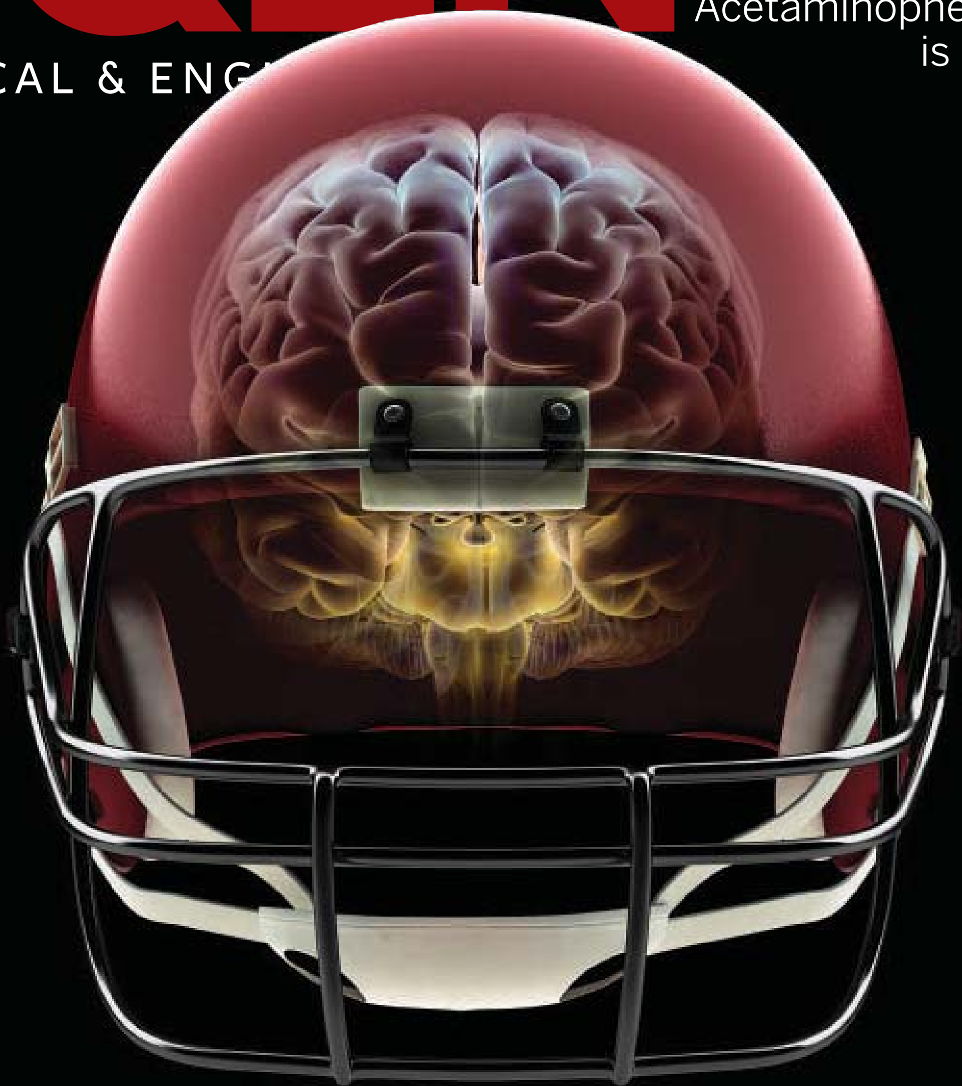
JULY 21, 2014

C&EN
CHEMICAL & ENG

PRIZING INNOVATION
Federal research agencies turn to competitions **P.23**

BELIEVE IT OR NOT
Acetaminophen's mechanism is still unclear **P.31**



GOING ON THE OFFENSIVE

New diagnostics could catch head trauma disease earlier **P.9**

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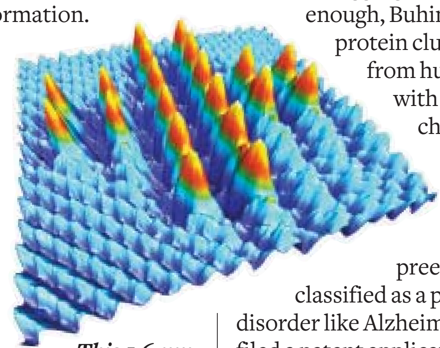
ATOM MANIPULATION CROSSES NEW THRESHOLD

In a teeny tiny display of patriotism, a team led by researchers at the University of Basel has created the world's smallest Swiss national flag out of ions (*Nat. Commun.* 2014, DOI: 10.1038/ncomms5403). To generate the flag's iconic cross, the scientists used the tip of an atomic force microscope (AFM) to pick up bromine ions scattered across a sodium chloride surface and move them one by one into formation. With the hope of one day creating atomic-scale electromechanical devices, physicists have been dragging single atoms around and repositioning them on surfaces with scanning probe tips since the 1990s. Usually, the atomic manipulations are carried out on metallic or semiconducting surfaces at very low temperatures. The Swiss cross, however, was generated on an insulating surface—sodium chloride—at room temperature. The researchers accomplished the more difficult task, says team leader Ernst Meyer, because of "tremendous progress" in the sensitivity and stability of AFMs. The team believes it succeeded in building the 20-ion cross because the NaCl-coated AFM tip it used had sodium ions at its apex: These positively charged particles were able to pick up the negatively charged bromines.—LKW

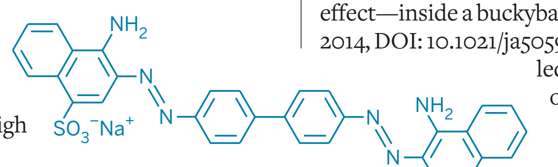


NAT. COMMUN.

