

Sustainable synthesis strategies towards amino acid based surfactants

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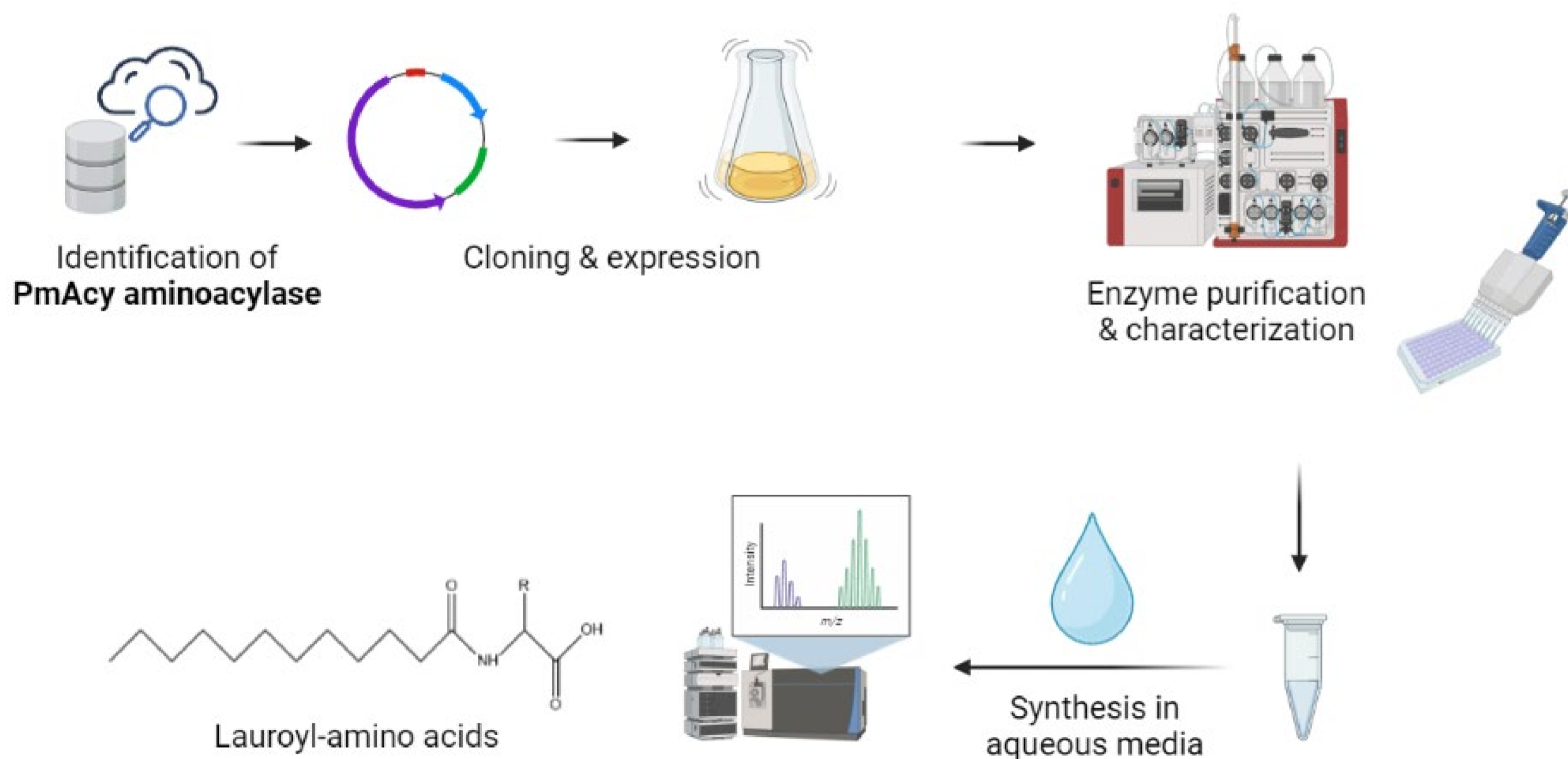
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Introduction

