

Interlocked molecules, origin of life and chirality : from synthesis to the analysis of chiral compounds.

IC²MMP

Institut de Chimie des Milieux et Matériaux de Poitiers



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UMR7285



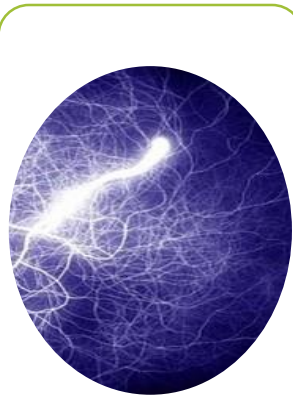
EBiCoM



Hydrasa



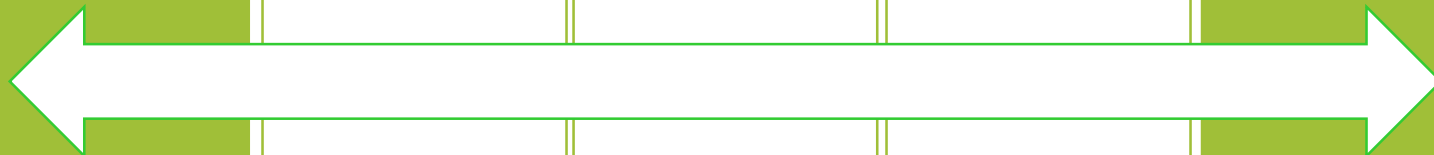
SAMCAT



MédiaCAT



Synthèse
organique

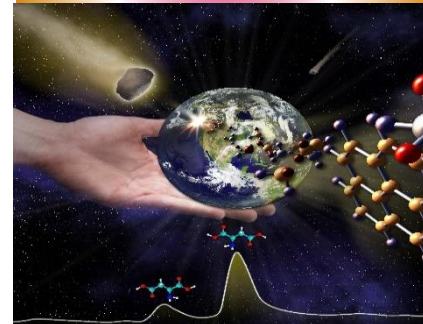
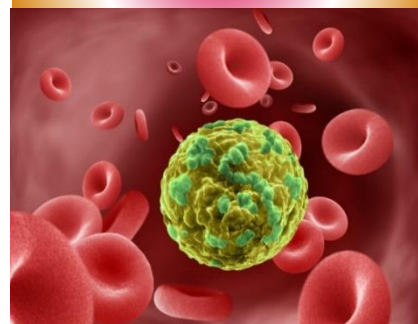
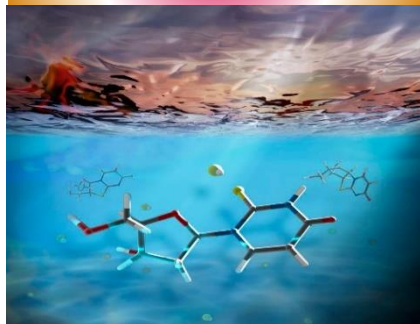
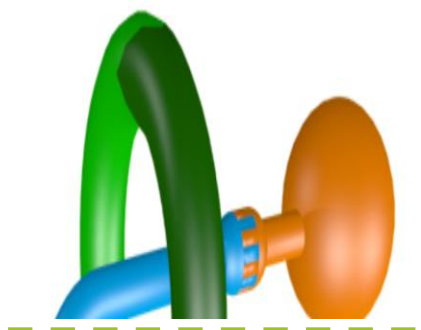


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UMR7285



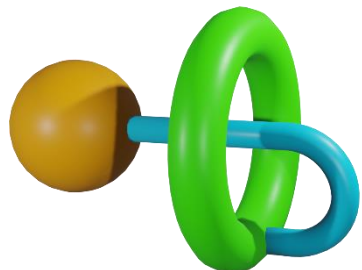
Axes thématiques transversaux



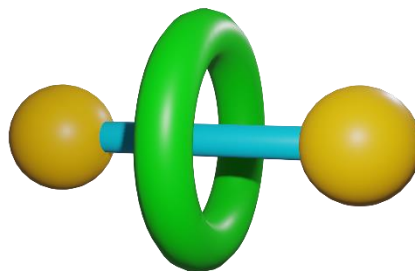
IC2MP

Institut de Chimie des Milieux et Matériaux de Poitiers

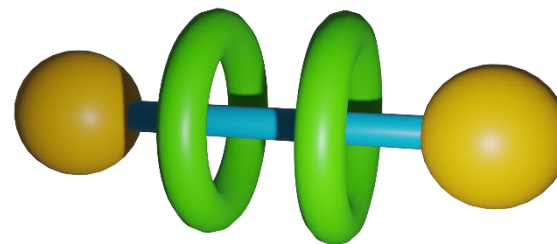
The rise of interlocked molecules



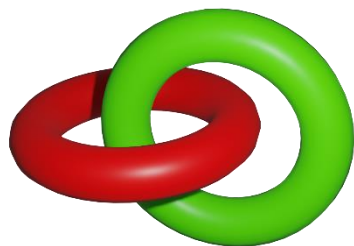
[1]rotaxane



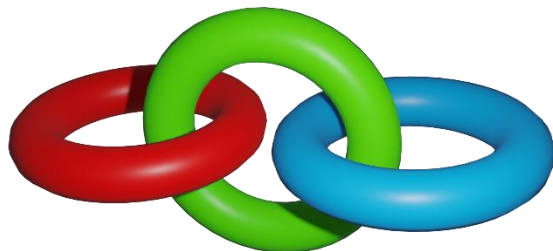
[2]rotaxane



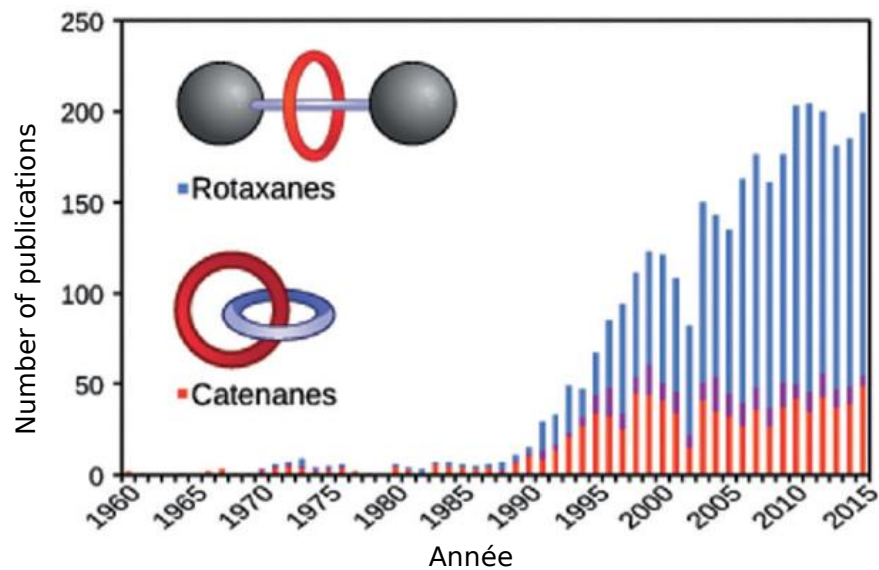
[3]rotaxane



[2]caténane

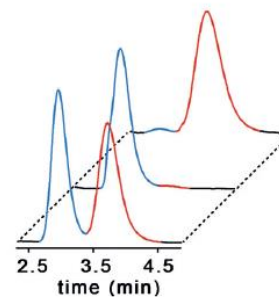
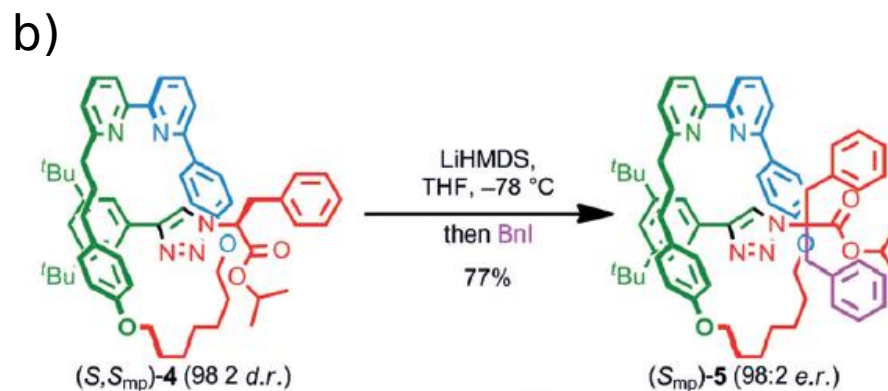
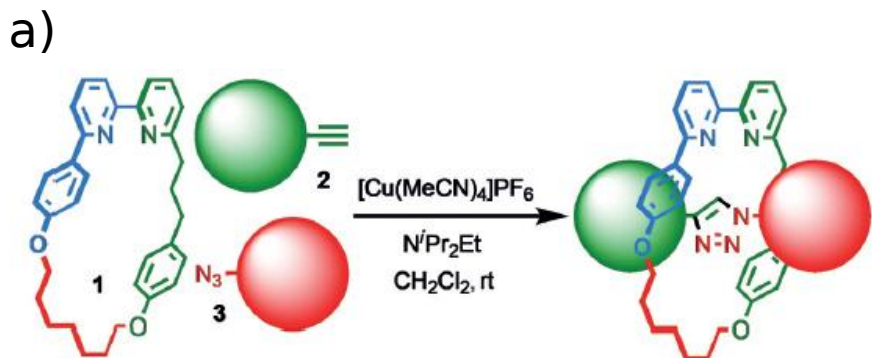
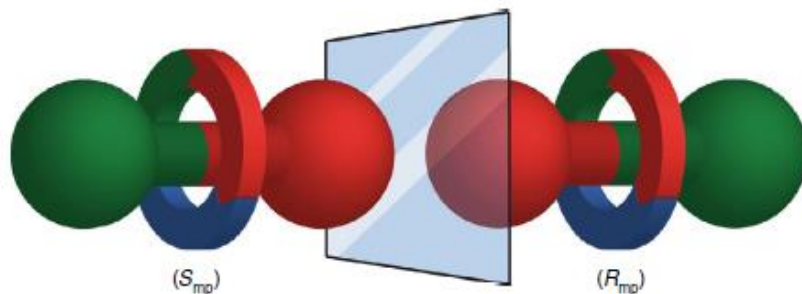


[3]caténane



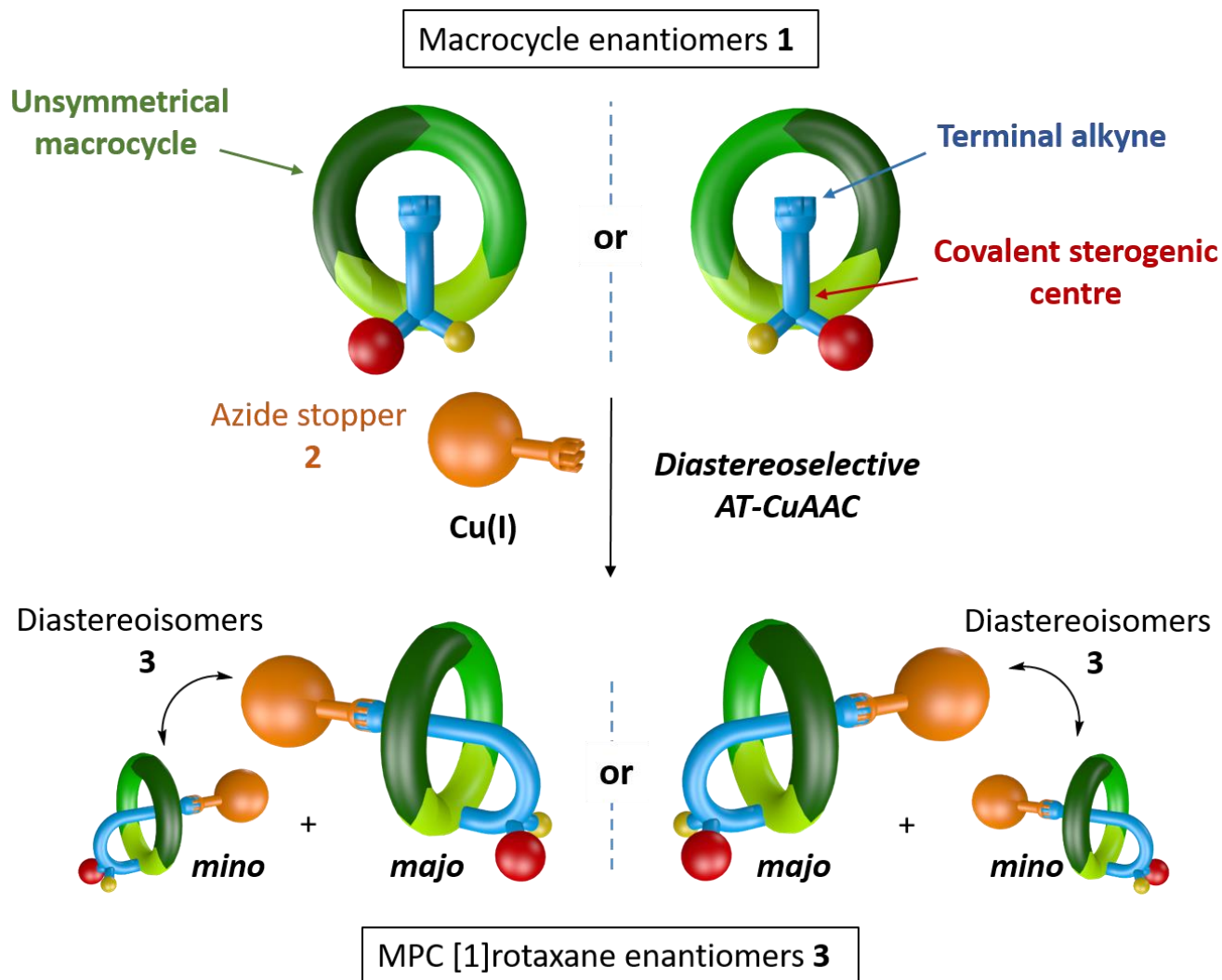
Stoddart, J. F. *Angew Chem. Int. Ed.* **2017**, 56 (37), 11094-11125

