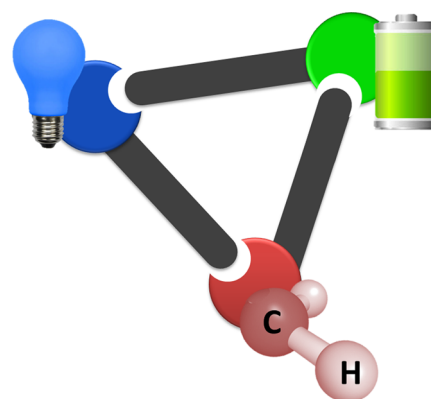


A Triple Crown of Sustainable Synthesis

Having just returned from a thoroughly enjoyable visit to Churchill Downs to watch the Kentucky Derby, I'm reminded of the optimism and interest every year at the prospects of the winning horse going on to take the Triple Crown. We gravitate to seeing patterns in threes, from book and movie trilogies to sets of lucky or unlucky occurrences to the dreaded third reviewer. You can even look it up on Wikipedia, where the so-called "rule of three" is "a writing principle that suggests that things that come in threes are funnier, more satisfying, or more effective than other numbers of things (or *omne trium perfectum* if you are more fluent in Latin than I am).¹

On the heels of our recent Outlook from Steve Ley's laboratory on new enabling technologies for synthesis,² particularly flow chemistry, this month's issue of *ACS Central Science* features its own Triple Crown of Outlooks centered on three forward-looking challenges and opportunities in synthesis from the view of sustainability: C–H functionalization, photocatalysis, and electrosynthesis. There is no doubt that we as a community have barely scratched the surface of chemical space and what is possible to make, but it is just as important that we push ourselves to pay attention to the limited elemental resources we have on our planet and make the molecules and materials we want and need for society in the most efficient, sustainable, and energy-conscious manner possible.

Against this backdrop, Hartwig and Larsen summarize recent advances and future prospects in C–H functionalization.³ Many times referred to by my more synthetic colleagues as the "unfunctional" group, hydrocarbons represent our most abundant source of organic feedstocks, and the selective transformation of C–H bonds to other functionalities offers a direct way to upgrade those feedstocks in a single step. Metal-based catalysis, particularly the use of coordination chemistry to achieve directed C–H functionalization, has been met with most success, but a growing set of traceless or even undirected C–H functionalizations promises to uncover new strategies for molecule construction. The other two Outlooks feature methods for synthesis that focus on sustainable energy input. Levin, Kim, and Toste write on the use of photoredox catalysis for transition metal mediated cross-coupling reactions, where solar energy can be harnessed to create flexible odd-electron



intermediates from excited-state reagents that are both stronger oxidants and reductants than their ground-state counterparts.⁴ The authors draw parallels from odd-electron organometallic reagents to provide a set of design principles for activating two-electron chemistry from elementary single-electron transfers. Finally, Horn, Rosen, and Baran outline electrochemistry as another emerging area for sustainable synthesis with a long and storied history that in the current age offers new opportunities to forego harsh, toxic, and often unselective reagents and replace them with electrodes that can achieve a highly specific and programmable redox bias.⁵ The authors highlight the utility of this synthetic approach in the context of synthesis of complex molecular architectures. Both photochemistry and electrochemistry offer approaches that are highly scalable, environmentally friendly, and tolerant of many functional groups.

We hope that you agree that these papers provide three keen visions for the continued growth in bond-making and bond-breaking reactions at carbon with sustainable feedstocks and reagents, each providing unique insight and guidance to their further advances in development and practice. We are eager to continue to provide these multi-pronged sets of Outlooks as a service to the community, so let us know if you have a good idea or three.

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Notes

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