Normandie Université

UNITÉ DE RECHERCHE
EN CHIMIE ORGANIQUE
ET MACROMOLÉCULAIRE

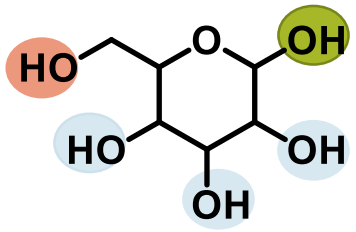
IRON CATALYSIS FOR THE OXIDATION OF UNPROTECTED SUGARS

Dr Laure Benhamou

Normandy Le Havre University

UNIVERSITÉ LE HAVRE NORMANDIE

- Traditional strategies

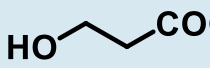


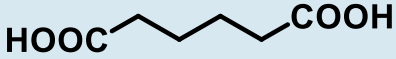
  - Polyfunctionality & Selectivity
  - Protection / Deprotection

- Green Chemistry & sugars exploitation

Fermentation

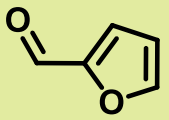
Alcohol: EtOH, *n*BuOH

3-HPA 

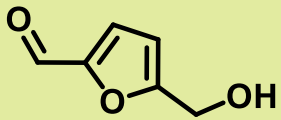
Adipic acid 

Dehydration

Aromatic derivatives



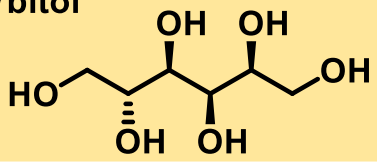
Furfural



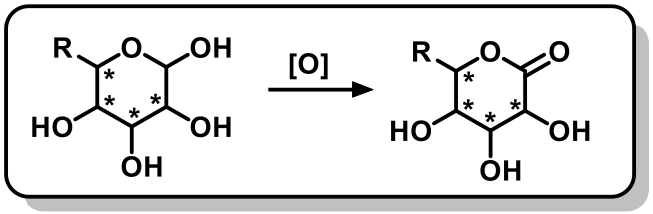
HMF

Hydrogenation

Hydrocarbons: benzene, xylene

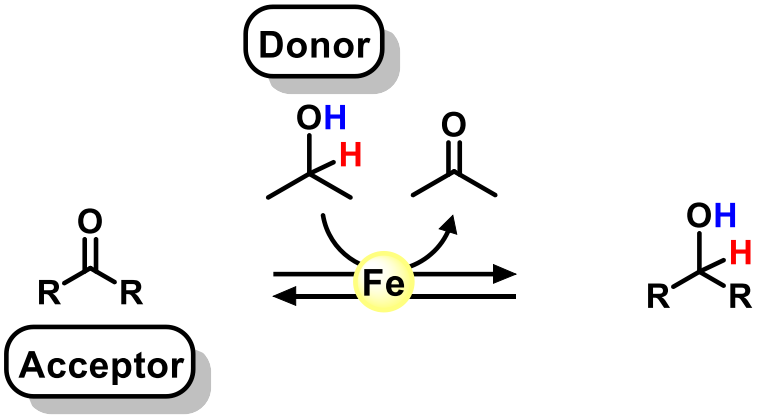
Sorbitol 

- Catalytic C1-oxidation of unprotected sugars
  - Traditional stoichiometric processes: halogen derivatives
  - Catalytic methodologies



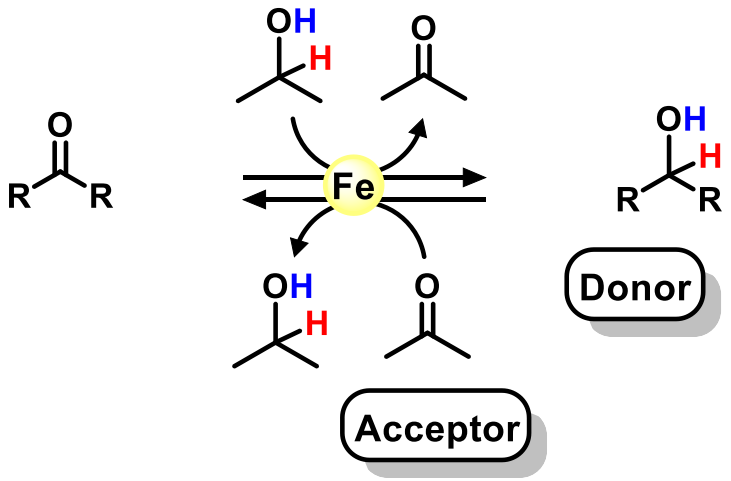
	Selected examples	Limitations
Biocatalysis	Gluconolactone industrial synthesis	Narrow range of tolerated substrates
Heterogeneous catalysis	Au / H_2O_2 / hv TiO_2 / O_2 / hv	Selectivity
Homogeneous catalysis	TEMPO / NaOCl Pd catalysis	Halogenated agent Selectivity