- Surfactants with acyl-amino or lipopeptide structure are mild & environmentally friendly
 - Synthesis from bio-based, renewable resources
- Technical synthesis relies on *Schotten-Baumann*-condensation reaction,
 - Disadvantage: Hazardous acyl chlorides needed in stoichiometric quantities
- Sustainable synthesis in accordance with "12 Principles of Green Chemistry" needed:
 - Peptide coupling-agent T3P for fatty acid activation (T3P classified as sustainable activating agent for peptide synthesis, recycling is possible)
 - Novel aminoacylase PmAcy for direct condensation of fatty acid and amino acids without use of protective groups

Novel aminoacylase PmAcy

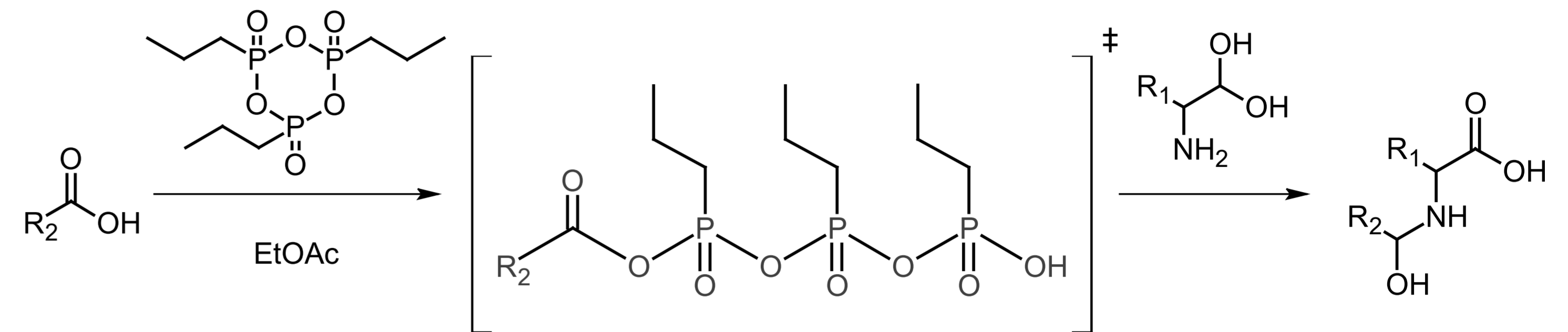
- Novel aminoacylase PmAcy from *Paraburkholderia monticola* was cloned and heterologously expressed in *E. coli*
- Enzyme purification achieved via Strep-tag affinity chromatography
- PmAcy is a highly temperature and pH stable enzyme
- The enzyme hydrolyzed long-chain acylamino acids with broad substrate acceptance
 - Suitable candidate for surfactant synthesis



