



HAL
open science

BIOCATALYTIC APPROACH TO CHEMOSELECTIVE ACYLATION OF SESQUITERPENE LACTONES FROM CHICORY: TOWARDS NEW ESTERS

Juan Rodriguez Mosheim, Francesca Ruggieri, Catherine Humeau, Philippe Hance, Nicolas Willand, Jean-Louis Hilbert, Egon Heuson, Renato Froidevaux

► **To cite this version:**

Juan Rodriguez Mosheim, Francesca Ruggieri, Catherine Humeau, Philippe Hance, Nicolas Willand, et al.. BIOCATALYTIC APPROACH TO CHEMOSELECTIVE ACYLATION OF SESQUITERPENE LACTONES FROM CHICORY: TOWARDS NEW ESTERS. BIOTRANS, Jun 2023, La Rochelle, France. hal-04562021

HAL Id: hal-04562021

<https://hal.univ-lille.fr/hal-04562021>

Submitted on 28 Apr 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

BIOCATALYTIC APPROACH TO CHEMOSELECTIVE ACYLATION OF SESQUITERPENE LACTONES FROM CHICORY: TOWARDS NEW ESTERS

J. Rodriguez Mosheim^a, F. Ruggieri^{a,b}, C. Humeau^c, P. Hance^{a,e}, N. Willand^b, J.L. Hilbert^{a,e}, E. Heuson^{*d} and R. Froidevaux^{*e}

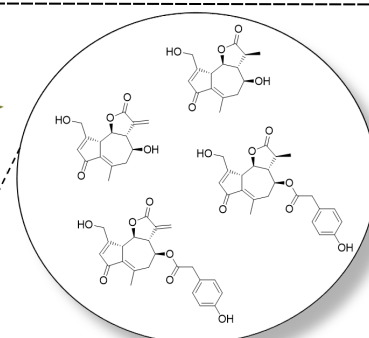
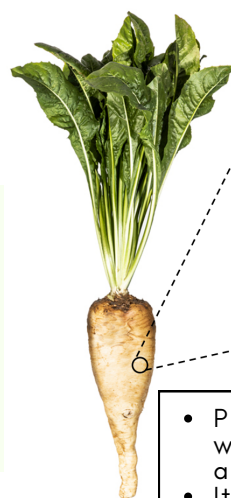
a. Univ. Lille, INRA, ISA, Univ. Artois, Univ. Littoral Côte d'Opale, EA 7394 - Institut Charles Viollette, France
 b. Univ. Lille, Inserm, Institut Pasteur de Lille, U1177—Drugs and Molecules for Living Systems, F-59000 Lille, France
 c. Univ. Lorraine, CNRS, UMR 7274 - Laboratoire Réactions et Génie des Procédés, F-54000 Nancy, France
 d. Univ. Lille, CNRS, Centrale Lille, Univ. Artois, UMR 8181—UCCS—Unité de Catalyse et Chimie du Solide, F-59000 Lille, France
 e. Joint Laboratory University of Lille—Florimond-Desprez CHIC4Health, F-59655 Villeuveuve d'Ascq, France

INTRODUCTION

- Terpenes are the largest family of natural compounds, with over 64,000 structures known.
- Sesquiterpene lactones (STL) are a very diverse group of terpenoids with 15-carbon skeletons commonly found in plants of the *Asteraceae* family. They serve as defence tools to help them cope with environmental stresses.
- STLs have shown a wide range of biological activities:



Anti-Inflammatory



Cichorium intybus

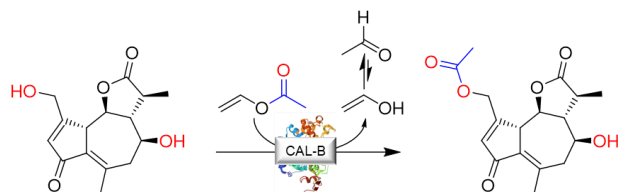
- Plant of the *Asteraceae* family widely cultivated in Belgium and in the north of France.
- Its root is rich in STLs such as lactucin (Lc), lactucopicrin (Lp) and their dihydro derivatives (DHLc, DHLp).