- Catalytic transfer hydrogenation (TH)
  - Alternative to direct hydrogenation



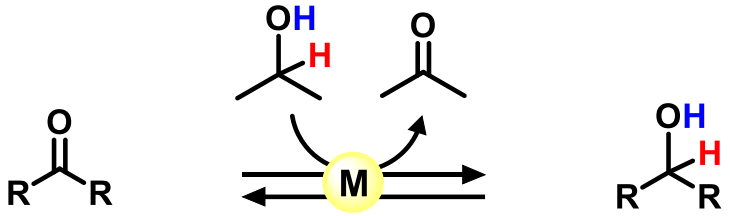
  - Simple set-up
  - Reversibility

- Catalytic transfer hydrogenation (TH)
  - Alternative to direct hydrogenation



- Simple set-up
- Reversibility
- Strong oxidant free

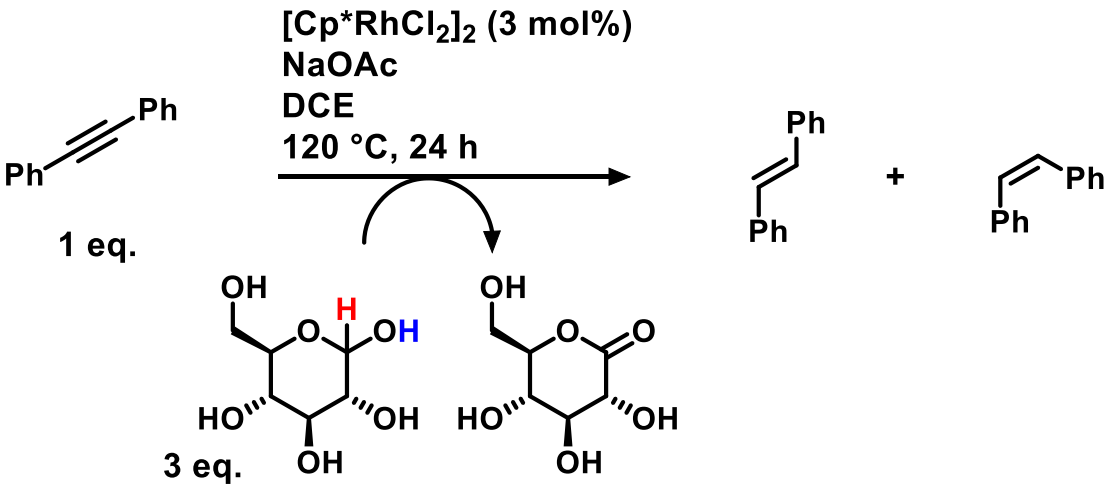
- Catalytic transfer hydrogenation (TH)
  - Alternative to direct hydrogenation



- Simple set-up
- Reversibility
- Strong oxidant free

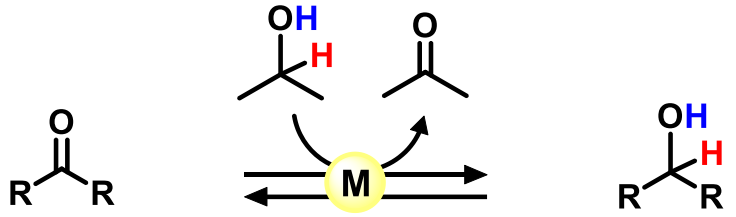
  - Sugar oxidation via catalytic TH : a noble metal matter?

Rhodium



S. Manna *et al. ChemSusChem* 2019, *12*, 3094

- Catalytic transfer hydrogenation (TH)
  - Alternative to direct hydrogenation



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  - Reversibility
  - Strong oxidant free

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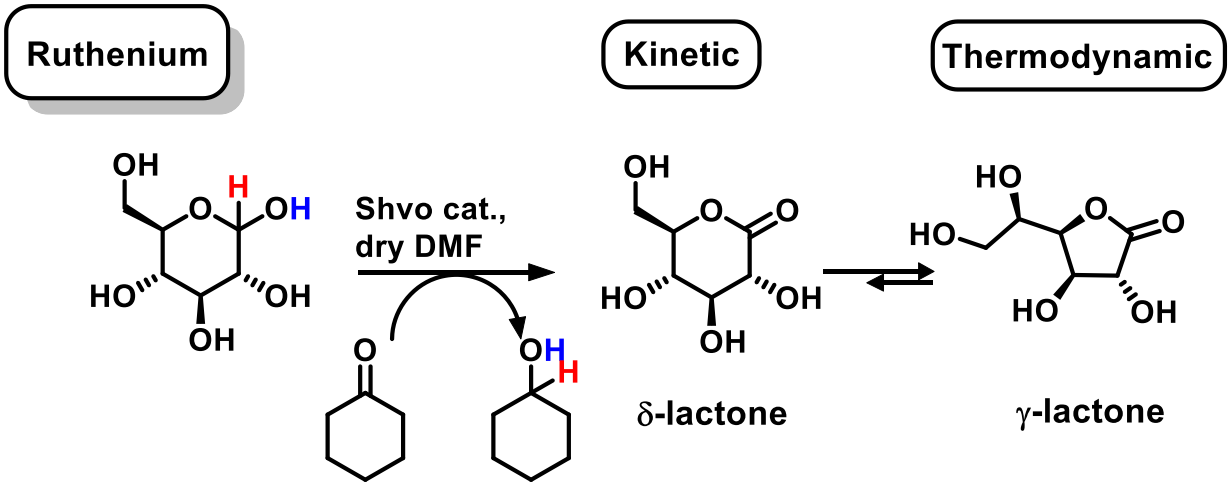
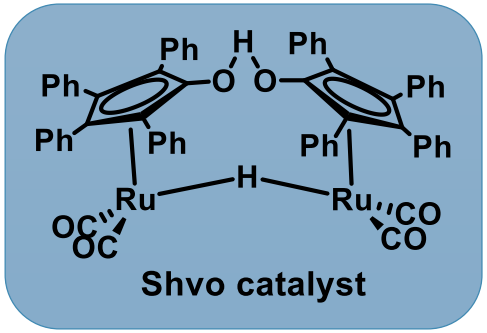
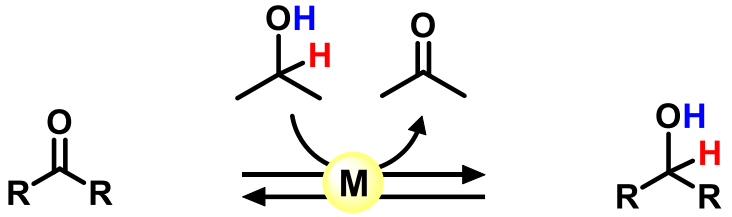




M. Bierenstiel *et al. Eur. J. Org. Chem.* **2004**, 1474

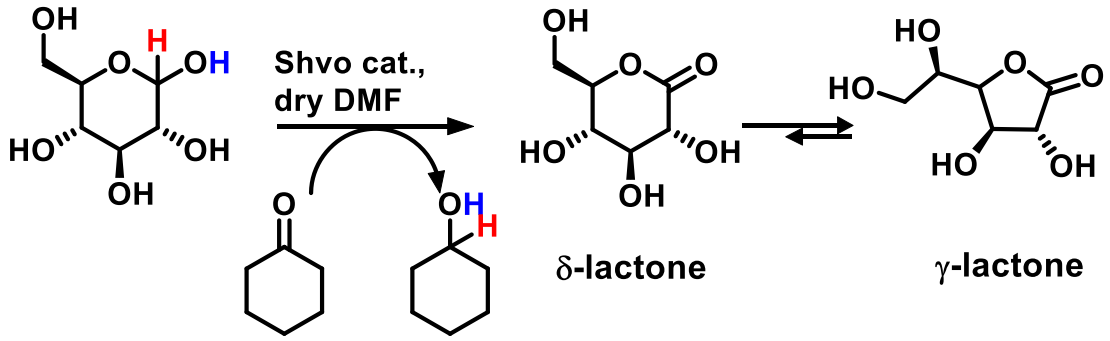
- Catalytic transfer hydrogenation (TH)
  - Alternative to direct hydrogenation



- Simple set-up
- Reversibility
- Strong oxidant free

  - Sugar oxidation via catalytic TH : a noble metal matter?

