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Upgraded Production of a Hydroxylactone Anhydrosugar by Cellulose Pyrolysis and its Application in the Synthesis of Biologically Active Compounds

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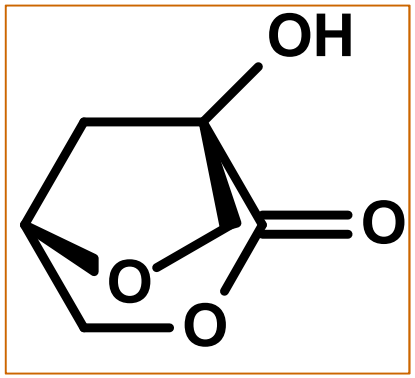
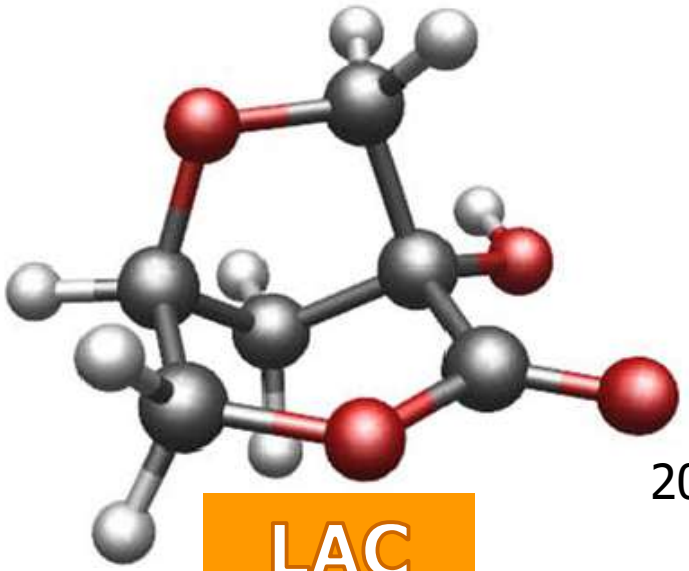
Provincia Autonoma di Trento,
CNR, Naples
Inst.Composite Biomedical Materials

LAC: a building block from biomass



CHIRAL

DERIVABLE from CELLULOSE



C6 MONOMER

LAC

1989: Discovered by Forneaux *et al* from pyrolysis of cellulose with $ZnCl_2$ - Mechanism proposed.

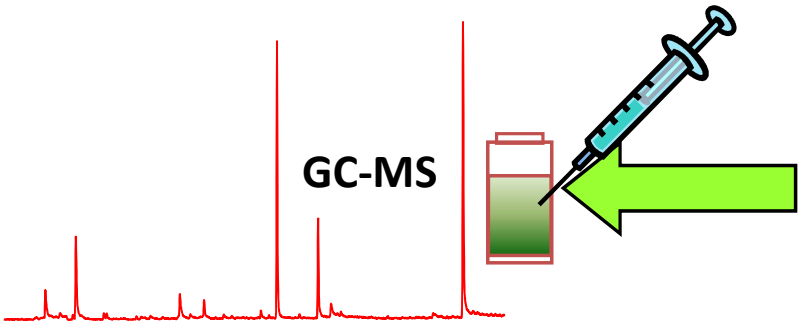
2007: Ri-descovered from pyrolysis of cellulose with nanopowders metal oxide ($Al_3(TiO_4)_2$)

