

Spotlights on Recent JACS Publications

■ CATALYTIC ALKENE HYDROSILYLATION MADE BETTER AND CHEAPER

Organosilicon compounds are not only an essential class of laboratory reagents, but also valuable industrial starting materials for products ubiquitous in daily life, such as sealants and coatings. Their preparation largely relies on the hydrosilylation of alkenes, a process requiring catalysts containing precious metals, like platinum.

The rapidly growing demand for silicone and the scarcity of precious metals present a challenge twice over. To overcome these obstacles, a team led by Hideo Nagashima has found an efficient, inexpensive, and, mostly importantly, practical solution based on non-precious metal catalysts (DOI: [10.1021/jacs.5b11311](https://doi.org/10.1021/jacs.5b11311)). The researchers develop two catalytic systems containing iron or cobalt pivalate and 1-adamantyl isocyanide for efficient and selective hydrosilylation of a broad range of substrates. They further demonstrate chemical modification and cross-linking of silicones, common transformations of significant industrial interest.

Unlike previously reported catalysts, these systems use hydrosiloxanes instead of hydrosilanes as coupling partners, considerably expanding the scope of functional organosilicon materials. Because they are stable and easy to handle, the new low-cost alternative catalysts hold vast potential to replace their platinum-based counterparts in both laboratory and industry applications of organosilicon compound synthesis.

Xin Su, Ph.D.

■ DISCERNING MECHANISMS OF NON-ENZYMATIC BIOSYNTHESIS

The biosynthesis of most natural products relies on enzymatic reactions, but non-enzymatic transformations—reactions independent of proteins—can play an important role as well. This is especially true for discoipyrroles A–D, a family of marine bacterial natural products with *in vitro* anticancer activity, that are assembled enzyme-independently from metabolite building blocks.

To elucidate the mechanism of this non-enzymatic formation of discoipyrroles, John MacMillan and Dominic Colosimo *in situ* monitor a model system with isotope-labeled starting materials using several advanced two-dimensional nuclear magnetic resonance (2D NMR) spectroscopies (DOI: [10.1021/jacs.5b13320](https://doi.org/10.1021/jacs.5b13320)). With the aid of various analytical techniques, the researchers identify a highly concerted three-component oxidative coupling process mediated by ambient oxygen.

This work demonstrates that isotopically enhanced 2D NMR spectroscopy is a straightforward and powerful tool for mechanistic studies in complex reaction systems. The results provide new and valuable insights into the largely unexplored aspects of non-enzymatic biosynthesis and can guide the optimization of total synthesis as well as the screening of bacterial libraries for similar natural products.

Xin Su, Ph.D.

■ FILLING THE KNOWLEDGE GAPS WHERE GRAPHENE INTERSECTS WITH BIOLOGY

Graphene—a single layer of carbon atoms arranged like honeycomb hexagons—has been extensively studied for its unique physical, mechanical, electrical, and chemical properties. In this Perspective, Yang Luo and colleagues discuss current research into how graphene and its oxides interact with biological systems, with potential for future antimicrobial applications (DOI: [10.1021/jacs.5b11411](https://doi.org/10.1021/jacs.5b11411)).

Despite a wealth of studies, exactly how these materials affect and often kill bacterial and mammalian cells remains controversial. The authors examine the predominant theories, including the importance of graphene's sharp edges, oxidative chemical interactions, and wrapping and trapping. By combing through sometimes contradictory results, they clarify evidence for each mechanism and point to areas where additional efforts to understand bio–graphene interactions should focus. The researchers call for systematic studies that control for size, shape, layer number, defects, oxidation, environment, and synthesis technique. Whether graphene can selectively kill pathogens while remaining nontoxic to mammalian cells has not yet been determined, the authors note. They suggest that future investigations should expand the range of microbes and materials studied as well as explore differences between normal and abnormal cells.

This work is a timely examination of research into graphene–microbe interactions. The authors tie together seemingly disparate results to relate materials' physical and chemical properties with biological effects and identify areas of need for future work.

