

Eco-friendly synthesis of (*R*)-3-hydroxydecanoic acid and analogues: New green pathway to highly potent elicitor(s) of plant immune system

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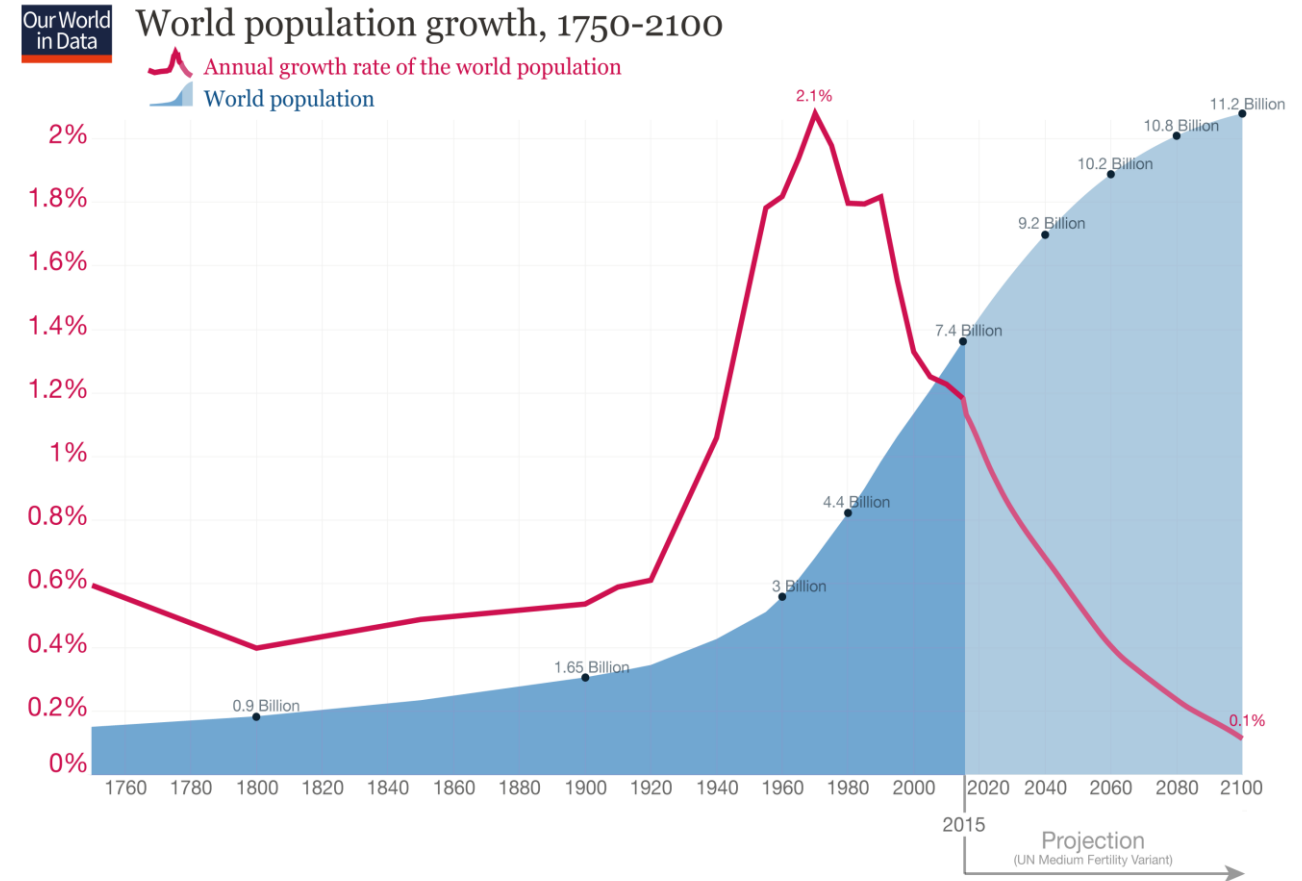
12 novembre 2021



Introduction

Context

- Challenge: Feeding a growing population without poisoning ecosystems (soil, water...)
- Elicitation (i.e., stimulation of plant immune system) could be an answer to ensure good productivity and to limit chemical treatments on fields?