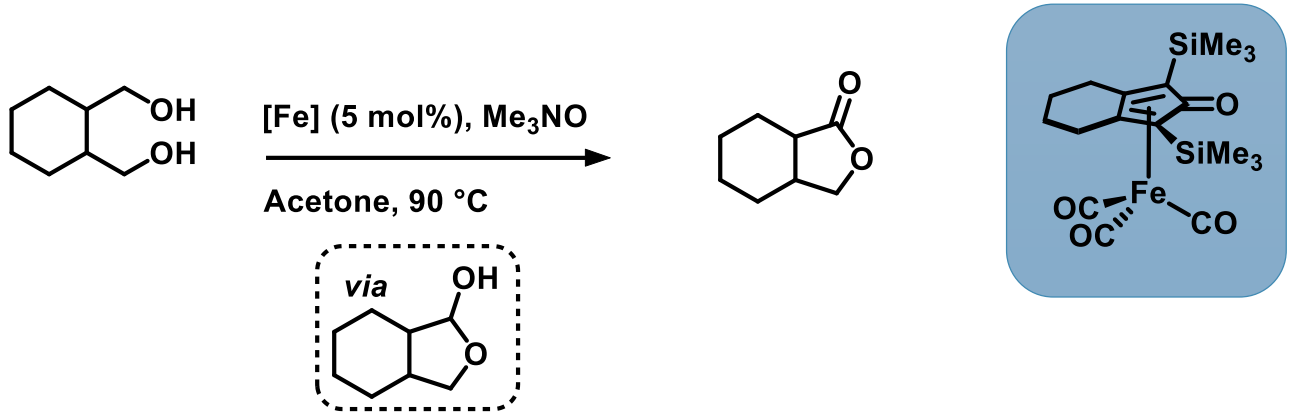
Ruthenium **Kinetic** **Thermodynamic**



- ✓ Excellent selectivity & activity
- ✓ Hexoses oxidation
- ✓ Mild conditions
- - Inert condition
- - Large excess of acceptor
- - Hazardous solvent
- - Precious metal

M. Bierenstiel *et al. Eur. J. Org. Chem.* **2004**, 1474

- Knölker catalyst

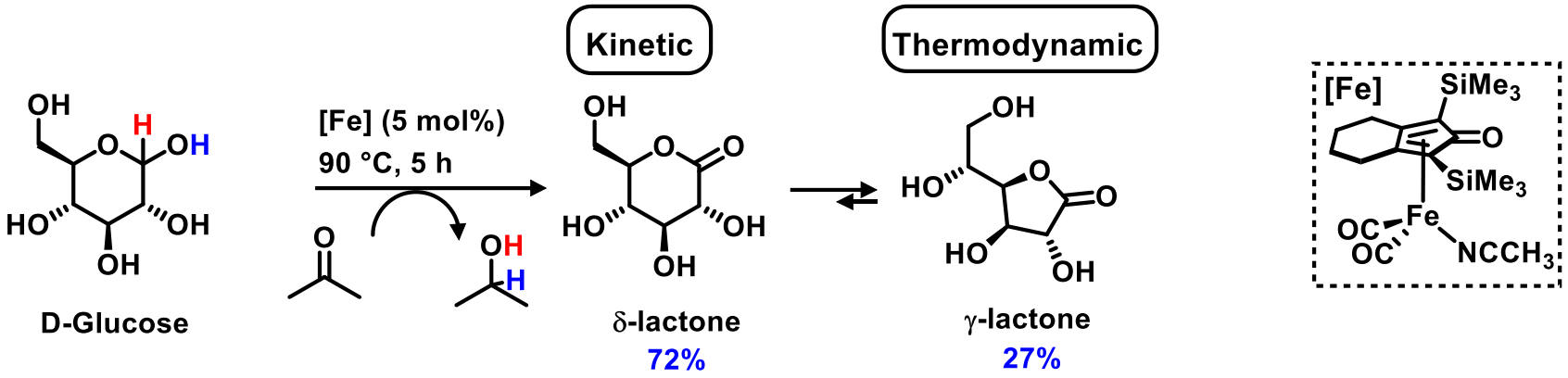


- Oxidation / reduction of alcohol/ketone derivatives
- Application in hydrogen borrowing transformation
- Analoguous to Shvo catalyst
- Air and moisture stable

Y. Tang *et al.*, *J. Org. Chem.*, 2020, **85**, 1823

Optimisation

- Preliminary test



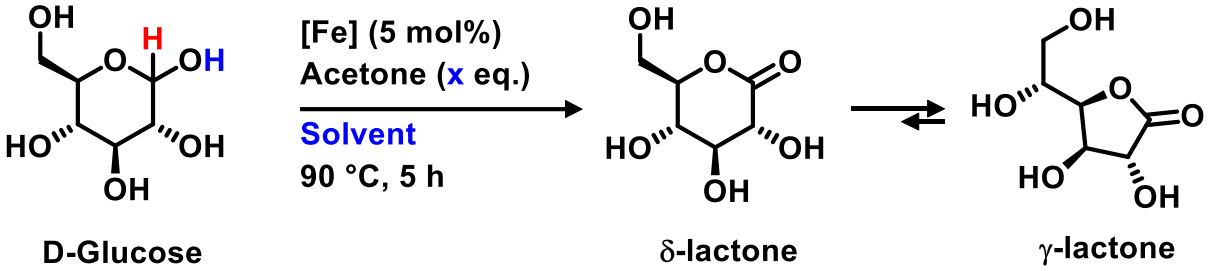
- Complete oxidation of glucose
- Chemo-selectivity for the more reactive anomeric position
- Base and strong-oxidant free
- Full isomerisation in 24 h (+ acetalisation product with acetone)

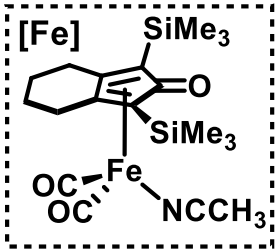
Decrease the amount of acceptor?

