently low toxicity to noninsect species may be the result of the pesticide's novel mode of action. Other insecticides, including the frequently used organophosphates and carbamates, also work by stimulating action at acetylcholine receptors. But there are two major classes of these receptors, distinguished by their different specificities. While the organophosphates and carbamates increase acetylcholine's effects on both types of receptor by inhibiting an enzyme that normally breaks down the neurotransmitter, imidacloprid specifically binds to the nicotinic receptor, so called because it preferentially binds nicotine. And that receptor is more common in insects than in other animals.

Imidacloprid was discovered by industrial chemists working "rationally" to find a nicotine derivative with just the right stability to last long enough to keep a pest insect population down, but not so long that it hangs around and pollutes the environment. But some efforts in the chemical industry still rely on the older, trial and error methods. Indeed, the two other major classes of chemical insecticides now in advanced development were discovered by more traditional techniques, such as screening thousands of soil samples for substances that deter insects.

It was just that kind of screening, for instance, that enabled chemists at Rhône-Poulenc's laboratories in Ongar, England, to discover that company's fiprole compounds, which are phenyl pyrazoles. A compound called fipronil is likely to be the first of these to come to market, and sales may begin in Europe as early as 1994, says spokesman Bruno Treppoz of the company's facility in Lyon, France. Rhône-Poulenc plans to file for registration with the EPA in the same year, although sales in the United States aren't likely before 1997.

Like nicotine, fipronil is a nerve poison, but this one blocks transmission of signals by the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). That novel mode of action may be one reason why fipronil is active against insects, such as the Colorado potato beetle and some cotton pests, that have become resistant to current chemical insecticides, says Rick Rowntree of Rhône-Poulenc's lab in Research Triangle Park. What's more, fipronil may have a greater specificity for the GABA receptors of insects than for those of mammals, a finding suggesting that it may have little toxicity for higher animals. Indeed, preliminary LD50 trials are bearing out that expectation, indicating, says Rowntree, that fipronil is "10, 20, or even 30 times less toxic than the compounds currently on the market."

So far, the only U.S. entry in the new pesticide sweepstakes comes from American Cyanamid of Princeton, New Jersey, which is developing a class of compounds called pyrroles, also identified by screening soil samples for compounds toxic to insects. Like the other new types of chemical insecticides, the pyrroles control a wide variety of insects, says Bob Farlow, Cyanamid's manager of insecticides for the United States. They appear to have an edge over imidacloprid and fipronil, however, in that the pyrroles are effective against mites, which are serious pests on citrus fruits, cotton, and ornamental plants, whereas the other two chemicals aren't.

But unlike imidacloprid and fipronil—and in fact all the major classes of insecticides currently in use—the pyrroles are not nerve poisons of some type. Rather than interfering with nerve cell function, the pyrroles work by inhibiting energy production in the mitochondria. Since cells of all higher organisms get the bulk of their energy from the mitochondria, active pyrroles would be widely lethal. But Cyanamid chemists were able to reduce that widespread toxicity by making an inactive "pro-insecticide" by attaching an oxygen-containing side-chain to the pyrrole ring. This chemical modification can be readily reversed by oxidase enzymes present in insect cells, says Farlow.

Mammals, on the other hand, are protected because they can't readily convert the pro-insecticide to the active molecule; they also rapidly excrete the pro-insecticide in feces. Nevertheless, even the modified compound remains acutely toxic to birds and some aquatic species, although Farlow maintains this should not be a problem if it is used according to package directions. It's supposed to be applied, for example, to foliage, which birds don't eat, rather than seeds, which they do. Cyanamid has just applied to EPA for an experimental use permit for its pro-insecticide, with sales planned in the United States and Europe by 1996 or 1997 if all goes well.

All this varied research work is good news for chemical insect control. But researchers won't be able to rest on their laurels. Experience predicts that, sooner or later, resilient insects will develop resistance to these new compounds. Yet the insecticide-makers can take satisfaction in having won another skirmish in the ongoing chemical warfare between humans and insect pests. And with rational design as their guide, the researchers can take heart that the next round will go their way, too.

–Anne Simon Moffat

Combatting the whitefly. Planted in soil treated with imidacloprid, the cabbages on the left thrived while the whitefly infestation retarded the growth of those on the right.