TEMASEK JUNIOR COLLEGE
JC2 Preliminary Examination
Higher 3

CHEMISTRY

9813/01

Paper 1

INSERT

21 September 2021

2 hours 30 minutes

INSTRUCTIONS

This insert contains information for Question 1. **Do not write your answers on the insert**.

Information for Question 1

Organic electrosynthesis experienced an early explosion of interest, with the formation of alkanes from carboxylate salts via electrolysis, first discovered and reported by Hermann Kolbe in 1848. Over the last century, however, despite obvious environmental benefits, only a limited set of practitioners have adopted the techniques. The following are abstracts from two research papers published by Baran and co-workers on electrosynthesis.

Abstract 1 (*Nature*, 2016, 533, 77–81)

New methods and strategies for the direct functionalization of C–H bonds are beginning to reshape the field of retrosynthetic analysis, affecting the synthesis of natural products, medicines and materials. The oxidation of allylic systems has played a prominent role in this context as possibly the most widely applied C–H functionalization, owing to the utility of enones and allylic alcohols as versatile intermediates, and their prevalence in natural and unnatural materials. Allylic oxidations (shown in Fig. 1.1) have featured in hundreds of syntheses.

Despite many attempts to improve the efficiency and practicality of this transformation, most conditions still use chromium- or selenium-based reagents or catalysts such as palladium or rhodium. Currently, no scalable and sustainable solution to allylic oxidation exists. This oxidation strategy is therefore rarely used for large-scale synthetic applications, limiting the adoption of this retrosynthetic strategy by industrial scientists. Here we describe an electrochemical C–H oxidation strategy that exhibits broad substrate scope, operational simplicity and high chemoselectivity. It uses inexpensive and readily available materials, and represents a scalable allylic C–H oxidation (demonstrated on 100 grams).

Fig. 1.1 illustrates allylic oxidation of a substrate via electrochemical method using carbon electrodes. Note that all arrows drawn are ‘reaction arrows’; arrows drawn touching the electrodes imply that the reactants interacted with the electrodes. Arrows intersecting each other imply that the reactants reacted with one another.

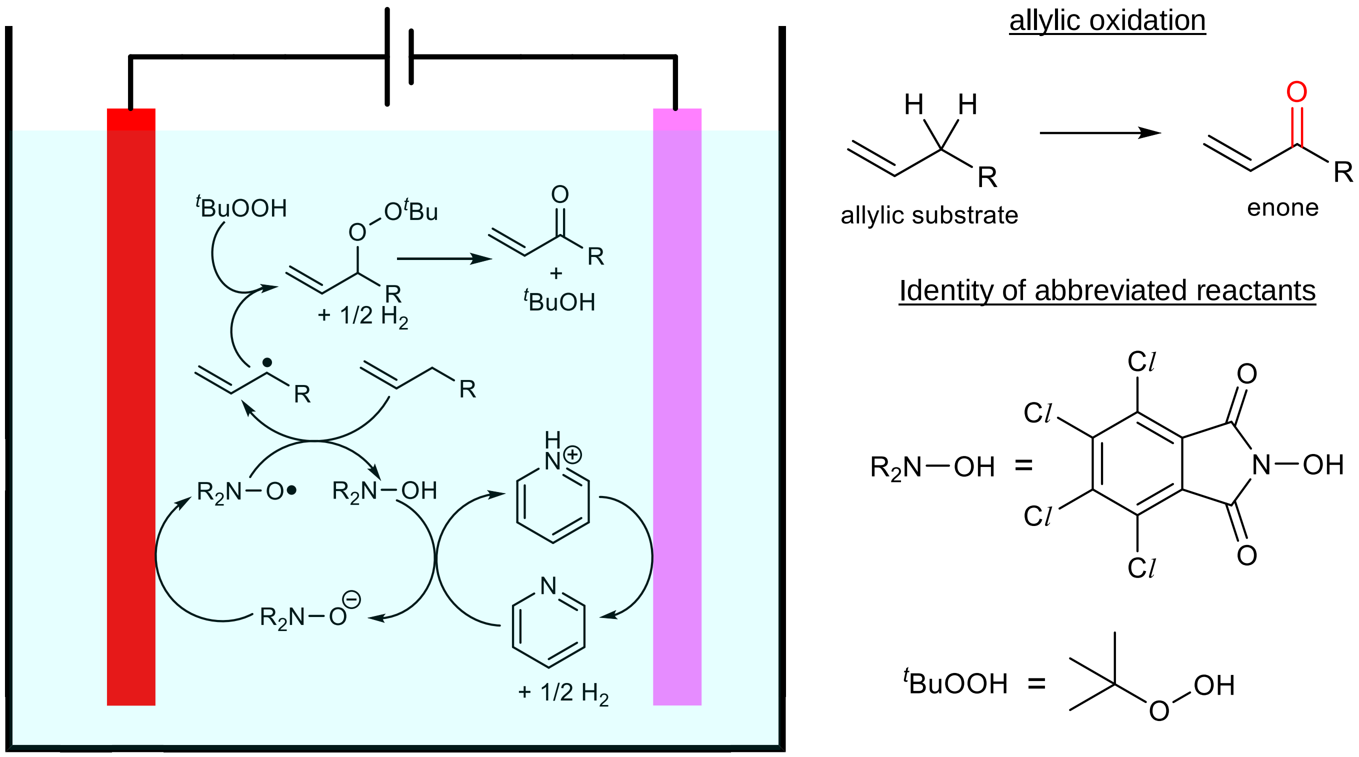
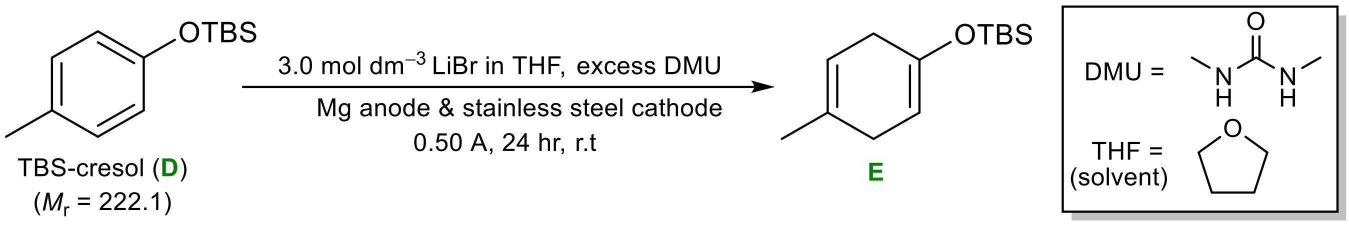


