Chemical Year In Review 2010

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C&EN produces 51 issues each year containing hundreds of articles on important research advances in chemistry. The annual Chemical Year In Review reveals our choices for some of the superlative achievements that we featured in 2010. It also provides an opportunity to reflect on the ramifications of these developments. Our choices, displayed in no particular order, are necessarily subjective and not intended to be comprehensive. Indeed, these discoveries represent only a few examples of the many ways in which chemists are pushing the boundaries of what we know and what we are capable of doing.

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A New Chlorophyll

Chlorophyll f, which absorbs light in the red spectral region, was discovered in cyanobacteria living in rocky structures called stromatolites on the west coast of Australia.

For the first time in more than 60 years, researchers found a new kind of chlorophyll, the magnesium porphyrin pigment used by plants and bacteria to catch sunlight and convert it into energy by means of photosynthesis (C&EN, Aug. 23, page 7; Science, DOI: 10.1126/science.1191127). The newly christened chlorophyll f was found in cyanobacteria living in rocky outcrops off the west coast of Australia by Min Chen of the University of Sydney and colleagues. It absorbs "redder" wavelengths of light than its five chlorophyll siblings, stepping beyond the visible region into the infrared range and thus widening the spectrum of light known to be harvested by photosynthetic organisms. Chlorophyll f differs slightly from other chlorophylls, primarily by having a formyl group at C-2 of the pigment's chlorin ring; all other chlorophylls have a methyl group at C-2. Chlorophylls a, b, c1, c2, d, and f differ slightly at C-2, C-3, C-7, and C-8, and chlorophylls c1 and
c2 lack the C20H39 phytyl group. The new pigment could possibly contribute to improving the efficiency of artificial photosynthesis and be exploited by scientists and engineers aiming to use biotechnology to produce renewable energy from sunlight, commented Robert Blankenship, a plant biologist at Washington University in St. Louis who studies photosynthetic reactions.

Finally, Palau'amine

With the help of a daring cyclization reaction, a team led by Phil S. Baran of Scripps Research Institute completed the first total synthesis of palau'amine, a marine natural product that has captivated synthetic chemists (C&EN, Jan. 11, page 5; Angew. Chem. Int. Ed., DOI: 10.1002/anie.200907112). Isolated from a sponge in waters near the island nation of Palau in the Pacific Ocean, palau'amine is a dauntingly complex alkaloid with eight contiguous stereogenic centers and many reactive nitrogen groups. Until the Baran group’s synthesis, "palau'amine's unprecedented hexacyclic ring system and its nasty physical properties had undermined total synthesis endeavors in leading laboratories worldwide," said Larry E. Overman, an organic chemist at the University of California, Irvine, who has worked toward the palau'amine synthesis. The biggest chemical challenge has been in recreating the molecule's strained core. After several failed attempts and two years of work, Baran, Ian B. Seiple, Shun Su, and colleagues used a cyclization strategy across the large ring of an intermediate to successfully make the natural product. Baran's team continues to work on an enantioselective version of the synthesis for obtaining gram amounts of material. "I don't see our synthesis as an end—I see it as a beginning," he said in January. In fact, in September, Baran's team reported a silver-catalyzed procedure inspired by its palau'amine quest that couples electron-poor heterocycles such as pyridines with arylboronic acids, a process tough to carry out with established Suzuki coupling chemistry (J. Am. Chem. Soc., DOI: 10.1021/ja1066459). 
A new synthetic strategy yields polypropylene oligomers with narrow molecular weight distribution, permitting formation of low-viscosity white oils such as the one shown. This process promises to boost the efficiency of polymer synthesis and produce materials with highly controlled polyolefin chain lengths and properties. The process, developed by Lawrence R. Sita, Jia Wei, and Wei Zhang of the University of Maryland, gives chemists access to previously unattainable oils and waxes that could be useful in specialty chemical applications, including detergents, lubricants, and plasticizers. "While millions of tons of linear α-olefins are produced each year based on ethylene, the corresponding and potentially more interesting derivatives based on propylene or higher α-olefins have not been prepared in a robust fashion," said polymer scientist Craig J. Hawker of the University of California, Santa Barbara. Sita's group combined two techniques in its strategy: Living Ziegler-Natta polymerization of propylene to form continuously growing single polymer chains on hafnium catalyst molecules, and chain-transfer polymerization that relies on diethylzinc to shuttle the chains back and forth to an inactive aluminum surrogate for temporary holding (C&EN, Feb. 15, page 13; Angew. Chem. Int. Ed., DOI: 10.1002/anie.200906658 and 10.1002/anie.201004709). "All three metals must act in concert to pull off the precise chemistry," Sita said. The process allows multiple polymer chains to grow at the same rate, giving exquisite control over polymer molecular weights to prepare block copolymers and add terminal functional groups, he added. Sita founded a company, Precision Polyolefins, to commercialize the technology.
Element 117 Created

