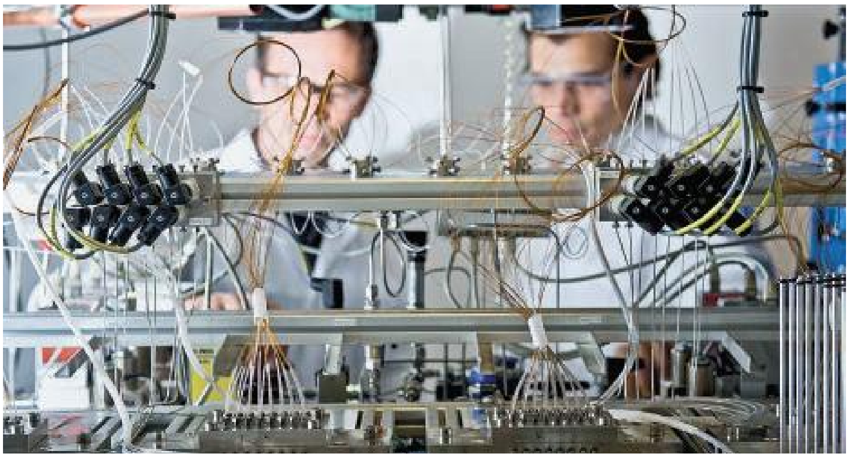
AVANTIUM



PARALLEL PROCESSING An Avantium Nanoflow unit, which can have up to 64 parallel reactors, can screen catalysts for making biobased molecules.

CATALYZING BIOBASED CHEMICALS

HIGH-THROUGHPUT-SCREENING FIRMS say their techniques are giving industrial biotech some competition

ALEXANDER H. TULLO, C&EN NORTHEAST NEWS BUREAU

OVER THE PAST DECADE, some of the most prominent initiatives in biobased chemicals and polymers—products such as DuPont Tate & Lyle's propanediol and NatureWorks' polylactic acid—were founded on fermentation. That these chemicals are being produced in quantities rivaling those of traditional petrochemicals speaks volumes for how far industrial biotechnology, white biotechnology, has come.

But officials at several companies that specialize in high-throughput experimentation say their methods have helped identify catalysts that enable economical production of new chemicals from biobased feedstocks. They see their firms harnessing techniques the chemical industry knows well—while simultaneously rejuvenating them.

One of these firms is Avantium, which provides high-throughput equipment and services for chemical and pharmaceutical clients. It has employed its technology to devise a route to furan dicarboxylic acid (FDCA), a chemical that, though yet to be produced commercially, is regarded as promising. FDCA was listed as one of the top 12 biobased building blocks in a seminal 2004 Department of Energy report.

Dirk den Ouden, director of new business development at Avantium, calls FDCA "the closest biobased alternative to terephthalic acid and isophthalic acid." Like those diacids, FDCA can be condensed with diols such as ethylene glycol to make polyester resins similar to polyethylene terephthalate (PET).

But to get to FDCA from sugar, a bifunctional furan is needed as an intermediate. Many chemists have pursued hydroxymethylfurfural (HMF) for this purpose. And given that HMF is a dehydrated sugar molecule, synthesizing it ought to be simple enough. But there's a catch. "The big drawback to HMF is that the molecule normally is not stable under the conditions that it is formed in," den Ouden says. "When you do the reaction, it reacts further, and you end up with not HMF but HMF degradation products."

Avantium threw itself at the problem in 2005. The company came up with a catalyst to make methoxymethylfurfural (MMF), a stable alternative to HMF, from glucose and fructose. It also developed a catalyst that converts MMF into FDCA. Avantium plans a pilot plant for 2011.

Avantium calls its furanic chemistry platform "YXY." The firm has teamed with NatureWorks, which has experience in commercializing biobased polymers. NatureWorks' parent, Cargill, has access to feedstocks.

Plastics based on FDCA and ethylene glycol "show extremely nice properties, in some cases better than PET," den Ouden suggests, without providing details. He sees fertile ground for FDCA-based polymers. Coca-Cola has been rolling out a "plant-based" PET beverage bottle, made with sugarcane-based ethylene glycol, and Coke officials are keen to eventually use an entirely bioderived polymer. But "biobased terephthalic acid is far, far away," den Ouden says.

Other companies are combining high-throughput screening and chemocatalytic methods to make existing petrochemicals. Rennovia was founded last year by Symyx Technologies veterans Thomas Boussie and Vincent Murphy, who jumped ship as that company spun off its high-throughput experimentation equipment business as Freeslate and merged with Accelrys (C&EN, April 12, page 6).

The pair tapped former Chemtura chief business officer Robert S. Wedinger as their firm's chief executive officer and then approached 5AM Ventures and Versant Ventures for funding. "We came up with paper chemistry that suggested we could get to adipic acid from glucose," Wedinger recalls. "That was the pitch we presented to the venture capital firms to get the funding." They landed $12 million.

Rennovia had good reason for choosing its raw material and target molecule. Each year, some 4.8 billion lb of adipic acid is produced globally as a raw material for nylon 6,6 and polyurethanes, according to Chemical Market Associates. Glucose is readily available, Wedinger says, noting that "corn syrup is shipped around by railcar."

THE COMPANY started the high-throughput screening of catalysts in December 2009. By February, scientists were making gram quantities of adipic acid. This year, they plan to run the process in a laboratory-scale pilot plant.

