that drive DNA ejection into the host are likely to be smaller than those resisting packaging, which may limit the role of pressure in DNA ejection. Berndsen et al. propose that relaxation of confined DNA may occur by a reptation-like mechanism, the time scales of which depend on the cube of genome length. If so, relaxation time scales would be even longer for bacteriophages and viruses with genomes longer than that of φ29 (e.g., λ, T4, T7, and herpes virus) (9). Because the time to complete packaging is expected to be similar for many of these systems (10), this potentially presents an even bigger challenge to their packaging motors. Interestingly, under certain conditions, T4 is also known to “unpackage” DNA (11), allowing its genome to exit the capsid in a controlled and reversible manner. It is tantalizing to speculate that this mechanism could allow the motor to “unjam” DNA.

A number of issues remain to be addressed. More precise measurements of relaxation times as a function of filling fraction will aid theoretical models of polymers, because such models often lack accurate relaxation time scales. It will also be important to connect the observed slow relaxation to the mechanism of the packaging motor and to the organization of the DNA inside the capsid. Another recent optical trap study (12) showed that the motor rotates DNA as it packages it, and that the rotation pitch changes as the capsid becomes filled. This is potentially related to the spool structure proposed for packaged DNA (13, 14). It may be possible to study the prerelaxation conformations of the packaged DNA with the help of recent advances in cryoelectron microscopy. Direct visualization of confined DNA motion by single-molecule imaging may shed additional light on the packaging process. This system illustrates how biological processes exist far from equilibrium and how their study can provide an unexpected testing ground for the underlying physical theories. ■

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CATALYSIS

Self-control tames the coupling of reactive radicals

Iridium complexes use two points of contact to control carbon-carbon bond formation

By Guy C. Lloyd-Jones and Liam T. Ball

Highly reactive or unstable chemical reagents are challenging to prepare, store, and safely handle, so chemists frequently generate them in situ from convenient precursors. In an ideal case, the rate of release of the reagent would be matched to the rate of its “capture” in the desired chemical reaction, thereby preventing the reagent from accumulating and minimizing any opportunity for decomposition. However, this synchronization is rarely achieved or even attempted: The rate of release is usually dictated by the conditions of the reaction (l), rather than being regulated by capture of the reagent. In this issue, Tellis et al. (2) on page 433 and Zuo et al. (3) on page 437 independently report the use of iridium photocatalysis (4, 5) to supply highly reactive radical coupling partners (R + ) to a nickel-catalyzed carbon-carbon bond-forming process (see the figure). Intriguingly, the two points of contact between the iridium and nickel cycles enforce autoregulated release of the radical, ensuring its efficient capture by nickel rather than its decomposition via other pathways.

Transition metal catalysts for the carbon-to-carbon coupling of complementary pairs of appropriately functionalized molecular building blocks are now a mainstay in modern organic synthesis, at least for unsaturated carbon sites (ones with double or triple bonds). Efficient coupling at saturated sites (“C sp3 ”, where the carbon has four single bonds) remains troublesome.

An important difference between these processes is that C sp3 coupling generates three-dimensional molecular architectures that are of key importance to the pharmaceutical, agrochemical, and materials industries (6).

There are three primary reasons that C sp3 reaction centers are ill-suited to coupling. First, it is the organic component transfers sluggishly to the metal catalyst. This problem precedes two more—the resulting organometallic species are frequently unstable, and also only slowly undergo the desired C-C bond formation (“reductive elimination”), exacerbating the instability problem (7). Cases of successful C sp3 couplings typically must address all three issues. The slow transfer is tackled by use of highly reactive C sp3 nucleophiles (the electron-rich component), which are inherently hard to control. The other two issues are suppressing side reactions at the metal center and accelerating the reductive elimination, which can be addressed through careful tuning of the metal catalyst (for example, altering its ligand sphere).

The reports of Tellis et al. and Zuo et al. offer an alternative and innovative solution to all three issues. The authors report high-yielding and selective formation of a new bond between an aromatic (benzenelike) ring and a C sp3 moiety (“R + ”) with an aromatic halide (“Ar-X”) coupling partner, and convenient precursor sources of the C sp3 component, in reactions that are simple to conduct and of substantial scope. At the heart of the new process is a photocatalyzed iridium complex ([Ir(III)]+) that oxidizes stable C sp3 precursors (R-Y, where Y is BF, K, CO, Cs, or H) to their corresponding organoradicals (R’), highly reactive species in which the sp3 carbon now bears an unpaired electron. The radical does not accumulate, but instead is captured by an aryl-nickel(II) complex that “awaits” its arrival. Not only does the use of an organoradical overcome the usual reluctance for formation of the

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The system is an example of an under-exploited approach in synthesis: “autoregulated release” of reactive intermediates by synchronization of multiple catalytic cycles, a phenomenon that is ubiquitous in biochemistry. This analysis also shows that, by modulating the relative concentrations of the two catalysts and by judicious choice of their initial point of entry into the system, the distribution of catalytic intermediates can be constrained to be predominantly in one or the other hemisphere of a cycle. This manipulation of the location of the so-called “catalyst resting state” provides wide-ranging opportunities for the development of novel catalyst systems for synthesis and for the installation of new modes of selectivity into ones already known (9).

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