This illustration shows the creation of element 117 from 48Ca atoms smashing into 249Bk atoms.

This year, scientists finally made the especially shifty superheavy element 117, a milestone for nuclear chemistry that completed the seventh row of the periodic table (C&EN, April 12, page 9; Phys. Rev. Lett., DOI: 10.1103/physrevlett.104.142502). The discovery helps clarify the still-fuzzy picture of the behavior of superheavy elements. It also bolsters the case for the existence of an “island of stability,” a cluster of superheavy elements with a “magic number” of protons and neutrons that have half-lives of minutes or days, rather than fractions of a second. Yuri Oganessian, director of the Flerov Laboratory of Nuclear Reactions at the Joint Institute for Nuclear Research, in Dubna, Russia, led the international team that created the new element.

Using a particle accelerator at Dubna, the researchers repeatedly smashed 48Ca atoms into a target coated with 249Bk. The two elements fused to produce two isotopes of the new superheavy element, 293117 and 294117, which were identified by their characteristic decay chains. Before element 117 can be named, the International Union of Pure & Applied Chemistry requires that the element’s creation be replicated by an independent team—a potentially lengthy process. For example, more than 10 years after it was created, element 112 finally received its official name and symbol this year. It’s now copernicium, Cn (C&EN, March 1, page 15; Pure Appl. Chem., DOI: 10.1351/pac-rec-09-08-20).

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Cellular Joystick

![Cellular Joystick](http://pubs.acs.org/ezp-prod1.hul.harvard.edu/cen/coverstory/88/8851cover.html?featured=1)
Decorators Acetyl coenzyme A, which cells use to deliver acetyl groups to proteins.

Scientists have known for decades that proteins can be acetylated on their lysine residues, but the modification was long seen as the poor cousin to phosphorylation, which can activate or deactivate countless processes in living cells. New research this year, however, revealed that acetylation is a master switch for a who's who of cellular functions in organisms as diverse as bacteria and humans. Knowledge of the widespread acetylation of important proteins will likely inspire drugmakers to target enzymes that can decorate or undress proteins with acetyl groups. Acetylation is probably best known for its role in controlling which genes in a cell are put into deep storage and which ones can be accessed by transcription machinery. Hints of acetylation's greater versatility came last year, when researchers including Chunaram Choudhary of the University of Copenhagen found that thousands of proteins with other functions are acetylated, including some involved in cell division and DNA repair (C&EN, July 20, 2009, page 37; Science, DOI: 10.1126/science.1175371). Then in February, a team including Guo-Ping Zhao of China's Fudan University and Kun-Liang Guan, now at the University of California, San Diego, revealed that acetylation controls glycolysis, tricarboxylic acid and urea cycles, fatty acid metabolism, and glycogen metabolism (C&EN, Feb. 22, page 11; Science, DOI: 10.1126/science.1179689 and 10.1126/science.1179687). "These are the fundamental pathways in a cell—how a cell gets its energy," Choudhary said. Furthermore, such acetyl decorations cover the evolutionary tree from bottom to top, he added.

Dendrimersomes Debut

Dendrimeromes Micrographs show polygonal, cubic, spherical, tubular, rodlike, helical, and disklike dendrimersomes. Colorized versions are shown in alternate rows.

Nanostructure Dendrimersome cross-section shows its cell-membrane-like bilayer.
Janus dendrimers are amphipilic, with nonpolar (red) and polar (blue) ends.

