

# 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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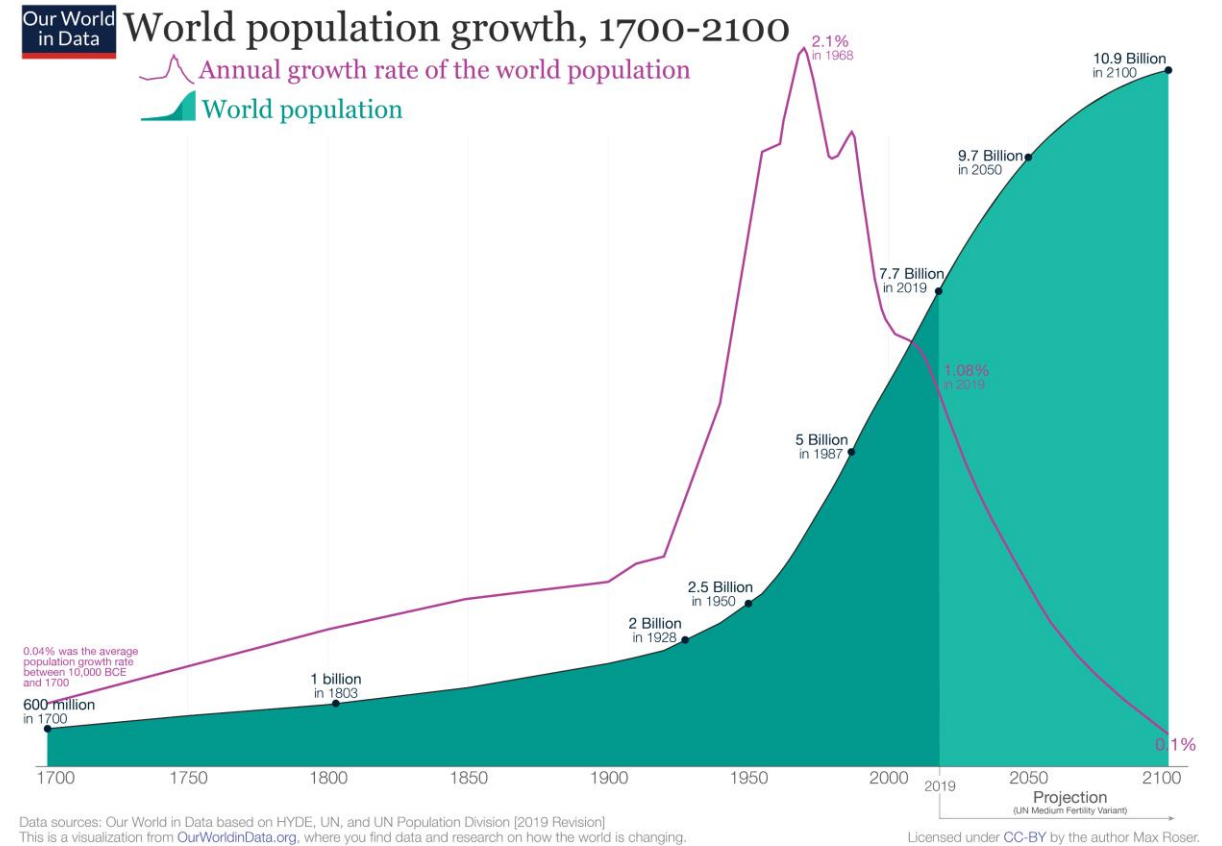
# Some words about ABI

- URD ABI is dedicated to biomass valorization
  - Pomacle, France (15 km East of Reims) on the site of biorefinery
  - Agricultural region
    - Vine
    - Wheat
    - Beetroot
    - Rapeseed
  - Multidisciplinary research unit
    - Biotechnology
    - Eco-process engineering
    - Green chemistry



