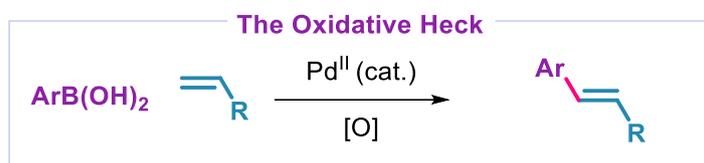
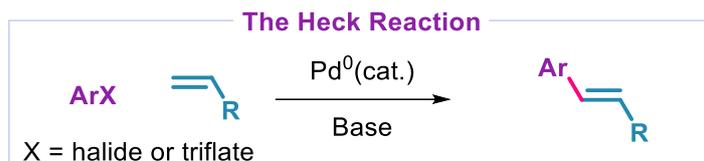


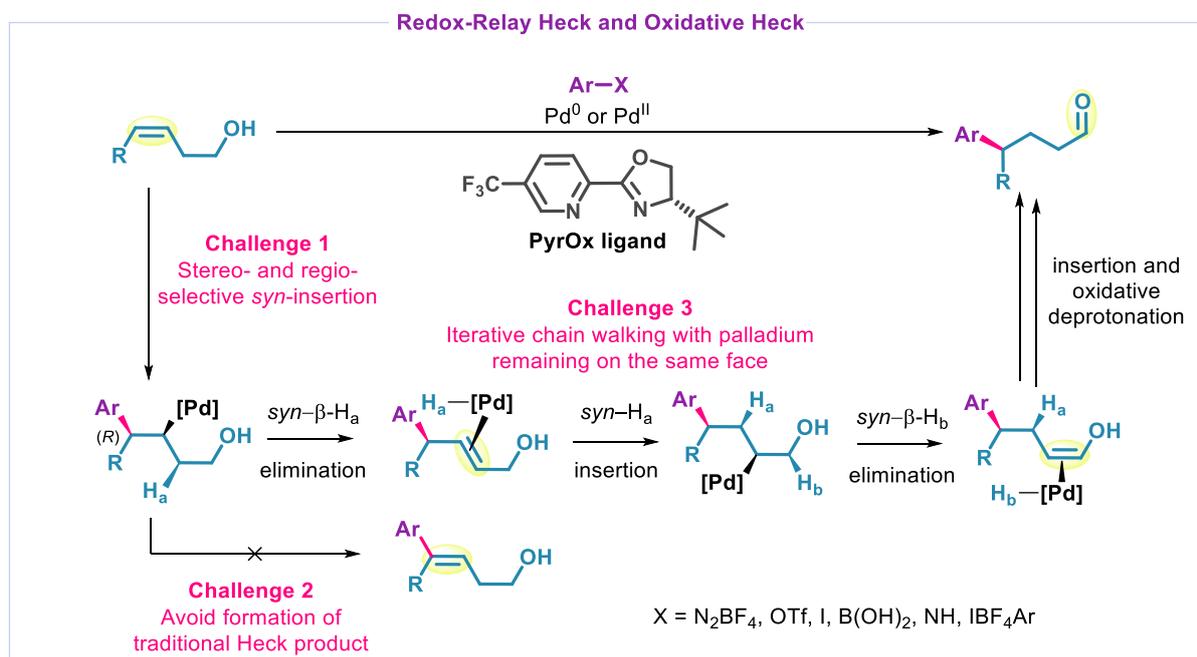
[O] What the Heck?!

Author: Dr Holly Bonfield

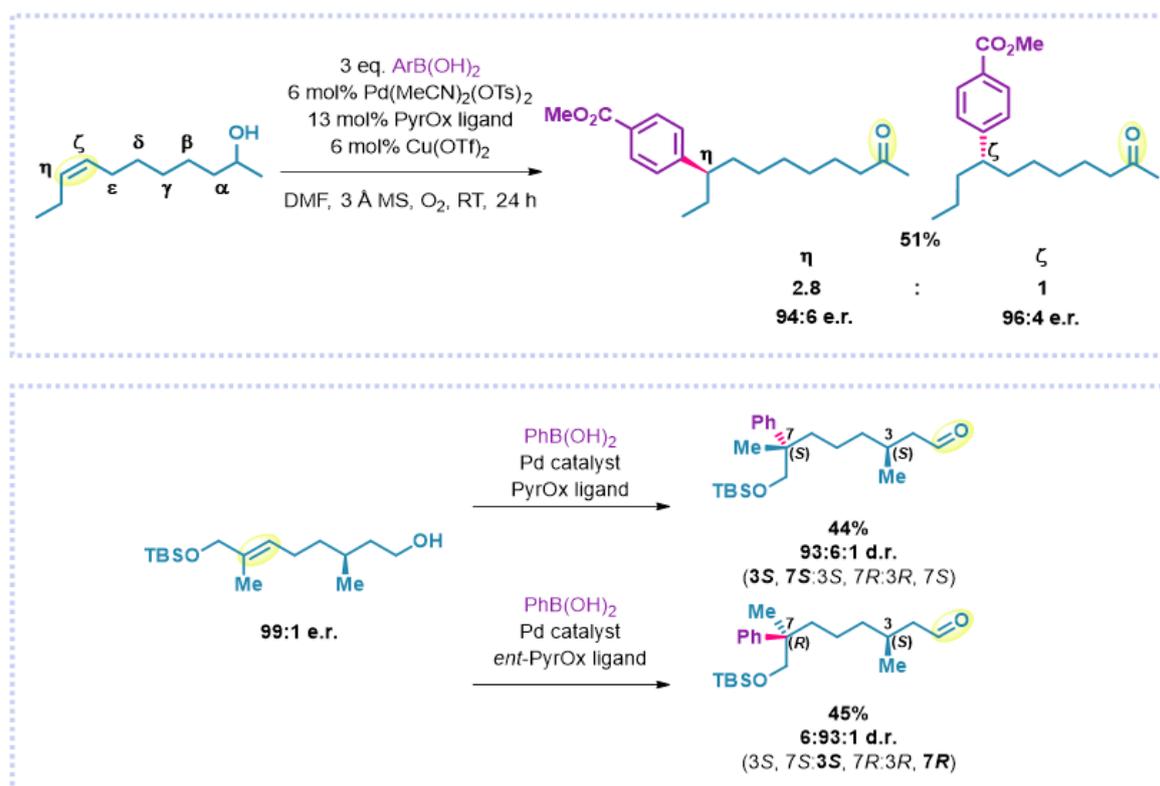
The Heck or Mizoroki-Heck reaction takes an alkene and an aryl halide or triflate, and, in the presence of palladium (0) and base, forms a more substituted alkene product. Since the initial publications on this reaction in 1971-72, many variants have also been reported. One example is the oxidative Heck. Here, an aryl boronic acid replaces the more traditional aryl halide or triflate. This requires the use of a palladium (II) catalyst and oxidant but forms similar types of products.



