SYNLETT Best Paper Award 2019: Electrochemical C(sp³)–H Fluorination

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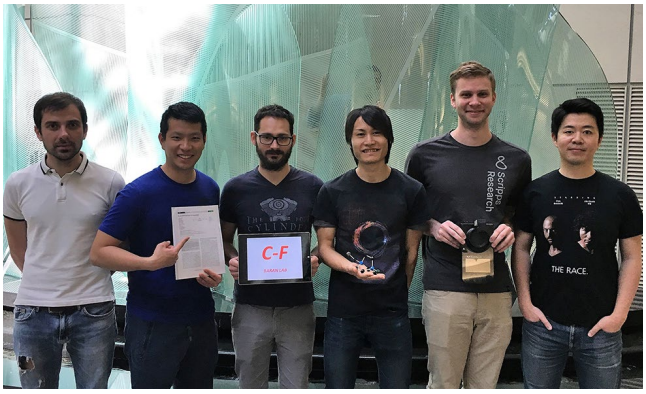
Background. Thieme Chemistry and the Editors of SYNTHESIS and SYNLETT present the 'SYNTHESIS/SYNLETT Best Paper Awards'. These annual awards honor the authors of the best original research papers in each of the journals, considering their immediate impact on the field of chemical synthesis.

Professor Phil S. Baran and co-workers from The Scripps Research Institute, USA, as well as from industrial companies in Ukraine, China and Japan, are the recipients of the SYNLETT Best Paper Award 2019. The authors are recognized for their stereospecific approach to alkylamines. Benjamin List, Editor-in-Chief of SYNLETT, noted: "This is a truly outstanding paper in which the authors apply electrochemistry as a rising technology to activate aliphatic C–H bonds, delivering highly important fluorinated molecules. In addition, the method is scalable, has a very large scope, and can be applied to late-stage functionalizations of pharmaceuticals and natural products. Awesome work!"

SYNFORM spoke with Professor Phil S. Baran, who was happy to share some background information regarding the prize-winning paper as well as current research activities ongoing in his group.



Left to right: Pavel Mykhailiuk, Hugh Nakamura, Byron K. Peters, Yu Kawamata, Solomon H. Reisberg, and Yusuke Takahira

Biographical Sketch

Phil S. Baran is a Professor in the Department of Chemistry at Scripps Research (USA). He completed his undergraduate education at New York University (USA) in 1997. After earning his Ph.D. at The Scripps Research Institute (TSRI) in 2001, he pursued postdoctoral studies at Harvard University (USA) until 2003, at which point he returned to TSRI to begin his independent career. He is currently the Darlene Shiley Professor of Chemistry. The mission of his laboratory is to educate students at the intersection of fundamental organic chemistry and translational science.

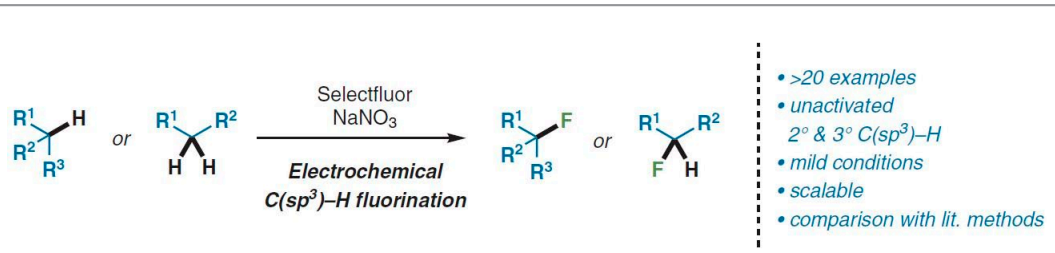
INTERVIEW

SYNFORM *Could you highlight the value of your award-winning paper with respect to the state-of-the-art, as well as the potential or actual applications?*

Prof. P. S. Baran Achieving site-selective exchange of a C–H bond for a C–F bond has value for those interested in making biologically active substances (for medicinal or agricultural uses for example). This is because such perturbations will often block those sites for metabolism or alter the physical and electronic properties of a substrate in a desirable way. One can envisage that this method for C–H fluorination could have utility in many subfields of chemistry and at small or large scales (Scheme 1).

SYNFORM *Can you explain the origin, motivations and strategy used for conducting the award-winning research?*

Prof. P. S. Baran This problem was initially brought to our attention by our collaborators (co-authors) at Eisai when they were experiencing difficulties in executing photochemical and chemical strategies for C–H fluorination. We simply wanted to see if electrochemical means for achieving such a transformation would be beneficial in certain contexts. It turns out that there are many cases, either in a medicinal or process setting, where this electrochemically driven radical process holds tangible advantages over the state-of-the-art.



Scheme 1

SYNFORM *What is the focus of your current research activity, both related to the award paper and in general?*

Prof. P. S. Baran Our lab is always interested in making complex things attainable more simply. It can be in the context of natural products (which more than half the lab continues to focus on) or unanswered challenges in medicinal/process chemistry (which we love exploring in collaboration with industrial colleagues). We are agnostic to the approach used to solve such problems and in this case electrochemistry seemed to be an underexplored avenue for C–H fluorination and one that has actual pragmatic benefits.

SYNFORM *What do you think about the modern role, major challenges and prospects of organic chemistry?*

Prof. P. S. Baran Organic chemistry has as bright of a future as it did several decades ago. Many new technologies emerge and some consistently believe that one of them will somehow diminish interest in this core area of the life sciences. Those predictions have so far been shown to be wrong. The number and quality of young scientists captivated by this field has not gone down over the past few decades. The desire of industry to hire such students has only increased. This trend will probably continue for years to come because organic chemistry is indelibly tied to human creativity and imagination. One can create, be artistic, explore, and the product of those efforts can often have direct and rapid impact in so many fields. The major challenge of organic chemistry, indeed its charm and appeal, continues unchanged: to access targets more quickly and more simply and to do so directly without waste. Aiming for ideality is fun because such an aspirational goal requires the invention of new strategies and methods.

SYNFORM *What does this award mean to you/your group?*

Prof. P. S. Baran We are humbled and honored to receive this recognition and the funds are being used to support our weekly group meetings, the slides of which can be found online.