## research highlights

### SYNTHETIC METHODS Olefin couplings

J.Am. Chem. Soc. 136, 1304-1307 (2014)



The presence of an olefin in a molecule opens up an almost bewildering array of potential transformations, ranging from simple addition reactions to more complex cross-metathesis protocols and cycloadditions. One particularly useful strategy is functionalization through a radical intermediate. In this way, unactivated olefins are converted into reactive radicals that subsequently combine with an appropriate acceptor. This approach has enabled functional groups such as halides, pseudo-halides and hydroxyl groups to be selectively introduced into unactivated olefins.

While working on the formation of the carbon framework of terpenes, Phil Baran and co-workers from the Scripps Research Institute in La Jolla hit upon a disconnection requiring the intramolecular coupling of an unactivated olefin with an enone. Inspired by previous work in the area, they examined the application of iron catalysts in the presence of a reducing agent (sodium borohydride) for the reductive coupling of these groups. After optimization of the reaction conditions, it was found that a simple iron(III) acetylacetonate complex combined with a much milder reducing agent (phenyl silane) not only resulted in excellent cyclization yields but also eliminated side reactions and left other functional groups intact. Intermolecular couplings could also be performed using this strategy and a range of electron-poor olefins — not just enones — could be used as the acceptors. Furthermore, with suitably arranged starting materials, these coupling reactions can be used to make cyclopropane derivatives.

The proposed reaction mechanism involves the generation of a tertiary radical on the unactivated double bond via an iron hydride species. This radical adds to the electron-poor olefin and the resulting intermediate re-oxidizes the iron catalyst; protonation from the solvent gives the final product. The scalability of the procedure was demonstrated by carrying out the reaction on gram scales and reaction times were generally short. The reaction is insensitive to oxygen or moisture, allowing it to be carried out in the open atmosphere without pre-dried solvents. Finally, like many radical reactions, sterically hindered products can be accessed in high yields, including vicinal quaternary centres. EB

### PHOTOCATALYSIS Water is the solution

Nature Commun. 5, 3145 (2014)

Biocatalysts show high selectivity and this is music to the ears of organic chemists. The higher the selectivity of a reaction,

Science 343, 61-65 (2014)

#### AZIRIDINE SYNTHESIS

# Protection not included

Nitrogen-containing functional groups are prevalent in natural products and biologically active compounds. The incorporation of nitrogen into a molecule during chemical synthesis is not always straightforward, but aziridines offer a potentially attractive route to this end. Their strained three-membered-ring structure and susceptibility to stereo- and regioselective chemistry makes aziridines very useful as intermediates in synthetic strategies. It is this reactivity, however, that also dictates the use of a nitrogen-protecting group during conventional aziridination procedures, which can subsequently lead to unwanted side reactions during deprotection steps.

A direct synthesis of aziridine products without the need for the nitrogen atom to be protected would, therefore, result in shorter and simpler synthetic approaches for nitrogen incorporation. Now, a team of researchers led by László Kürti and John Falck at the University of Texas Southwestern Medical Center and Daniel Ess at Brigham Young University in Utah have developed a simple, chemoselective and stereospecific procedure for the catalytic aziridination of olefins without N-protection. In the key step of the reaction, quantum mechanical



calculations have predicted that a rhodium nitrene electrophile is formed from the reaction of a O-(2,4-dinitrophenyl)hydroxylamine aminating agent with a homogeneous rhodium catalyst in trifluoroethanol. Using this intermediate, the stereospecific N-H aziridination of a diverse range of mono, -diand tri- substituted olefins, and di, -tri- and tetra-substituted styrenes was demonstrated. These transformations were all achieved in good yields under ambient conditions without the need for external oxidants. Alternatively, by using an N-alkylated nitrogen source, the stereospecific N-Me aziridination of di- and tri- substituted olefins and styrenes could be also be achieved in good yields under mild conditions. As a further demonstration of the utility of this strategy, a selection of the resulting aziridines were subjected to regioselective ring-opening reactions to give pharmaceutically active target amines — such as methoxy- and azido-amines — in excellent yields.