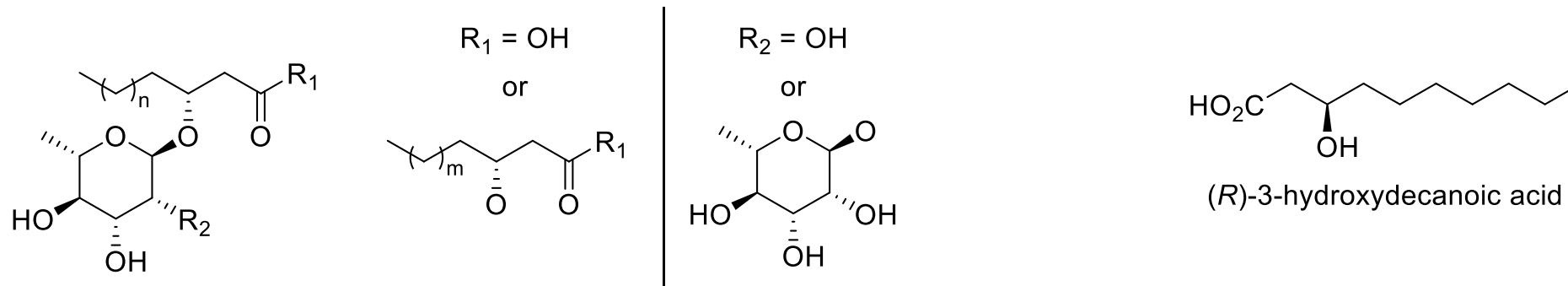
# Context

- 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
- Which molecules for elicitation?



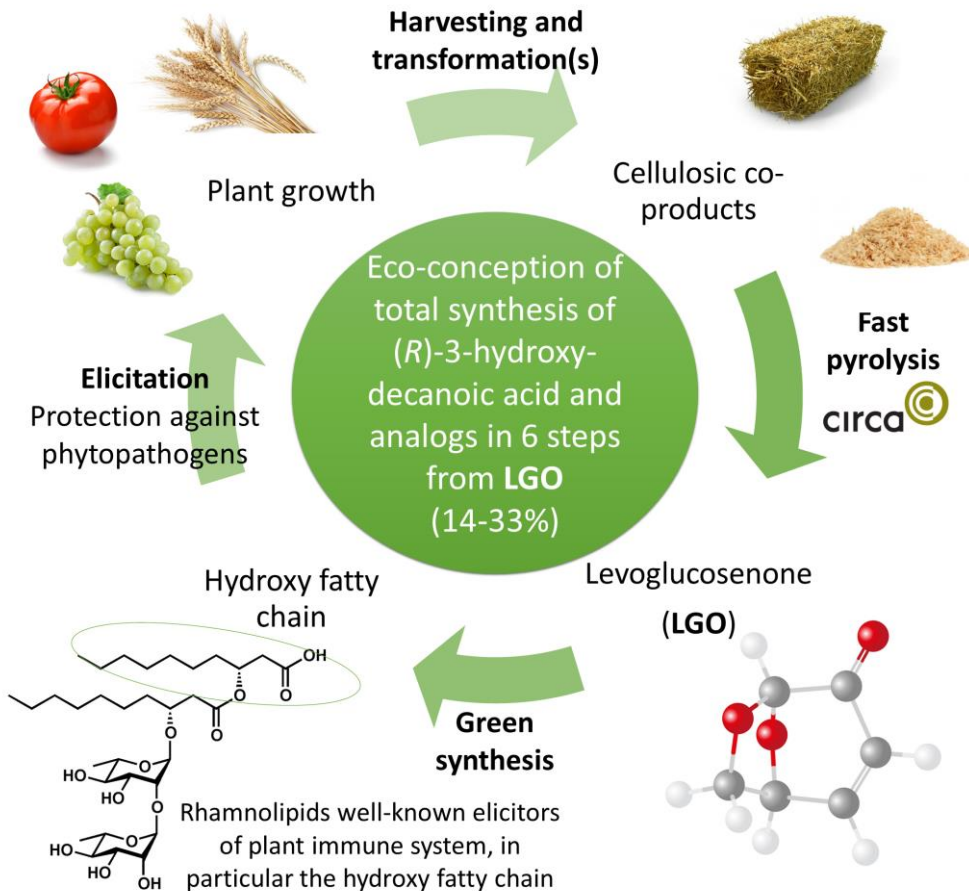
# Rhamnolipids

- Rhamnolipids proved to have eliciting properties
- 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

# Levogluconenone



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

Process advantages:

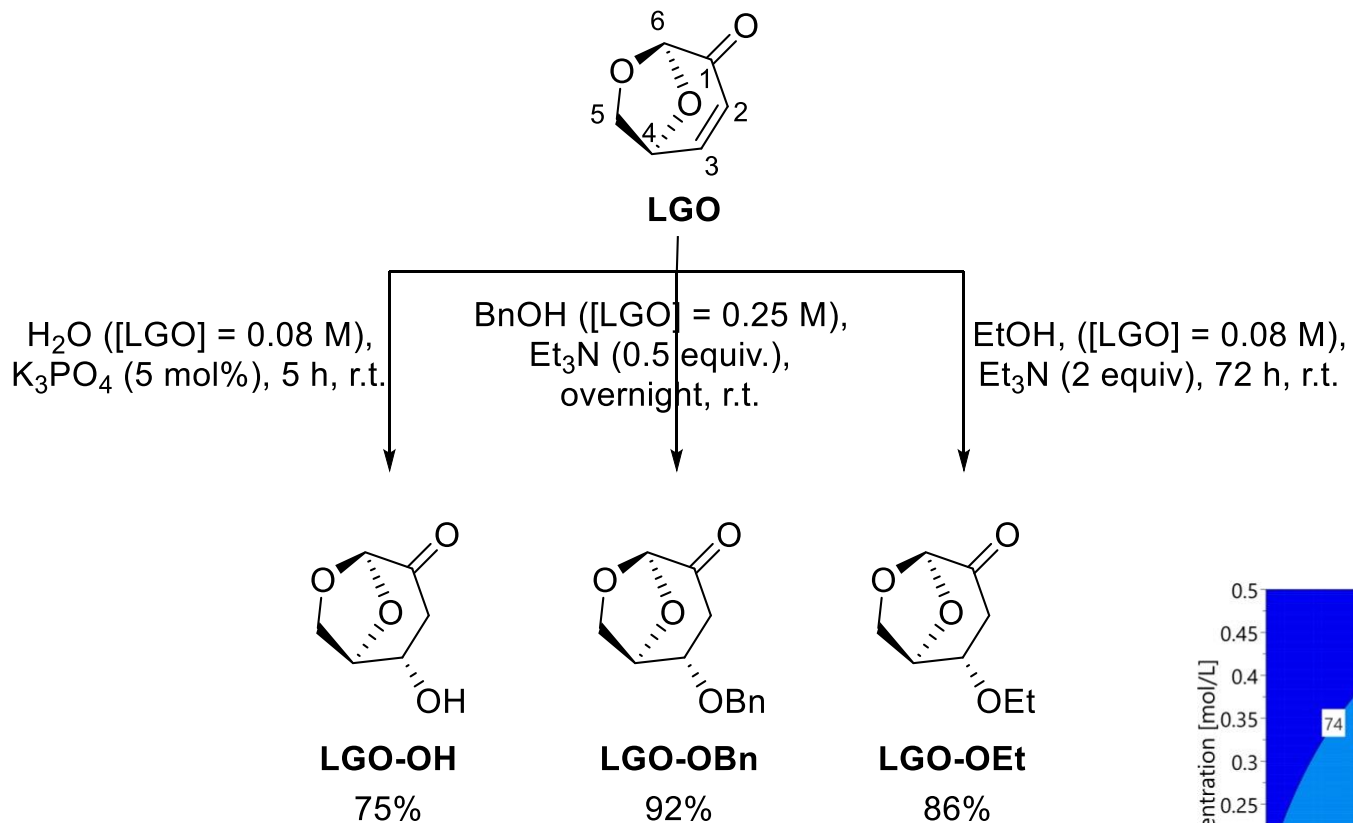
- From biomass
- Selectivity **LGO**, water and biocoal
- Energy neutral

Levogluconenone advantages:

- Chiral
- Multifunctional
- High reactivity

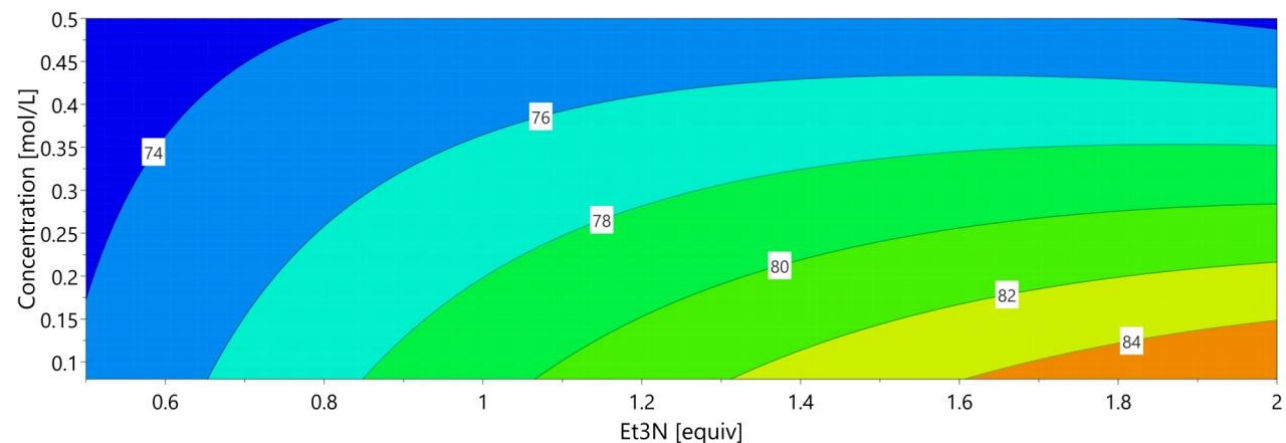
Design an eco-friendly synthetic route from bio-based **LGO** toward (*R*)-3-hydroxydecanoic acid & analogues

# Oxa-Michael addition

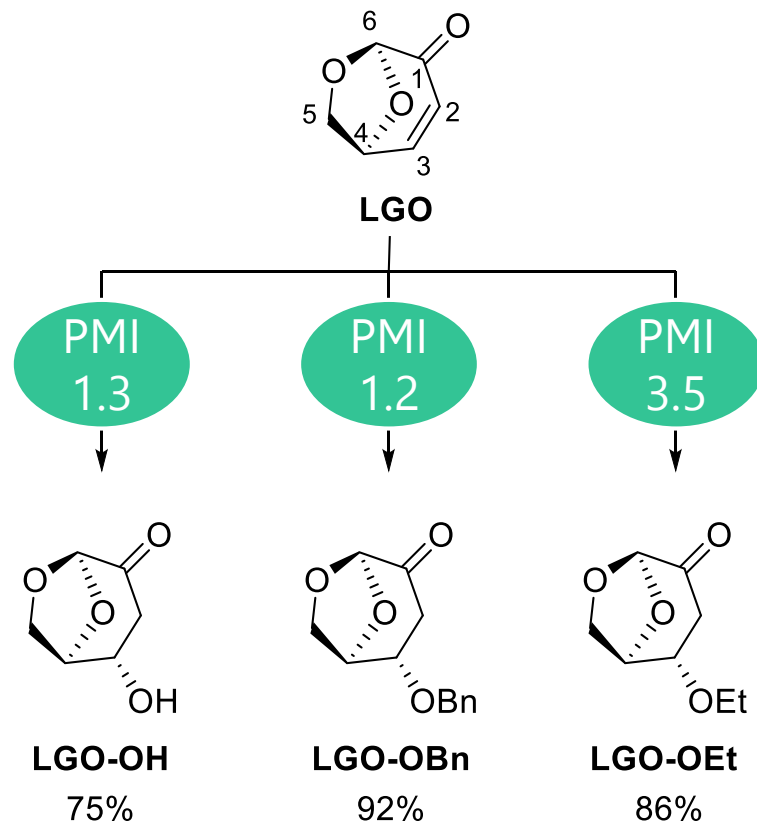


Diot *et al.* 2020    Kawai *et al.* 1995

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



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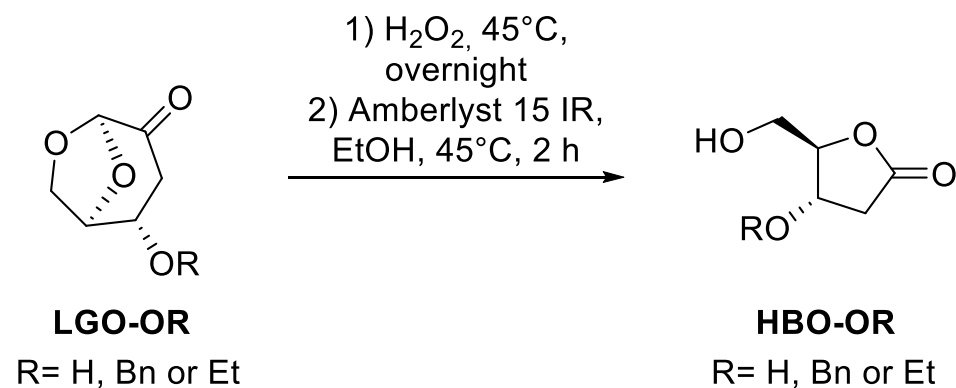