Chirality in rotaxanes



Goldup, S. M. *Angew. Chem. Int. Ed.* **2018**, 57, 14806-14810

Diastereoselective Synthesis of [1]Rotaxanes



Chem. Sci. 2020, 12, 2521-2526

Diastereoselective Synthesis of [1]Rotaxanes

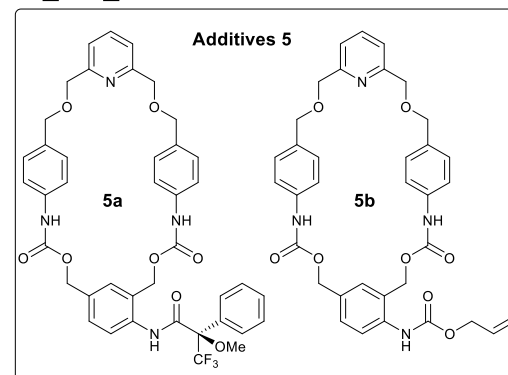
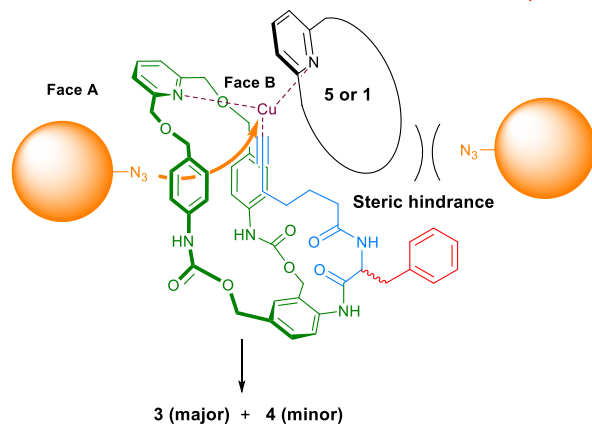
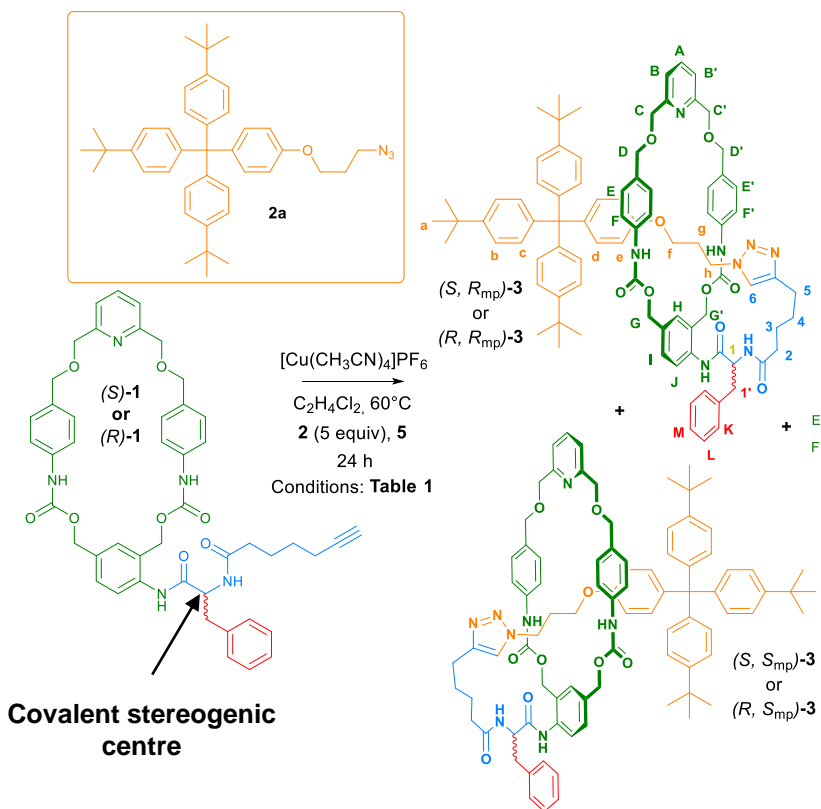
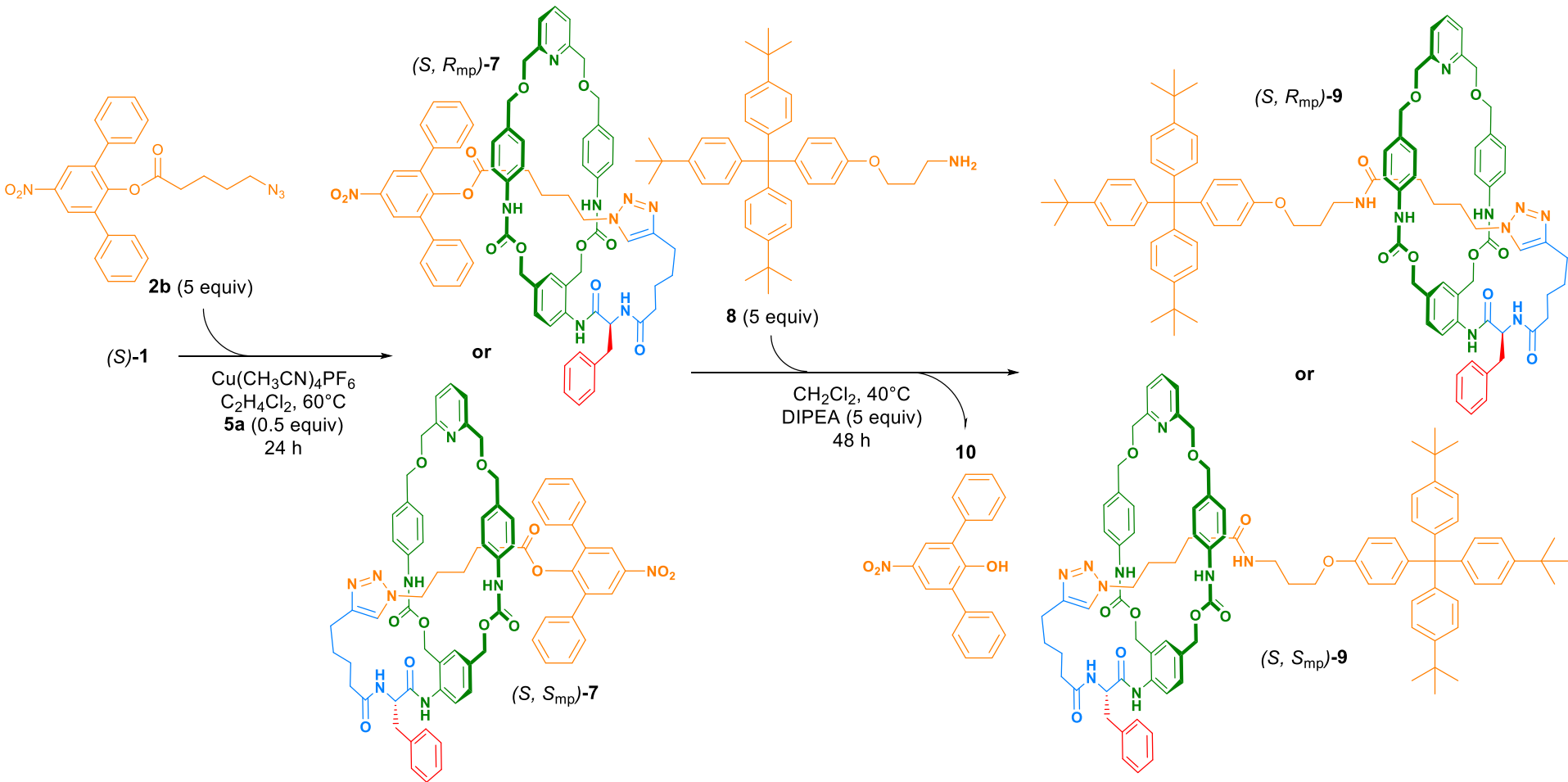


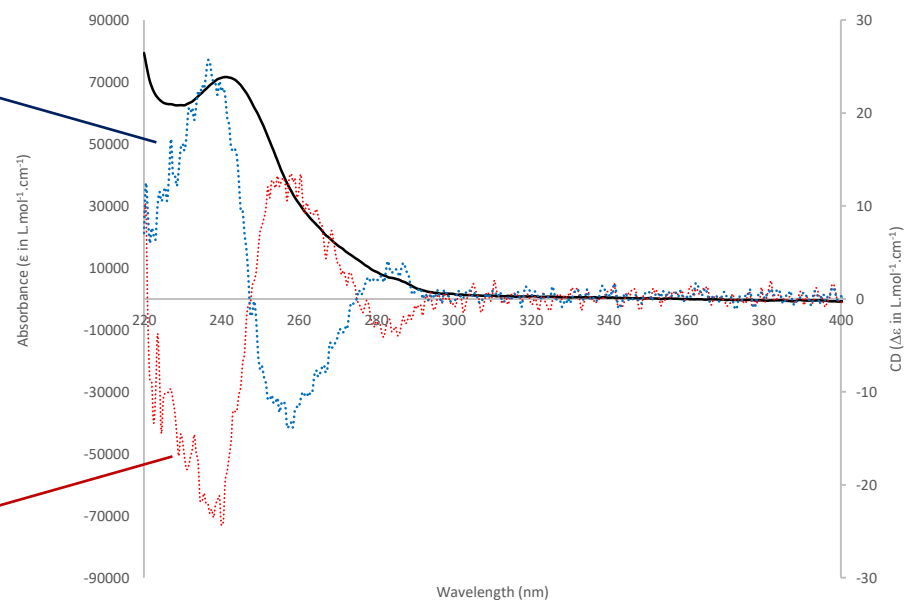
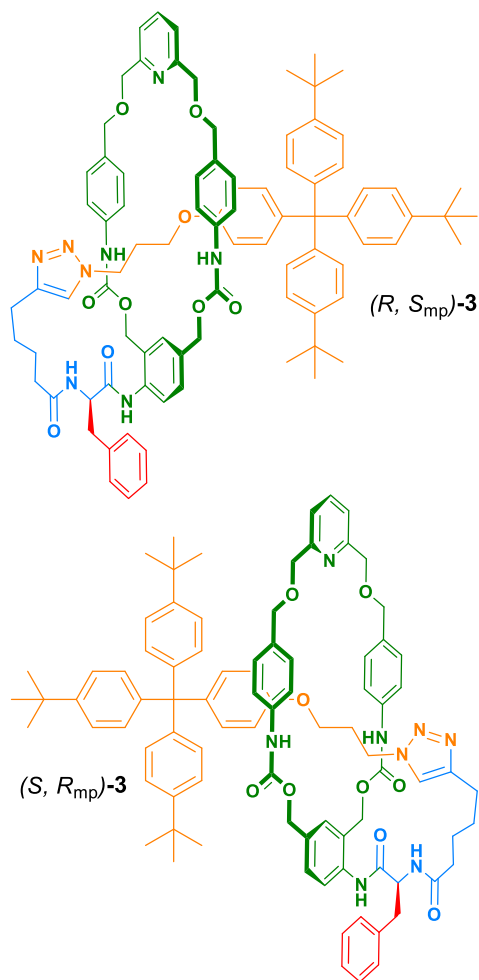
Table 1 Reaction conditions used for the diastereoselective synthesis of the [1]rotaxane **3**

Entry	Cu(I) equiv.	Additive (equiv.)	3/4 ratio ^c	Conversion (%)	Yield (%) ^d
1	0.5	None	8/2	50	29
2	0.75	None	8/2	75	35
3	1	None	1/1	100	33
4	0.95	None	1/1	95	33
5	1 ^a	None	7/3	100	44
6	1	5a^b (1)	8/2	100	48
(S)-1 7	1	5a^b (0.5)	8/2	100	45
8	1	5a^b (0.25)	7/3	100	40
9	1	5b^b (0.5)	8/2	100	31
(R)-1 10^e	1	5a^b (0.5)	8/2	100	46

Diastereoselective Synthesis of [1]Rotaxanes



Diastereoselective Synthesis of [1]Rotaxanes



CD spectra of (S, R_{mp}) -3 (red dashed) and (R, S_{mp}) -3 (blue dashed). Absorbance spectrum (black). Measured in CH_2Cl_2 ($C = 10^{-4}$ M) at $20^\circ C$.

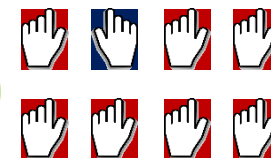
Chirality **2021**, *33*, 773-782 with J Crassous, G. Pieters and P. L. Polavarapu

Emergence of homochirality on Earth: an abiotic scenario

Early Earth
(racemic)



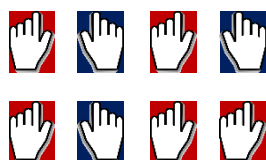
Asymmetric autocatalysis with ee amplification



Current Earth
(homochiral)

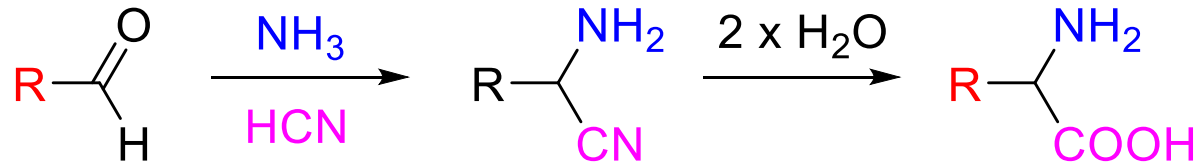


Symmetry breaking



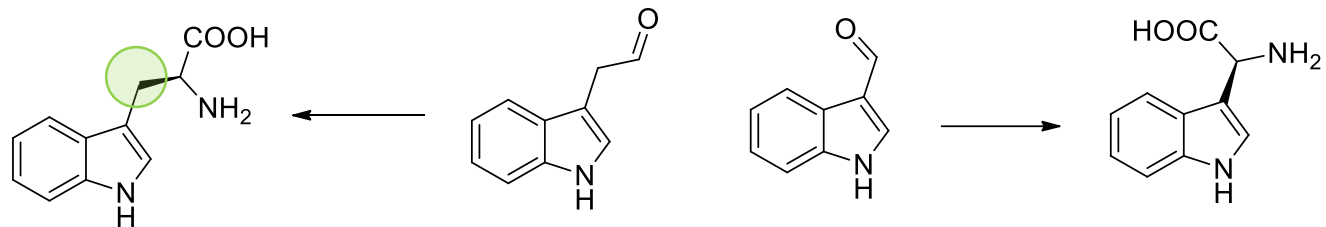
Chance or determinism?

