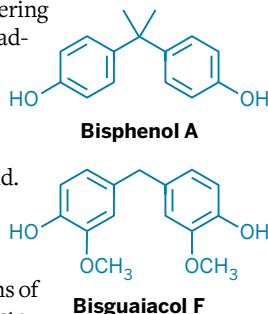


## BUILDING TISSUE LAYER BY LAYER

Just as there is a relationship between the structure and function of molecules, scientists suspect there is a relationship between structure and function of tissues and cells. Probing the latter relationship requires the ability to assemble tissues with specific structures. Zev J. Gartner and coworkers at the University of California, San Francisco, do this by attaching single-stranded DNA to cells and using DNA hybridization to direct tissue assembly. They pattern a surface with DNA sequences to which cells with complementary sequences adhere via DNA hybridization. They wash away excess cells and repeat the process with other DNA-labeled cells, growing tissue layer by layer. They then cleave the tissue from the surface and transfer it to a three-dimensional cell culture matrix where it continues to grow. The team is using the method to grow components of human mammary glands, sourcing cells from discarded tissue from breast reduction surgeries. Eventually, the researchers hope to grow tissues that could provide a more physiologically relevant screening platform for drug assays and studying breast cancer, Gartner said. It's not clear, however, how well the tissue growth process will scale up.—CHA

## PAPERMAKING WASTE COULD FIX BPA PROBLEM

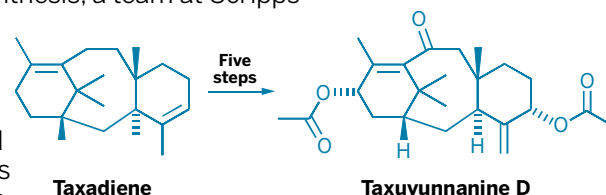
Lignin waste and the dangers of bisphenol A (BPA) seem like two unrelated problems. But not to Richard P. Wool and Kaleigh H. Reno. Instead, the University of Delaware chemical engineering professor and graduate student, respectively, see the first problem as a solution to the second. Every year, the pulp and paper industry produces millions of tons of lignin waste as a by-product. This material is usually incinerated. But a group led by Wool and Reno have developed a process for turning two aromatic alcohols that make up lignin—vanillyl alcohol and guaiacol—into a compound that could be used to replace BPA as a monomer that provides rigidity to plastics.



This week's selections are from the ACS national meeting, which took place on March 16–20 in Dallas.

## TAKING CUES FROM NATURE EN ROUTE TO PACLITAXEL

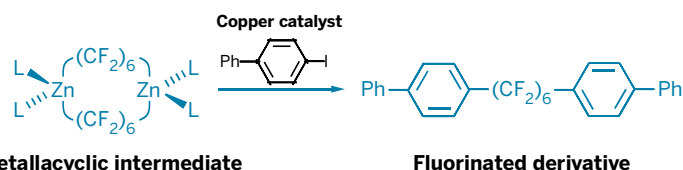
No one is better than nature at making the cancer drug paclitaxel (Taxol). But synthetic chemists would like to learn from nature. By mimicking the early steps in paclitaxel's biosynthesis, a team at Scripps Research Institute, La Jolla, Calif., has potentially come up with a way to create analogs of paclitaxel that are unavailable via bioengineering. These could turn out to be powerful drugs as well. A team led by Phil S. Baran synthesized the natural product (–)-taxuyunnanine D in just five steps from taxadiene. The transformation mimics the first three of eight oxidations that occur biosynthetically when taxadiene is converted to paclitaxel. Taxuyunnanine D, Baran said, could ultimately be used as an intermediate en route to paclitaxel. The challenge for Baran's group was to control the order of the three oxidations. It's a tough task, Baran explained, because taxadiene is a strained, doubly unsaturated hydrocarbon that is "spring-loaded" for oxidation at several spots at once. Through computational modeling, developing a seldom-used chromium reagent, and conducting hundreds of reactions, Baran's team executed the early steps of paclitaxel's biosynthesis (*J. Am. Chem. Soc.* 2014, DOI: 10.1021/ja501782r).—BH



