Converging Trends Brings Organic Electrochemistry To The Front Line Of Drug Discovery

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In a case of "back to the future", chemists at Scripps collaborating with instrument engineers at IKA have unveiled a powerful tool for electrifying chemistry to achieve complex reactions. The ElectraSyn is expected to change approaches to 3D-molecules, late-stage derivatization, and focused library construction, while promoting environmentally conscious chemistry. The teaser graphic here is from Ref. 5 in the text that follows.

The tableau was reminiscent of a Steve Jobs presentation. Phil Baran unveiled the iPad's conceptual equivalent for organic electrosynthesis. Déjà vu: the renaissance of a venerable technique, dating to the harnessed primal sparks in a tangle of wires at the hands of Faraday. It is now embodied into a sleek, standardized and almost hand-held smart reactor called the ElectraSyn 2.0, launched by IKA in close association with Baran (Refs.1,2), and well documented on YouTube for all to see in the recent ACS Fall national meeting keynote presentation: "Your Chemistry has Potential".

The significance of this development to the course of drug discovery becomes evident upon examination of the trends that converged in its development. Drug hunters have been laboring to: a) stake out new chemical real estate with more complex, 3D chemical structures via novel annulations yielding exocyclic or macrocyclic hybrid structures; b) achieve late-stage functionalization in parallel microsyntheses, including hard to implement C-H reactions; c) capitalize on microfluidic systems for continuous flow synthesis and purification, including up to kilogram scales for key fragments; and d) lower the impurity and environmental waste product burdens by resorting to heavy metal-free, greener chemistry.

To quote from Baran's summarizing conclusions, "electrochemical methods possess many benefits over traditional reagent-based transformations, such as high functional group tolerance, mild conditions, and innate scalability and sustainability." A teaser graphic from Baran's papers, used as introduction to this report, encapsulates the salient features of an approach for modernizing the practice of medicinal chemistry. The ElectraSyn combines them, together with the requisite miniaturized hardware and a software interface intended to accelerate the planning and execution of electrochemical syntheses.

By no means strangers to enabling drug discovery, Baran's group at Scripps continues the syndication of an international collaborative effort to make the case for electro-organic synthesis and to refine specific applications based on the ElectraSyn (Ref. 3). They have already offered up compelling studies in key publications, including a massive compilation in Chemical Reviews. These foreshadowed or coincided with the unveiling of the bench top resource (Refs. 4,5,6). Beyond Baran and the IKA mini-reactor, it is also fair to acknowledge that electrochemical applications in organic and medicinal chemistry, including new syntheses of heterocyclics, have advanced at a significant but slower pace, which will now gain acceleration (Refs. 7,8,9).

The graphic below, Figure 1A (Ref. 6), illustrates the scope of chemistry, superimposed on a historical timeline. Stay tuned for future developments.

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