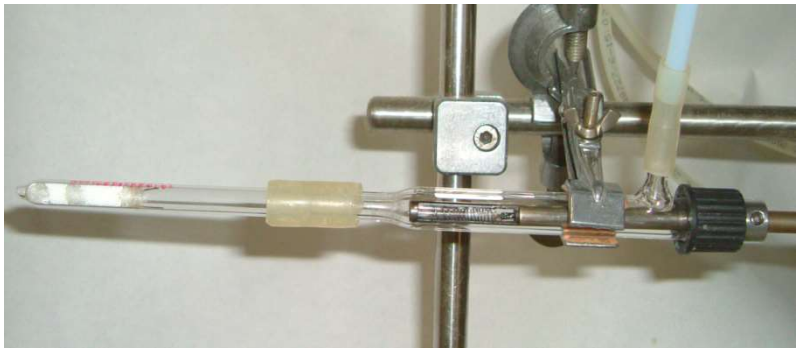
Functional groups HYDROXYLACTONE

R.H.Furneaux et al., *J.Chem.Soc.*. **1988**, *1*, 49

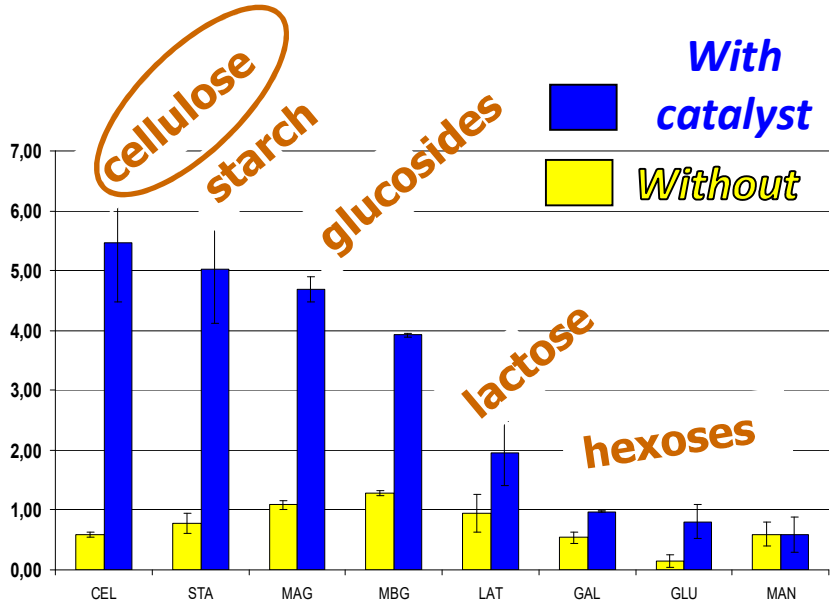
D.Fabbri et al. *Green Chem.* **2007**, *9*, 1374