Prebiotic synthesis of amino-acids: Strecker or not Strecker?



Question n°1 : **Where the aldehydes come from?**

Question n°2 : **Why aromatic amino-acids contain a CH₂?**

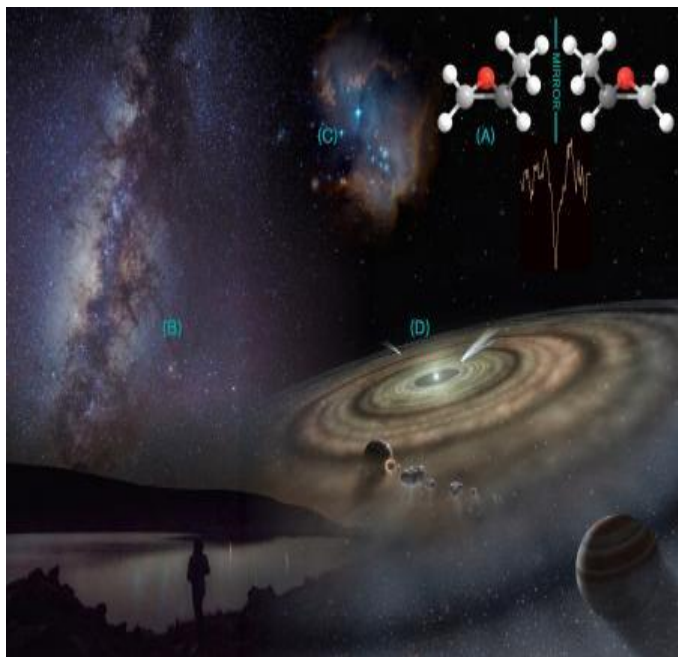


Question n°3 : **Is there any stereoselective Strecker reaction in water?**

Question n°3 : **How amino-acids polymerize in water?**

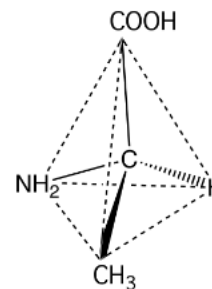
Homochirality and life

- Targets in interstellar media

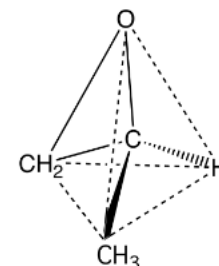


P. Poinot - C. Geffroy
Q. Remaury

204 identified molecules from 2 to 70 C
gaz phase (McGuire 2018)



Alanine

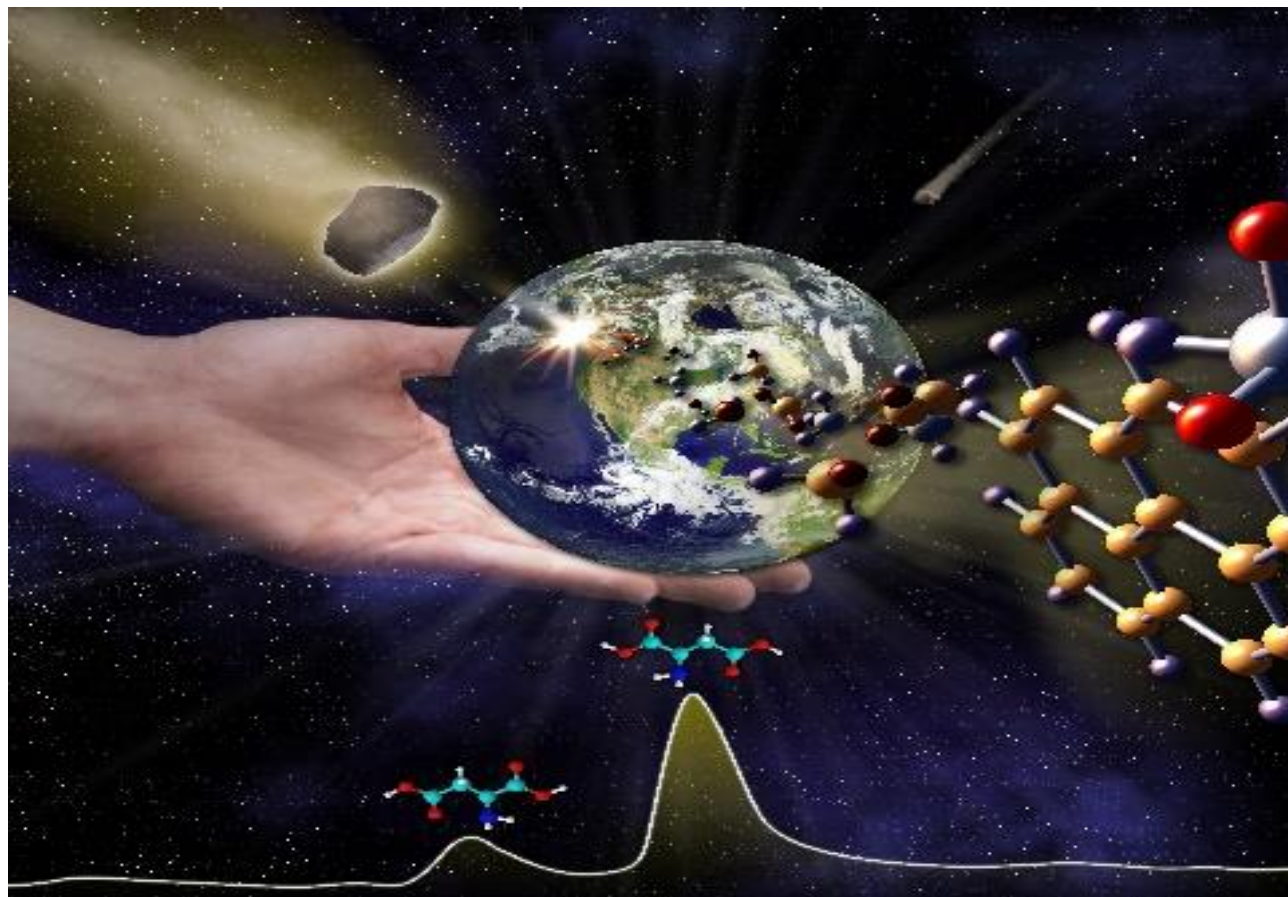


Propylene oxide

80 amino acids
solid phase

- Analytical challenges

Laboratory analyses



One LC-MS Analytical Approach

Extraction

Work-up

Characterization

Crush Meteorite

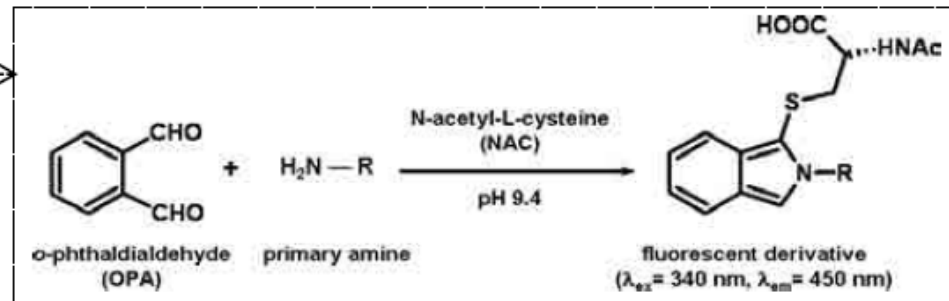
Solvent Extraction

Acid Hydrolysis

Desalting

OPA/NAC Derivatization

UPLC-HRMS



Our Analytical Approach

Extraction

Crush Meteorite

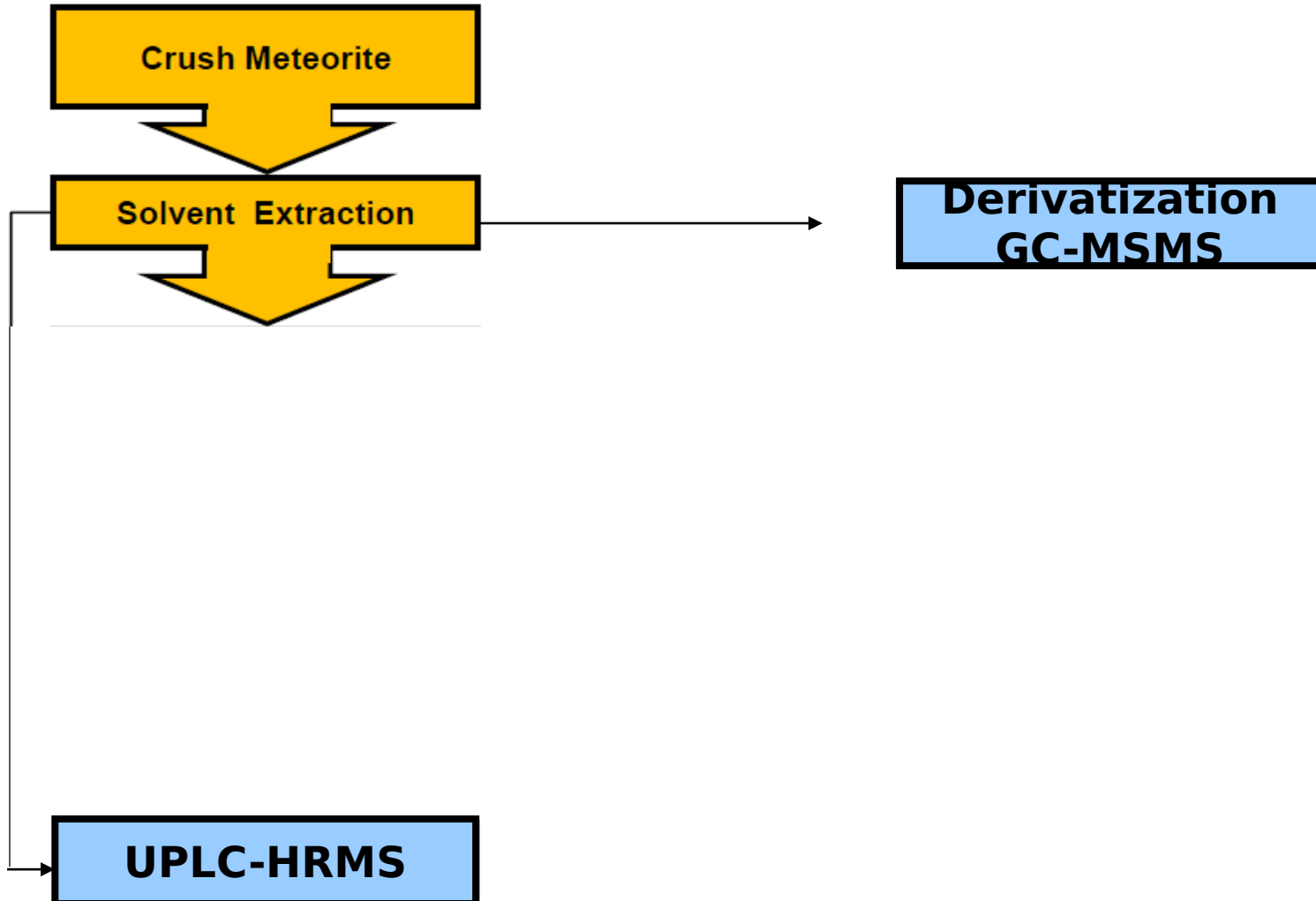
Solvent Extraction

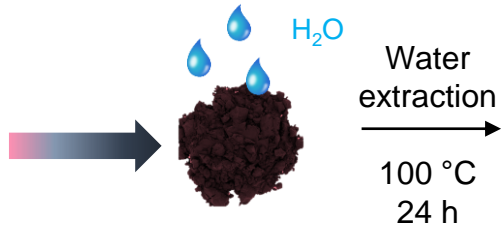
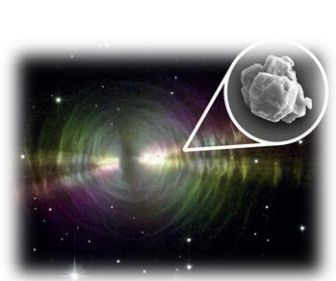
Work-up