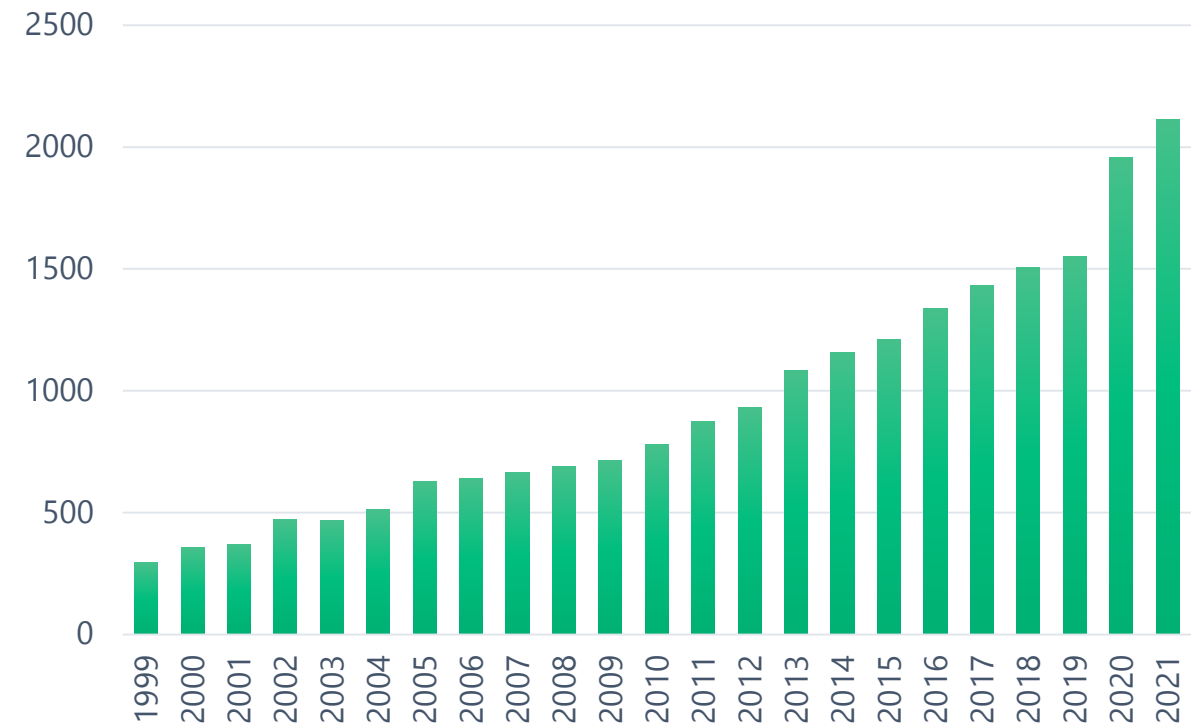
Data sources: Up to 2015 OurWorldInData series based on UN and HYDE. Projections for 2015 to 2100: UN Population Division (2015) – Medium Variant. The data visualization is taken from OurWorldInData.org. There you find the raw data and more visualizations on this topic.

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Elicitation

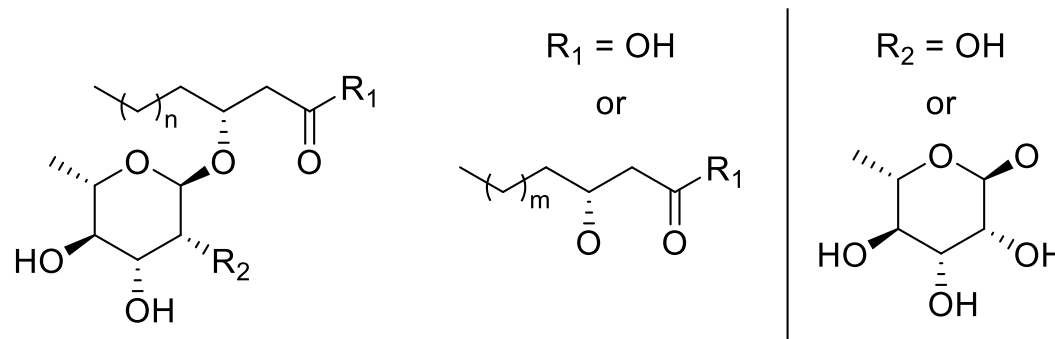
- Recent field of research
- MAMPs (Microbe-Associated Molecular Patterns) and PAMPs (Pathogen-Associated Molecular Patterns)
- Rhamnolipids proved to have eliciting properties

Number of publications over the time
source : Sciencedirect for elicitation of plant immune system

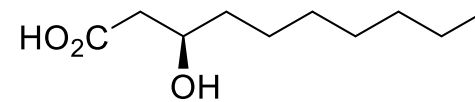


Rhamnolipids

- Family of numerous amphiphilic molecules produced by various microorganisms
- Can be recognized by plant immune system.



- Recently, (*R*)-3-hydroxydecanoic acid was identified as a very efficient elicitor



(*R*)-3-hydroxydecanoic acid

R. Schellenberger, *et al.* *PNAS*. **2021**, *118*, 39, e2101366118.

Levoglucosenone

Levoglucosenone (**LGO**) was generated through flash pyrolysis of cellulosic wastes.



