Ahmad Bachir, 13/04/2022

Hayashi, K.; Griffin, J.; Harper, K. C.; Kawamata, Y.; Baran, P. S. Chemoselective (Hetero)Arene Electroreduction Enabled by Rapid Alternating Polarity.
J. Am. Chem. Soc. **2022**, jacs.2c02102. https://doi.org/10.1021/jacs.2c02102.

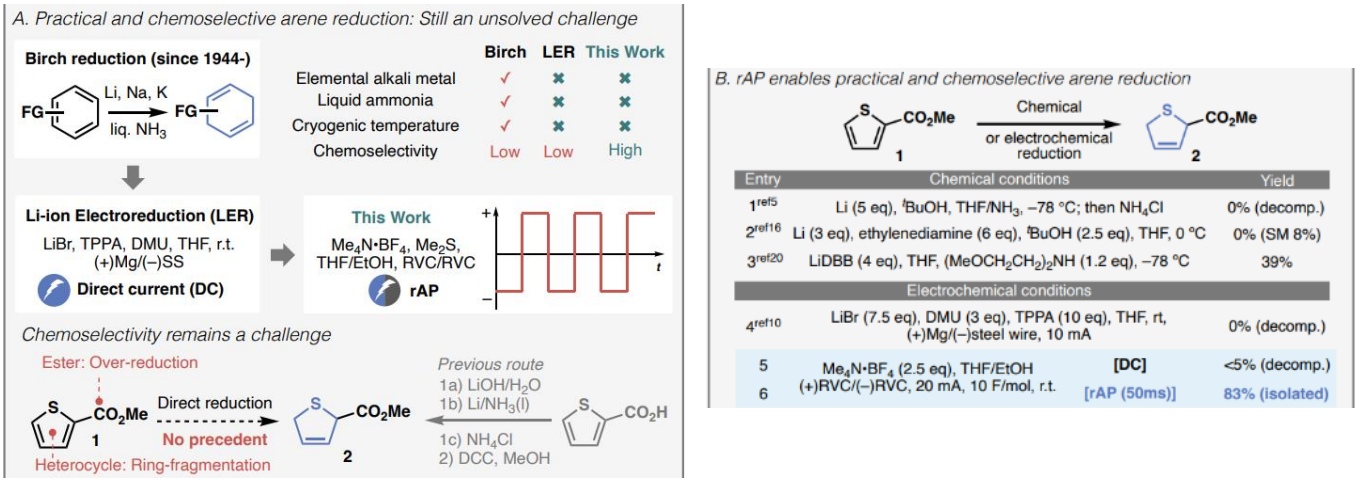

Figure 1: *A) On the left: A comparison showing the advantageous of the rAP synthetic method over previous reported methods (mainly Birch and LER),* ***B)*** *On the right: Scheme showing the yield obtained from several methods of a specific arene reduction, revealing the non-efficiency and the use of harsh conditions compared to the rAP synthetic path.*

Who are the corresponding authors and what are their research areas?

Phil S. Baran is an organic chemist, interested in recreating valuable natural products in the lab via total synthesis, and he is looking for original type reaction to achieve his goal.

What is the main claim of the article?

A demonstration of several examples of arene reduction without resorting to strong reducing agent (i.e., alkali metals) that can cause total reduction. In addition to that, they showed the possibility of scaling-up the synthesis.

How is it demonstrated?

Using rapid alternating polarity (50 ms, 10 Hz) between two electrodes, Phil Baran and co-workers were able to achieve the reduction of arenes. The reason behind this specific process is not fully understood, but they claimed that by suppressing the hydrogen ions reduction in the medium one could increase greatly the chemoselectivity toward the partially reduced desired product. By ^{1}H-NMR, they were able to provide evidence for the importance of altering the polarity rapidly by just repeating the reaction using DC method. The crude showed a significant increase with the amount of the desired product in the case of rAP over the DC one.