Derivatization
GC-MSMS

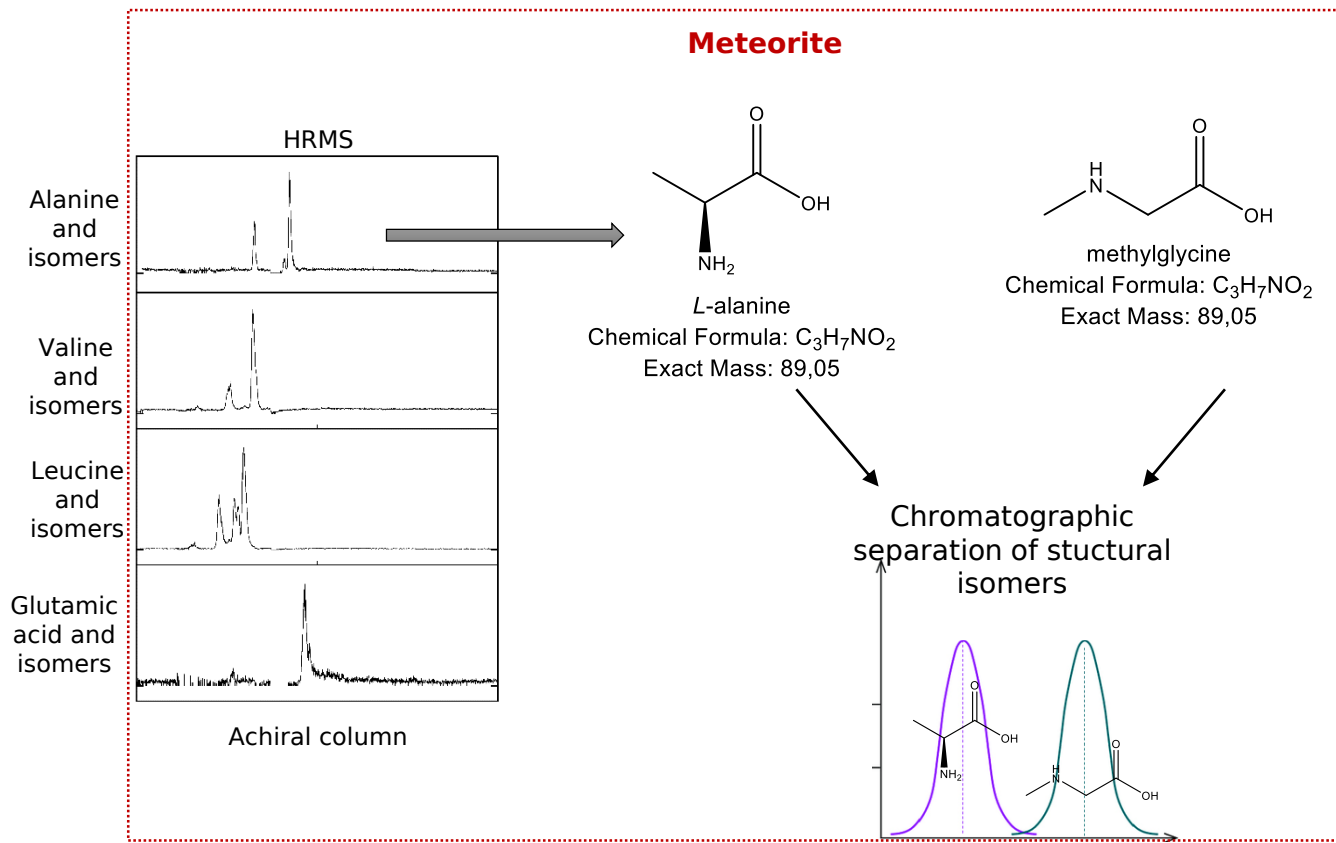
Characterization

UPLC-HRMS





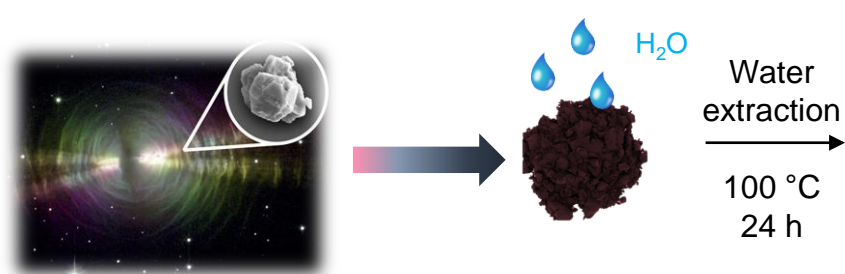
AMINO ACIDS HRMS ANALYSIS



AVANTAGES:

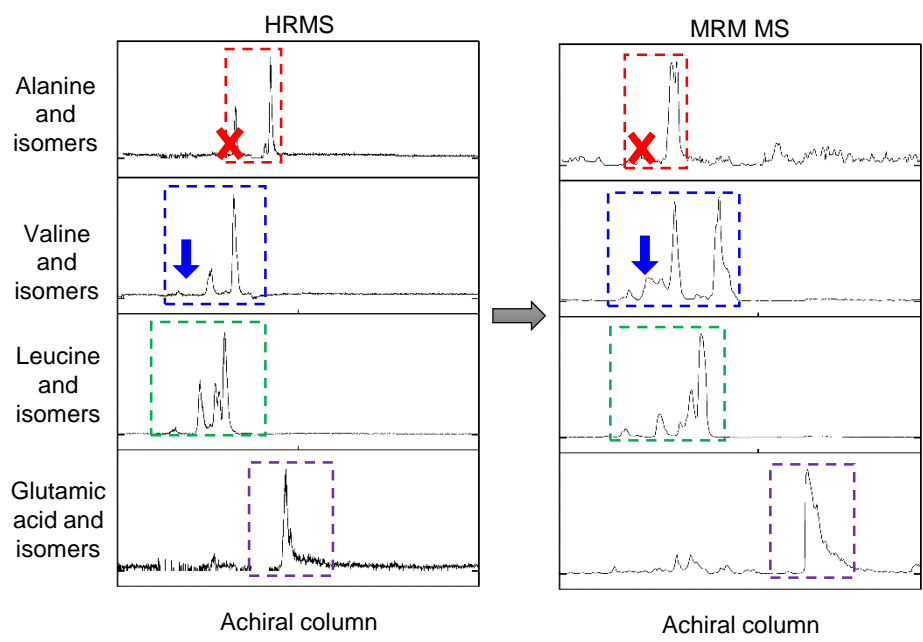
- ✓ No pretreatment
- ✓ No HCl hydrolysis
- ✓ No derivatisation

Eddhif et al. 2018 *Talanta* **179**, 238-245.



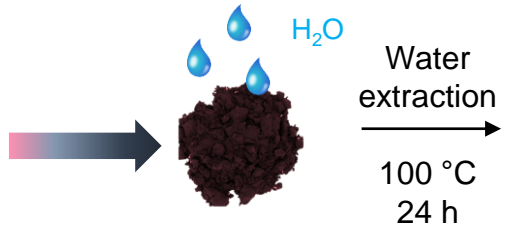
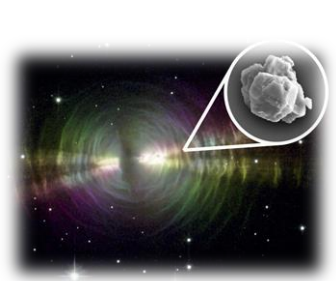
AMINO ACIDS MRM ANALYSIS

Meteorite

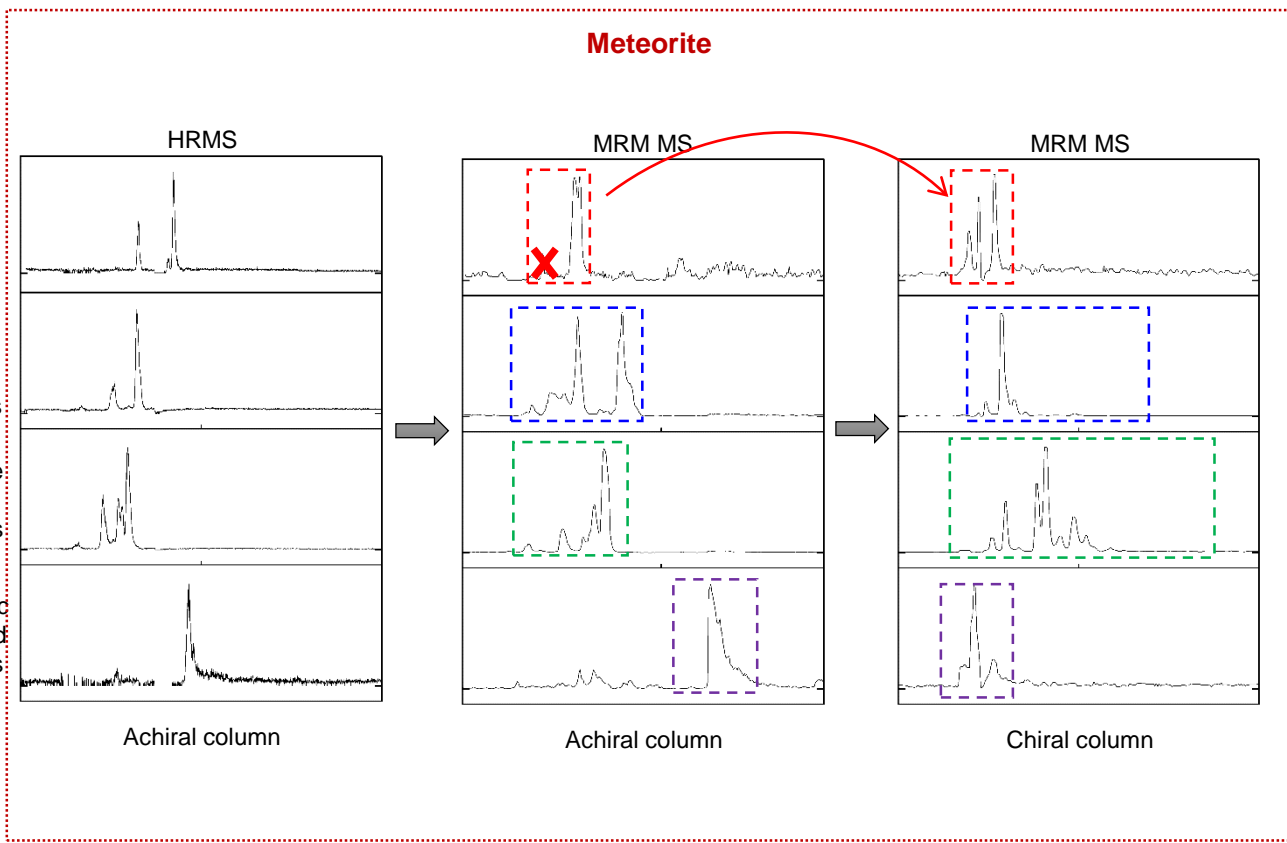


SIM HRMS → MRM MS

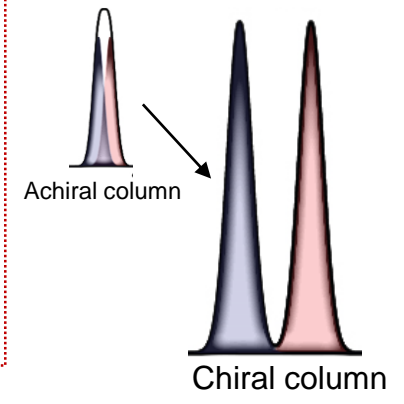
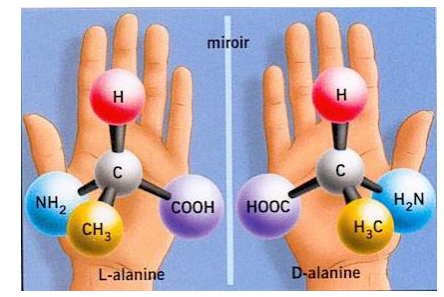
- ✓ Increase **selectivity** (limit identification errors)
- ✓ Improve **sensitivity** in complex matrices
- ✓ Detection of **10⁻¹⁴ mol** ($\approx 10^{-12}$ g) of amino acids in the injected meteorite extracts

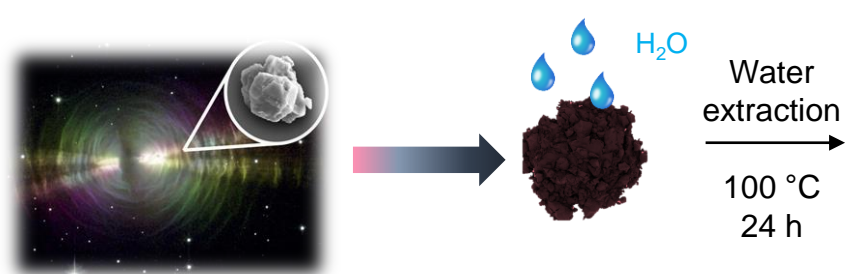


AMINO ACIDS MRM ANALYSIS

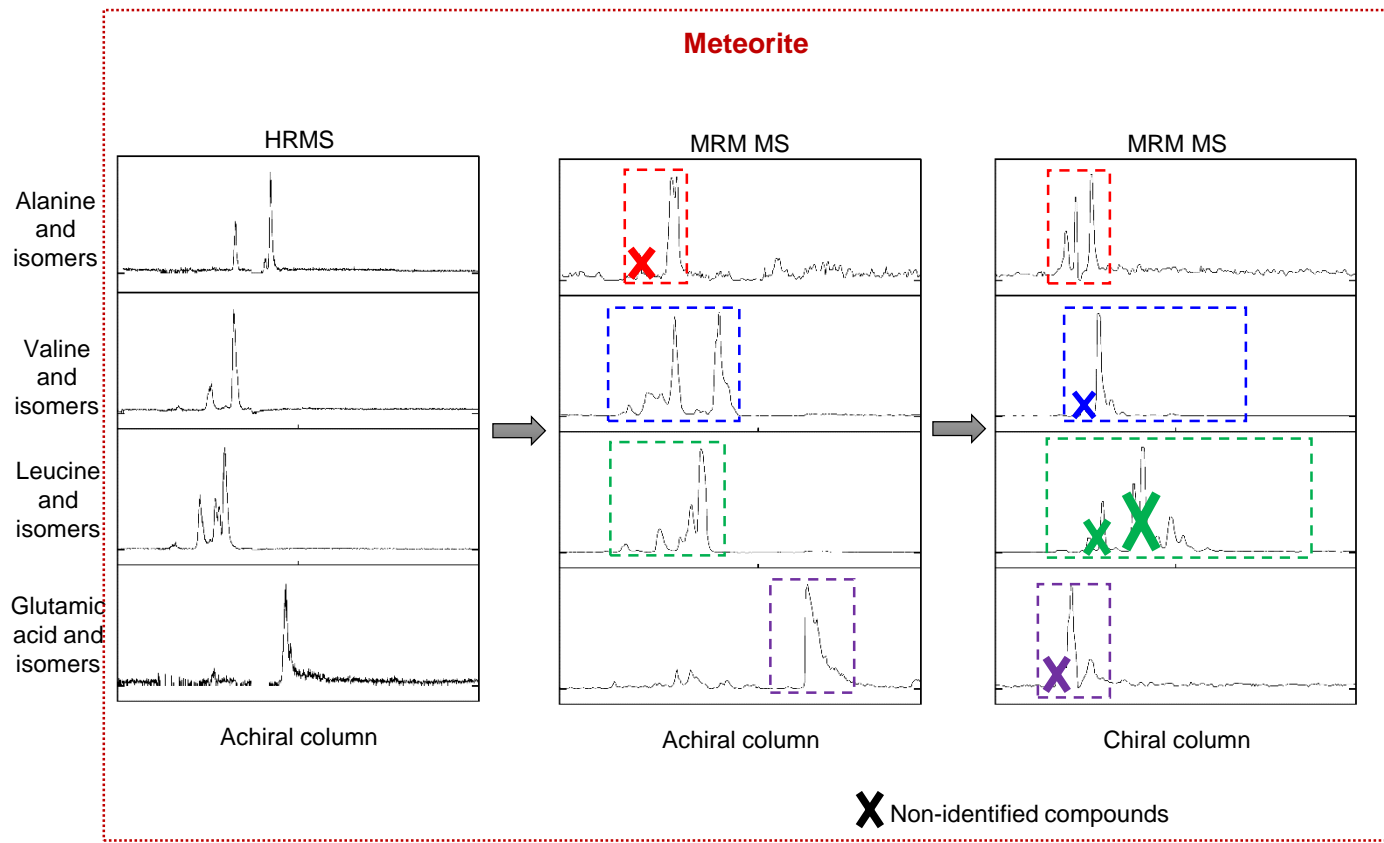


Chirality of amino acids : amino acids form two stereoisomers that are mirror images of each other