Diot *et al.* 2020    Kawai *et al.* 1995

- 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

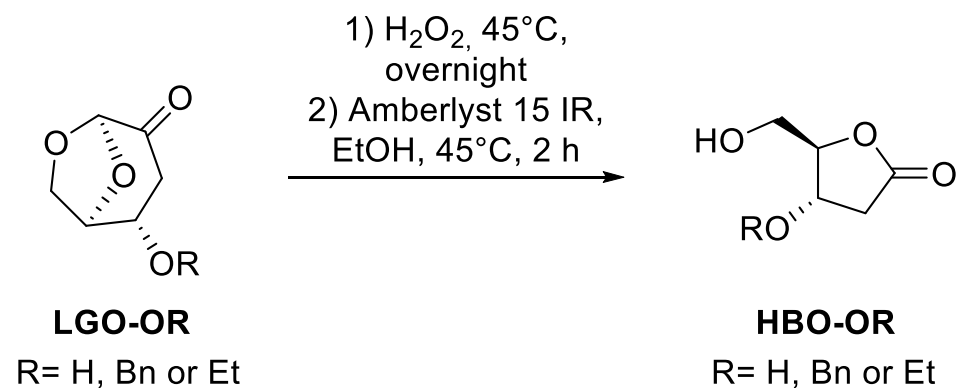


| R  | Yield |
|----|-------|
| H  | 99%   |
| Bn | 93%   |
| Et | 97%   |

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



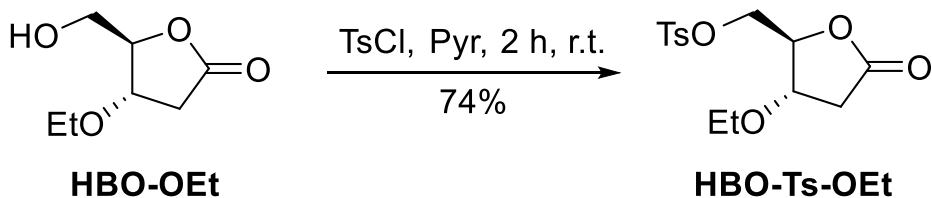
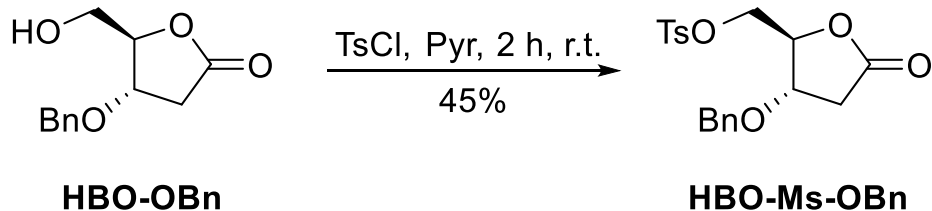
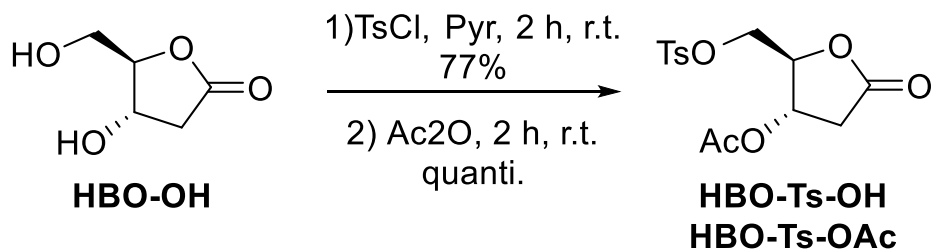
# Baeyer-Villiger Oxidation