Surfactant synthesis with T3P

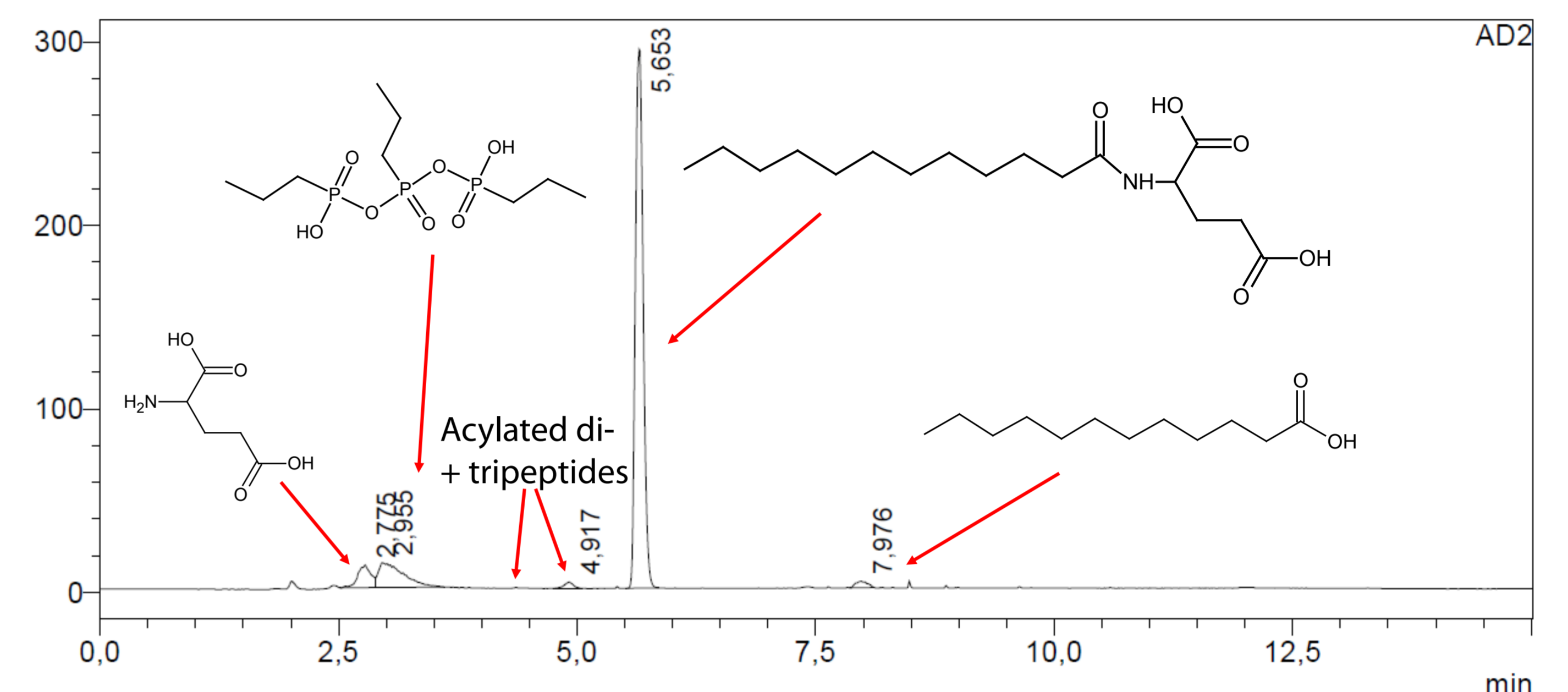
Two-step synthesis strategy employed:

- Priming of fatty acid with coupling-agent
- Nucleophilic substitution of coupling agent with amino acid