The role of analytical pyrolysis
Preliminary screening

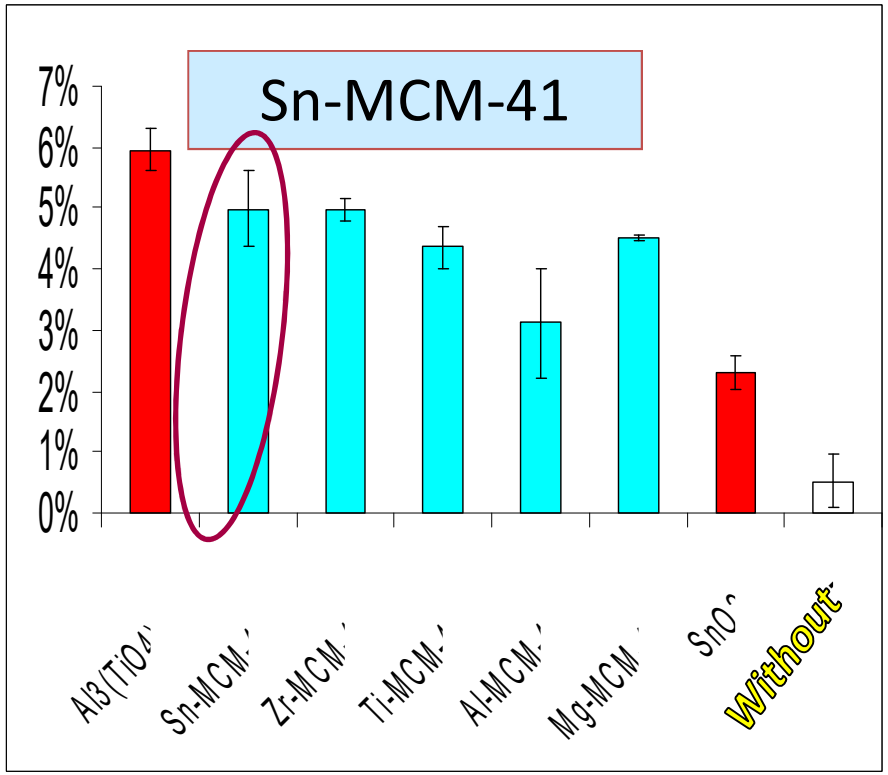




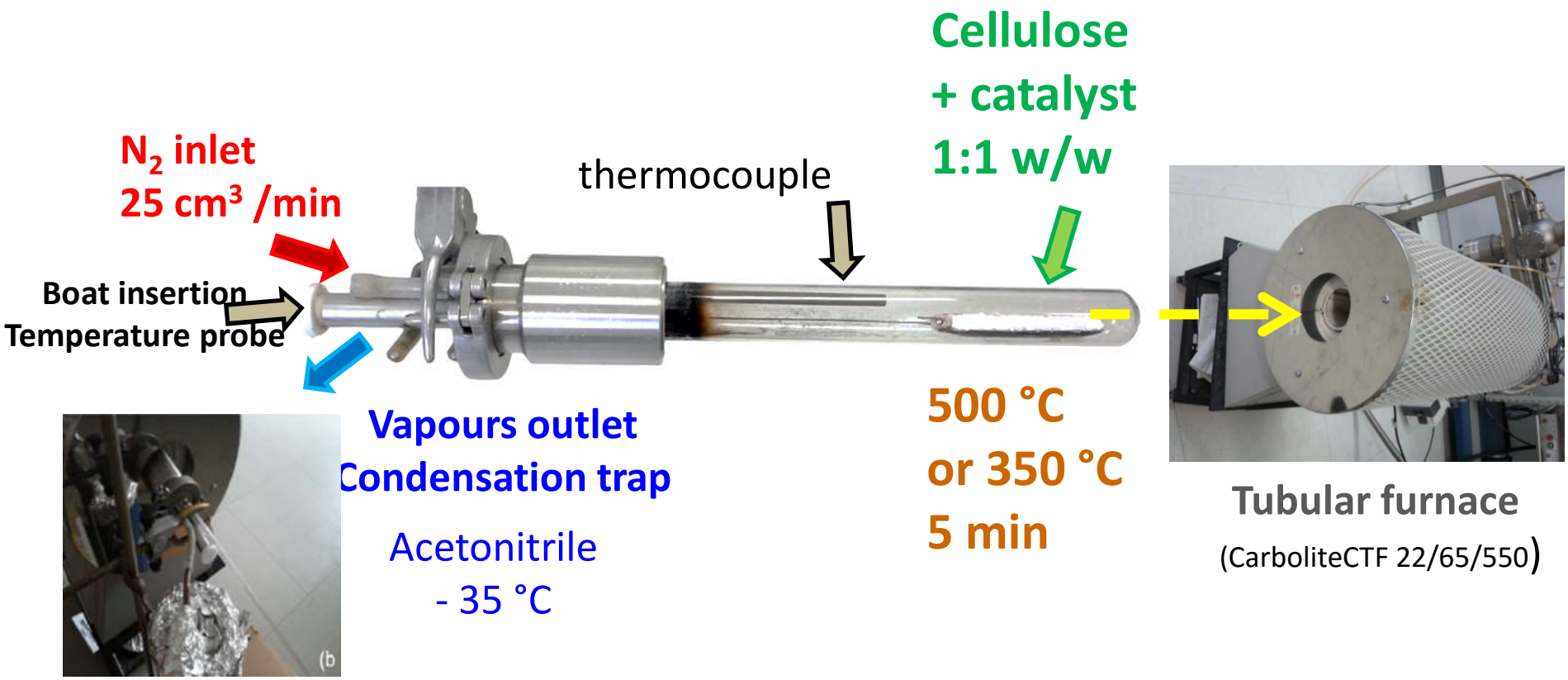
LAC yields



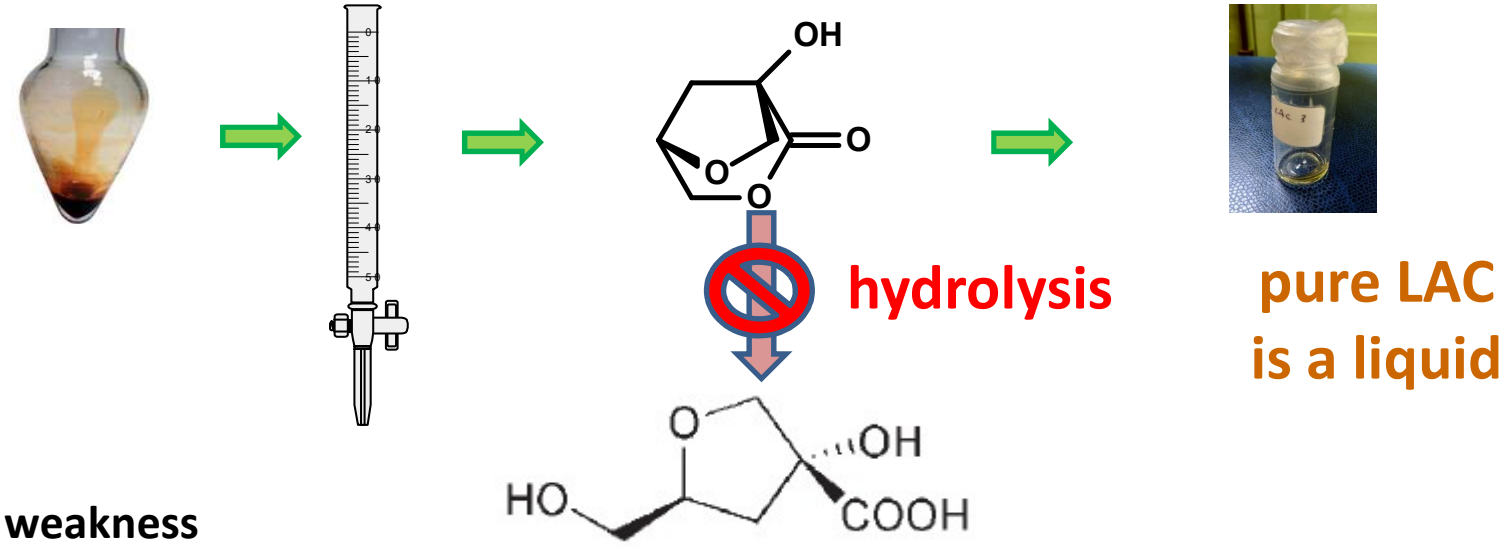
C.Torri et al. JAAP **2009**, *84*, 25



Scale-up: bench pyrolyser



LAC purification
Liquid chromatography