Chemists found this year that when highly branched bifunctional organic compounds called Janus dendrimers are added to water, the dendrimers magically self-assemble into tiny bubbles and other nanostructures called dendrimersomes. The nanostructures could prove more useful for biomedical and other applications than similar nanostructures made from phospholipids and polymers. Dendrimers are repetitively branched molecules, and Janus dendrimers are two-faced versions, with polar groups on one side and nonpolar groups on the other. Virgil Percec of the University of Pennsylvania and coworkers found that Janus dendrimers can self-assemble in water into elaborate dendrimersomes that adopt vesicle, tube, and disk shapes, among others (C&EN, May 24, page 7; Science, DOI: 10.1126/science.1185547). The shapes can accommodate guest molecules and could therefore have a variety of applications, including drug delivery, gene transfer, imaging, and cosmetics. Some of the dendrimersomes' favorable characteristics, such as long-standing stability, size uniformity, biomembrane-like dimensions, and ease of derivatization, could give the materials advantages over previously developed synthetic vesicles, such as liposomes and polymersomes. "This is truly groundbreaking work," said Donald A. Tomalia, who discovered dendrimers in 1979 and is a professor at Central Michigan University. "It's the first step toward a huge family of dendrimersome structures." Tomalia and coworkers believe it will eventually be possible to use Janus dendrimers with specific sizes, shapes, and surface
chemistries as building blocks to create dendrimersomes with customized structural and functional characteristics.

Baker's team envisioned an enzyme that could catalyze the intermolecular Diels-Alder reaction of the diene 4-carboxybenzyl trans-1,3-butadiene-1-carbamate (left in active site) and the dienophile N,N-dimethylacrylamide (right in site).

**Build Your Own Enzyme**

Chemists designed and built from scratch the first enzymes capable of catalyzing the versatile intermolecular Diels-Alder cycloaddition reaction, raising the bar for complex chemical transformations performed by de novo-designed enzymes (C&EN, July 19, page 5; Science, DOI: 10.1126/science.1190239). A team led by David Baker of the University of Washington built the Diels-Alderases specifically for catalyzing the reaction of the diene 4-carboxybenzyl trans-1,3-butadiene-1-carbamate and the dienophile N,N-dimethylacrylamide. The researchers used Rosetta computational design methodology and the RosettaMatch program to design and screen enzymes with the right shape and composition to align the reactants and couple them to form a chiral cyclohexene ring. Starting from millions of theoretical active sites, Baker and coworkers used modeling and their scientific intuition to narrow the field to 84 enzyme candidates, for which they synthesized and expressed genes to obtain purified enzymes. Of those, two demonstrated Diels-Alderase activity. Fine-tuning amino acids in the active sites boosted the enzymes' activity so that they outperform catalytic antibodies currently used for Diels-Alder reactions. Although the activity of the new enzymes is still a far cry from that of native enzymes, the work might one day lead to industrially useful biocatalysts that operate more efficiently or work under greener conditions than is currently possible.

**United Ubiquitins**

Protection Scheme In the MRC Laboratory's synthesis, a C-terminal thioester in an amine-protected donor ubiquitin (orange) reacts with deprotected lysine in an acceptor ubiquitin (yellow) to form a native isopeptide-bonded product, which is deprotected to yield a diubiquitin (orange and yellow). The protecting groups are pink, and the thioester, deprotected lysine, and isopeptide bond are shown in ball-and-stick representations.
Researchers demonstrated this year that previously inaccessible ubiquitin protein chains could be synthesized, making it possible to study their functions (C&EN, Oct. 11, page 36). Ubiquitin chains containing two or more protein units linked via isopeptide bonds play key biological roles, including marking unwanted proteins for disposal. But there are seven homogeneous ubiquitin chain types, and only three of them could be synthesized enzymatically and studied before. David Komander, Jason W. Chin, and coworkers of the MRC Laboratory of Molecular Biology, in Cambridge, England, used genetic engineering and chemical synthesis to create two previously unobtainable ubiquitin chains, K6 and K29 (Nat. Chem. Biol., DOI: 10.1038/nchembio.426). Chuan-Fa Liu of Singapore's Nanyang Technological University and coworkers used native chemical ligation to develop a chemical synthesis of a K48 chain (Chem. Commun., DOI: 10.1039/c0cc01382j). And Ashraf Brik of Ben-Gurion University of the Negev, in Israel, and coworkers used native chemical ligation to synthesize all seven homogeneous ubiquitin chain types (Angew. Chem. Int. Ed., DOI: 10.1002/anie.201003763). These syntheses, which each yielded diubiquitins, will enable scientists to structurally analyze and identify the roles and selectivities of the different chain types. "There will be a lot of interest in the ubiquitin community in getting access to these chains," commented synthetic protein chemist Tom W. Muir of Rockefeller University. "This is high-impact stuff because the field just has not had access to these reagents—period."