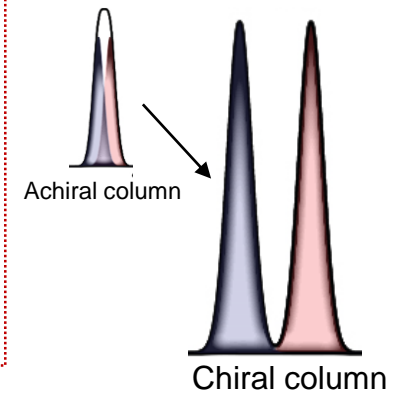
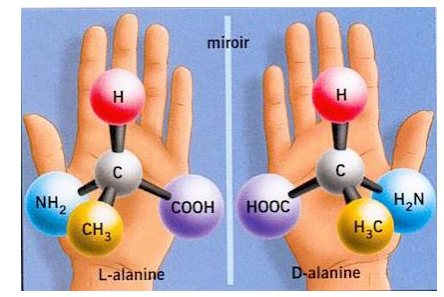




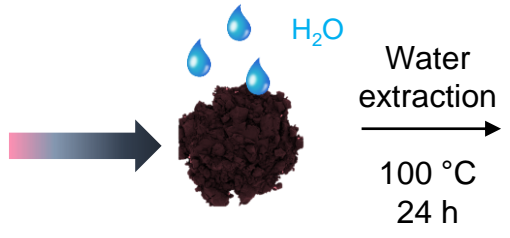
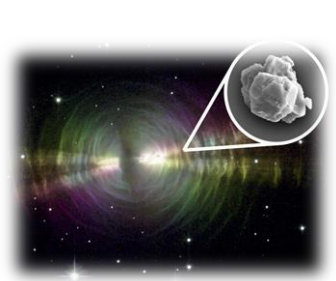
AMINO ACIDS MRM ANALYSIS



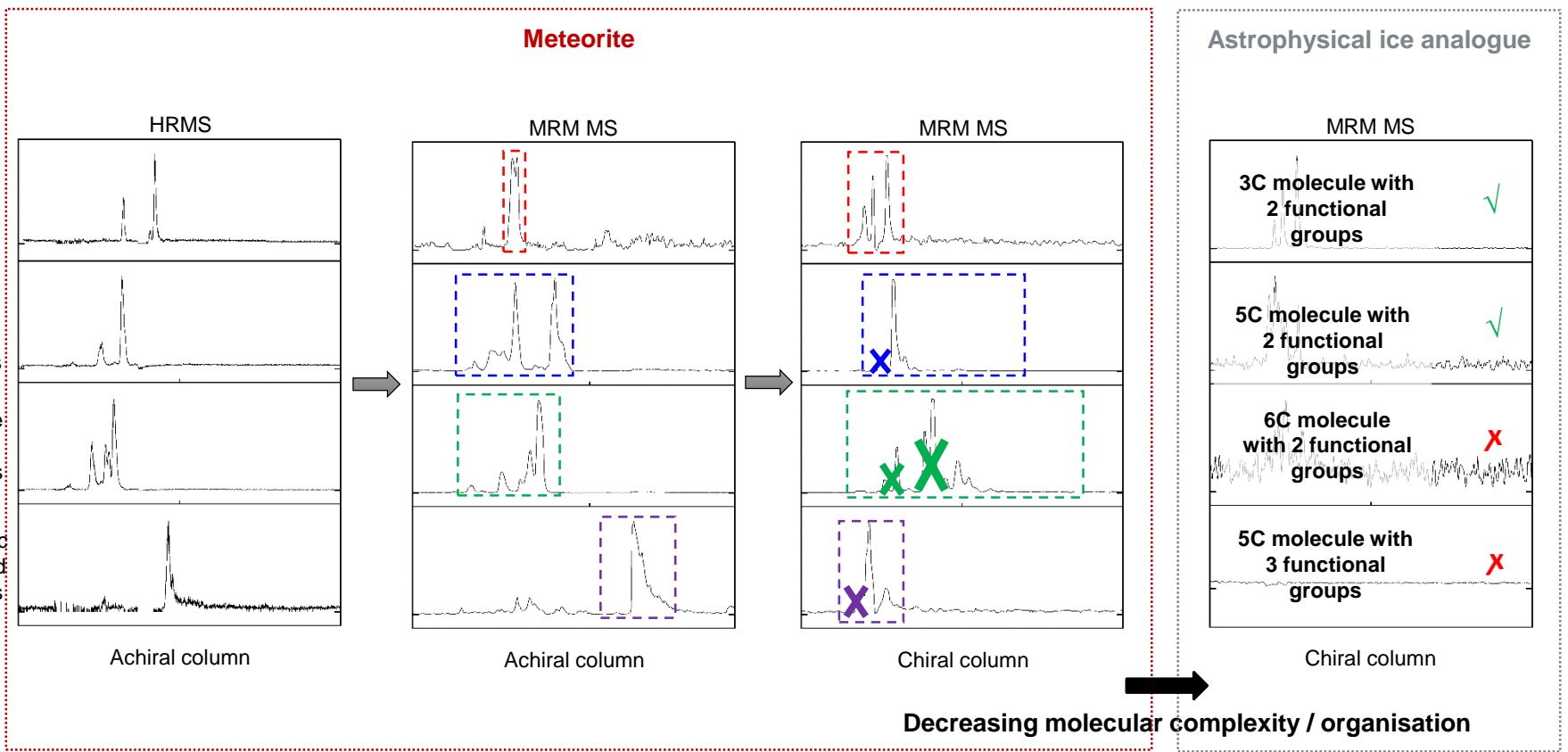
Chirality of amino acids : amino acids form two stereoisomers that are mirror images of each other



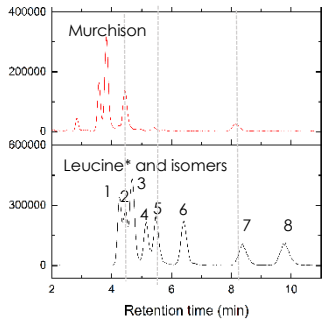
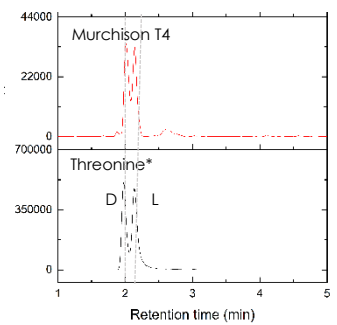
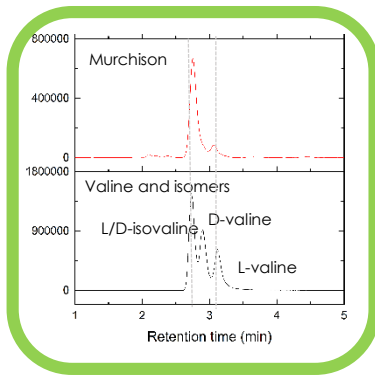
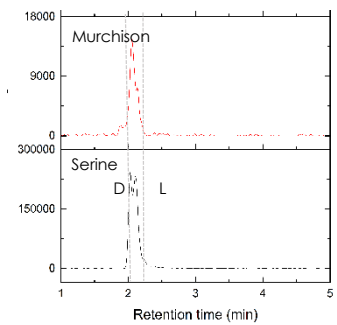
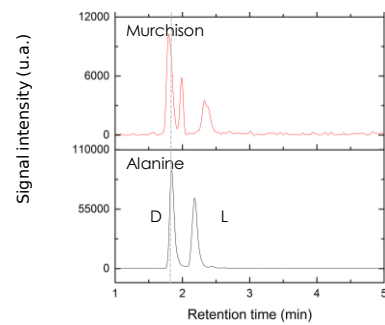
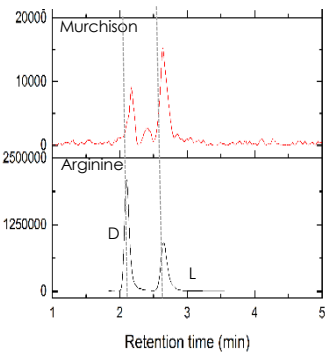
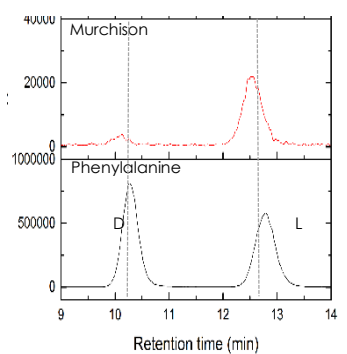
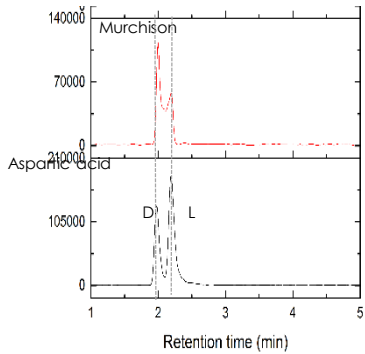
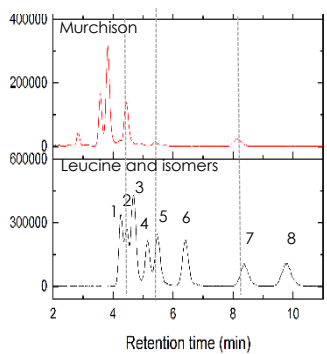
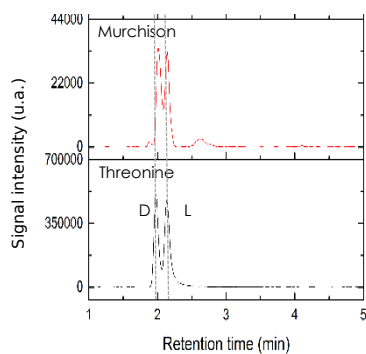
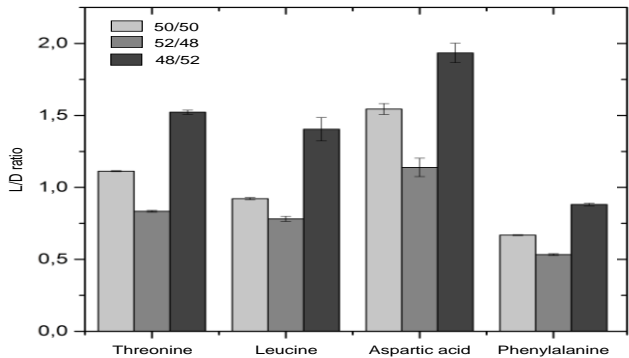
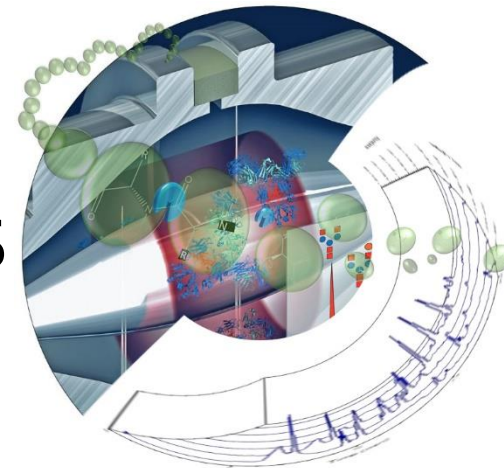
Serra et al. Talanta submitted