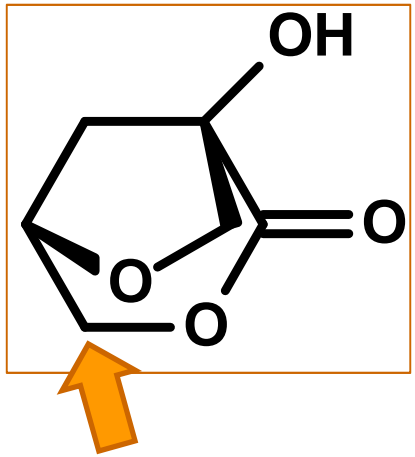
➢ **Observed weakness**

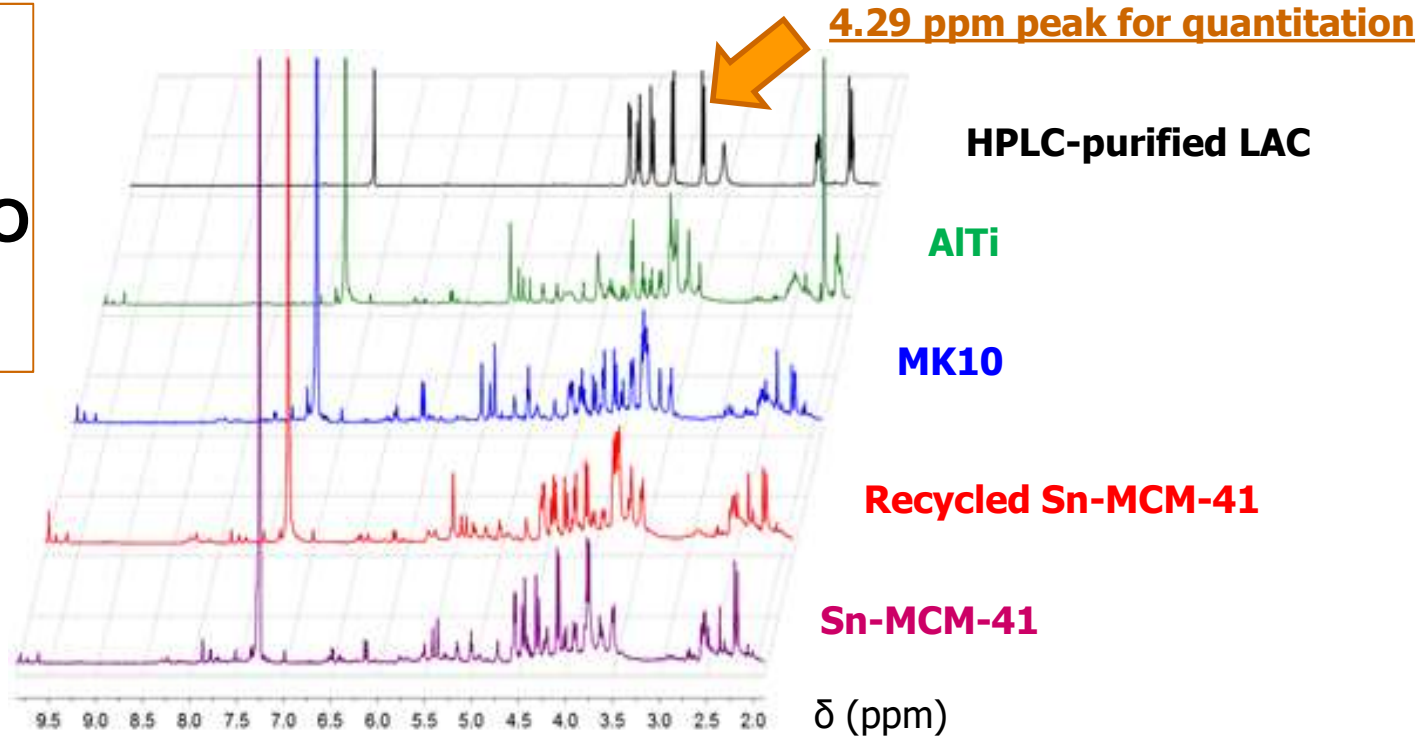
- **Polar Silica gel** its acidity down-grade LAC ➔ **rapid chromatography**
- **Normal cyano phase** allowed a major recovery ➔ **expensive**
- **Non-polar reversed phase**, water as co-eluent ➔ **hydrolysis of lactone**