This 5.6-nm-wide Swiss cross, made of bromine ions (orange) on a sodium chloride surface (blue), is stable at room temperature.

SPOTTING PREECLAMPSIA EARLY

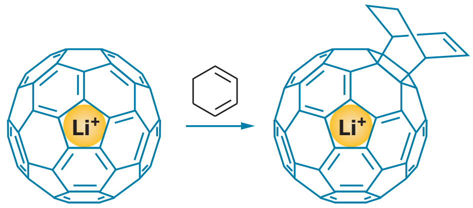
Once preeclampsia sets in during pregnancy, the only way to stop the risk of harm is to deliver the baby, no matter how premature. However, detection yardsticks—high blood pressure and high protein levels in urine—are not necessarily specific to preeclampsia or easy to monitor in the developing world. According to a study, a color-change urine test with the dye Congo Red might complement established tests to provide a clear early picture of preeclampsia (*Sci. Transl. Med.* 2014, DOI: 10.1126/scitranslmed.3008808). Irina A. Buhimschi of Nationwide Children's Hospital in Columbus, Ohio, and colleagues used Congo Red to test the idea that misfolded proteins play a role in preeclampsia. Alzheimer's disease researchers have long used Congo Red to detect misfolded aggregates of amyloid-β. Sure enough, Buhimschi's team found protein clumps in urine samples from hundreds of women with preeclampsia. Biochemical data suggest the clumps may play a role in the disease's development, so Buhimschi thinks preeclampsia should be classified as a protein-misfolding disorder like Alzheimer's. The team has filed a patent application on their diagnostic technology. "The diagnostic potential is really big—depending on how specific it turns out to be for preeclampsia," says Robert Moir, who studies amyloid-β at Harvard Medical School.—CD



Congo Red

SPEEDING UP C_{60} CYCLOADDITIONS

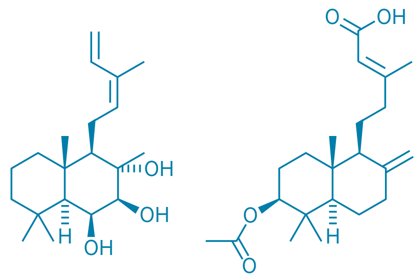
To get more zip out of Diels-Alder reactions, chemists often employ a Lewis acid catalyst to starve the cycloaddition's dienophile of electron density as it seeks out the electron-rich diene. One problem with this approach is that a heteroatom is needed in the dienophile to coordinate with certain Lewis acids, such as lithium ions. This coordination adds a steric component to the reaction, making it difficult to separate electronic and steric effects when teasing out the intricacies of the reaction. Seeking a way to remove steric effects from their study of the Diels-Alder reaction, chemists in Japan decided to put their lithium ion in a spot where it could exert only an electronic effect—inside a buckyball (*J. Am. Chem. Soc.* 2014, DOI: 10.1021/ja505952y). Researchers led by Ken Kokubo of Osaka University and Yutaka Matsuo of the University of Tokyo found



that C_{60} with an encapsulated lithium ion reacts with 1,3-cyclohexadiene (shown) about 2,400 times as fast as empty C_{60}. Kinetic and computational studies indicate that the lithium ion lowers the energy of the transition state and stabilizes the reactant complex and the product through favorable molecular orbital interactions.—BH

GOLDENROD COMPOUND MASKS BITTERNESS

Scientists have discovered a compound extracted from the Canada goldenrod plant that binds to human bitterness receptors (*J. Nat. Prod.* 2014, DOI: 10.1021/np5001413). Bitterness-masking compounds are a hot research focus because they could be important in developing foods or medicines that people would otherwise reject as too bitter-tasting. The human tongue contains the TAS2R family of bitterness receptors, and their active sites are popular binding targets. A. Douglas Kinghorn of Ohio State University and colleagues screened extracts from Canada goldenrods, which had been shown to inhibit one of the human bitterness receptors, hTAS2R31. They isolated a number of compounds, including a new labdane diterpenoid, called solidagol. Another of these compounds, 3β-acetoxycopalic acid, directly inhibited hTAS2R31 activity and is the first labdane diterpene shown to have this property, the authors report. The group then used computational modeling to show how this compound binds to the active site of the receptor. The compound, they say, "might be a potential source for the development of bitterness-masking dietary supplements or agents."—EKW



Solidagol **Bitter-masking compound**