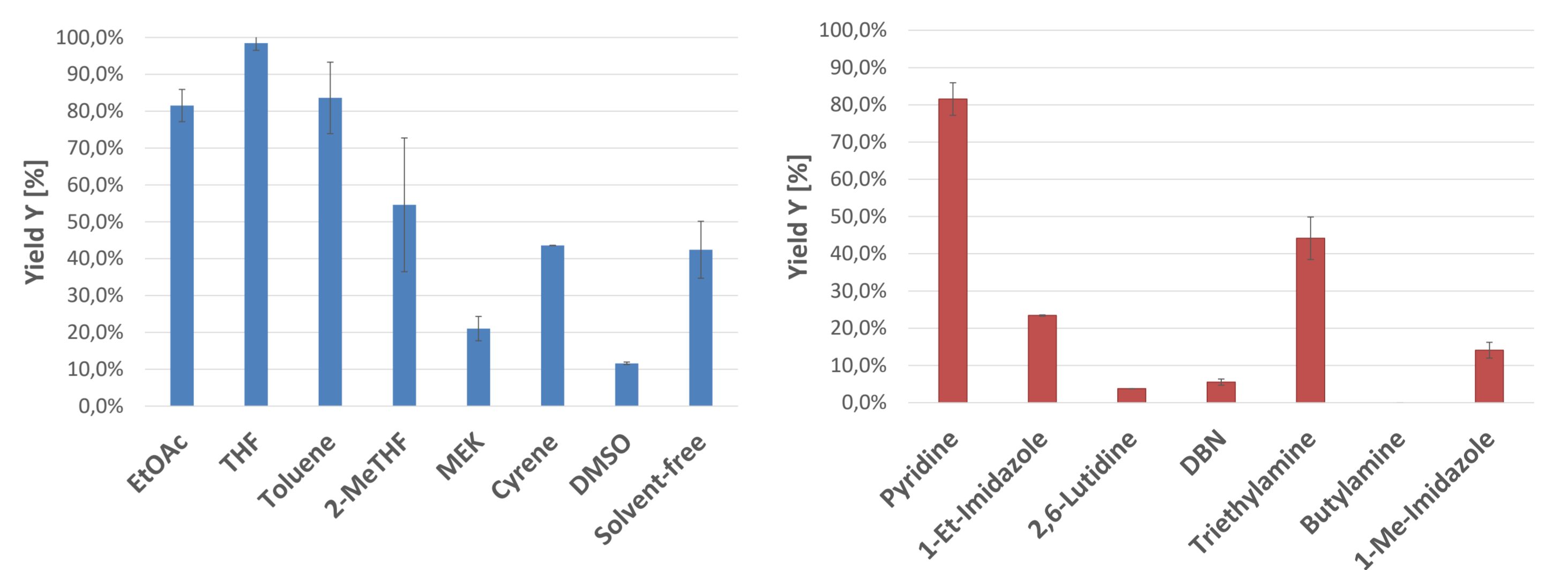


- Example lauroylglutamate synthesis: Good yields were achieved

Small amounts of acylated di- and tripeptides visible

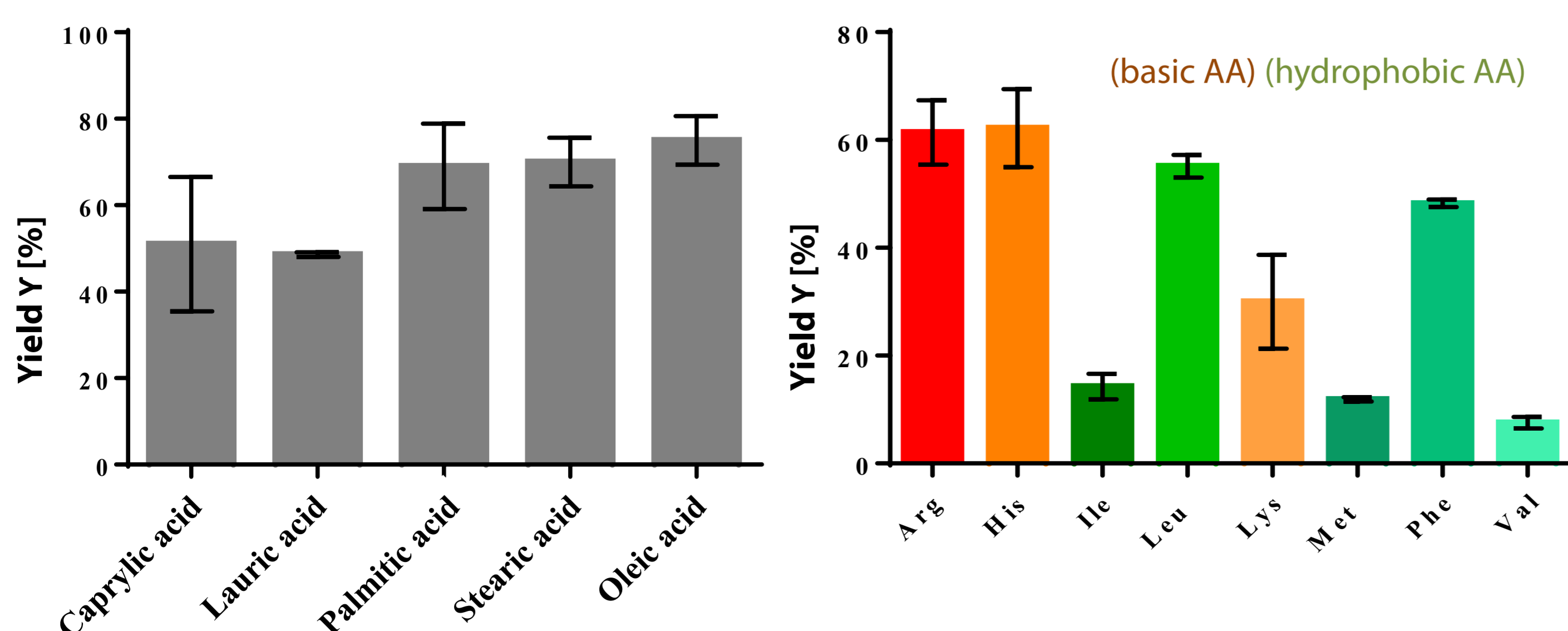
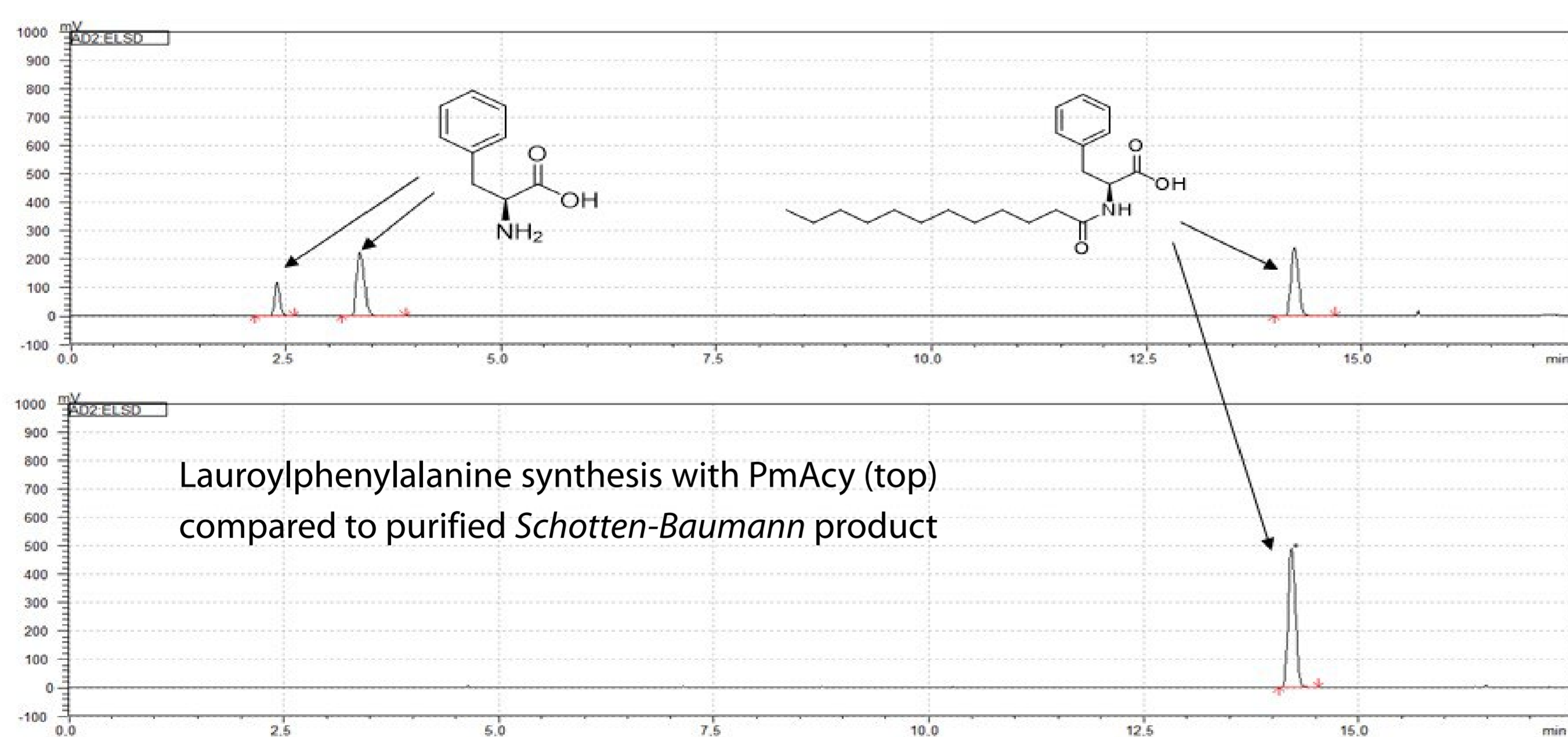


- Solvent-free reaction conditions possible
 - Better reaction in solvents, ethyl acetate suitable as green solvent
- Reaction needs stoichiometric amounts of base - best yield with pyridine
 - Ongoing search for green alternative