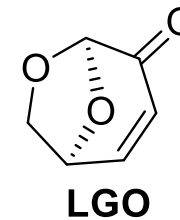
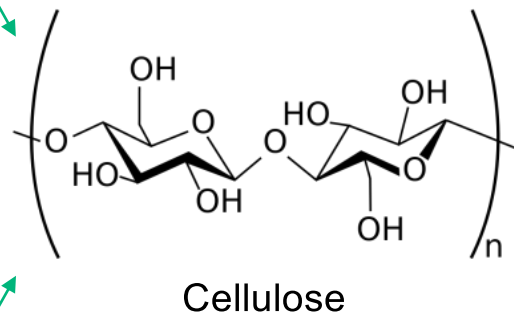
Sawdust



Used paper



Straw



Process advantages:

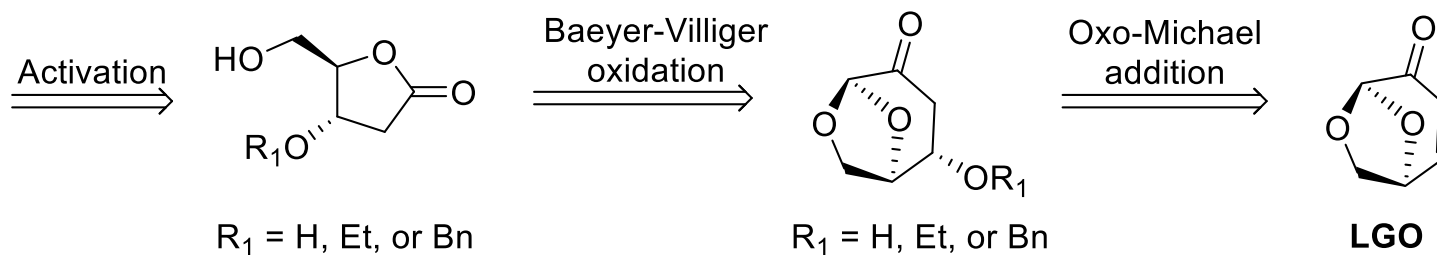
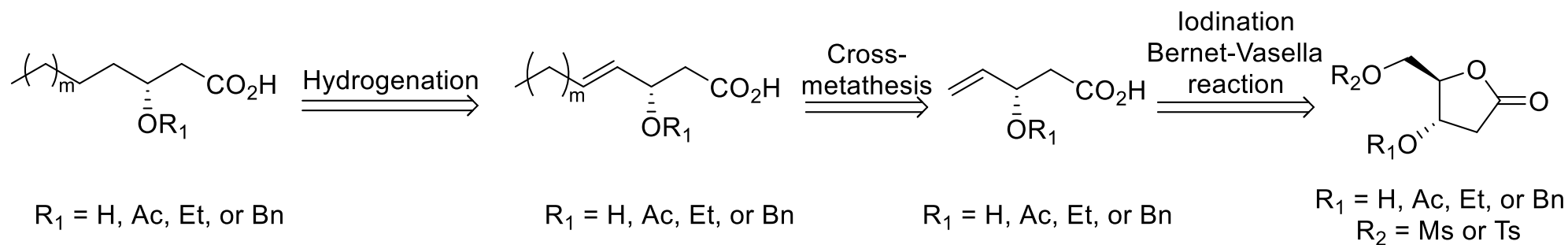
- From biomass
- Selectivity LGO, water and biocoal
- Energy neutral

Levoglucosenone advantages:

- Chiral
- Multifunctional
- High reactivity

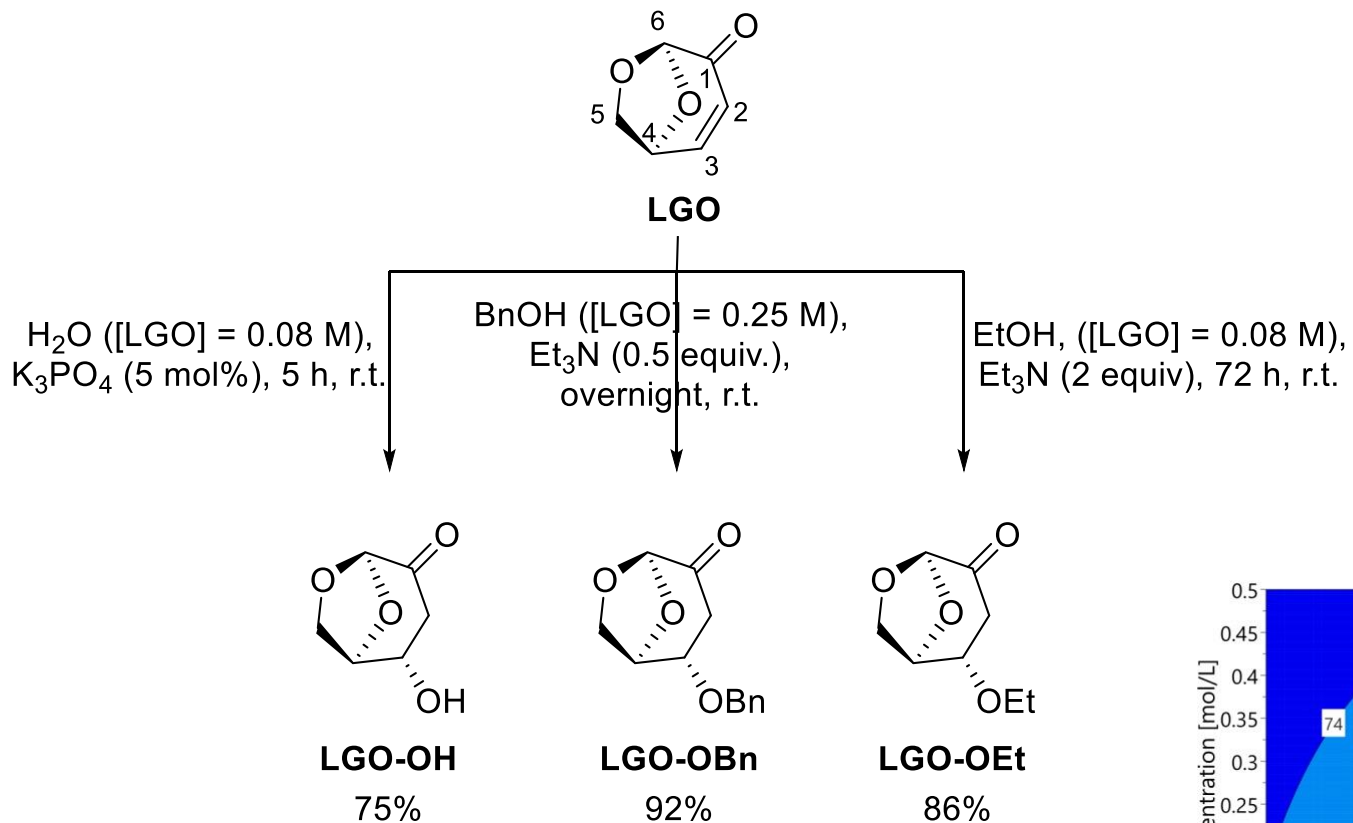
Goal

- Design an eco-friendly synthetic route from bio-based levoglucosenone toward (*R*)-3-hydroxydecanoic acid & analogues



