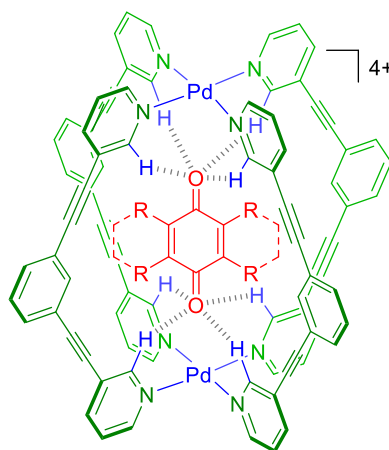


## Turning Capsule Catalysis Inside Out: Novel Approaches Utilizing Innately-Polarized Pd<sub>2</sub>L<sub>4</sub> Scaffolds

Dr. Paul J. Lusby, *University of Edinburgh, Joseph Black Building, David Brewster Road, Edinburgh, EH9 3FJ, UK* ([Paul.Lusby@ed.ac.uk](mailto:Paul.Lusby@ed.ac.uk); [www.lusby.chem.ed.ac.uk](http://www.lusby.chem.ed.ac.uk))

Substrate pre-organization remains the paradigm for bio-inspired catalytic strategies using supramolecular capsule systems. The scarcity of capsule-catalyzed annulation reactions ( $A+B\rightarrow C$ ) highlights the limitation of this approach—while co-encapsulation can give significant acceleration, product inhibition frequently halts turnover.<sup>1,2</sup> In this talk, two novel and distinct methods for realizing capsule-catalyzed annulation processes will be described, both involving the host-guest chemistry of simple Pd<sub>2</sub>L<sub>4</sub> assemblies (Figure 1).<sup>3</sup>



**Figure 1.** A Pd<sub>2</sub>L<sub>4</sub><sup>4+</sup> host-guest system.

In the first part we will show that the inhibition problems synonymous with capsule-mediated Diels-Alder (DA) reactions can be overcome by avoiding mechanisms that rely on entropic effects.<sup>1,2</sup> Instead, innately-polarized metallo-organic structures have been utilized to increase substrate reactivity using electronic activation.<sup>3</sup> This approach reveals remarkably efficient DA catalysts, combining excellent activity ( $k_{\text{cat}}/k_{\text{uncat}} > 10^3$ ) and efficient turnover (TONs  $> 10^3$ ). We will also demonstrate that cavity confinement of the transition state alters the intrinsic chemo, regio and diastereoselectivity of several DA reactions, indicating that this method retains the most appealing aspects of capsule catalysis.

In the second part we will describe an “*exo*-catalytic” approach, wherein substrates remain entirely in the bulk-phase, instead the capsule switches the behavior of a “redox co-factor” guest. This method has been used to catalyze an  $sp^3$ - $sp^2$  C–C bond cross-coupling that involves the C–H activation of one of the reaction partners.

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