➢ **Final conditions for gram-scale purification**

Column LC (silica gel, hexane /EtOAc gradient elution) of the soluble portion from dichloromethane suspension of bio-oil and further purification by filtration on active charcoal.

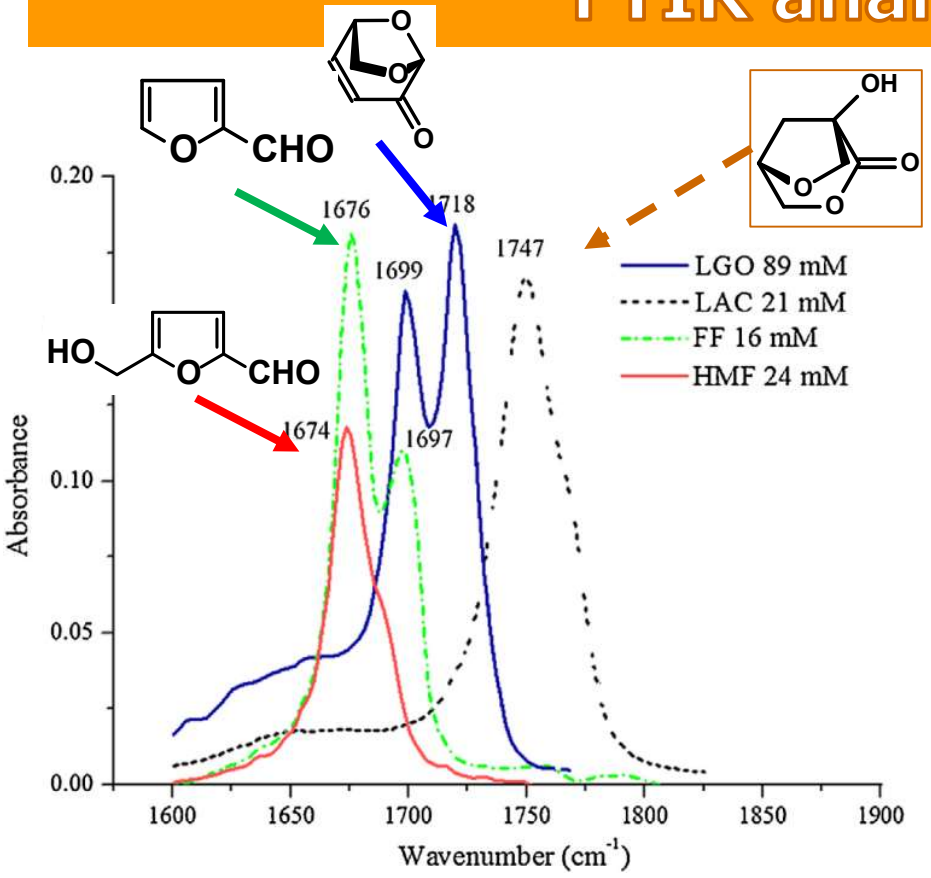
Quantitation of LAC in bio-oil by NMR analysis

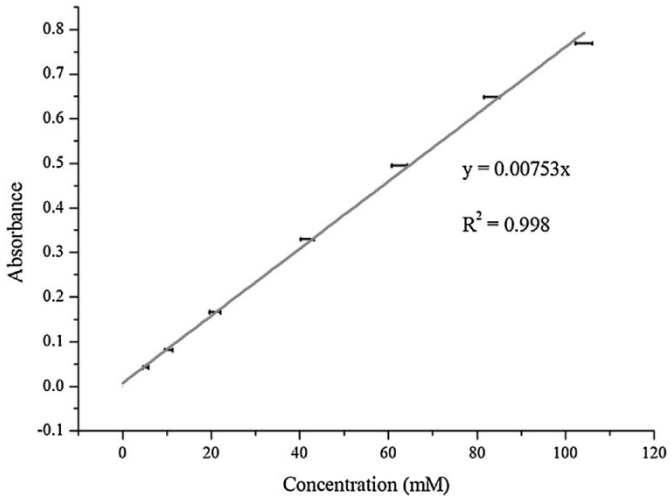




^{1}HNMR spectrum (1.5 mg mL^{-1} in $CDCl_3$, 400 MHz) of pure LAC and bio-oil samples from cellulose pyrolysis in the presence of the indicated catalysts.

