# Tag-Assisted Peptide Synthesis (TAPS) – Development of a continuous liquid-phase process

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## TAPS vs. SPPS

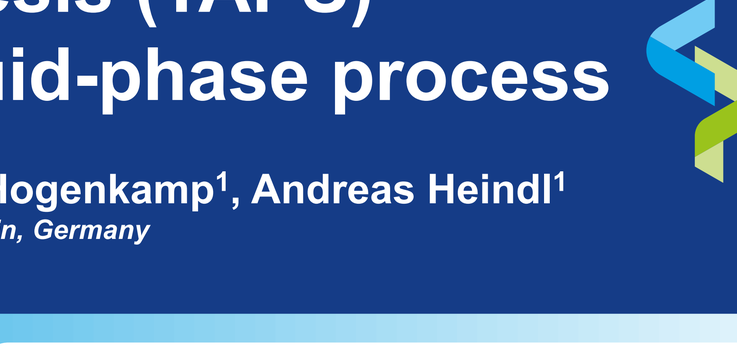
**Advantages:**

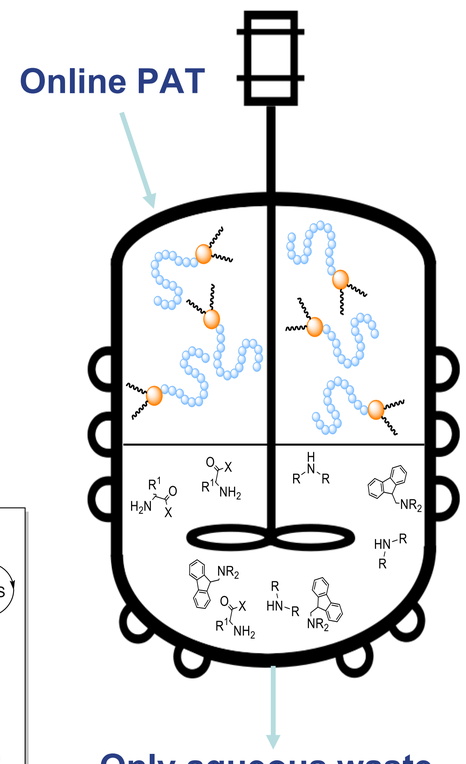
- Green solvents (TAPS) compared to DMF (SPPS)
- Excess of amino acids up to 99% reduced
- Replacement of piperidine by low toxic to non-toxic amines
- Direct IPC and online PAT monitoring
- Aqueous washing compared to very large DMF volumes in SPPS
- Drastic reduction of PMI (~90% lower solvent amount)
- Cost savings due to lower solvent / RM consumption / better quality
- TAPS can better handle difficult sequences

## TAPS Principle

**Synthesis Cycle:**

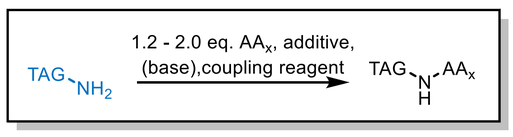
- Fmoc-Amino Acid coupling
- *In Situ* Fmoc deprotection
- Aqueous wash, to waste
- Organic solution retained
- Ready for next cycle

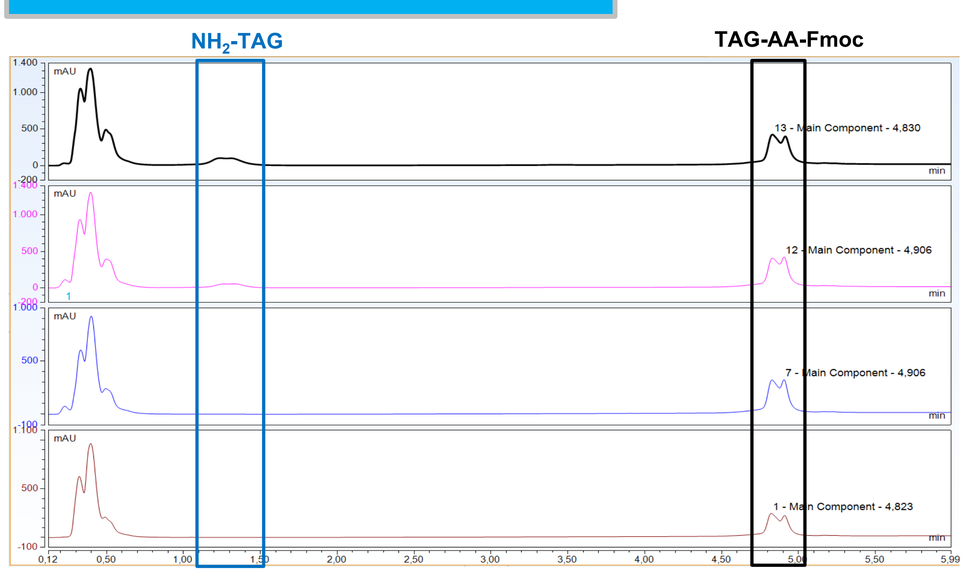



## Development History - Coupling Chemistry

- **Coupling reagent choice**
  - By-products water soluble
  - Very fast reaction kinetics
  - No pre-activation necessary