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation

- Solvent screening



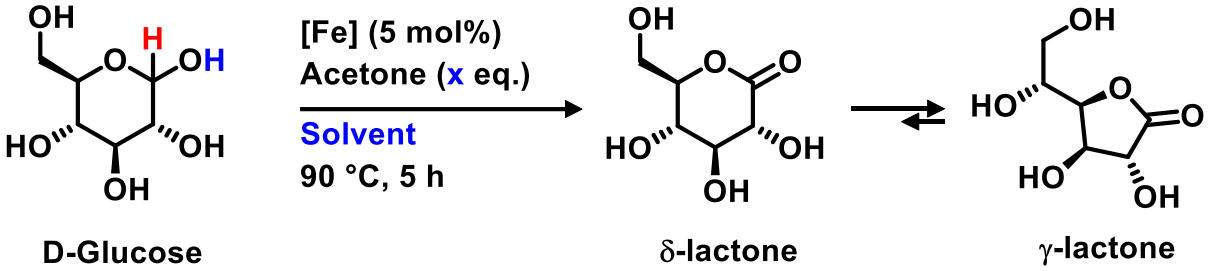


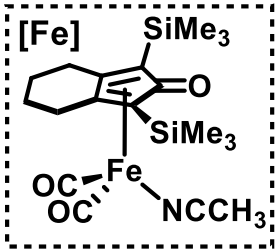
Solvent	Acetone (Eq.)	Lactone Yield (%)
H_2O	10	0
CH_3CN	10	0
CH_3CN	100	0
HFIP	10	0

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation

- Solvent screening



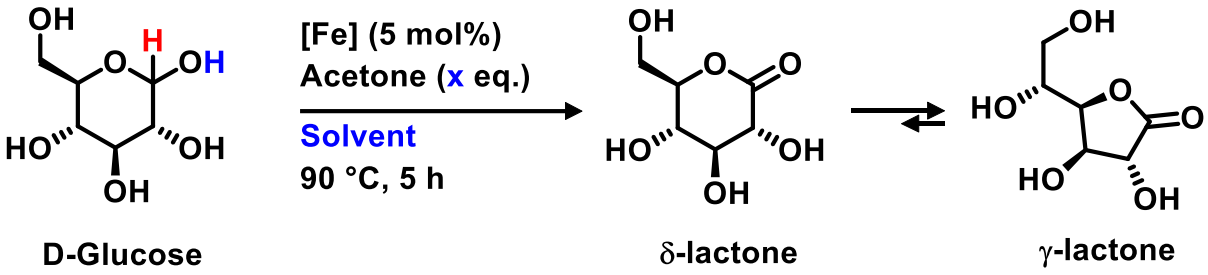


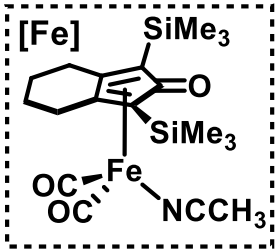
Solvent	Acetone (Eq.)	Lactone Yield (%)
H_2O	10	0
CH_3CN	10	0
CH_3CN	100	0
HFIP	10	0
CF_3CH_2OH	10	40
*t*BuOH	10	90
*t*BuOH	9	58
*t*BuOH	7	50

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation

- Solvent screening





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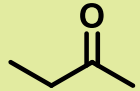
*t*BuOH	7	50
*t*BuOH	5	75

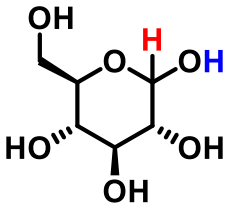


bp = 80 °C

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

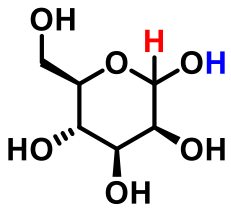
Optimisation | Scope

- Hexoses



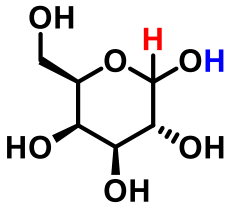
D-Glucose

> 98 %
> 98 %



D-Mannose

> 98 %
> 98 %



D-Galactose

	24 h
54 %	> 98 %
35 %	85 %

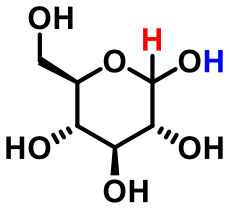
Condition A: acetone, 5 mol% [Fe], 90 °C, 5 h

Condition B: 10 eq. acetone, *t*BuOH, 5 mol% [Fe], 90 °C, 5 h

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

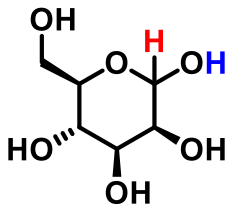
Optimisation | Scope

- Hexoses



D-Glucose

> 98 %
> 98 %



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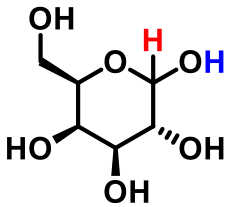
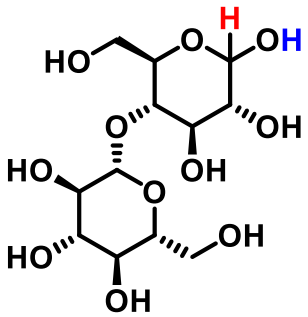


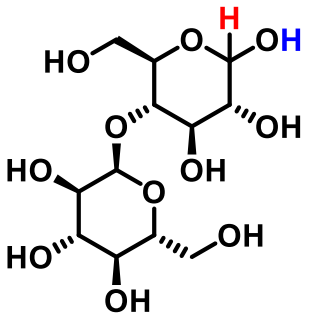
D-Galactose

24 h
54 %	> 98 %
35 %	85 %

Solubility issue?