Quantitation of LAC in bio-oil by FTIR analysis





FTIR Calibration curve for LAC quantification, at c= 2÷104 mM.

Carbonyl C=O region

Levoglucosenone, Furaldehyde, Hydroxymethylfuraldehyde , LAC

I.Mancini et al., JAAP **2014**, *11*, 2985.

LAC yields from Sn-MCM-41

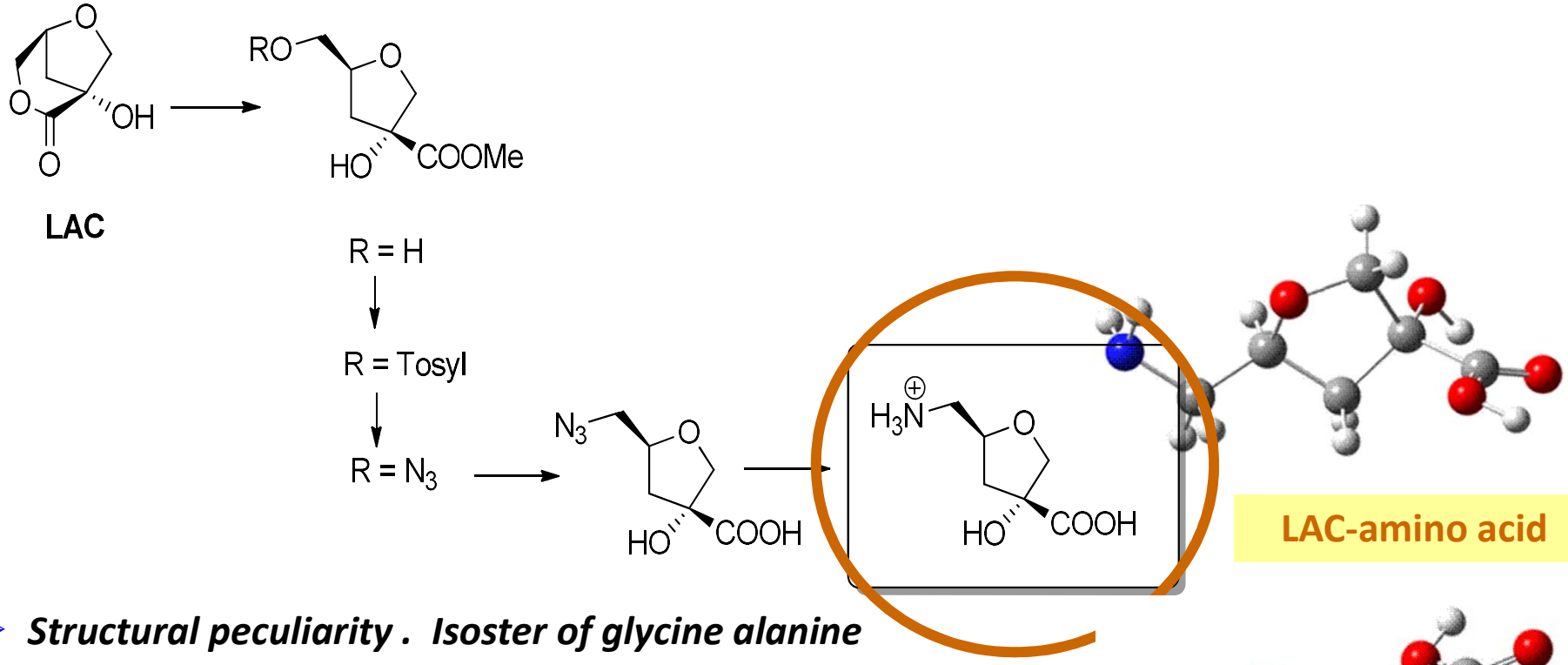
Catalyst	LAC concentration (wt.%)			Yield of LAC from cellulose (wt.% ±0.1%)
	^{1}HNMR	FT-IR		
Sn-MCM-41	27.6 ± 0.4	28.1 ± 0.3 (27.0 ± 0.3)	500 °C (350 °C)	7.6
Recycled Sn-MCM-41	26.8 ± 0.5	27.3 ± 0.3 (25.4 ± 0.3)		7.3