A Wire For Spying On Cells
A nanoFET just 200 nm long approaches (left) and slides into a cell (right).

Tapping into the inner workings of a cell got significantly more sophisticated this year, thanks to a nanoscale field-effect transistor bioprobe (C&EN, Aug. 16, page 9; Science, DOI: 10.1126/science.1192033). The new device, known as a nanoFET, uses a kinked silicon nanowire coated with a phospholipid bilayer to monitor electrical signals—for example, from neurons firing or cardiac cells driving a beating heart. The probe could also be outfitted with auxiliary bioactive molecules to measure the expression of nucleic acids or proteins. The use of nanoFETs "represents the first totally new approach to intracellular studies in decades, as well as the first measurement of the inside of a cell with a semiconductor device," said Harvard University's Charles M. Lieber, who spearheaded the work. "Our breakthrough allows for the first time the capability to interface directly digital electronics with living cells in a way that literally blurs the distinction between these two information-processing units of life." The device's key component is the silicon nanowire that Lieber's team coaxed into growing with an elbow-shaped kink. In addition to controlling the shape, the researchers can modulate the amount of impurities in the silicon as it grows so that portions of the nanowire adopt metallic properties. Although previous examples of nanoscale FETs were made on flat substrates, Lieber's three-dimensional design allows the entire nanoFET to slip into a cell.

Carbon Takes Chemistry And Physics Nobels
VERSATILITY  Heck, Negishi, and Suzuki couplings have been used to make various fine chemicals.

[Diagram of Heck reactions, Negishi coupling, and Suzuki coupling]

Me = methyl

See experts react to the awarding of the Nobel Prize in Chemistry to Richard Heck, Ei-ichi Negishi and Akira Suzuki.

Have a look at experts reacting to the winners of the 2010 Nobel Prize in Physics.

 Physics Nobel Laureates Geim (left) and Novoselov.
Andre Geim

Peelled Off Geim and Novoselov obtained these planar films of graphene, each about 2 μm across, by repeatedly peeling layers from graphite. The thinnest layer in this STM image is about 30 atoms thick.

In what many scientists in the chemical community called "long overdue" recognition, the 2010 Nobel Prize in Chemistry was awarded to Richard F. Heck, Ei-ichi Negishi, and Akira Suzuki for discovering and developing palladium-catalyzed cross-coupling reactions (C&EN, Oct. 11, page 7). In these reactions, palladium complexes are used to catalyze the formation of carbon-carbon bonds, a widely used synthetic strategy to make complex molecules employed as materials, pharmaceuticals, and other specialty chemicals. "It is hard to overestimate the importance of these processes in modern-day synthetic chemistry," said Massachusetts Institute of Technology's Stephen L. Buchwald. The pioneering chemistry discovered by Heck in 1968 uses palladium to wed aryl halides with olefins. In 1977, Negishi used palladium to catalyze couplings of organozinc reagents with organohalides. Two years later, Suzuki began developing palladium-catalyzed couplings of organoboron compounds with organohalides. "To practicing synthetic chemists in industry and academe, these names are familiar," added Victor Snieckus of Queen's University, in Ontario. "Many of us have run Heck, Negishi, and Suzuki reactions with our own hands."