D-cellobiose

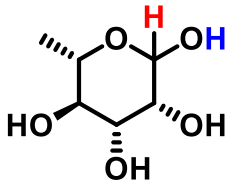


D-maltose

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation | Scope

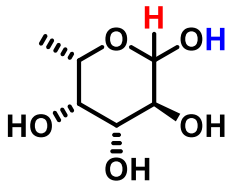
- Deoxy-sugars & pentoses



L-Rhamnose

> 98 %

94 %



L-Fucose

> 98 %

90 %

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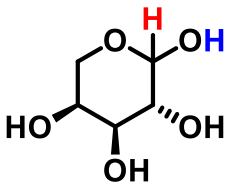
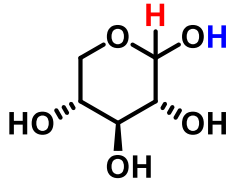


L-Arabinose

> 98 %

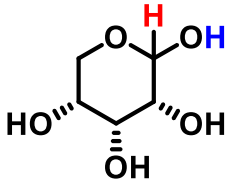
> 98 %



D-Xylose

> 98 %

> 98 %



D-Ribose

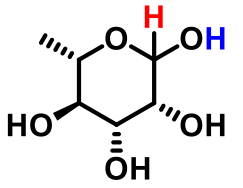
-

> 98 %

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation | Scope

- Deoxy-sugars & pentoses



L-Rhamnose

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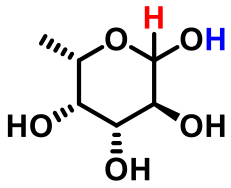
94 %



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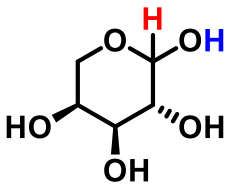
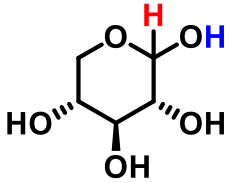


L-Arabinose

3 h

> 98 %
> 98 %

-
90 %

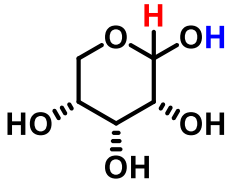


D-Xylose

3 h

> 98 %
> 98 %

98 %
90 %



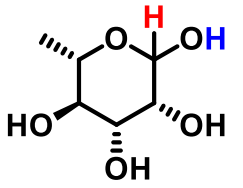
D-Ribose

-
> 98 %

D. Branquet, *et al. Green Chem.* **2022**, *24*, 7682.

Optimisation | Scope

- Deoxy-sugars & pentoses



L-Rhamnose

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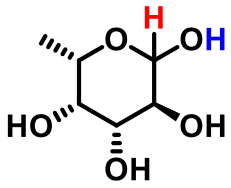
94 %



L-Fucose

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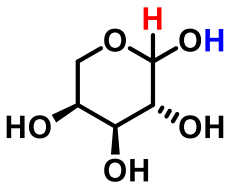
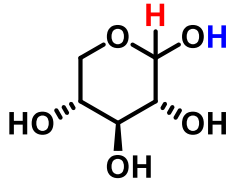


L-Arabinose

3 h
> 98 %
> 98 %

-
90 %

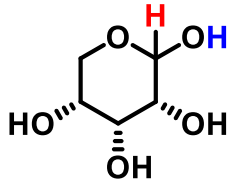


D-Xylose

3 h
> 98 %
> 98 %

98 %
90 %

500 mg
82 %
93 %



D-Ribose

-
> 98 %

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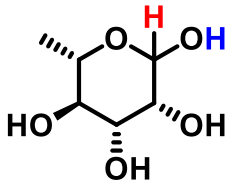
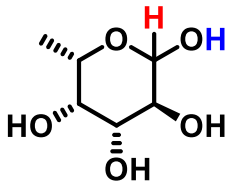
Optimisation | Scope

- Deoxy-sugars & pentoses



L-Rhamnose

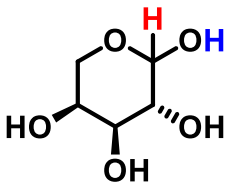
> 98 %
94 %



L-Fucose

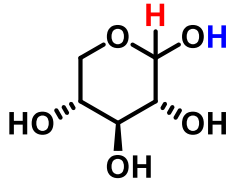
> 98 %
90 %

- ✓ Excellent selectivity & activity
- ✓ Hexoses & pentoses oxidation
- ✓ Mild conditions
- ✓ Greener solvent
- ✓ Earth abundant metal
- - Excess of acceptor



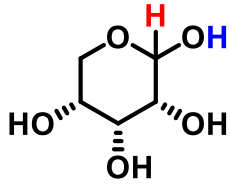
L-Arabinose

3 h	
> 98 %	-
> 98 %	90 %



D-Xylose

3 h		500 mg
> 98 %	98 %	82 %
> 98 %	90 %	93 %



D-Ribose

-
> 98 %

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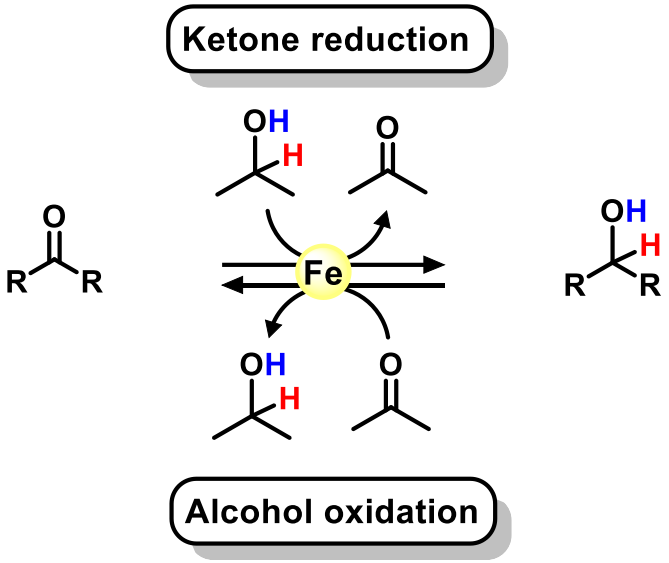
- Transfer hydrogenation



– Reversible process

– Excess of hydrogen donor / acceptor (often used as solvent)