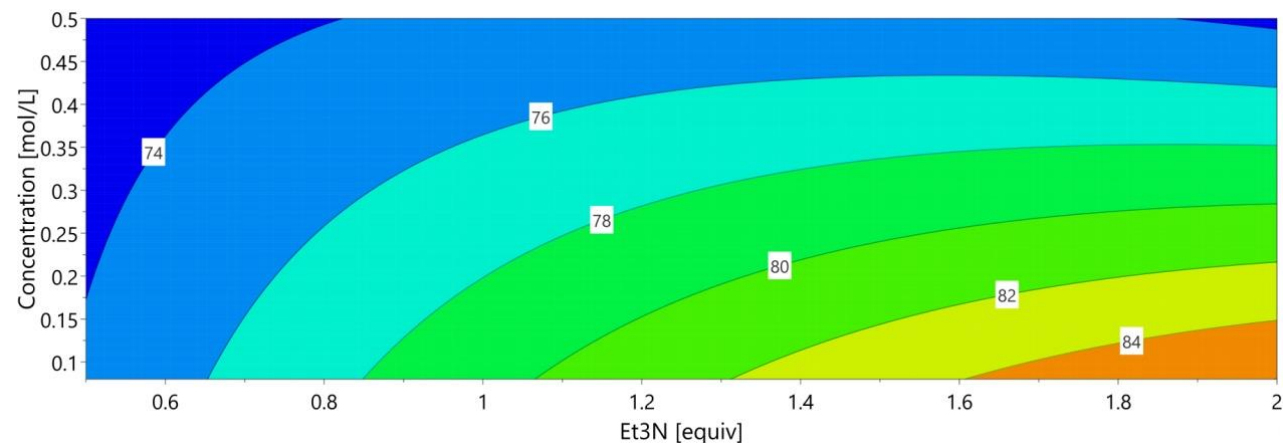
Results & Discussion

Oxa-Michael addition

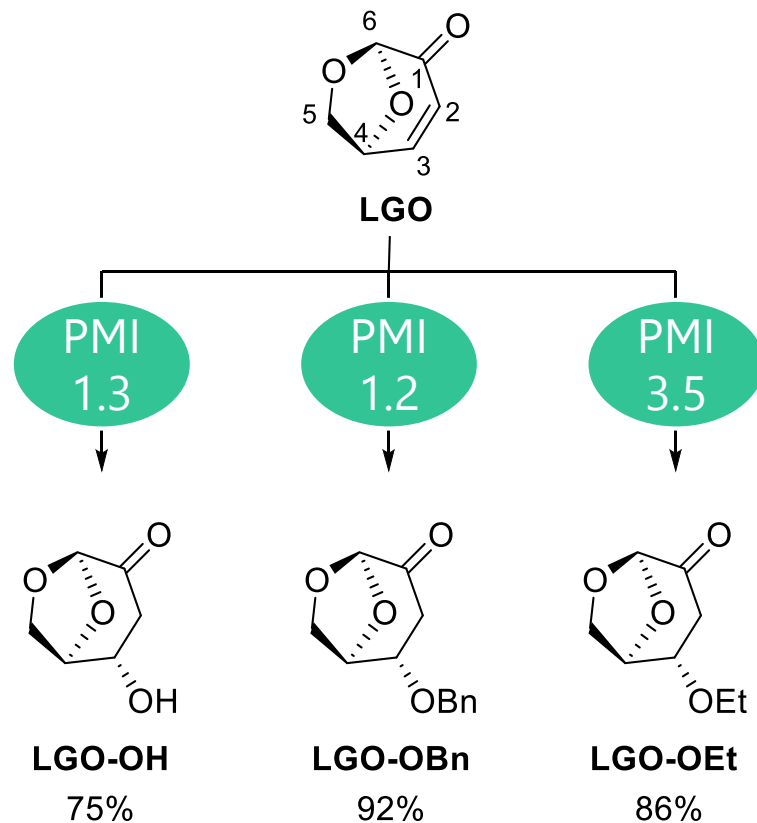


Diot *et al.* 2020 Kawai *et al.* 1995

- Total selectivity due to chirality of **LGO**
- Reaction in water or in recyclable solvents
- High yield



Oxa-Michael addition

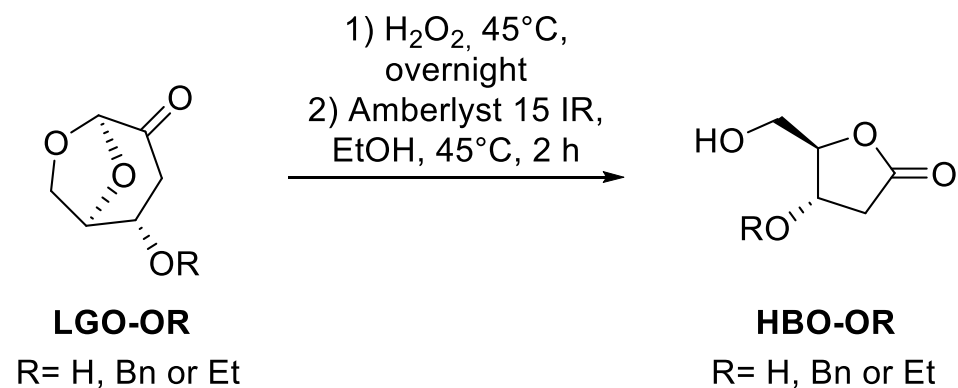


Diot *et al.* 2020 Kawai *et al.* 1995

- Total selectivity due to chirality of **LGO**
- Reaction in water or in recyclable solvents
- High yield
- Low waste generation

PMI = Process Mass Intensity
Sum of masses of all species entering in the reaction (except water) over the mass(es) of desired product(s)