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

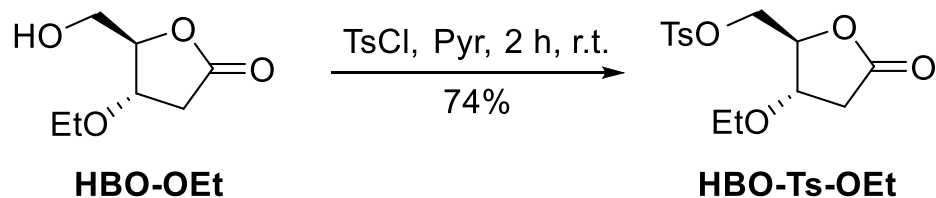
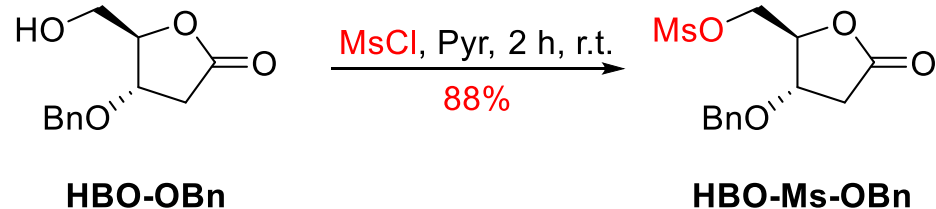
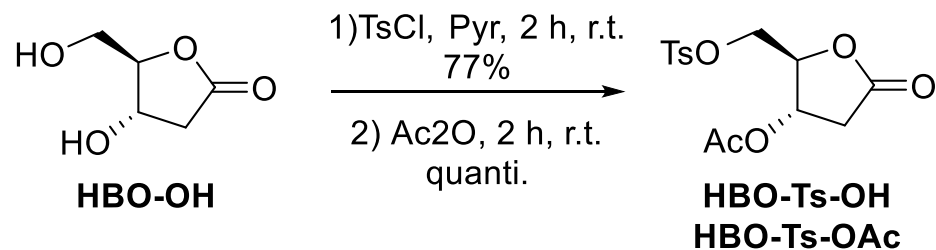
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# Activation of primary alcohol



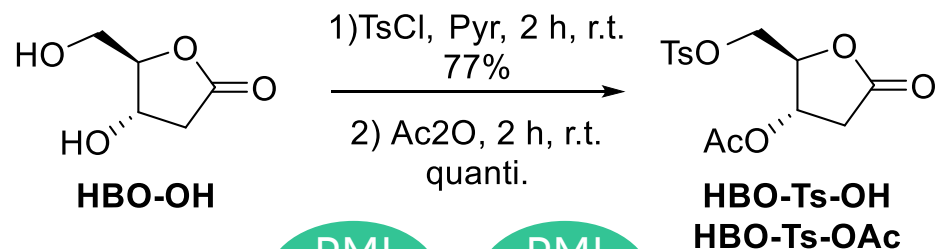
- No need of purification over silica gel
- Efficient « one-pot, two-steps » strategy for **HBO-Ts-OAc**
- Good yield from **HBO-OH** and **HBO-OEt** but moderate from **HBO-OBn**
  - Steric hindrance?

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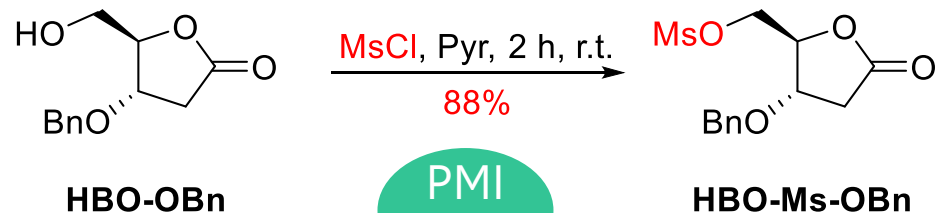
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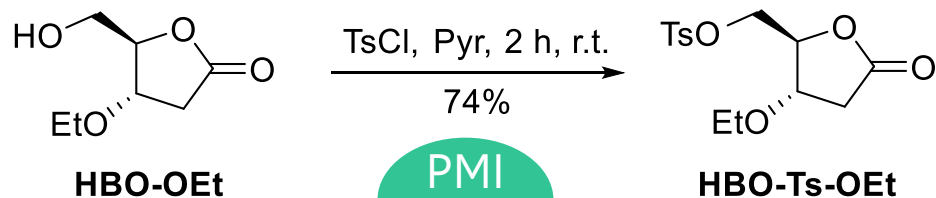