Fig. 1.1

Abstract 2 (*Science*, 2019, 363, 838–845)

Reductive electrosynthesis has faced long-standing challenges in applications to complex organic substrates at scale. Here, we show how decades of research in lithium-ion battery materials, electrolytes, and additives can serve as an inspiration for achieving practically scalable reductive electrosynthetic conditions for the Birch reduction. Specifically, we demonstrate that using a sacrificial magnesium anode, combined with a cheap and non-toxic proton source (DMU), and an overcharge protectant inspired by battery technology can allow for multigram-scale synthesis of pharmaceutically relevant building blocks. We show how these conditions have a very high level of functional-group tolerance relative to classical electrochemical and chemical dissolving-metal reductions. Finally, we demonstrate that the same electrochemical conditions can be applied to other dissolving metal–type reductive transformations.

A typical reductive electrosynthesis using 10 g TBS-cresol (**D**) as the substrate is given in the equation below alongside with the reagents and conditions. Fig. 1.2 presents the intermediate species (**D1** to **D3**) in the reduction; the two curly arrows drawn touching the cathode imply that the species interacted with it.



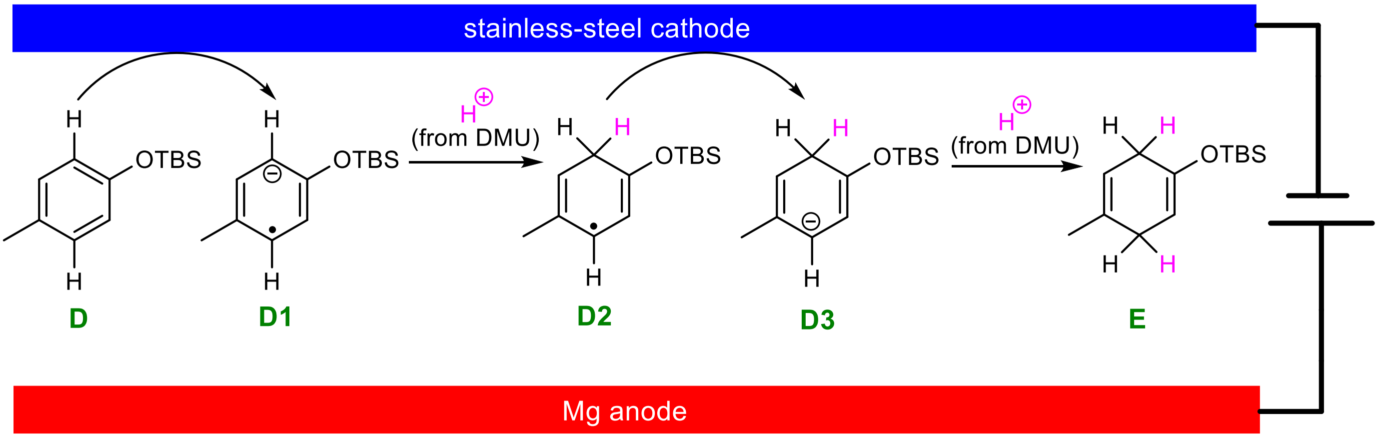


Fig. 1.2

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Copyright Acknowledgements:

Abstract 1	© Horn, J. H., Rosen, B. R., Chen, Y., Tang, J., Chen, K., Eastgate, M. D. & Baran, P. S. Scalable and sustainable electrochemical allylic C–H oxidation. *Nature*, **533**, 77–81. (2016)
Abstract 2	© Peters, B. K., Rodriguez, K. X., Reisberg, S. H., Beil, S. B., Hickey, D. P., Kawamata, Y., Collins, M., Starr, J., Chen, L., Udyavara, S., Klunder, K., Gorey, T. J., Anderson, S. L., Neurock, M., Minteer, S. D. & Baran, P. S. Scalable and safe synthetic organic electroreduction inspired by Li-ion battery chemistry. *Science*, **363**, 838–845. (2019)