The isolation and characterization of graphene—a one-atom-thick sheet of carbon atoms arranged in a honeycomb pattern—won the 2010 Physics Nobel for Andre K. Geim and Konstantin S. Novoselov of the University of Manchester, in England. In 2004, Geim and Novoselov worked out a surprisingly simple method for exfoliating graphite by folding adhesive tape against tiny crystals of the compound and peeling apart the tape repeatedly. The team showed that not only could single sheets of graphene be isolated, but the sheets also remain stable at room temperature. Graphene has quickly become a top choice for computing and electronics applications, as well as for advanced composite materials.
Halogenase Success

Fermented Fluorine By replacing a gene in the bacterium S. tropica with one for the fluorinase enzyme, researchers have biosynthesized a fluorinated version of salinosporamide.

\[
\begin{align*}
\text{S-Adenosyl-L-methionine} & \quad \text{Fluorinase, } F^- \\
\text{5'-Fluorodeoxyadenosine} & \quad \text{Fluorosalinosporamide}
\end{align*}
\]

Met = methionine, A = adenine, CoA = coenzyme A

View Enlarged Image
Fermented Fluorine A culture of the colorful bacterium S. tropica (top) was used to make fluorosalinosporamide (bottom).

Weerawat Runguphan

This periwinkle plant was engineered to produce "hairy roots" that are removed and transferred to cell-culture medium where they continue to grow and express chlorinated natural products.

Efforts this year to introduce halogenase enzymes into bacteria and plants could make it easier to produce halogenated pharmaceuticals. In one instance, scientists reprogrammed a deep-sea microbe to make a fluorinated version of an anticancer drug candidate (C&EN, Feb. 1, page 7; J. Nat. Prod., DOI: 10.1021/np900719u). The achievement marks the first time scientists have managed to insert the gene for a fluorinase enzyme into a host organism to generate a fluorinated metabolite. Organofluorine compounds play an important role in medicinal chemistry: About 15% of all pharmaceuticals include at least one fluorine atom to improve bioavailability and efficacy. Although halogenated natural products are common, organofluorine versions are rare, with only five examples reliably known. David O'Hagan at Scotland's University of St. Andrews in collaboration with Alessandra S. Eustáquio and Bradley S. Moore of Scripps Institution of Oceanography replaced the chlorinase gene in the marine bacterium Salinispora tropica with the fluorinase gene from the soil bacterium Streptomyces cattleya. The researchers then used the engineered bacterium to make a fluorinated version of salinosporamide A, which is a chlorinated natural product drug in clinical trials. In a related report, a team led by Sarah E. O'Connor of Massachusetts Institute of Technology engineered the Madagascar periwinkle to express halogenase enzymes from soil bacteria. This modification expands the plant's ability to biosynthesize complex natural products to include chlorinated and brominated analogs (C&EN, Nov. 8, page 13; Nature, DOI: 10.1038/nature09524). The development could make it easier to produce desirable halogenated pharmaceuticals in plants rather than in engineered bacteria or by way of elaborate multistep chemical syntheses. "We are in an exciting new phase in metabolite engineering," O'Hagan told C&EN. "It is clear that the tools are developing to selectively halogenate natural products by biotechnological, rather than chemical, methods."

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20.Dec.10
Nanostructure Dynamics

A 4-D electron tomography method provides a 3-D view of this carbon nanotube spiral (orange and yellow), shown here against an artistic background, as it wiggles and moves. The braceletlike structure has a radius of about 620 nm.

Time-resolved electron tomography captures this carbon nanotube structure undergoing ultrafast morphological changes from various viewing angles.

High-resolution imaging of nanoscale objects jumped from three dimensions to four this year when researchers debuted 4-D electron tomography (C&EN, June 28, page 11; Science, DOI: 10.1126/science.1190470). The technique, which provides a dynamic view of complex microscopic objects undergoing subtle transient motions and structural changes, could have wide-ranging applications in materials and biological sciences. Some of the limitations imposed by studying 2-D projections of 3-D specimens, which is the norm in electron microscopy, can be overcome by recording multiple 2-D projections at different angles and using the data to construct 3-D images. But the 3-D structural information obtained is still limited because it is a time-averaged representation of the sample as a static object in an equilibrium state. To sidestep the time-averaging issue, Oh-Hoon Kwon and Chemistry Nobel Laureate Ahmed H. Zewail of California Institute of Technology used laser-driven ultrafast electron microscopy technology pioneered by Zewail's group to integrate time resolution into electron tomography. The team developed a stroboscopic procedure for producing images with nanoscale spatial resolution and femtosecond temporal resolution. In a demonstration study, the researchers generated a time-lapse series of tomographic images and assembled them into videos, thereby capturing a ring-shaped carbon nanotube structure wiggling and "breathing" in response to sudden laser heating pulses.