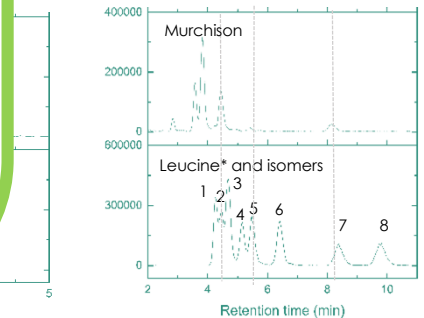
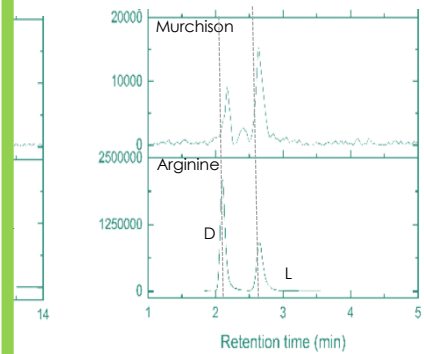
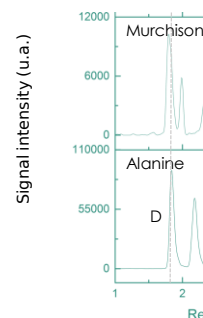
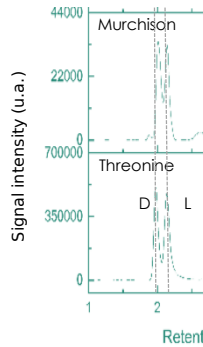
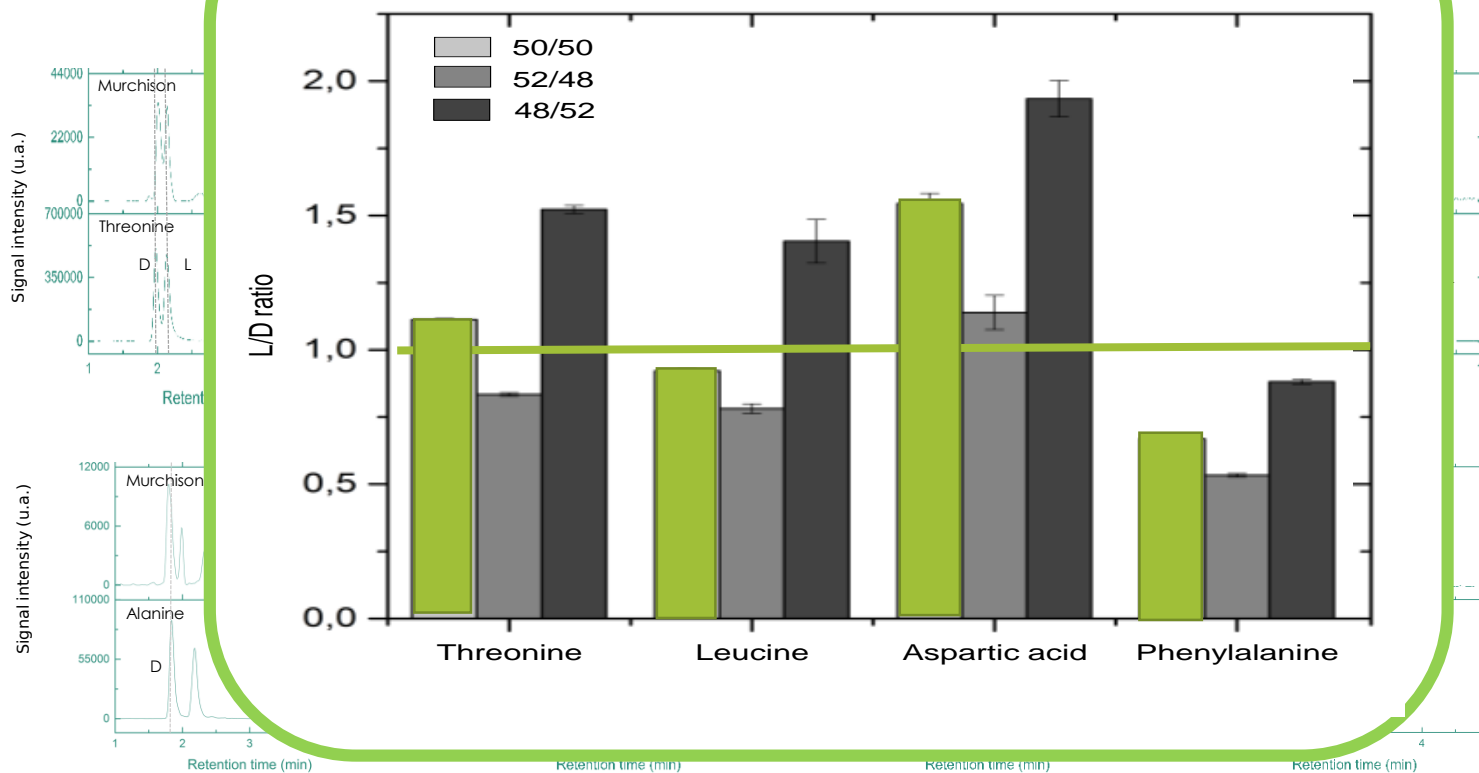
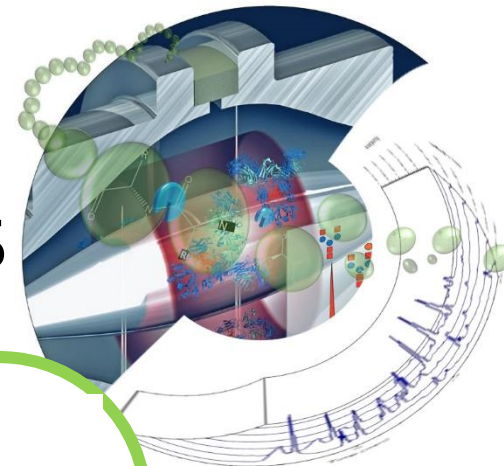
AMINO ACIDS MRM ANALYSIS



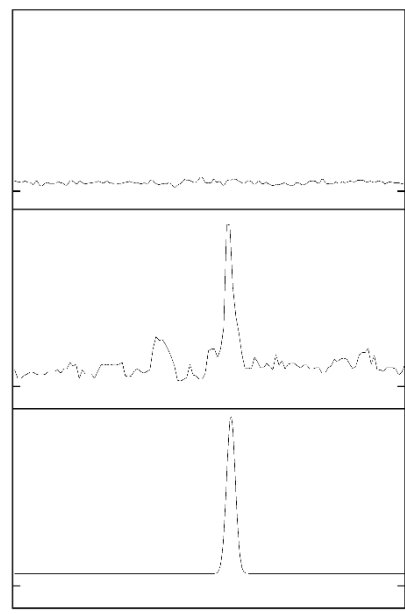
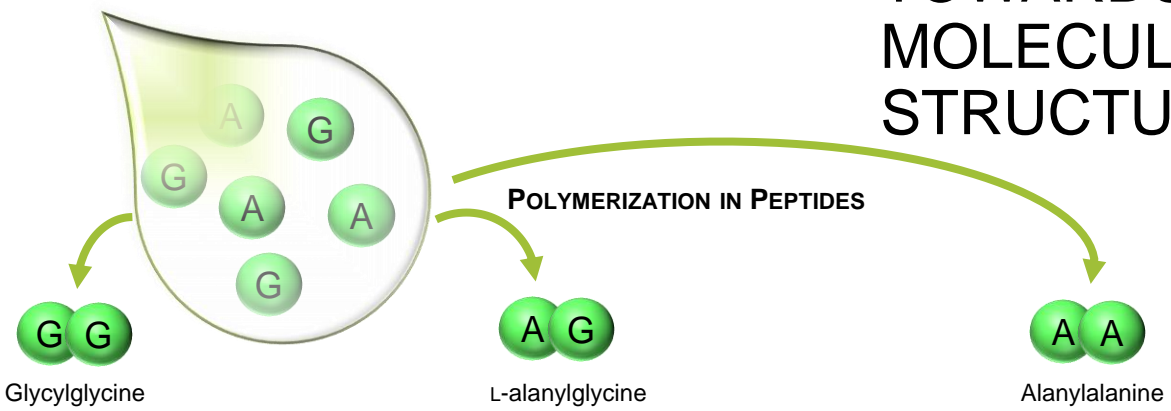
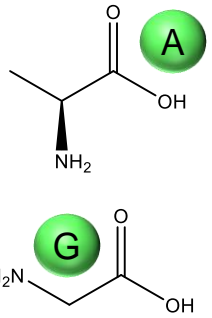
CHIRAL ANALYSIS



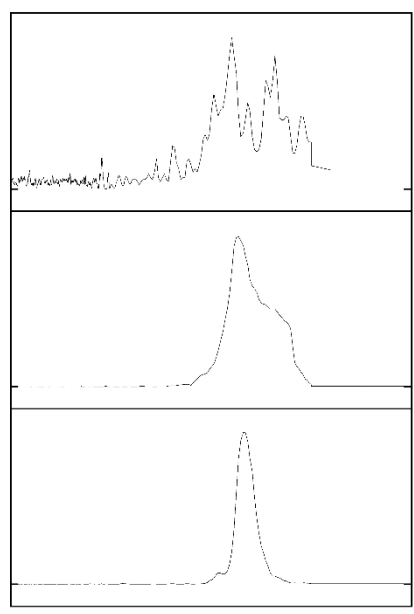
CHIRAL ANALYSIS



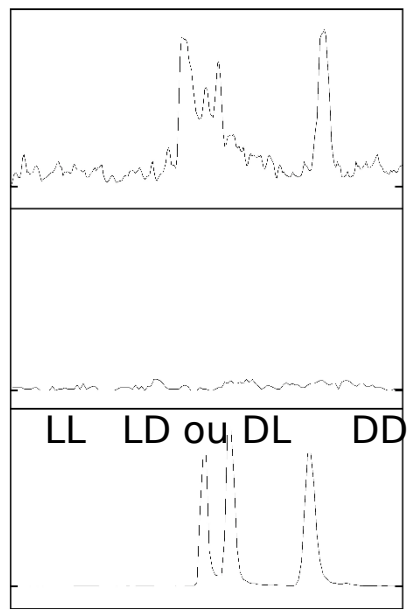
TOWARDS ORGANIZED MOLECULAR STRUCTURES



MRM MS – chiral column



MRM MS – chiral column



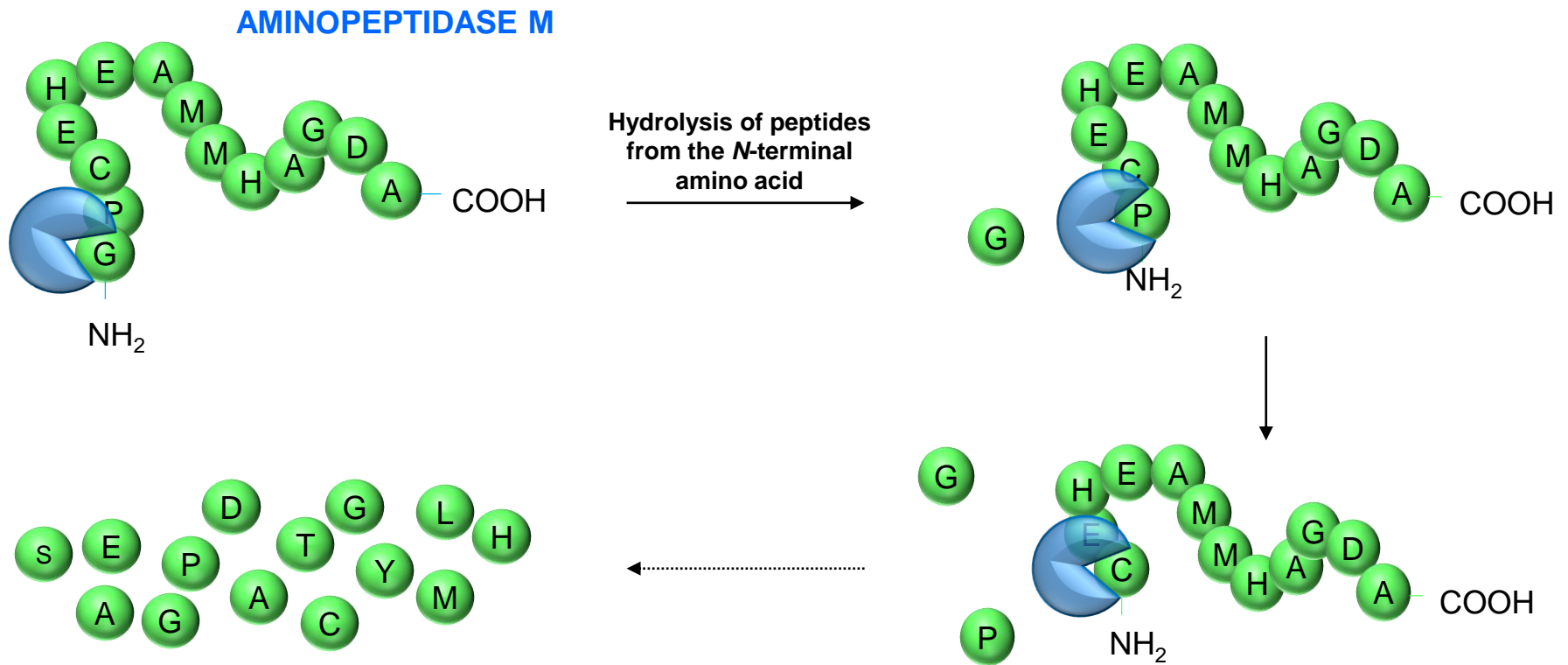
MRM MS – chiral column

Astrophysical ice analogue

Meteorite

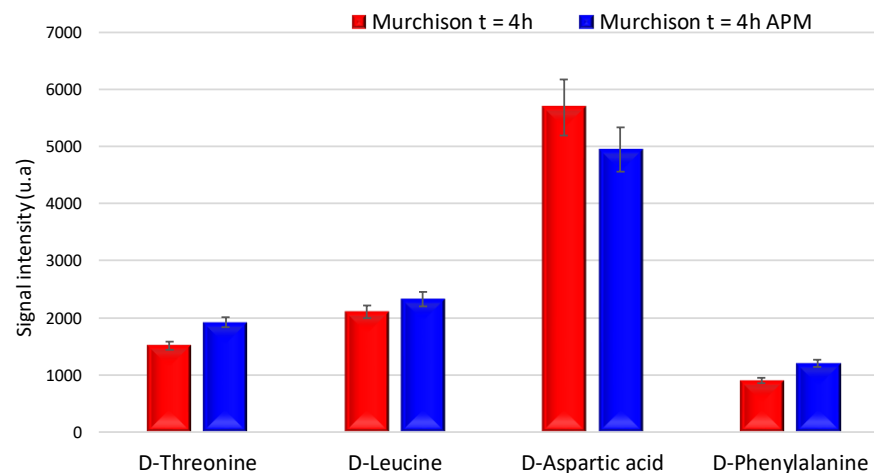
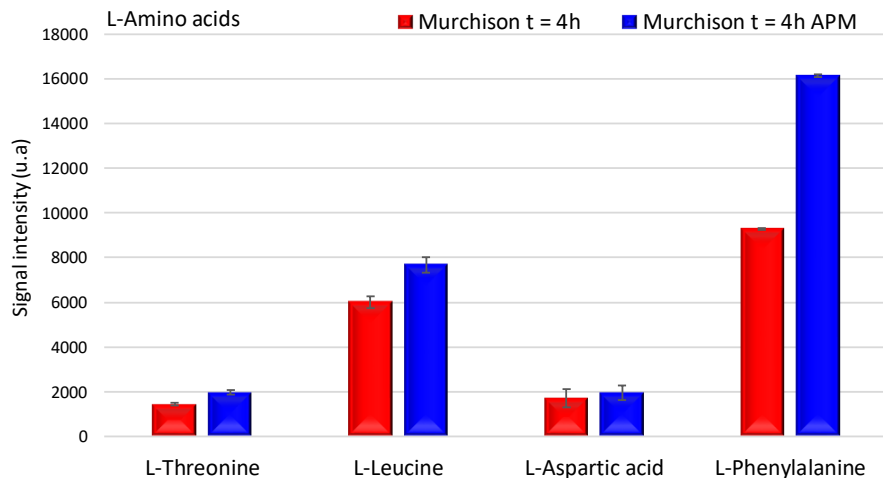
Standard

