UC SANTA BARBARA

Hes·so
Haute Ecole Spécialisée de Suisse occidentale
Fachhochschule Westschweiz
University of Applied Sciences and Arts Western Switzerland

Master of Science HES-SO in Life Sciences

Oxidations and applications under green chemistry conditions

Emilie Buchs

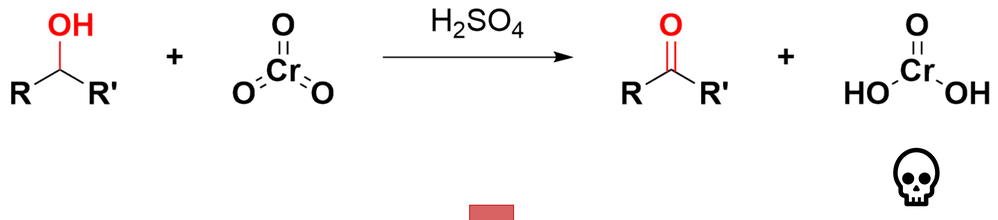
CHEMICAL DEVELOPMENT & PRODUCTION

HEIA-FR

Advisor: Prof. Dr. Ludovic Gremaud // In collaboration with **University of California, Santa Barbara** (Prof. Dr. Bruce Lipshutz)

DESCRIPTION

Alcohol oxidation constitutes a key synthetic step in various chemical industries [1]. Current methods often involve environmentally detrimental conditions, utilizing stoichiometric amounts of chromium or manganese salts and resulting in the generation of toxic wastes for a simple hydrogen transfer [2]. In this context, we address the need for a more sustainable , inexpensive and reliable method to carry out this key transformation with a particular interest for large scale application for the pharmaceutical industry.

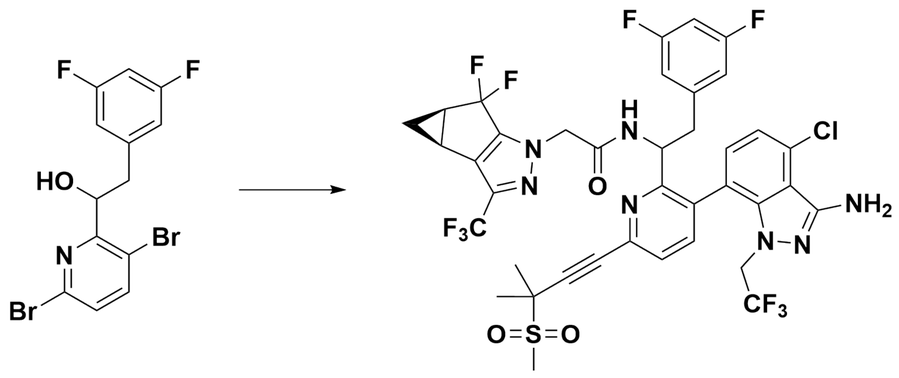


.

Objectives

The aim of this project was to develop alcohol oxidation processes that are

- Sustainable
- Economical
- Applicable to a broad range of compound
- Relevant to the industry

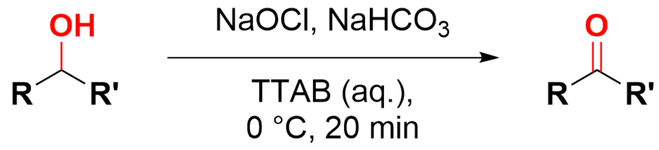


Lenacapavir [3, 4]

Anti-HIV drug from Gilead Sciences

RESULTS

Hypochlorite oxidation

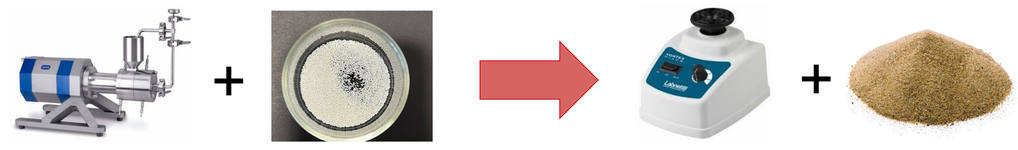


Thermal chemistry

- Fast reaction < 1h
- Tertiary amine compatible
- Sustainable and inexpensive reagents

- Overoxidation of primary alcohols
- Oxidation not selective

Mechanochemistry

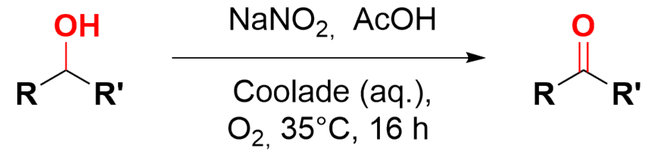


- Very fast reaction < 1 min
- Sustainable and inexpensive reagents
- No need for special equipment

