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Spotlights on Recent *JACS* Publications

ONE "LIGHT" MOVE, TWO GAINS

Dehydrogenative cross-coupling is a highly desirable synthetic approach toward C−C bond formation, as it does not require additional functionalization of subcomponents. Reactions of this type often involve the use of stoichiometric sacrificial oxidants, which leads to low atom economy, and possible generation of toxic wastes.

Now Li-Zhu Wu and co-workers develop a catalytic system for cross-coupling reactions by taking advantage of visible light as a clean energy input (DOI: 10.1021/ja408486v). It not only avoids using any sacrificial oxidants, but also yields hydrogen gas, a useful energy resource, as the sole byproduct. This strategy relies on catalytic amounts of a photosensitizer and a ruthenium-based catalyst on graphene, and uses water as solvent. Its efficacy is demonstrated by the excellent yields of coupling reactions between a variety of isoquinoline and indole substrates.

This novel reaction, namely cross-coupling hydrogen evolution, offers a potential solution for highly efficient, clean, and atom-economic C−C bond formation. Hydrogen generation becomes a great added value once it is employed in mass production of chemicals. This work may also inspire the development of alternative methods for practical hydrogen evolution.

Xin Su, Ph.D.

FOLLOWING PROTEIN MOVES WITH LOW MAGNETIC FIELDS

The ability to generate very strong magnetic fields has allowed scientists to generate high-quality nuclear magnetic resonance spectroscopy data on large molecules, such as proteins, with enhanced sensitivity and resolution. However, such experiments yield dynamic information within only a narrow range of frequencies, preventing scientists from fully understanding how protein dynamics influence function. Now, Fabien Ferrage and colleagues have measured protein movements that are accessible only at lower magnetic fields, but with all the benefits of high-field spectrometry (DOI: 10.1021/ja409820g).

To obtain this unprecedented dynamic insight, the researchers develop a custom probe for use in a 600 MHz NMR spectrometer. The magnetic field felt by a sample is highly dependent on the sample's location within the spectrometer above the magnet. Ferrage's probe, with a burst of air, can shuttle a sample up and down within the probe, covering 50 cm, moving it from a magnetic field of 14.1 to 0.5 T and back, all within about 150 ms. The system allows researchers to enjoy the increased sensitivity and resolution of high-field magnetic spectroscopy, while also exploring a protein's dynamic range at previously inaccessible time scales.

The researchers test their approach on ubiquitin, which has the flexibility to bind with a variety of partners, and map its ^{15}N relaxation at multiple magnetic fields. They find extensive nanosecond motions within ubiquitin that may be important to the protein's function.

Erika Gebel Berg, Ph.D.

UNIVERSAL DNA TEMPLATE FOR SMALL MOLECULE SCREENING

Xiaoyu Li and colleagues report a new way to streamline the screening of large libraries of compounds for drug discovery using a universal DNA template (DOI: 10.1021/ja409936r).

To screen small molecules for drug discovery with high throughput, researchers often use DNA-encoded chemical libraries. In such libraries, DNA sequences are conjugated to compounds and used as tags to identify, amplify, and select them. For example, a lead candidate for treating chronic obstructive pulmonary disease was recently identified using the method. But this approach usually requires generating a unique DNA template sequence for each of the screened compounds, which can number in the millions.

Now Li and co-workers offer a more efficient way to generate these libraries by using a single DNA template. It directs reactions to prepare entire DNA-encoded libraries from reagent DNAs. This universal template relies on deoxyinosine, a base that can pair with any of the four canonical nucleobases. The method could help accelerate drug discovery against a variety of biological targets.

Deirdre Lockwood, Ph.D.

NEW OLIGO PROBES ARE FIT TO BE BRIGHT

Fluorogenic nucleic acid probes, key to hybridization-based fluorescence microscopic RNA imaging, typically include both a fluorophore and quencher. The two make the probes highly responsive—off when single-stranded, on in a duplex—but not terribly bright, limiting their use in rapid add-and-record experiments. Now Oliver Seitz and colleagues report a probe design that is both responsive and bright enough to be used without washing (DOI: 10.1021/ja410674h).

The team has developed quencher-free DNA forced intercalation (FIT) probes containing the intercalating dye, thiazole orange (TO), and/or its oxazolopyridine analogue, JO. These probes fluoresce only in nucleic acid duplexes, where they intercalate between base pairs. Probes containing two TO moieties are very responsive but are relatively dim; probes containing one JO moiety are bright but have low responsiveness. But probes containing both dyes exhibit high brightness and high quantum yield as TO transfers its excitation energy to the brighter JO via FRET.

The authors use the TO/JO probe to detect *oskar* mRNA in *Drosophila* ovaries by both confocal and wide-field microscopy in just 1.5 h, without laborious washing and amplification steps. "We expect that the TO/JO FIT-probes should prove useful in other RNA imaging endeavors including RNA imaging in live cells," they conclude.

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