Jenny Morber, Ph.D.

■ DOUBLE-SWITCHING DNA

The DNA double helix is one of the most iconic structures in science, but it is not the only shape DNA can take. DNA can also form a series of complex globular structures known as quadruplexes, which form via the stacking of four guanine bases in guanine-rich sequences. Scientists analyze structurally distinct quadruplexes so they can better understand their biological roles and manipulate them for nanotechnology applications.

Jean-Louis Mergny and colleagues now show that, under specific conditions, quadruplexes can act as double switches, taking on different structures sequentially (DOI: [10.1021/jacs.5b13130](https://doi.org/10.1021/jacs.5b13130)). The investigators demonstrate that when a quadruplex in a sodium-rich solution is treated with small amounts of potassium ion, its structure switches from an antiparallel to a parallel formation within seconds to minutes. Then, in the presence of potassium or strontium at low concentrations, the quadruplex turns to a different antiparallel structure, followed by a second switch into a parallel fold.

The authors say, “DNA systems are biological relevant targets, can be used in nanotechnology applications, and are

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valuable methodological tools for understanding DNA quadruplex folding, notably at low cation concentrations. We demonstrate that this behavior is not restricted to a narrow set of sequences but can also be found for other G-quadruplex-forming motifs, arguing for widespread applications.”

Rajendrani Mukhopadhyay, Ph.D.

■ GOING WITH THE FLOW: LIQUID–LIQUID PHASE TRANSITION IN SILICON CARBIDE

Like water, liquid silicon displays polyamorphism, a quality characterized by discontinuous structural changes. In particular, liquid silicon can undergo a liquid–liquid phase transition (LLPT) when it is supercooled, leading this amorphous material to transition from a high-density liquid to a low-density one based on structural changes that alter bonding characteristics. Although carbon has also been suggested to undergo a LLPT, its existence has not yet been proven.

In a new study, Hui Li and co-workers investigate the potential of a LLPT in a material that combines these two elements, liquid silicon carbide (SiC) (DOI: [10.1021/jacs.5b13467](https://doi.org/10.1021/jacs.5b13467)). Using molecular dynamics simulations, the researchers test the response of this material when it is confined inside various nanosized slits at different pressures. By adjusting the size and pressure parameters, they observe the SiC transition from a bilayer liquid into a trilayer one, evidence of a LLPT.

Further investigation shows that the distribution of Si and C atoms bonded to four or five neighboring atoms changes dramatically during this layering transition, causing this effect. Additional results suggest that, under high pressures, SiC's LLPT is mainly confinement-induced, but it is mainly pressure-induced under low pressures. The authors propose that these findings could guide the fabrication of 2D SiC, a promising material for electronic and other applications.

Christen Brownlee

■ COMPLEX DITERPENOID CRACKED WITH INGENIOUS CASCADE COUPLING

Chromodorolides A–E belong to a class of marine natural products isolated from sea slugs, and the molecules possess various intriguing bioactivities. These structurally complex natural products are rearranged diterpenoids from marine sponges. With 10 contiguous stereocenters, they represent a daunting total synthesis target.

Now, a team led by Larry Overman has tackled this challenge, accomplishing the total synthesis of (–)-chromodorolides B in 21 steps, the first breakthrough in this class of diterpenoids (DOI: [10.1021/jacs.6b00541](https://doi.org/10.1021/jacs.6b00541)). The elegance of their synthetic route lies in an unprecedented photoredox-catalyzed cascade consisting of intermolecular radical conjugate addition, cyclization, and fragmentation, making two carbon–carbon bonds and three stereocenters all at once.

The fused ring systems found in chromodorolides are also widely present in other rearranged spongian diterpenoids, so the reported method, especially the radical cascade, provides a useful toolbox for their total syntheses. Further understanding of cascade coupling may lead to convenient synthetic access to complex stereochemical scaffolds in both natural products and medicinal chemistry.

Xin Su, Ph.D.