The compound, bisguaiacol F, is structurally similar to BPA, but it has some differences, including two pendant methoxy groups. These groups, the researchers said, should keep bisguaiacol F from binding to estrogen receptors, where scientists think BPA wreaks havoc. The Delaware researchers used Environmental Protection Agency software to evaluate bisguaiacol F for safety and Wool's twinkling fractal theory of the glass transition to predict that its mechanical and thermal properties would be similar to those of BPA.—BH

## TEACHING ZINC A NEW TRICK

Metallacyclobutanes hold a special place in synthetic chemistry as intermediates in the olefin metathesis reactions that have revolutionized the way chemists make small molecules and polymers. David A. Vicic of



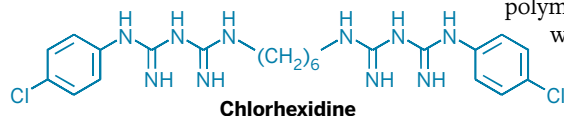
L = ligand, Ph = phenyl

Lehigh University reported that his group has taken a step toward using this approach to make new types of fluorinated small molecules and polymers. The key, he suggested, is using metallacyclic zinc reagents bearing fluoroalkyl groups. Current routes to fluorinated metallacycles use tetrafluoroethylene gas, which works well for adding C<sub>2</sub>F<sub>4</sub> and C<sub>4</sub>F<sub>8</sub> units via radical addition reactions. But the gas is hard to handle and leaves a significant environmental footprint. Vicic and his team developed an alternative metathesis route using metallacyclic dizinc reagents that incorporate C<sub>3</sub>F<sub>6</sub> and longer fluoroalkyl units into molecules without directly using tetrafluoroethylene (*Organometallics* 2013, DOI: 10.1021/om401016k). The team prepared the reagents from diethylzinc and I(CF<sub>2</sub>)<sub>n</sub>I (n = 3, 4, or 6). The fluoroalkyl units can be transferred via a copper-mediated

process to aryl iodides to form bicyclic fluorinated organometallic ring systems or ring systems with perfluoroalkyl linkers (shown). These compounds could serve as skeletons for medicinal or materials applications. The Lehigh team has filed a provisional patent on the method.—SR

## CORRALLING A CATTLE INFECTION

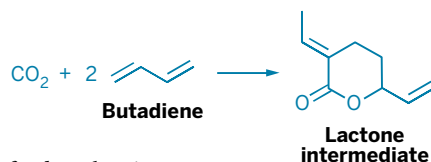
Ranchers may have cause to rejoice if a drug delivery system that works in cell cultures pans out in cattle. Researchers at Kansas State University have designed a treatment that they hope will eradicate liver abscesses caused by *Fusobacterium necrophorum*, a scourge that affects 12–32% of livestock. The microbe lives harmlessly in cows' rumina, but aggressive feeding strategies push it into the liver, delaying the animals' growth. What's more, slaugh-



terhouses must discard infected tissue, costing the beef industry an estimated \$29.9 million in 2011 alone. Antibiotics effective against *F. necrophorum* can be toxic to healthy cells, so professor Stefan H. Bossmann, graduate student Sebastian O. Wendel, and colleagues searched for a cloaking strategy. They loaded the antibiotic chlorhexidine into *Micrococcus luteus*, a microbe frequently found on human teeth and skin. To target the abscesses, they inserted the modified microbes into neutrophil granulocytes, which are white blood cells that respond to inflammation and then undergo apoptosis. This cell death process also degrades *M. luteus*, releasing the antibiotic. In cell cultures, *F. necrophorum* did not survive the targeted treatment. The team next plans to test their strategy in rodents. Biological cloaking isn't a new idea, but applying it to this case is smart, noted molecular release expert Catherine J. Murphy of the University of Illinois, Urbana-Champaign. She looks forward to seeing results of animal studies.—CD