Wedinger hopes to have a commercial development unit up and running in 2012 or 2013. It's at this scale, he says, when one of the advantages of the chemocatalytic approach kicks in. "We can use equipment that already exists," he says.

Rennovia plans to fully commercialize the process by 2014. The scale that Wedinger has in mind for the first plant, 300 million lb per year, is similar to a petrochemical adipic acid plant. He hopes to find a partner to help cover the cost of building it.

Wedinger says he is confident with such

a large unit because his process is more economical than the petrochemical route to adipic acid with oil prices at $60 per barrel. Additionally, the only intermediate is glucaric acid, which could become a lucrative secondary market, he says.

RENNOVIA ISN'T the only company pursuing adipic acid from biobased sources. Carlsbad, Calif.-based Verdezyne announced in February that it has proved the concept of making adipic acid from yeast, using alkanes, plant-based oils, or sugars as raw materials. Verdezyne estimates that it has a cost advantage of more than 20%, depending on feedstock, versus petrochemical routes.

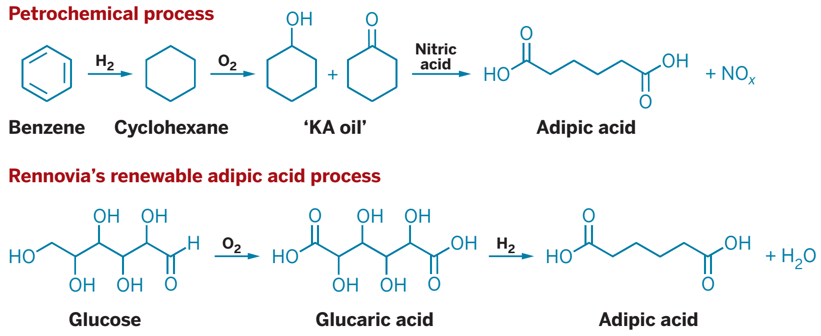
Wedinger contends that the chemocatalytic approach to making chemicals has advantages over biotechnology. "The industry has a lot of infrastructure in place," he says. "You have engineers who know how to design processes chemocatalytically." Of the 100 largest volume organic chemicals, he points out, more than 90 are made using chemocatalysis.

In addition to being well established, chemical catalysis offers technical advantages, Wedinger says. "You have more degrees of freedom. You can increase the pressure. You can increase the temperature. You can change the pH. With fermentation, you have limitations because you have to keep the bugs alive." Plus, Wedinger says, chemical catalysis is more efficient for producing at an industrial scale. "You get better space-time yield than you do in fermentation," he notes.

Proponents of industrial-scale fermentation counter that the field is advancing at a rapid rate. "Tinkering with DNA is getting easier by the day," notes Mark Bünger, research director for the biofuels and biomaterials intelligence practice at the R&D consulting firm Lux Research. And like chemocatalysis, fermentation has been taking advantage of high-throughput experimentation.

ALTERNATIVE ROUTE

Rennovia says its biobased route to adipic acid saves money



Although he concedes that chemocatalysis has the edge in efficiency, largely because of past industrial experience, Bünger is biased toward biocatalysis. Biotechnology, he says, is more flexible. With new genetic tools making it easier to identify useful metabolic pathways or tailor them from scratch, he adds, biocatalysis offers the most potential to get a process to the ideal "crossroads": taking in as many feedstocks as possible, including second-generation sources such as forestry and agricultural waste, and turning them into a virtually limitless number of useful materials and fuels.

OVER THE PAST DECADE, Dow Chemical, DuPont, and other companies have been overcoming their own preference for chemical catalysis and putting increased emphasis on biotechnology, Bünger points out. "They have had a bias, but it is a bias that they are trying to break."

Avantium's den Ouden doesn't dispute the biotech trend. But he says tools such as high-throughput screening are making chemocatalysis a viable alternative. "For the last decade or so, the attention was focused a lot more on white biotechnology," he says. "But maybe the trend is to revisit these chemically engineered processes." Organizations such as Pacific Northwest National Laboratory and the agribusiness giant Archer Daniels Midland have recently purchased equipment and contracted services from Avantium, respectively, to work on biomass.

Sascha Vukojevic, business development manager for key accounts at the Heidelberg, Germany, high-throughput research firm HTE, says he has seen a ramp-up in research on chemocatalytic routes to biobased chemicals. "Five years ago, there weren't many calls for biobased materials in the request pipeline," he says. "In the last two or three years, we have seen that the requests have increased."

Last year, for example, HTE wrapped up a program with French chemical maker Arkema to make acrolein and acrylic acid, normally propylene derivatives, from glycerin. Arkema says the high-throughput-screening collaboration enabled it to do in a "matter of months" what normally would have taken more than two years.

Vukojevic says HTE has other projects in the pipeline. Although he declined to disclose them, he noted that the projects are in chemicals as well as fuels based on bioderived synthesis gas and other biobased feedstocks.

Given the high-throughput screening infrastructure already installed at chemical companies, Vukojevic says, it's a good bet that many companies have internal R&D programs that outsiders don't know about. "High-throughput these days is a well-established tool, just like a gas chromatograph or any other tool that you use in professional R&D," he says.

Avantium's den Ouden expects industrial biotechnology and chemocatalytic processes will coexist and even complement each other. Enzymatic technology could be used to free up sugars from all kinds of biomass, and then when those sugars are available, companies like his could chemically convert them. "There is a lot to be gained by making very strong combinations," he says. ■