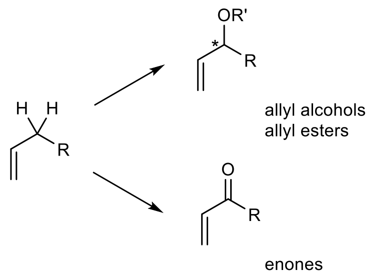
Sustainable, Fast and Safe Aerobic Allylic Oxidations of Olefins to Enones

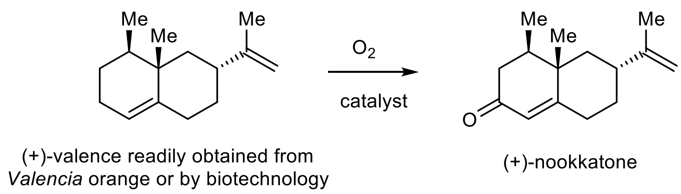
This PhD is hosted by the LGPC (Catalytic Process Engineering Laboratory – UMR 5285 (CNRS-CPE-UCBL), 3 rue V. Grignard, 69100 VILLEURBANNE under the supervision of Laurent Vanoye (lva@lgpc.cpe.fr) and Alain Favre-Réguillon (afr@lgpc.cpe.fr).

Background: New methods and strategies for the direct functionalization of C–H bonds are used extensively in synthetic organic chemistry.[1] Among them an oxidation reaction of special interest is the allylic oxidation into allyl alcohols or enones owing to their utility as versatile intermediates and their prevalence in natural and unnatural materials. The starting olefinic starting materials are readily available as cheap bulk chemicals and many interesting ones such as terpenes are available from renewable sources. The resulting oxidation products are attractive synthetic intermediates, or they may be used directly, for example, as flavor compounds or drugs.[2]

Several methods are available for the allylic oxidation of alkenes to allyl alcohols or allyl esters, and enantioselective methods have received special attention.[3] On the other hand, limited procedures are available for the direct transformation of alkenes to enones. Despite many attempts to improve the efficiency and practicality of this transformation, the majority of conditions still use stoichiometric amounts of highly toxic reagents (chromium or selenium).[4] Metal-catalyzed methods have been developed but require a large excess of *tert*-butyl hydroperoxide as oxygen source.[5] These requirements are problematic and currently, no scalable and sustainable solution to allylic oxidation into the corresponding enone exists.



For more than ten years, the LGPC has developed new experimental setup and used innovative catalysts to perform selective aerobic oxidation under safe conditions. Homogenous[6] and heterogeneous[7] metal-catalysts have been used as well as photochemistry[8] in flow with a focus on alcohols, aldehydes and alkenes oxidation. Currently the selective transformation of (+)-valence into (+)-nooktkatone, the principal fragrance of component of grapefruit aroma is being studied.



Work plan: We propose in this PhD to optimize and generalize this valuable, scalable and sustainable allylic C-H oxidation into enones. Optimization of the experimental conditions (temperature, O_2 pressure, residence time, catalyst, co-catalyst, solvent and concentration of the substrate) and kinetic modelling will be performed through the use of a lab-scale flow chemistry setup. Scope and limitations of this reaction will also be evaluated on different substrate, among them cycloalkenes, terpenes, terpenoids and steroid derivatives.

Profile: Master or equivalent degree in chemical engineering, physical chemistry or catalysis. The funding of this PhD will depend on the candidate success to obtain a 3-years Doctoral grant from the "Doctoral school of chemistry of the University of Lyon" (https://www.edchimie-lyon.fr/).

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1 *Curr. Opin. Chem. Biol.*, 2019, 49, 25-32; *Org. Biomol. Chem.*, 2019, 17, 5475-5489
2 *Synthesis*, 2013, 45, 1421-1451
3 *Nature*, 2017, 547, 196-200
4 *J. Steroids Horm.* Sci., 2016, 7, 2 1000171
5 *Green Chem.*, 2019, 21, 3629-3636
6 *Org. Lett.* 2019, 21, 10134−10138
7 *React. Chem. Eng.*, 2019, 4, 550
8 *ChemPhotoChem* 2019, 3, 122 –128