Proteomics strategy to Search for peptide sequences



Lange et al. (JPR, 2021)

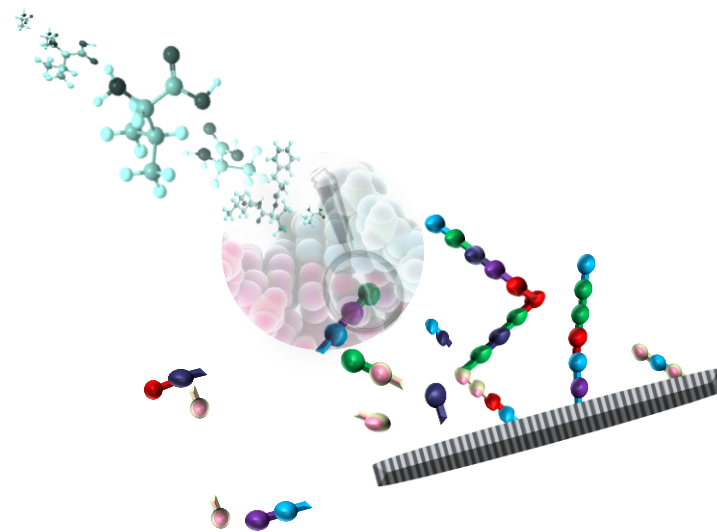
Proof of concept on Murchison meteorite



	Amino acid	L/D ratio t = 4h APM / L/D ratio t = 4h
Murchison	Threonine	1.08
	Leucine	1.16
	Aspartic acid	1.34
	Phenylalanine	1.30

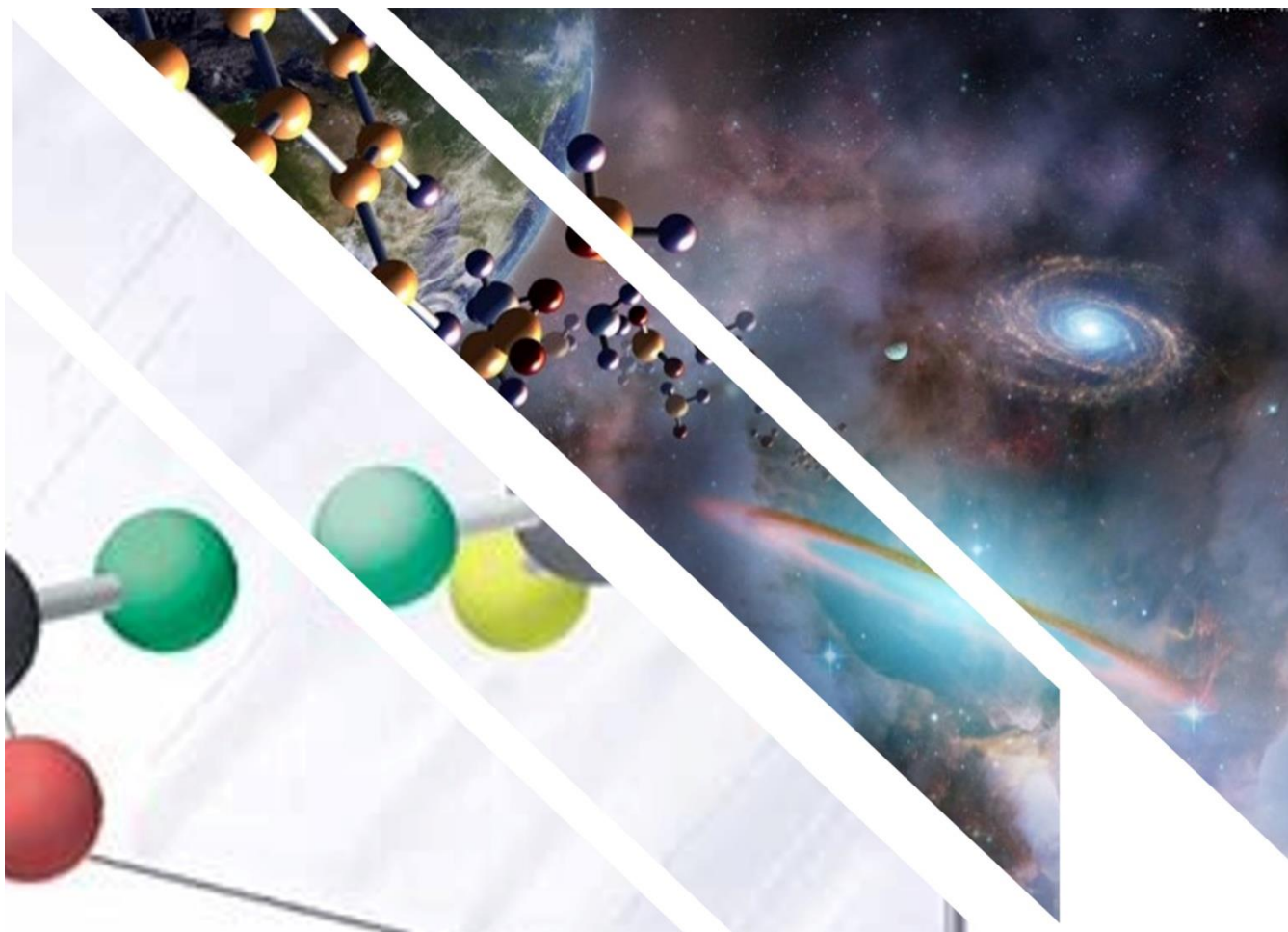
→ Increase of some L- and D-amino acids in the presence of APM

→ **Murchison may contain extra-terrestrial peptide sequences involving either L- or D-amino acids**

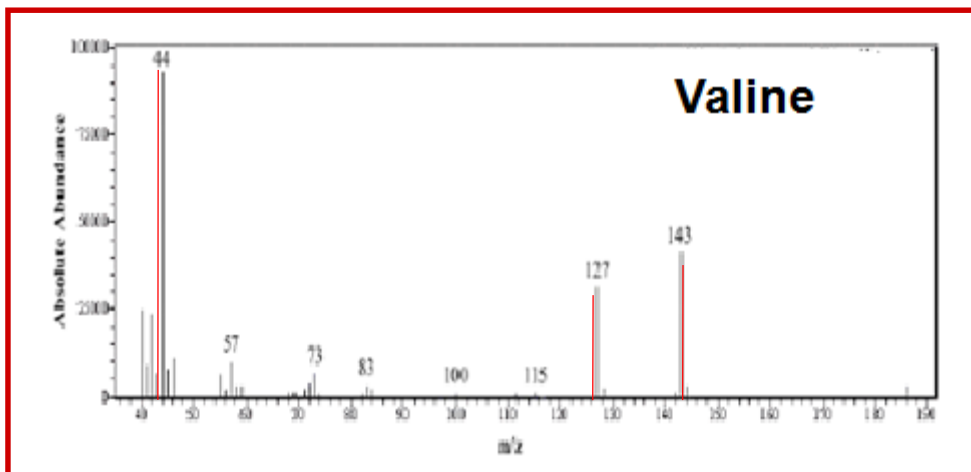
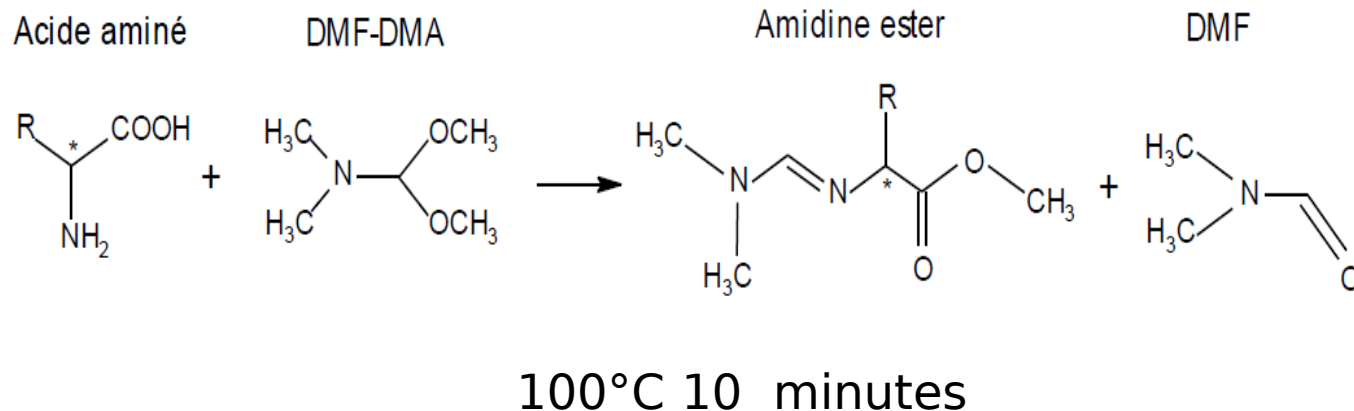


Lange et al. 2021 *Journal of Proteome Research* **20**, 1444-1450

In situ analysis



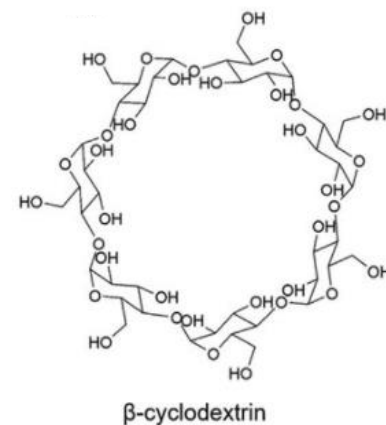
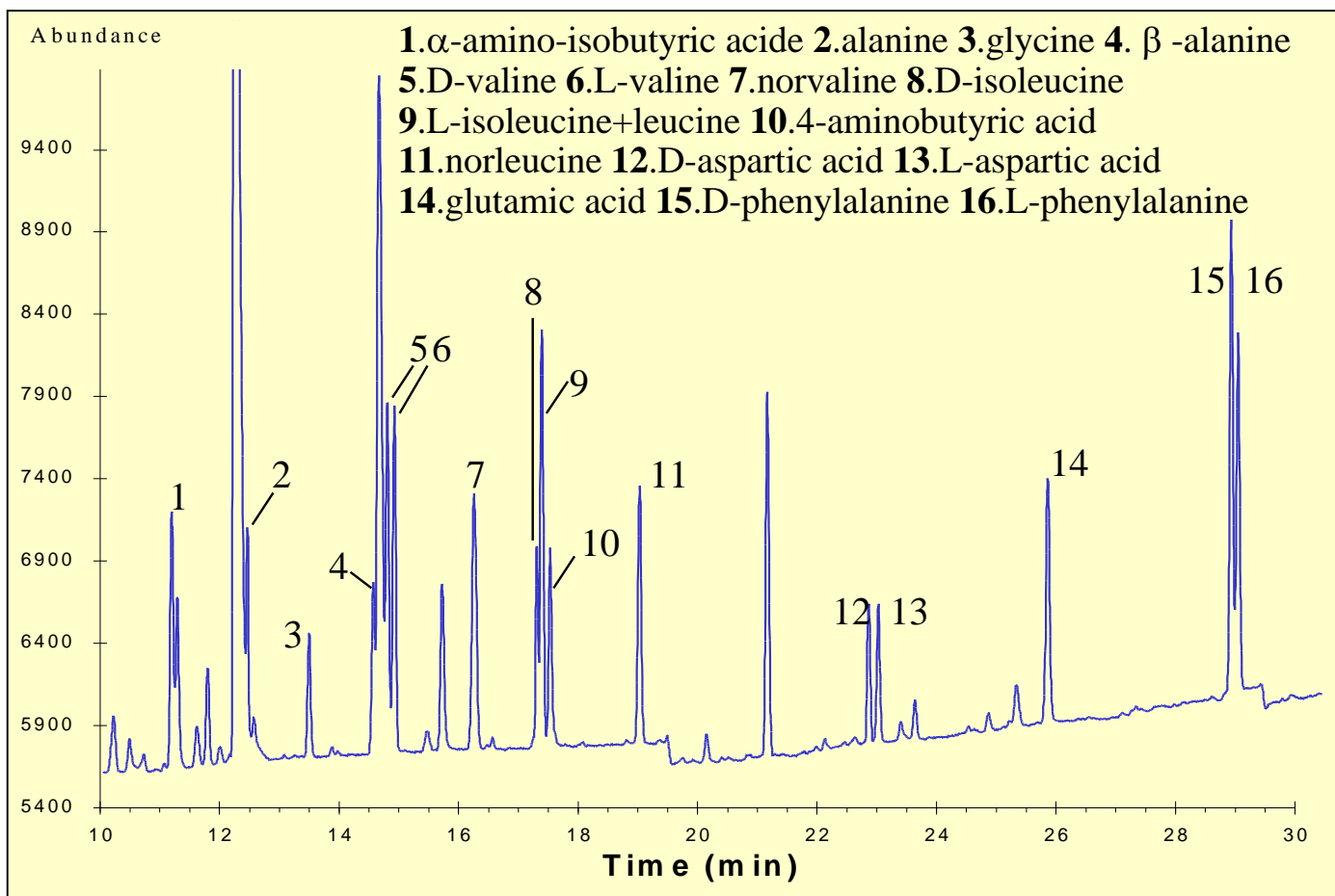
ORGANICS ?: *DERIVATIZATION today*