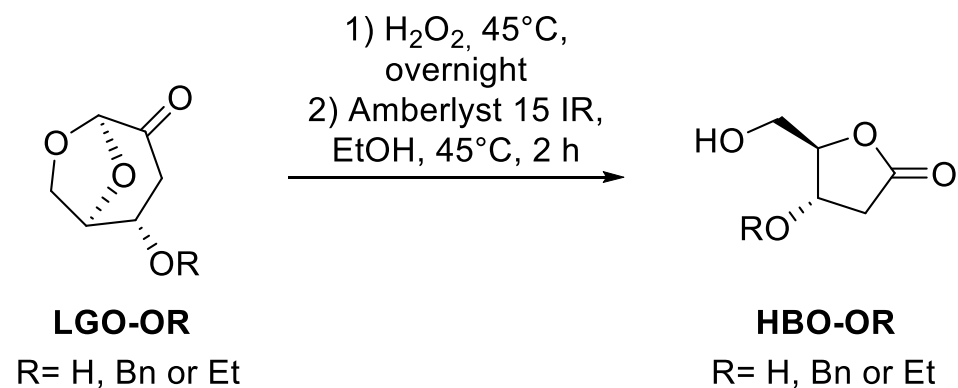
Baeyer-Villiger Oxidation



R	Yield
H	99%
Bn	93%
Et	97%

- Total regioselectivity due to acetal moiety of **LGO**
- First step is solvent free and 2nd is performed in ethanol
- Excellent yields >90%
- Recyclability of the acidic resin
- Mild conditions
- No need of purification over silica gel

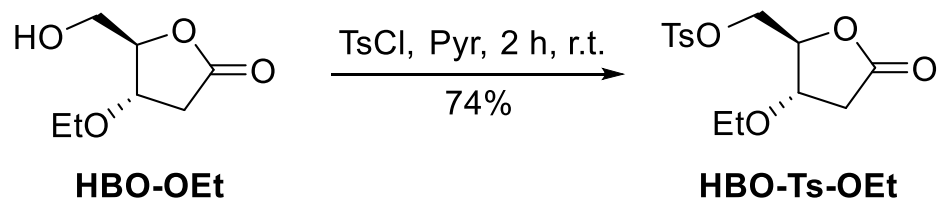
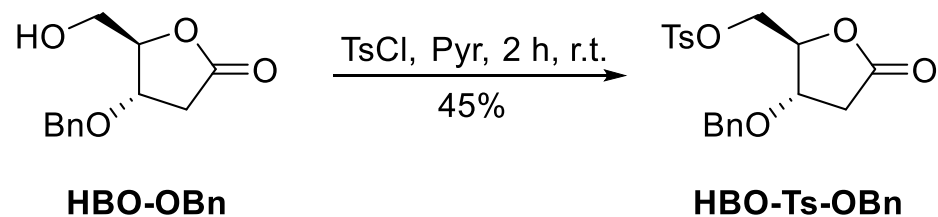
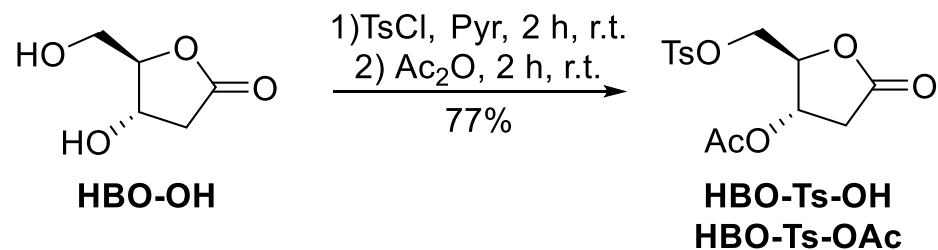
Baeyer-Villiger Oxidation



R	Yield	PMI
H	99%	7.6
Bn	93%	5.1
Et	97%	6.4

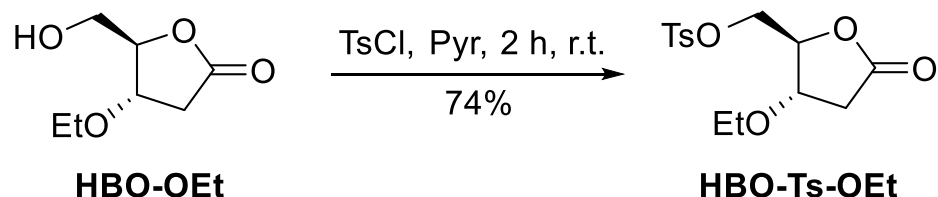
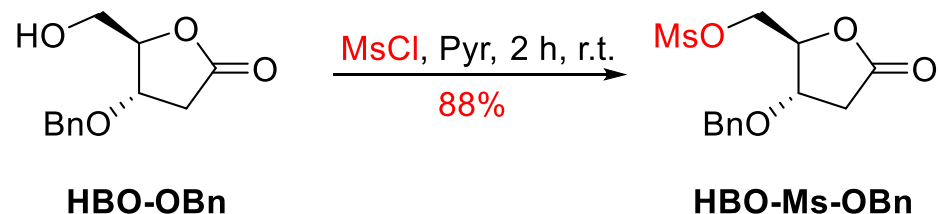
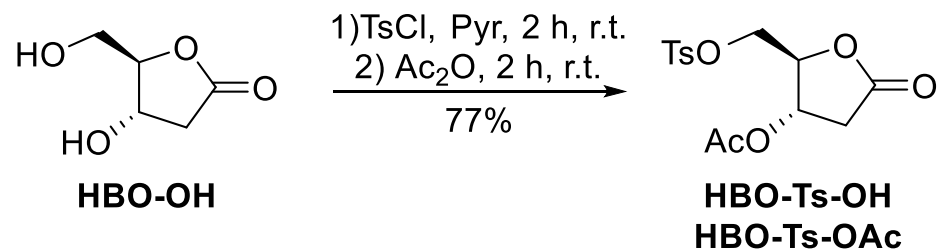
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Activation of primary alcohol