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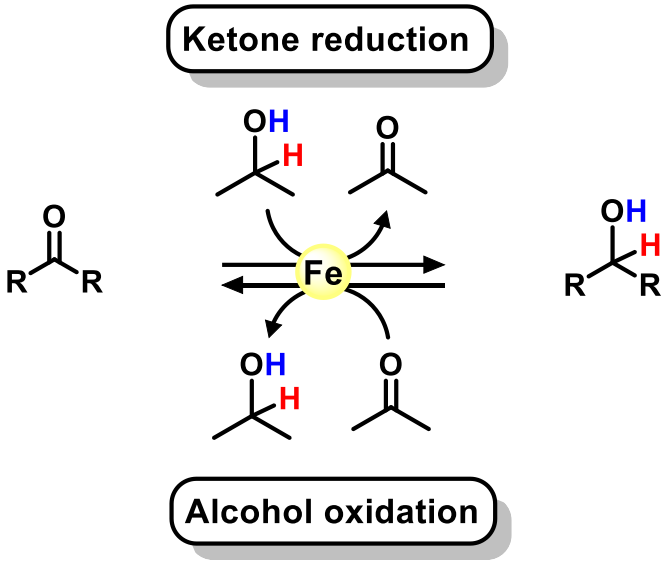
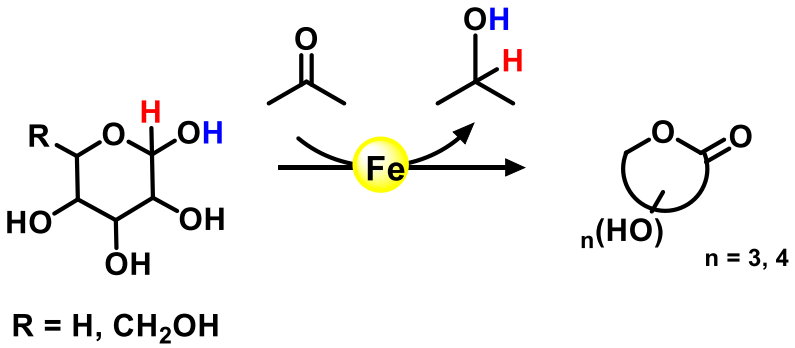
- Transfer hydrogenation



– Reversible process

– Excess of hydrogen donor / acceptor (often used as solvent)

- Oxidation of unprotected sugar via transfer hydrogenation



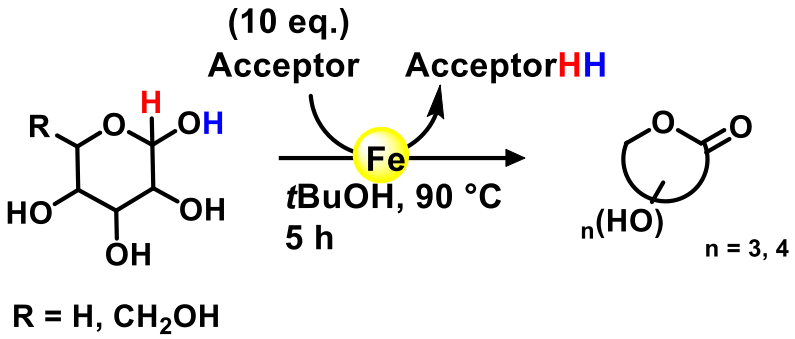
– Stable lactone – Irreversibility

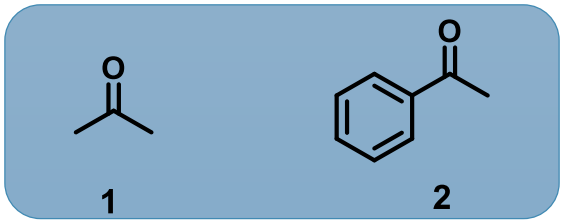
– Stoichiometry of the acceptor?

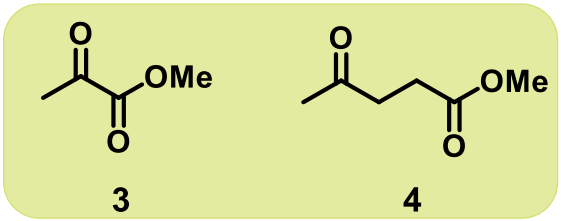
– Increase the range of acceptors

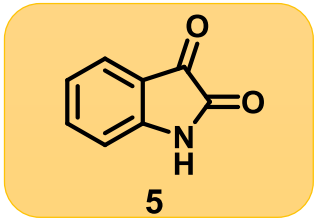
Optimisation | Scope | Acceptor stoichiometry

- Screening of acceptors









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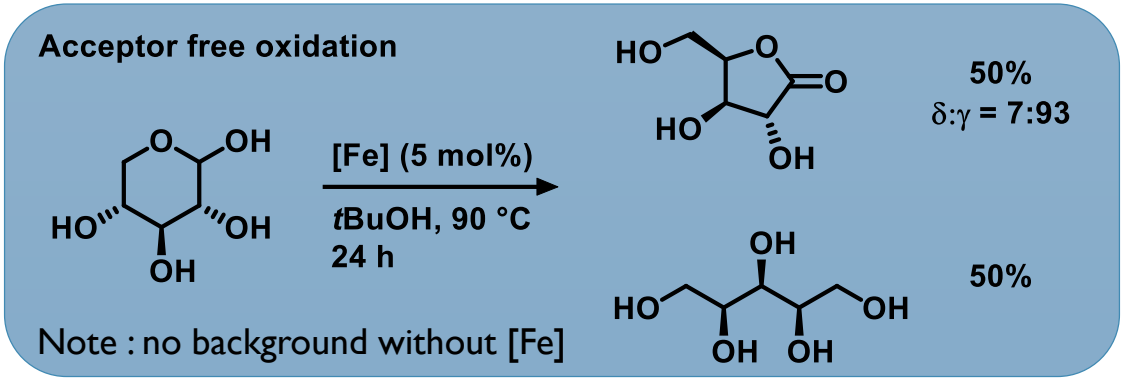
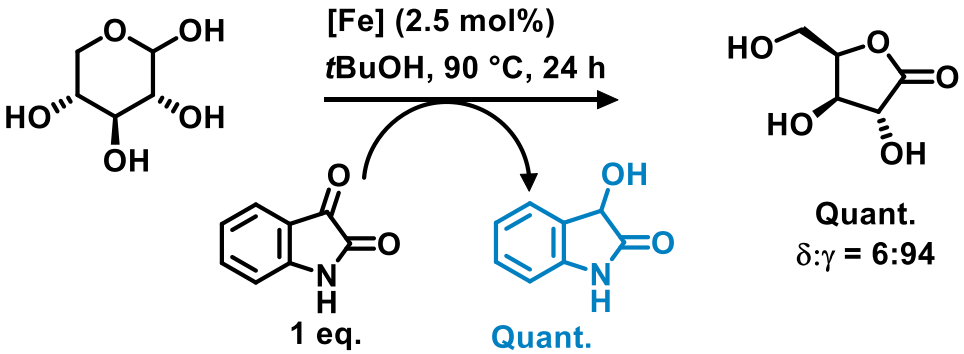
Optimisation | Scope | Acceptor stoichiometry