LAC yields from montomorillonite

Catalyst	Pyrolysis T	FT-IR LAC conc. Wt%	Yield of LAC from cellulose (wt.% ±0.1%)
MK10	500 °C	18.6 ± 0.2	4.8
MK10	350 °C	24.1 ± 0.3	-

Industrially available, low cost, regenerable

LAC derivatives
Synthesis of a new amino acid

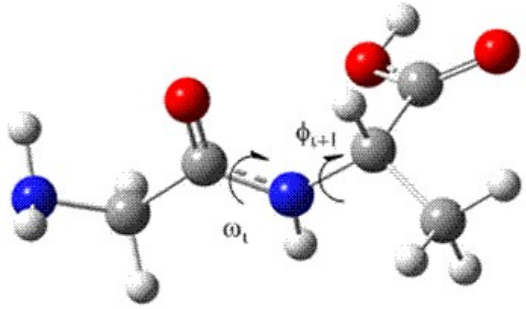


LAC-amino acid

➢ ***Structural peculiarity . Isoster of glycine alanine***

It is comparable to H-Gly-Ala-OH dipeptide, with the peculiarity of assuming a restricted conformation.

Replacement for the Gly-Ala residue in a peptide sequence can be interesting in peptidomimetics studies .



Glycine-Alanine

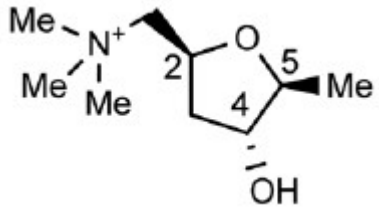
A. Defant et al. *Amino Acids* **2011**, *40*, 633.