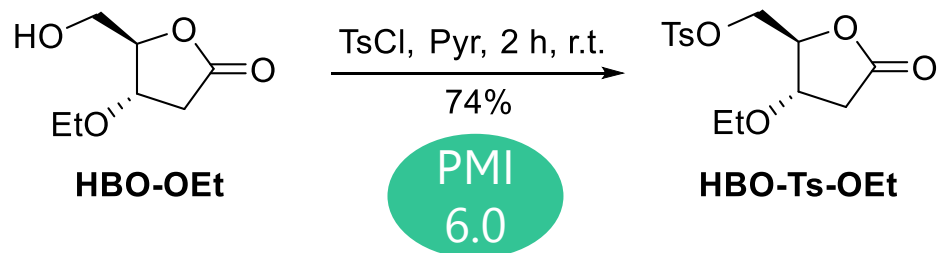
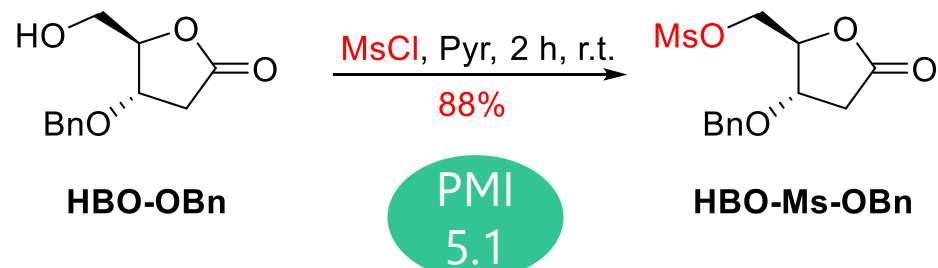
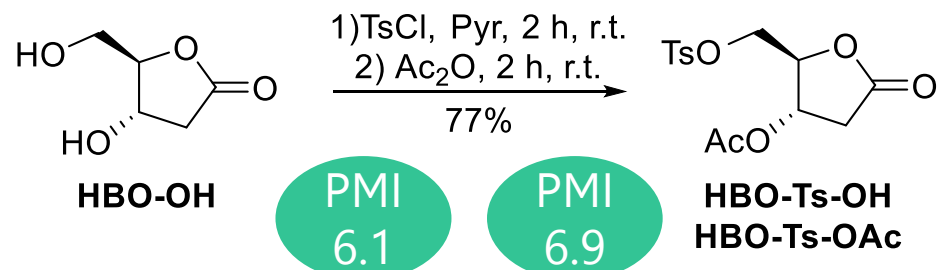
- No need of purification over silica gel
- Efficient « one-pot, two-steps » strategy for **HBO-Ts-OAc**
- Good yield from **HBO-OH** and **HBO-OEt** but moderate from **HBO-OBn**
 - Steric hindrance?

Activation of primary alcohol



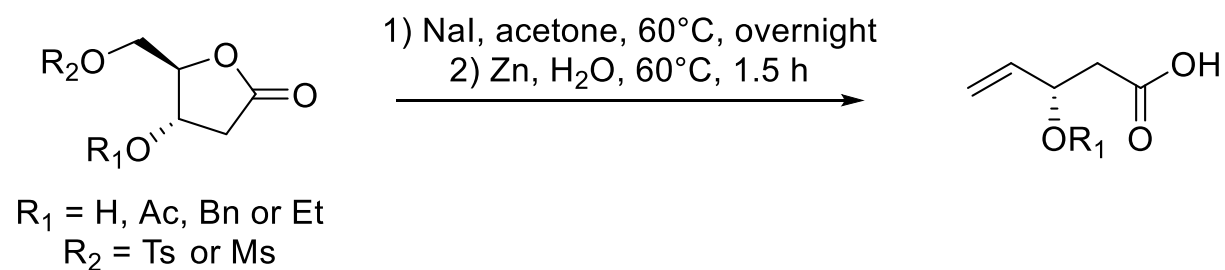
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- Good yield using mesyl chloride instead of tosyl chloride from **HBO-OBn**