- Competitive disproportionation of xylose



- Stoichiometry - Isatin



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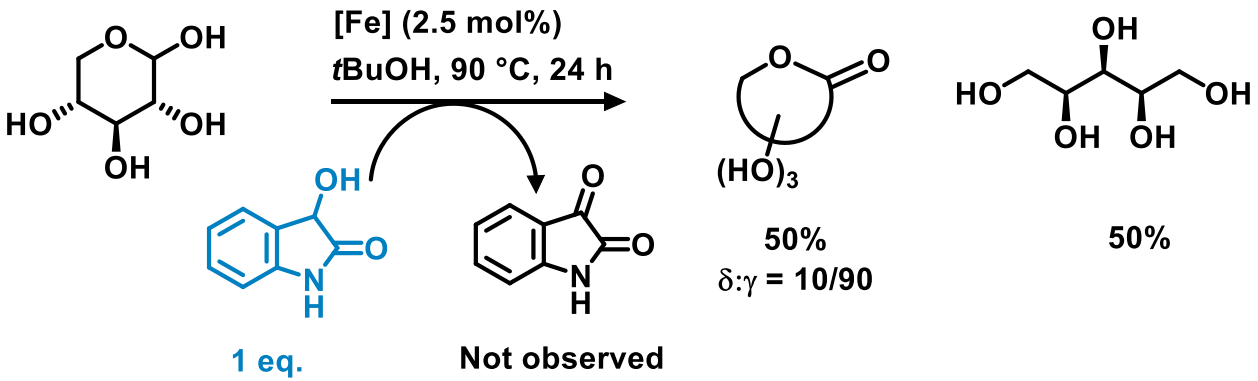
- 3-hydroxyoxindole as donor?



- Disproportionation favoured
- Irreversibility of the transfer hydrogenation process with isatin

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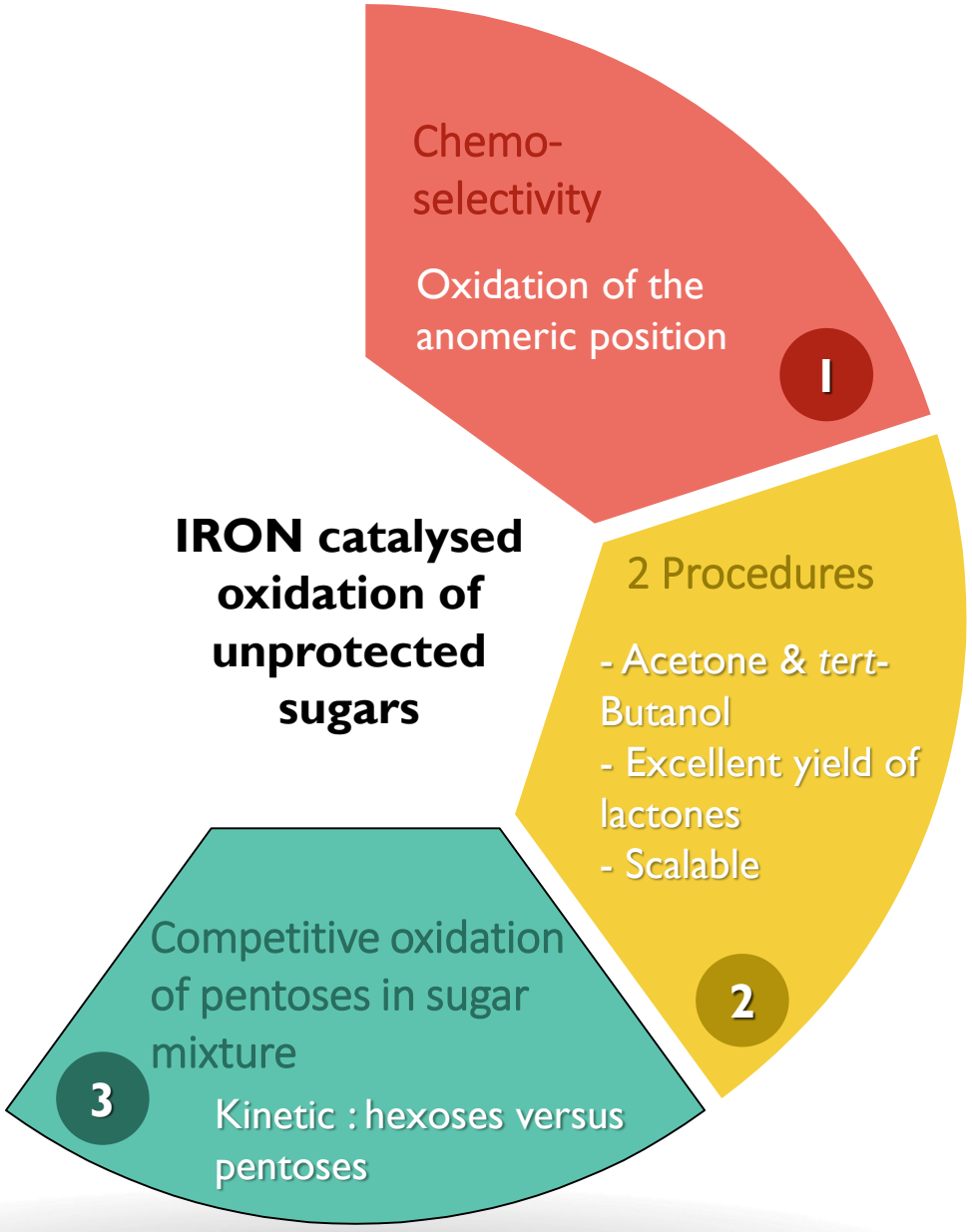
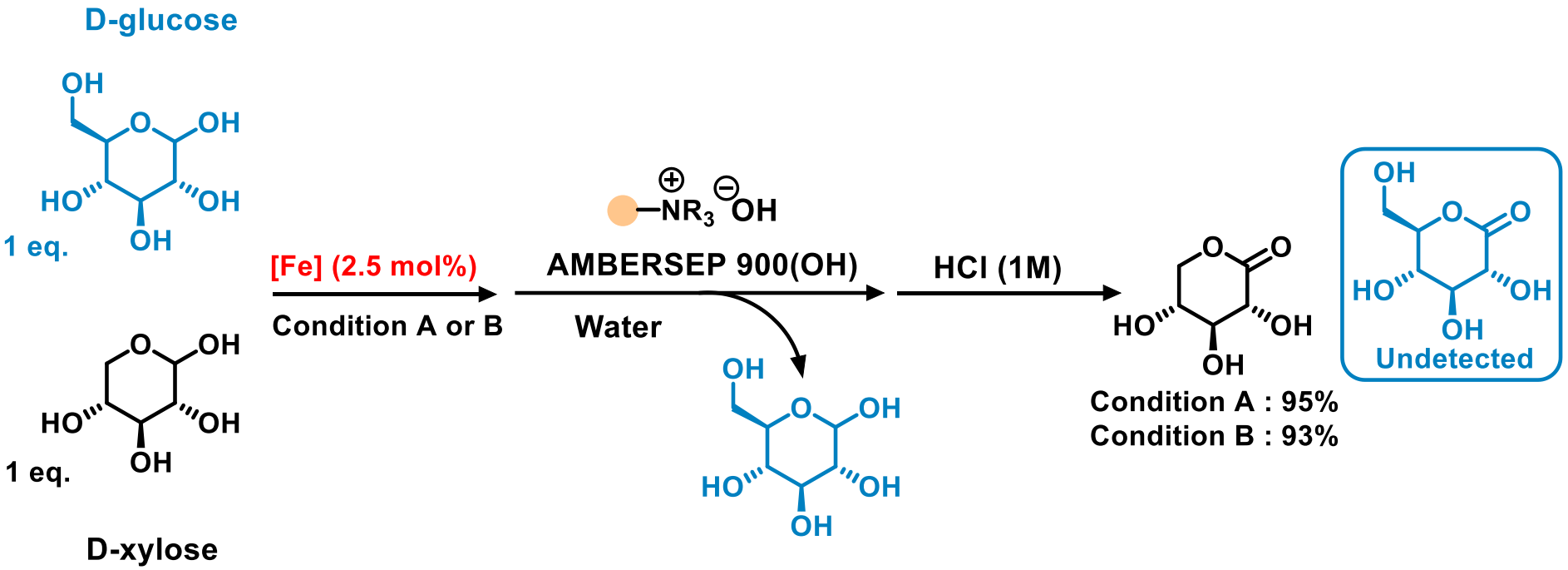