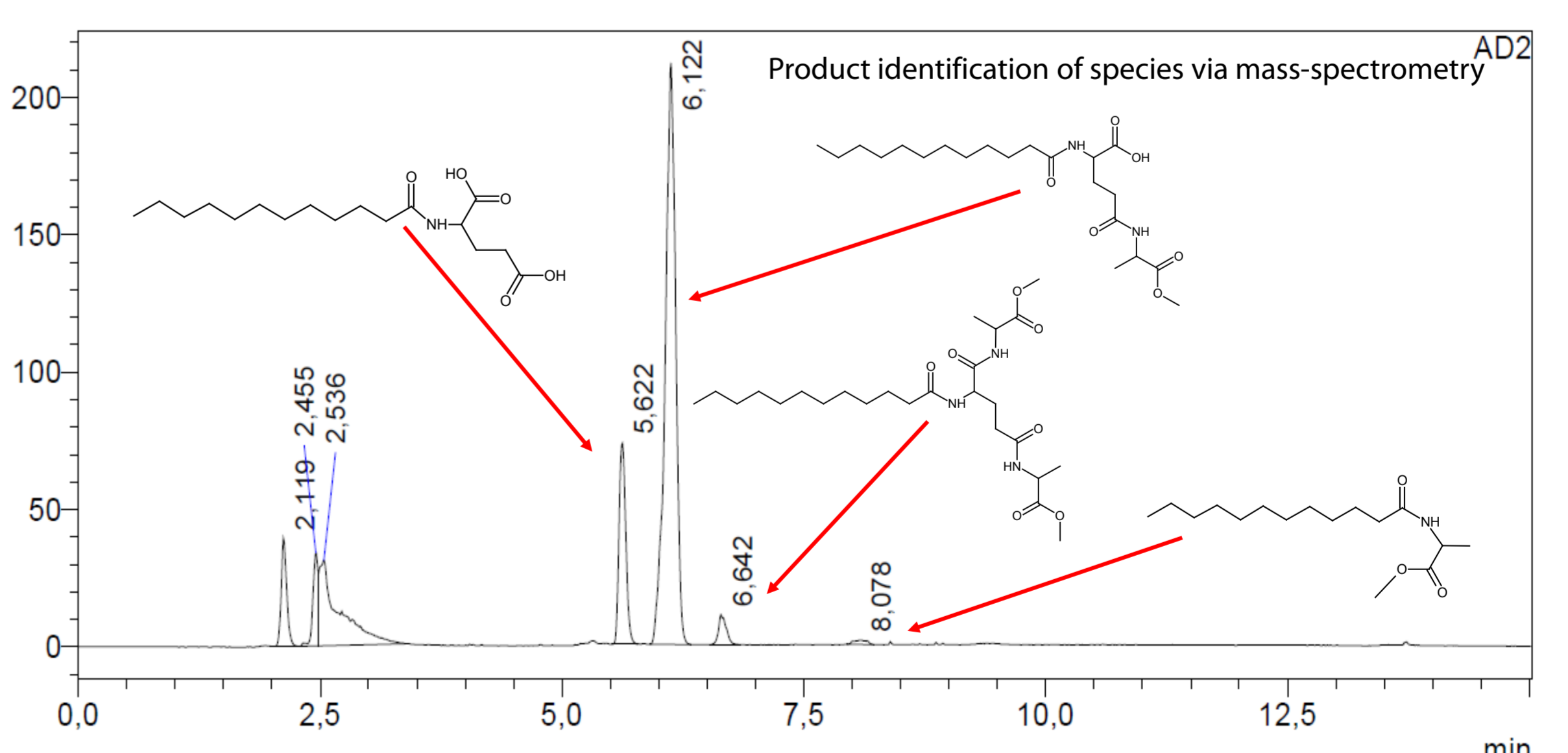
Surfactant synthesis with PmAcy

- Successful synthesis of acylamino acids was verified with PmAcy
- Broad acceptance of fatty acids with different chain length
- Good synthesis results with basic and some hydrophobic amino acids



Follow up: Acylated dipeptides

- T3P coupling of lauroylglutamate with alanine methyl ester successful
 - Multi step synthesis possible, but more side products with non-protected AA



Conclusions

- PmAcy is a promising enzymatic alternative to *Schotten-Baumann* synthesis
 - Broad range of fatty acids and amino acids at high yields
- Two-step synthesis of N-acyl amino acids T3P successful under green reaction conditions
 - High yields of desired product and with few di- / oligopeptide by-products
 - Method shows promise for synthesis for tailor made acyl peptides for specialized applications