its similarity with muscarine

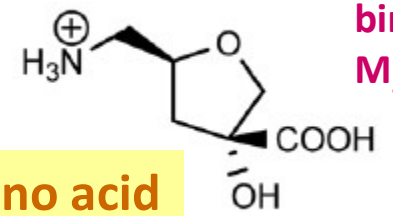
Amanita muscaria

It.wikipedia.org

muscarine



LAC-amino acid



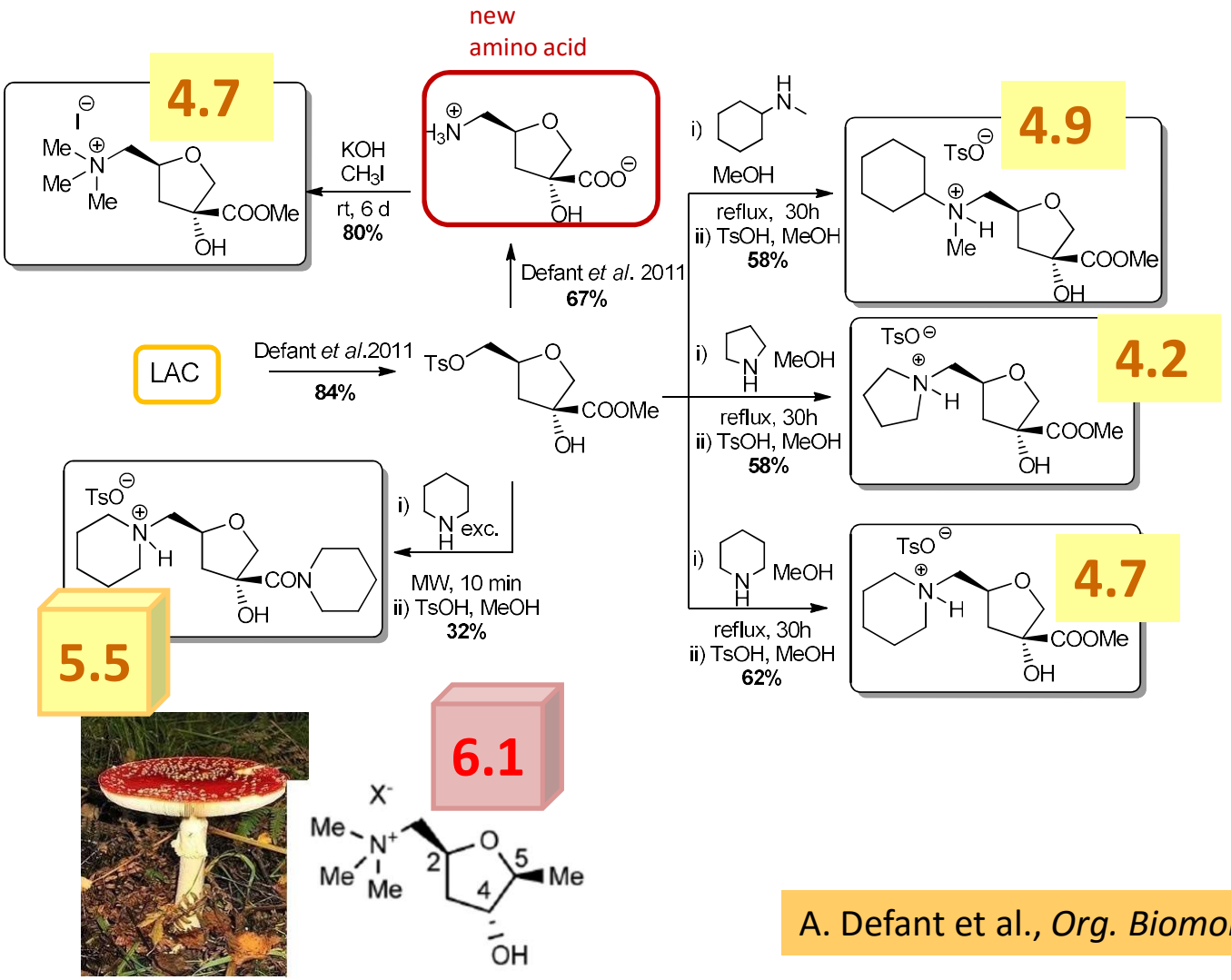
Muscarinic receptors

Muscarine is an agonist of the acetylcholine neurotransitter due its binding with muscarinin receptors M_1-M_5.

The LAC-derived aminoacid has a strong structural similarity with the alkaloid muscarine.

Compounds mimicking muscarine activity are of interest in drug design in order to achieve new selective agents in the therapeutic treatment of various disease (Alzheimer's, glaucoma).

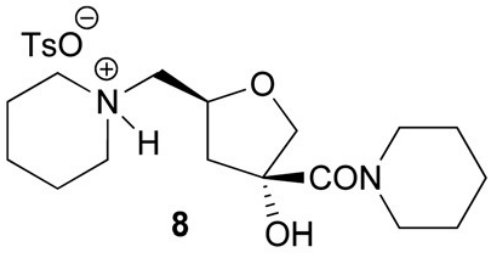
Synthesis and activity of muscarin-like compounds

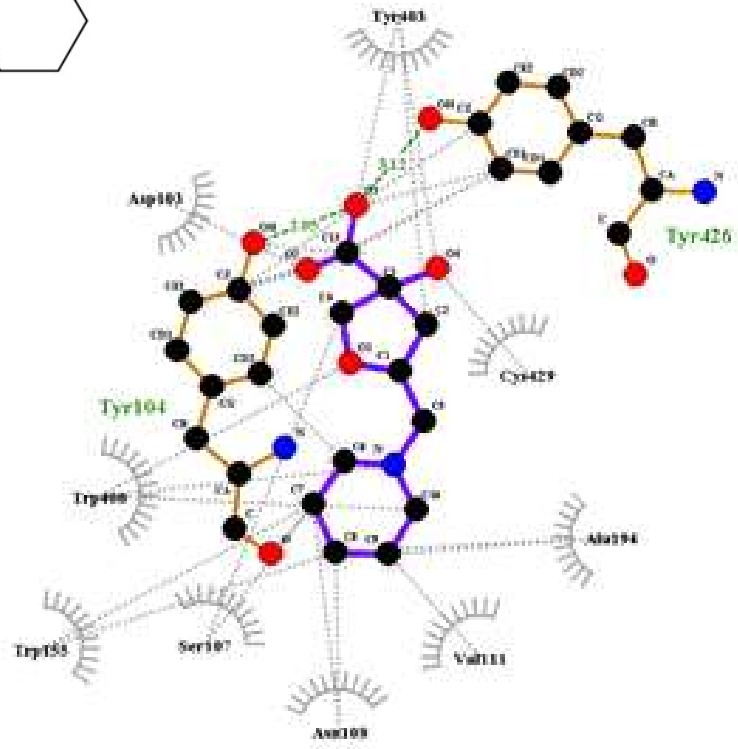


X.X
Binding data with receptor
M2
(cardiac function)

A. Defant et al., *Org. Biomol. Chem*. **2015**, *13*, 6291.

LAC-muscarinic interaction with hM2 receptor





Docking calculation of the complex between the most experimentally active compounds with hM_2 subtype (3UON PDB.file): view of the interactions in the receptor site.