Chemo-selectivity
Oxidation of the anomeric position
1
IRON catalysed oxidation of unprotected sugars
2 Procedures
- Acetone & tert-Butanol
- Excellent yield of lactones
- Scalable
2
Competitive oxidation of pentoses in sugar mixture
3
Kinetic : hexoses versus pentoses

- Sugars mixture



- Purification using an anion exchange resin
- Excellent yields of xylonolactones using procedure A and B

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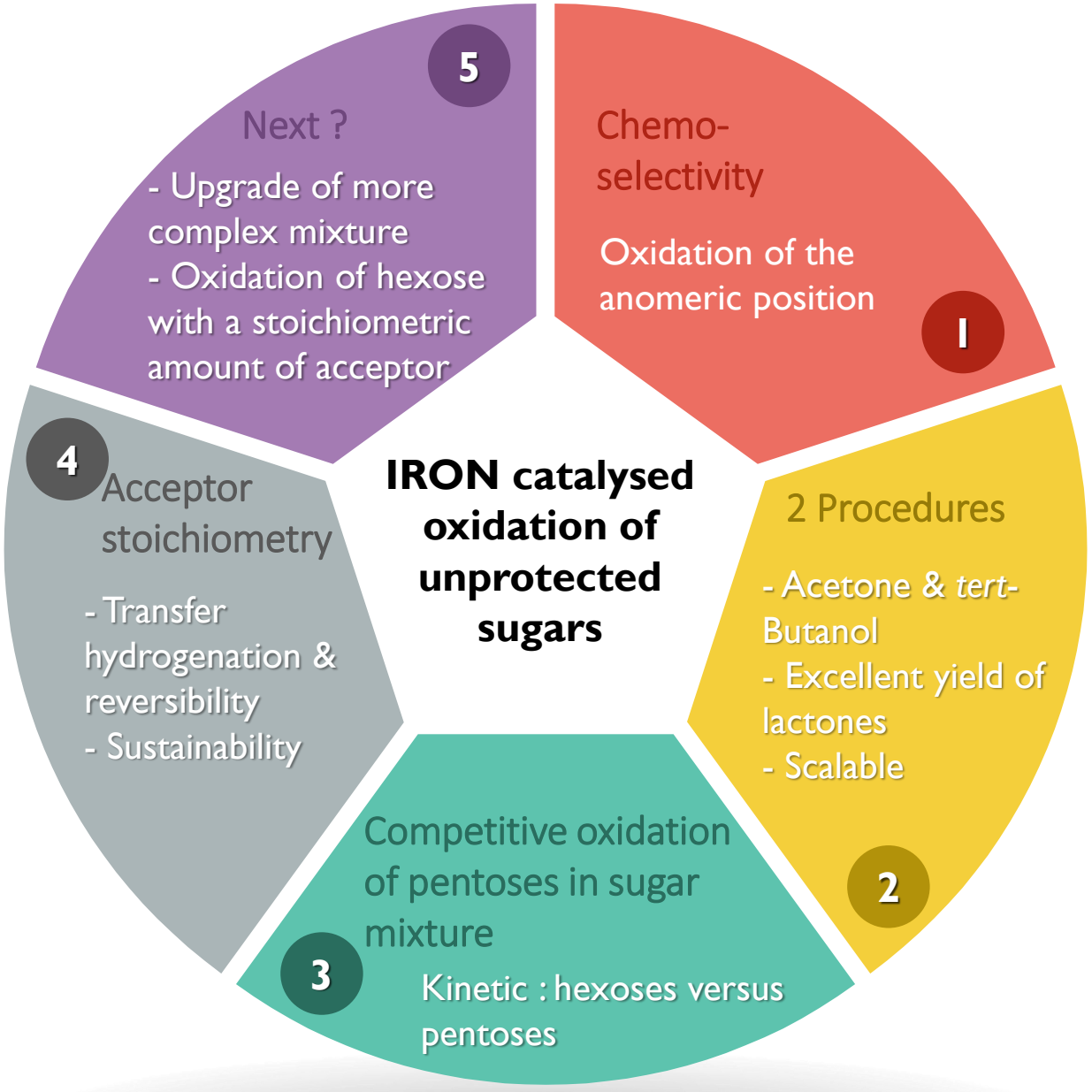
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Competitive oxidation of pentoses in sugar mixture
Kinetic : hexoses versus pentoses
4
Acceptor stoichiometry
- Transfer hydrogenation & reversibility
- Sustainability
5
Next ?
- Upgrade of more complex mixture
- Oxidation of hexose with a stoichiometric amount of acceptor

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  - Dr Nicolas Hucher
  - Dr Catherine Taillier
  - Prof. Vincent Dalla
  - Prof. Arnaud Martel (DFT calculations)