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Spotlights on Recent *JACS* Publications

ENHANCED STABILITY OF METAL–ORGANIC POLYHEDRA ASSEMBLED IN SILICA PORES

Owing to their intriguing molecular architecture, metal–organic polyhedra (MOPs)—also known as molecular polyhedra, nanoballs, and nanocages—have attracted much attention in recent years. MOPs have numerous potential applications, ranging from biological self-assembly to adsorption and catalysis. But these applications are hindered because MOPs are prone to hydrolysis in the presence of even trace levels of water, and they tend to aggregate, which compromises their performance.

Now, researchers led by Lin-Bing Sun and Jian-Rong Li report a new method for improving the stability and dispersion of MOPs (DOI: 10.1021/jacs.6b01207). The authors synthesize metal–organic polyhedra within the cavities of a mesoporous silica framework and find that, in doing so, they are able to minimize aggregation and boost their hydrolytic stability. They also find that the silica-confined metal–organic polyhedra have greater adsorption capacity, catalytic activity, and recyclability compared with their unconfined counterparts. The new approach may pave the way for the development of MOPs for myriad applications that had previously been out of reach due to the challenges of poor stability and aggregation.

Christine Herman, Ph.D.

GREATER EFFICIENCY IN POLYKETIDE SYNTHESIS

Polyketides—biologically active and structurally complex secondary metabolites—are ubiquitous in human medicine. Their synthesis is usually accomplished through fermentation, as their de novo construction often requires a large number of redox transformations and protecting group manipulations, resulting in routes that are too lengthy to be of commercial relevance.

In this Perspective, Michael Krische and co-authors describe methodology developed in his group that reinvents the chemistry of polyketide construction (DOI: 10.1021/jacs.6b02019). They have developed processes for the direct catalytic upgrade of lower alcohols to higher alcohols in a stereo- and site-selective fashion. By taking advantage of the intrinsic reducing properties of alcohols, this method readily couples carbon–carbon bond formations with the modulation of oxidation states, merging redox reactions and C–C bond construction into a single step. Site-selectivity for primary alcohol modification streamlines or eliminates steps devoted to protection/deprotection in the functionalization of glycols or higher polyols.

The enantioselective C–H functionalization of alcohols has enabled a step-change in efficiency, as demonstrated in dramatically simplified syntheses of several iconic type I polyketides. This approach is likely to find broad application well beyond polyketide construction, given the prevalence of chiral alcohols in chemical synthesis and the ability of these methods to assemble complex carbon skeletons without using hazardous metallic reagents, discrete redox reactions, or protection/deprotection steps.

Xin Su, Ph.D.

"MOLECULAR GLUE" MAKES ENZYMES ATP-RESPONSIVE

The essence of targeted therapy is when a drug compound acts specifically at the site of disease. One way to achieve that goal is by using targeting molecules, such as antibodies. Alternatively, researchers can exploit the unique biochemical conditions in diseased tissue. Here, Takuzo Aida and colleagues describe one such approach (DOI: 10.1021/jacs.6b02664).

Aida's team has developed a series of "molecular glues", linear polymers containing both guanidinium ion (Gu^+) and boronic acid (BA) "pendants", which release their cargo in response to high levels of adenosine triphosphate (ATP)—a cellular energy molecule found in abundance in tumor tissue.

The team tests their Gu_mBA_n polymers using fluorescently labeled trypsin, a proteolytic enzyme, as a model cargo. Gu_mBA_n efficiently binds trypsin in solution, suppressing its fluorescence and enzymatic activity. Micromolar concentrations of ATP reverse those effects, restoring, for instance, the enzyme's ability to separate human cells from plastic culture dishes.

Now the authors can test their design in the presence of actual drug compounds. "As Trp/Gu_mBA_n conjugates may potentially be sensitive to ATP-rich (>100 μM) tumor tissue, *in vivo* pharmacological studies may furnish interesting results," the authors conclude.

Jeffrey M. Perkel

HANDY LITTLE CAGE EATS AND REGURGITATES CARBON MONOXIDE

Metal–organic frameworks (MOFs) are porous cage-like molecules that consist of metallic junctions and organic linkers. They are increasingly studied for applications from gas storage to drug delivery, because researchers can control the size and chemistry of their chambers.

Jeffrey Long and his team have created an iron-based MOF that preferentially adsorbs carbon monoxide (CO) at very low pressures, even in the presence of other gases, and importantly, exhales the CO back again (DOI: 10.1021/jacs.6b00248). Most previously studied materials either bind CO so weakly that other gases are also adsorbed or bind CO so strongly that adsorption is irreversible. Here, selective, reversible binding results from a unique spin state change mechanism that holds CO strongly in one state and much more weakly in another. Only a few MOFs have previously been reported to display this kind of reversible spin transition and retain porosity, and none have been able to accommodate "guests" like CO.

This material demonstrates unprecedented selectivity for CO adsorption over other gas molecues, making it useful for fuel cell technologies and in the production of ammonia, iron, steel, alcohols, polymers, and more. Additionally, because mere trace amounts of CO induce changes in the structural, electronic, and spectral properties of the MOF, the authors envision its use for chemical identification and sensing.

Jenny Morber, Ph.D.

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