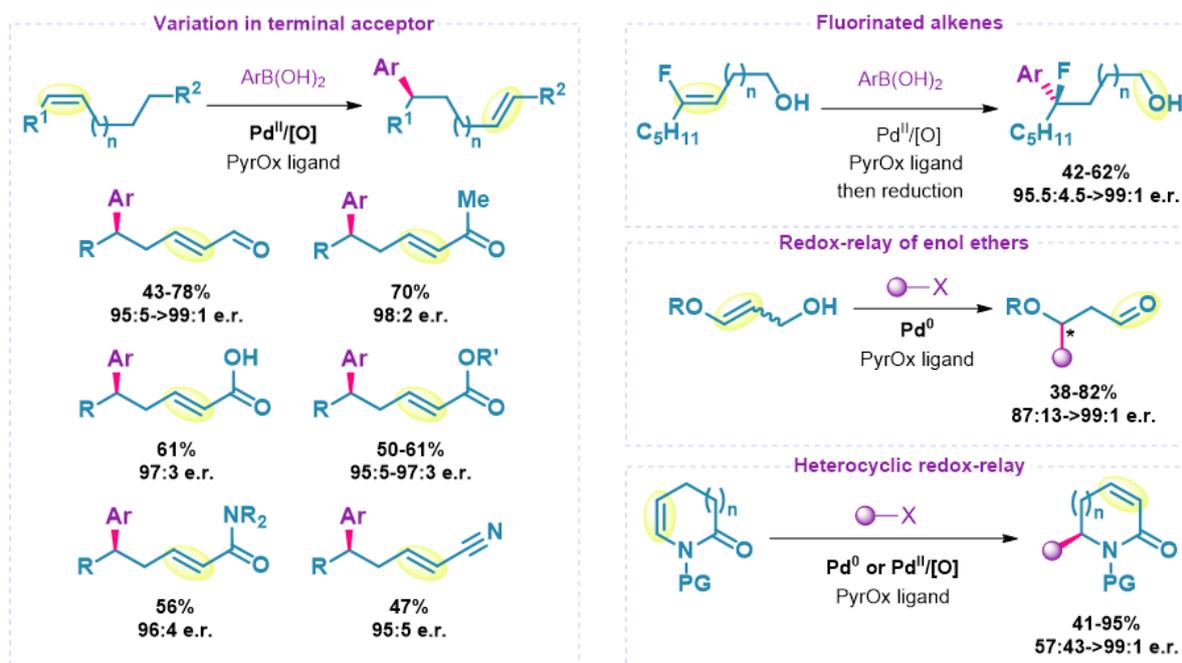
A more recent development in this area is the redox-relay Heck and oxidative Heck reaction, pioneered by Sigman and co-workers.¹ Here, reaction of an acyclic alkenol substrate leads to formation of an aldehyde containing a remotely located stereocentre, which is obtained in high enantioselectivity through use of a chiral PyrOx ligand. The palladium catalyst initially inserts into the alkene, analogous to a standard Heck reaction, but instead of eliminating, to form the traditional Heck product, a site selective *syn*- β -hydride elimination occurs. This reforms the alkene, but the alkene is now repositioned one carbon closer to the alcohol. A subsequent series of *syn*-migratory insertion/*syn*- β -hydride elimination steps, referred to as the *relay*, ultimately leads to the desired aldehyde product, with the alcohol acting as a terminal acceptor for the process. It was later shown that a secondary alcohol can also be used, generating the corresponding ketone.



It has since been shown that this migration can occur over long distances,² and through pre-existing stereocentres,³ delivering the desired products in high diastereoselectivity, with the particular diastereomer dictated by the enantiomer of ligand used.



Other terminal acceptors, beyond a primary or secondary alcohol, can be successfully used in the transformation, delivering the corresponding alpha, beta-unsaturated products.¹ Reaction success has also been reported with fluorinated alkenes, and the redox-relay can also be performed on enol ethers. In 2018, Sigman and co-workers reported the first example on a heterocyclic substrate, focusing on lactams.



1. H. E. Bonfield, D. Valette, D. M. Lindsay, M. Reid *Chem Eur. J.* **2021**, *27*, 158.
2. T.-S. Mei, E. W. Werner, A. J. Burckle, M. S. Sigman, *J. Am. Chem. Soc.* **2013**, *135*, 6830.
3. T.-S. Mei, H. H. Patel, M. S. Sigman, *Nature* **2014**, *508*, 340.