## CO<sub>2</sub> PLUS OLEFINS YIELDS POLYMERS

Carbon dioxide has attracted attention as an inexpensive renewable carbon



feedstock to incorporate into polymers. But the low reactivity of CO<sub>2</sub> has impeded progress in copolymerizing it with olefins. Kyoko Nozaki of the University of Tokyo described a strategy to overcome the copolymerization barrier. It hinges on cobbling together CO<sub>2</sub> and a pair of butadiene molecules via a palladium-catalyzed reaction to form a lactone intermediate. The work builds on the Nozaki group's palladium-catalyzed olefin copolymerization reactions and work by other groups to form lactones from CO<sub>2</sub> and epoxides to make polycarbonates.

When mixing ethylene with CO<sub>2</sub>, a thermodynamic barrier favors ethylene coupling and polyethylene formation, bypassing the less reactive CO<sub>2</sub> and failing to achieve copolymerization, Nozaki explained. But

when using a 1,3-diene, such as butadiene, she said, the palladium catalyst tips the conditions in favor of coupling CO<sub>2</sub> and two diene molecules together. Free-radical polymerization of the resulting lactone leads to high-molecular-weight poly(lactones)—a new class of polymers. The process also works when using two different 1,3-dienes, such as butadiene and isoprene, which leads to new terpolymers (*Nat. Chem.* 2014, DOI: 10.1038/nchem.1882).—SR

## GUT MICROBES BRING OUT BEST IN COCOA

People have been stating—and overstating—the health benefits of cocoa ever since Aztec emperor Montezuma II drank it obsessively in the 1500s, according to John W. Finley, a food scientist at Louisiana State University. “We wanted to peel into the science further,” he said of studies his research team conducted on how human gut microbes break down the tasty treat. The researchers first “digested” cocoa samples with solutions mimicking human stomach acid and enzyme-filled small intestine fluid. Then they collected what remained—undigested fiber and large polyphenols—and added the components to a mix of fecal bacteria such as *Bifidobacterium* and *Clostridia* to simulate conditions in the human colon. Using mass spectrometry, the team determined that the fiber broke down

into short-chain fatty acids. And the polyphenols reduced to small, absorbable molecules, such as vanillic acid, that scientists have shown can protect heart cells against inflammation. These results don't prove that cocoa is good for the heart, Finley said, but “that's where we're headed.” The report in Dallas came on the heels of a March 17 announcement by Brigham & Women's Hospital, in Boston, that it will lead a \$20 million clinical trial to test whether cocoa extract pills can reduce the risk of stroke and cardiovascular disease.—LKW

## PAPER MASS SPEC POISED TO SPEED UP DRUG ANALYSIS

Paper spray mass spectrometry provides comparable results to conventional liquid chromatography/mass spectrometry for measuring drug properties, according to Ryan D. Espy, a graduate student with



RYAN ESPY

R. Graham Cooks at Purdue University. Paper spray is an MS method that requires no sample preparation beyond simply spotting the sample on a piece of paper. It could reduce the amount of time and resources needed to study administered drugs' fate in the body. Such pharmacokinetic analysis is an integral part of the drug development process. Paper spray requires just 10  $\mu$ L of blood. Working with scientists at AbbVie, a pharmaceutical research company, Espy dosed rats with tamoxifen and then used paper spray MS and LC/MS to measure drug concentrations in blood samples. The maximum drug concentration measured by both techniques was almost identical: 42 ng/mL by the paper spray method and 43 ng/mL by LC/MS. But the paper spray approach was much faster: A set of 50 samples took eight hours to run with LC/MS, but only 40 minutes with paper spray MS.—CHA

*For paper spray mass spectrometry, a blood sample is spotted on a paper substrate, shown here in a cartridge.*