PMI 6.1

PMI 6.9



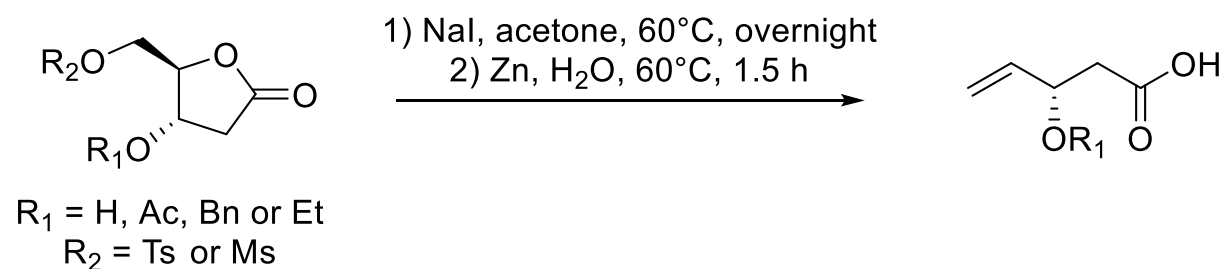
PMI 5.1



PMI 6.0

- No need of purification over silica gel
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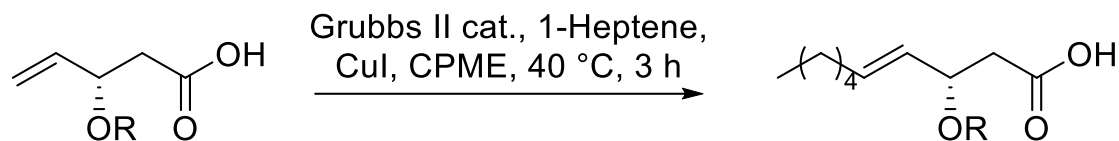
# Bernet-Vasella reaction



| R <sub>1</sub> | 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

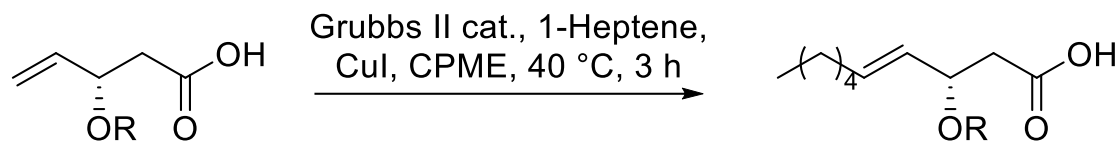
# Cross-metathesis homologation



| R  | Cat (mol%) | Concentration (mol.L <sup>-1</sup> ) | 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
- Required purification over silica gel

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| 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

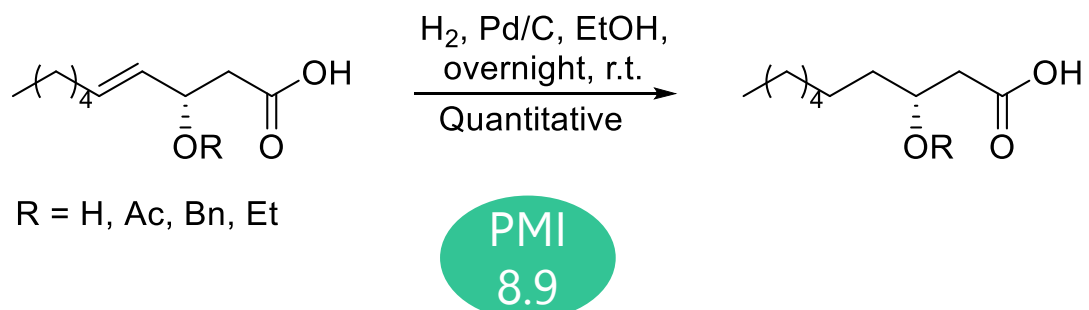
PMI  
106.9

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



# Metrics comparison with other 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 messages

- Synthesis of library of 3-(*R*)-hydroxydecanoic acid analogs 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

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Thanks for  
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Levogluosenone

Merci pour votre attention.

Thank you for your attention.

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Research Scientist

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