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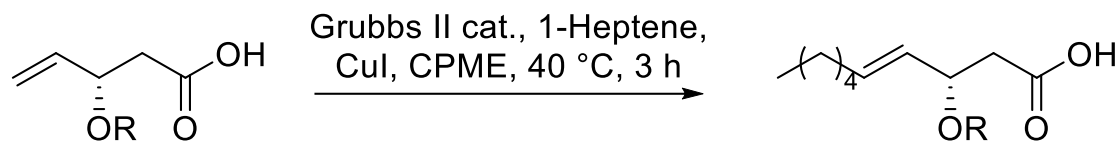
Bernet-Vasella reaction



R ₁	Yield	PMI
H	91%	14.6
Ac	98%	10.2
Bn	95%	8.0
Et	98%	11.1

- « One-pot, two-step » reaction
- Excess of reagent was limited at 1.2 for NaI and 1.5 for freshly activated Zn
- Excellent yield
- No need of purification over silica gel
- Limited waste generation

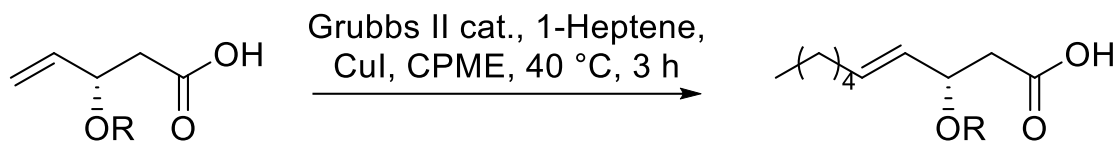
Cross-metathesis homologation



R	Cat (mol%)	Concentration (mol.L ⁻¹)	Yield (%)
H	2.4	0.1	46
Ac	4.8	0.1	62
Bn	4.8	0.1	47
Et	4.8	0.25	60

- Versatility of the procedure
- Use of CPME, a green solvent
- Moderate yields
- Starting material can be recovered, particularly with benzyl substitute (corrected yield 88%)
- Required purification over silica gel

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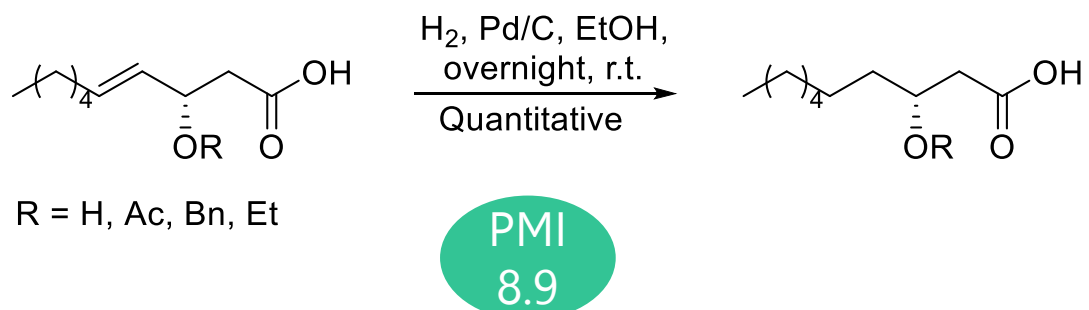
PMI
106.9

PMI
79.6

PMI
41.5

PMI
21.8

Hydrogenation



- Quantitative yield
- No need of purification over silica gel
- No debenylation when ethanol was used as solvent
- Switch to ethanol/acetic acid (95:5) allow total deprotection
- Limited waste production

Conclusions

Metrics comparison with others reported procedures

- Calculation for (*R*)-3-hydroxydecanoic acid

- PMI

This process
Average: 25
Range: 1.3 – 107

Bauer's process
Average: 101
Range: 4 – 347

Menhour's
process
Average: 276
Range: 25 – 1194

- Ecoscale

This process
Average: 77
Range: 47-87

Bauer's process
Average: 61
Range: 38-72

Menhour's
process
Average: 42
Range: 5-78

Take home message

- Synthesis of hydroxy fatty acid from cellulosic waste
- Thinking about usage of solvents
 - Reduction by concentrated media and/or « one-pot two-steps » procedures
 - Usage of bio-based solvents
 - No use of halogenated solvent
- Reduction of number of purification over silica gel
- Ensuring eco-friendliness through calculation of green metrics

Acknowledgements

Enzo Petracco (Master2 internship)



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Thanks for
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Levogluconone

Merci pour votre attention.

Thank you for your attention.

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