- API not easily converted
- Not scalable

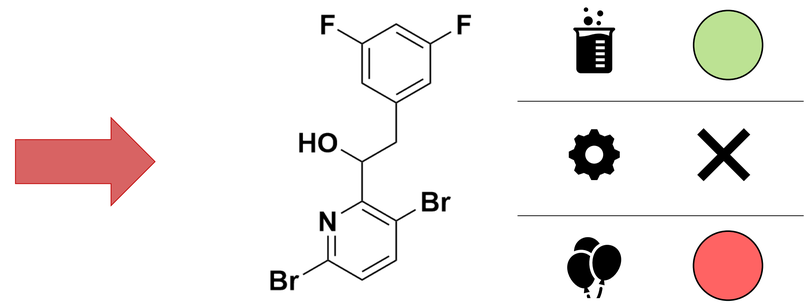
Aerobic oxidation

Thermal chemistry



- Safe use of oxygen (aqueous medium)
- Recyclable aqueous medium
- No overoxidation of primary alcohols
- Selective oxidation

- Longer reaction time < 24 h
- Incompatible with amines



CONCLUSION

- Further optimisation necessary for Lenacapavir oxidation
- Scale-up to increase attractiveness
- Explore mechanochemical route

- Three sustainable oxidation strategies developed and optimized
- Protocols tested on various alcohols (APIs included)
- Hypochlorite oxidations ideal for tertiary amines but not selective
- Aerobic oxidation, selective but incompatible to tertiary amines
- Lenacapavir oxidized under hypochlorite conditions (untested in mechanochemistry)

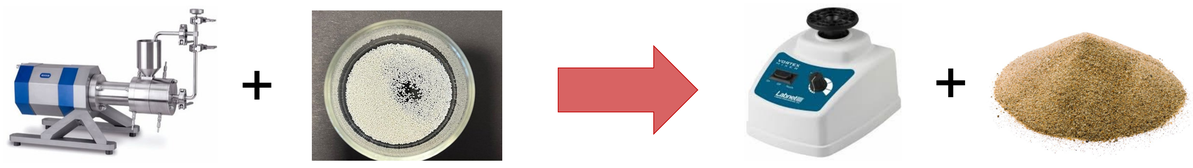
Thank you to
- HES-SO master
- Fondation Vincent Merkle
- Swiss Benevolent Society of New York

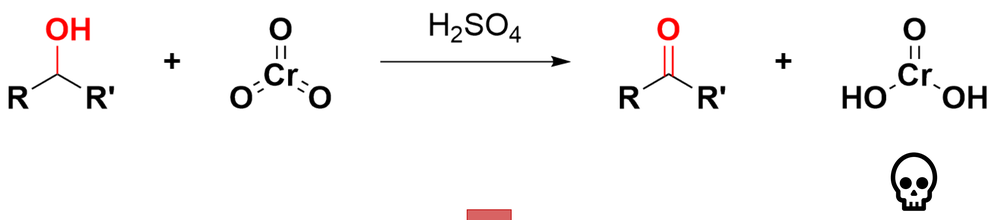
For their financial support

[1] Parmeggiani, C.; Cardona, F. *Green Chem.*, **2012**, 14, 547-564.
[2] Rabasso, N. Réactions d'oxydation in Chimie organique; 2nd ed.; de Boeck, 2009 ; pp 185-228.
[3] Lenacapavir Synthesis Highlight, https://drughunter.com/.
[4] Caravez, J et *al*. *J. Org. Chem* **2024** *89* (6).

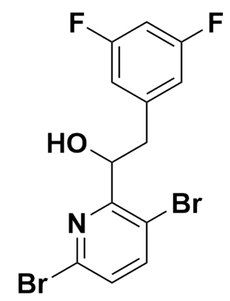
SWISS UNIVERSITIES APPLIED SCIENCES AND ARTS

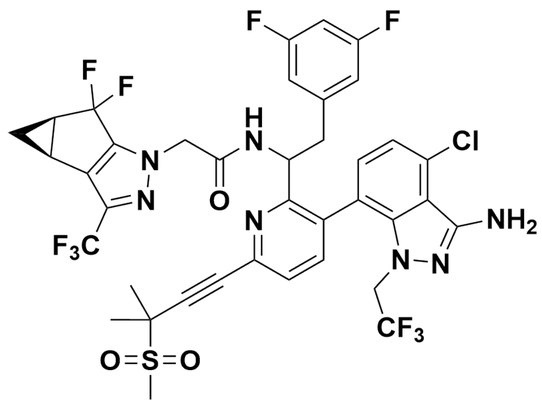
MLS | MASTER OF SCIENCE IN LIFE SCIENCES





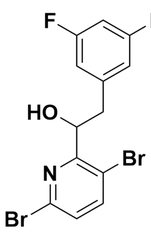
- Sustainable
- Economical
- Applicable to a broad range of compound
- Relevant to the industry





Lenacapavir

HIV drug from Gilead Sciences



- Fast reaction < 1h
- Tertiary amine compatible
- Sustainable and inexpensive reagents

- Overoxidation of primary alcohols
- Oxidation not selective

- Very fast reaction < 1 min
- Sustainable and inexpensive reagents
- No need for special equipment

- API not easily converted
- Not scalable

- Safe use of oxygen (aqueous medium)
- Recyclable aqueous medium
- No overoxidation of primary alcohols
- Selective oxidation

- Longer reaction time < 24 h
- Incompatible with amines