Chemoselective acylation of DHLc catalyzed by lipase B from *Candida antarctica* (Novozym 435)

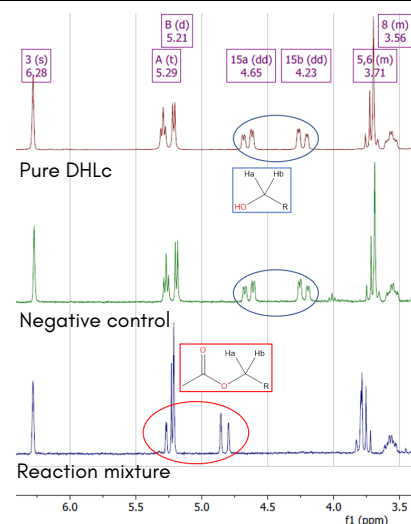
Pre-print



Scan me



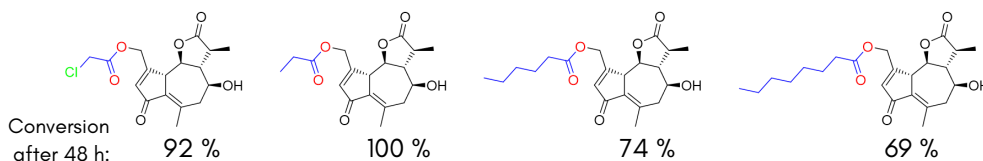
- 10 mM DHLc, 100 mM acyl donor, 2 mg N435, MS 5 Å, 37 °C, 35 RPM, 1 mL MTBE:ACN (3:1)
- **100 % conversion** in 24 h
- Pure product after filtration and concentration under vacuum (8 mbar)
- Complete chemoselectivity was observed for the primary allyl alcohol
- No hydrolysis of the lactone was observed at any time, neither spontaneous nor biocatalytical
- Acetic acid was also compatible as an acyl donor, giving 76 % conversion after 48 h



Ester derivatives of DHLc synthesized from their corresponding vinyl esters via the same protocol

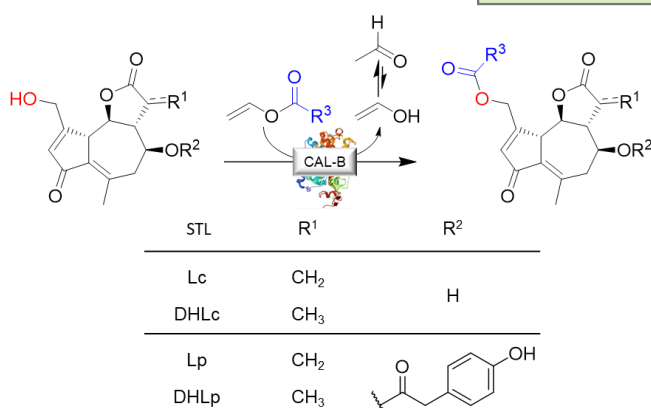
With short acyl chains (until propionate), the selectivity was due to the intrinsic reactivity of both hydroxy groups.

With longer chains such as those from vinyl hexanoate and octanoate, steric hindrance became significant and only the primary hydroxy group could reach the acyl enzyme carbonyl function. The reaction rate was also slower.



Applicable to other STLs from chicory

- 100 % conversion
- Complete selectivity



Binding modes & interactions between DHLc and N435

- The main enzyme-substrate interactions involving STLs and the different acyl donors are hydrophobic. Important residues at the cavity entrance (Ile189-285 and Val154) interact with the cycloheptene ring and the methyl group.
- Nevertheless, H-bonds were observed between the lactone and residues in the oxyanion hole
- Aliphatic acyl chains with a degree of flexibility tend to be preferred due to their better positioning over the hydrophobic wall of the cavity