AVANTAGES:

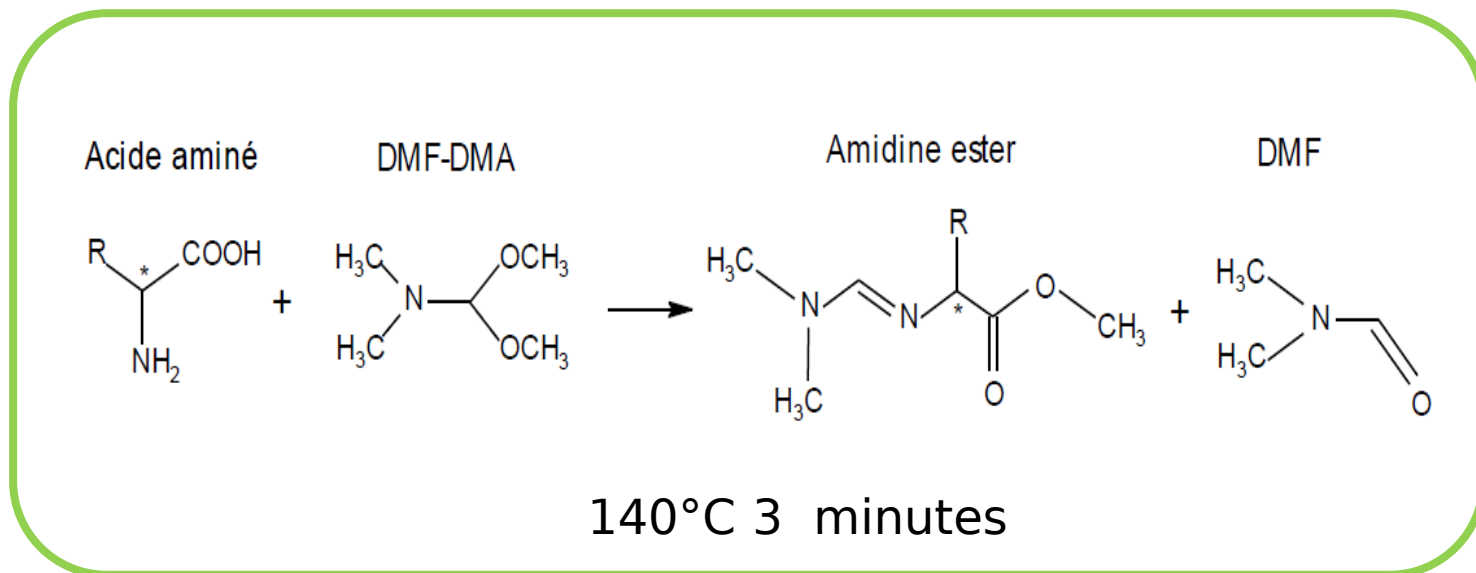
- ✓ One step reaction
- ✓ High temperature
- ✓ No purification step
- ✓ Non specific
- ✓ Sensitive
- ✓ Less characteristic mass spectra
- ✓ **Chirality measurement**

C. Rodier et al 2002 Chirality **14**, 527-532



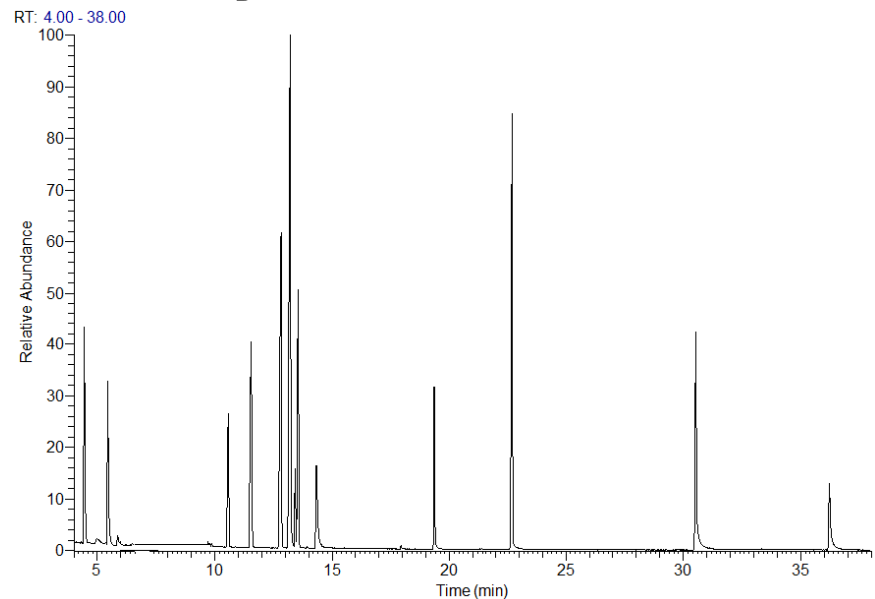
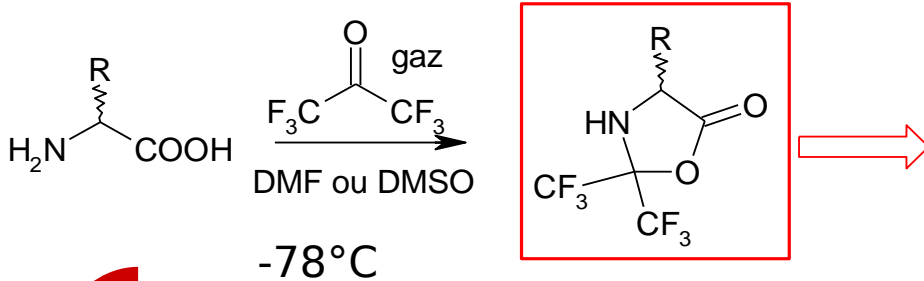
GC/MS analysis of the amino acids standard mixture (100mM each). A 10 m x 0.25 mm Chirasil-Dex fused-silica WCOT column, operated in the split mode (1 :100) was programmed at 4°C/min from 70°C (held 5min) to 170°C with an inlet internal helium pressure of 19.5 kPa.

ORGANICS ? : *DERIVATIZATION today*

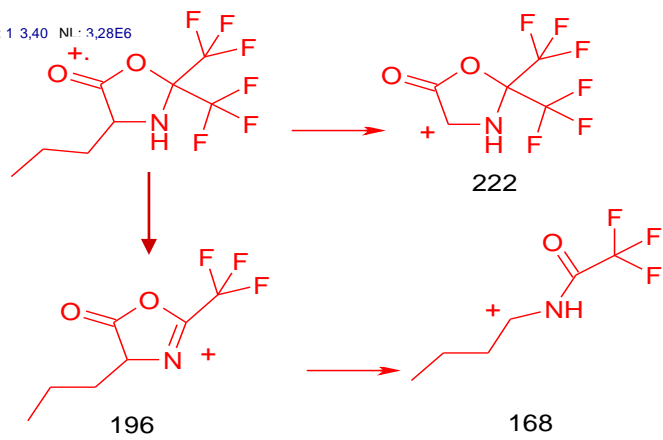
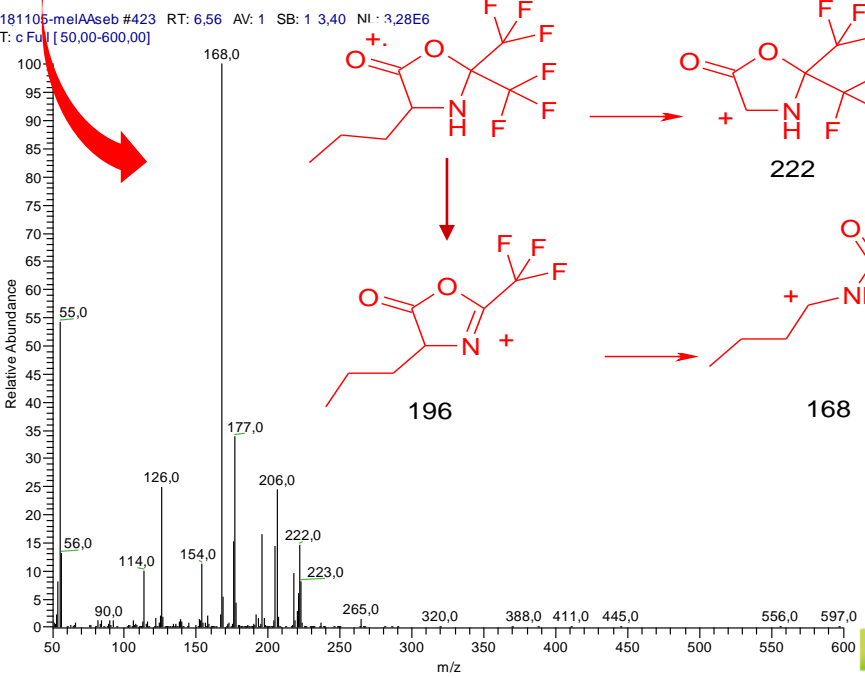


Racemisation,,,,

ORGANICS ? : DERIVATIZATION day after tomorrow



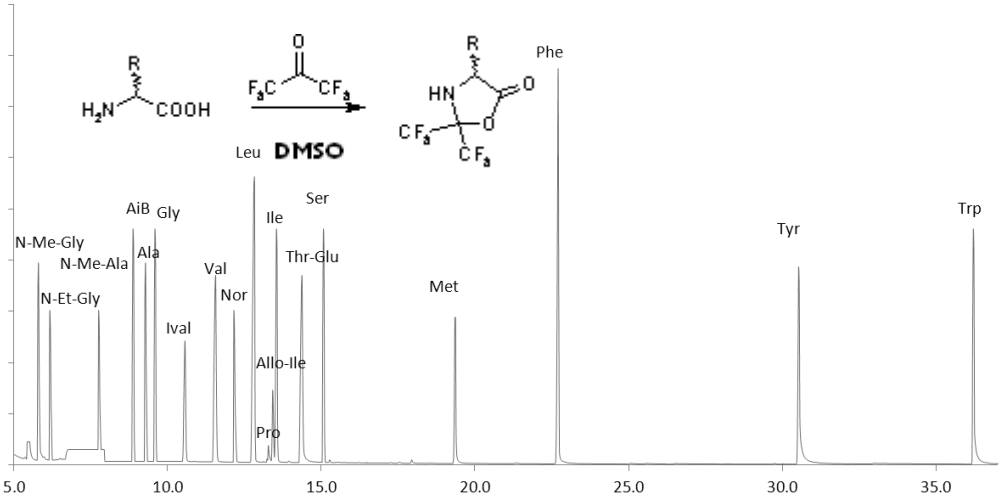
11 over 17 proteinic Amino Acids



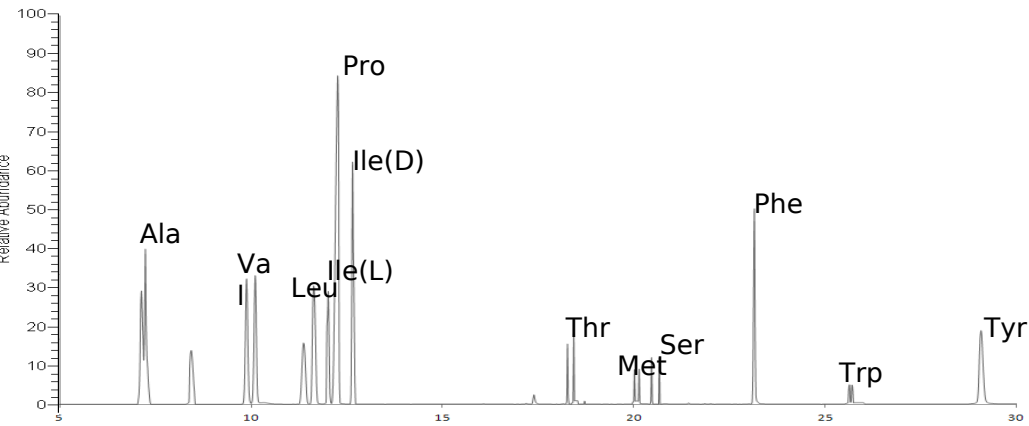
ORGANICS ? : **DERIVATIZATION** day after tomorrow

One step One pot
Low temperature

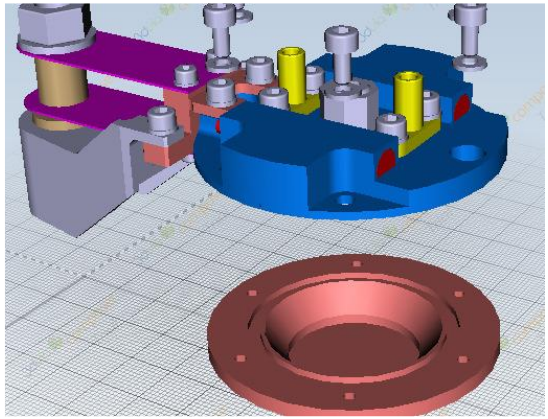
No liquid
Volatile derivatives
Separation 19 AA
Enantiomeric separations 8/11 AA



TIC of 19 HFA (L) derivatives on cpsil5 column.



TIC of 11 HFA (L,D) derivatives on γ -cyclodextrine column.
L forms eluted first



Geffroy-Rodier et al. 2012 Journal of chromatography **1245**, 158-166