Figure 2: Scheme showing the IKA ElectraSyn 2.0 device dedicated for organic chemistry synthesis using electrochemistry. (https://www.ika.com/en/Products-Lab-Eq/Electrochemistry-Kit-csp-516/ElectraSyn-20-Package-cpdt-20008980/).

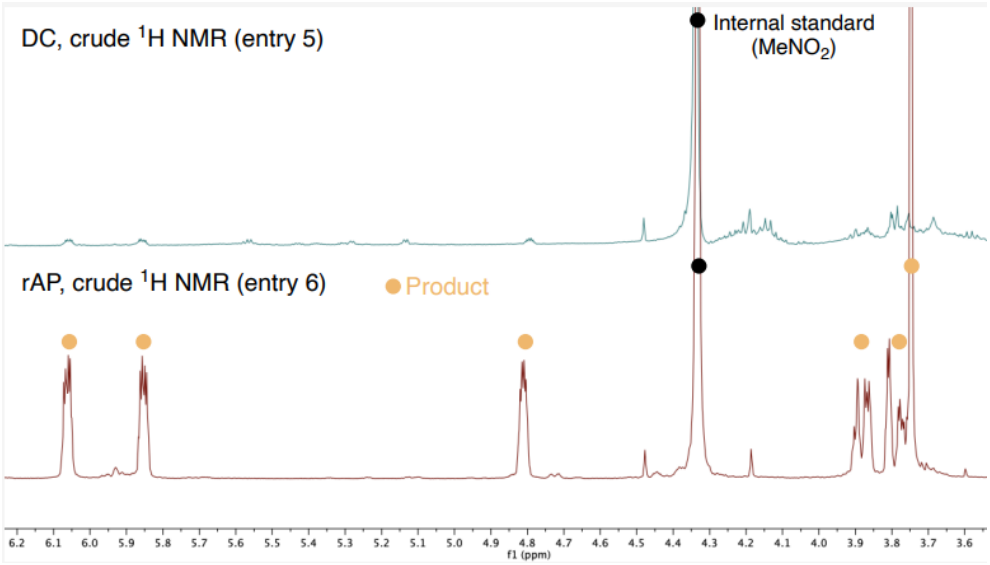

Figure 3: Scheme illustrate the difference between the crude obtained from DC method and rAP. Signals with oranges dots represent the peaks that belongs to the desired product. Using $MeNO_2$ as internal standard indicates clearly the advantageous of rAP over DC one where only trace of the desired product is observed.

What are the typical experimental conditions?

The reaction was performed at 0°C or ambient temperature in ElectraSyn reaction vial, 1 equivalent of the aromatic substrate is dissolved in 1.5 ml THF and 1.5 ml of ethanol and 2.5 equivalent of tetramethylammonium tetrafluoroborate as electrolyte followed by the addition of 3 equivalent of DMS as electron donor to avoid the oxidation of the product. Reticulated vitreous carbon (RVC) electrode is used for anode (+) and cathode (-). Reactions were performed under Argon even though not all reactions are air-sensitive but only in some cases.

Which are the key related papers?

1) Kawamata, Y.; Hayashi, K.; Carlson, E.; Shaji, S.; Waldmann, D.; Simmons, B. J.; Edwards, J. T.; Zapf, C. W.; Saito, M.; Baran, P. S. Chemoselective Electrosynthesis Using Rapid Alternating Polarity. *J. Am. Chem. Soc.* **2021**, *143* (40), 16580–16588. https://doi.org/10.1021/jacs.1c06572.

Additional comments, including additional elements of interest

Conceptual: Even though the mechanism of such chemoselectivity induced by rAP is not fully understood, the concept and the exploration in the field of organic synthesis is relatively original to what has been done in the

past. For sure, this will pave the way toward more investigations in terms of theoretical electrochemical study and new strategies of organic synthesis that might appear impossible using classical organic chemistry.

Practical: Phil Baran and co-workers showed many different examples of arene reduction with impressive high yields. Here, I enclosed only one example and intended to highlight more on the originality of their works related to arene reduction control.