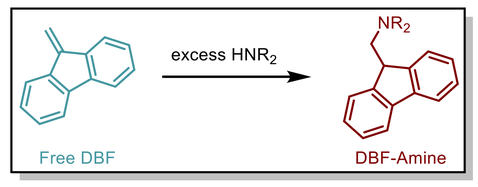


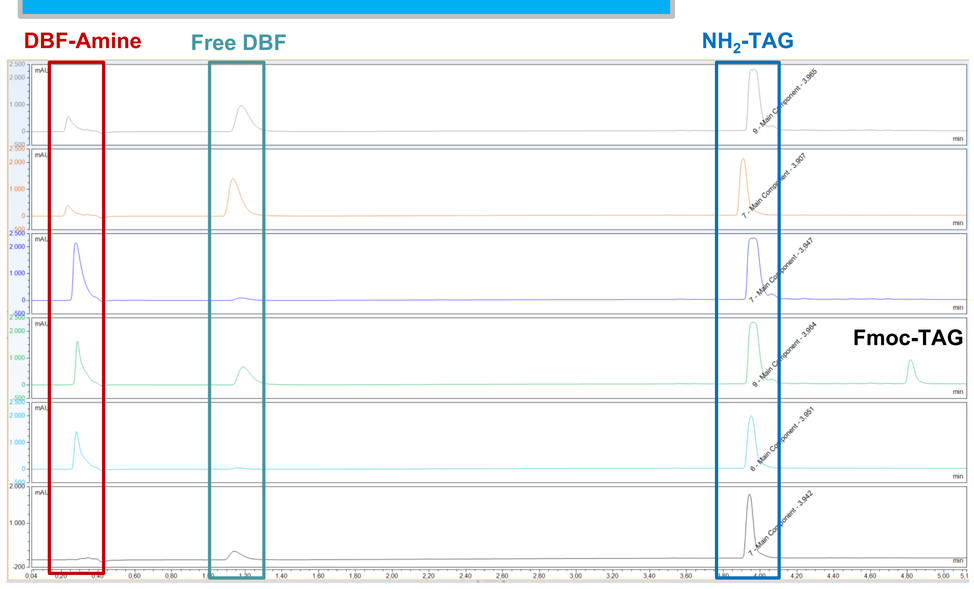




Note: TAG features stereocenter. Forms diastereomers after loading with amino acids

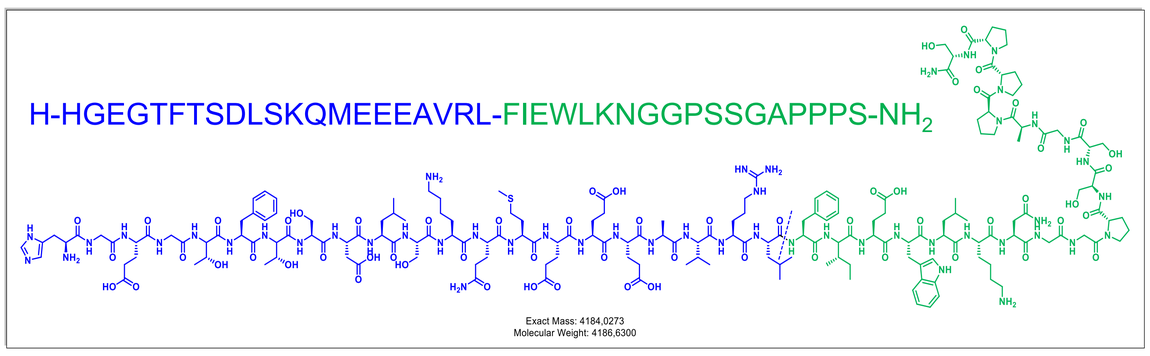
## Development History - Fmoc Deprotection

- **Amines with three main features:**
  - Fast deprotection (high basicity)
  - DBF scavenging (high nucleophilicity)
  - Water soluble (efficient work-up)



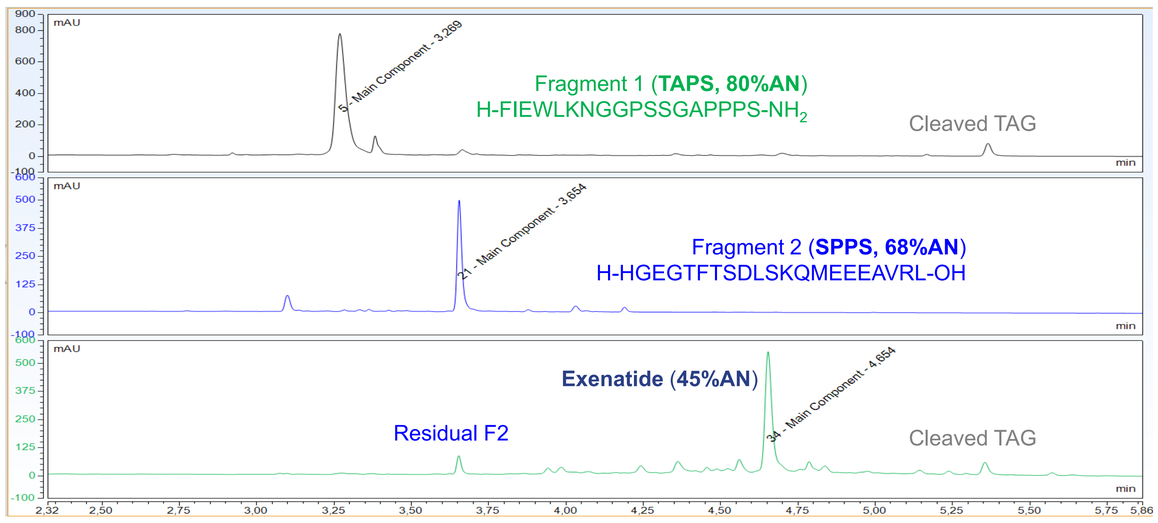

## Case Study - Exenatide



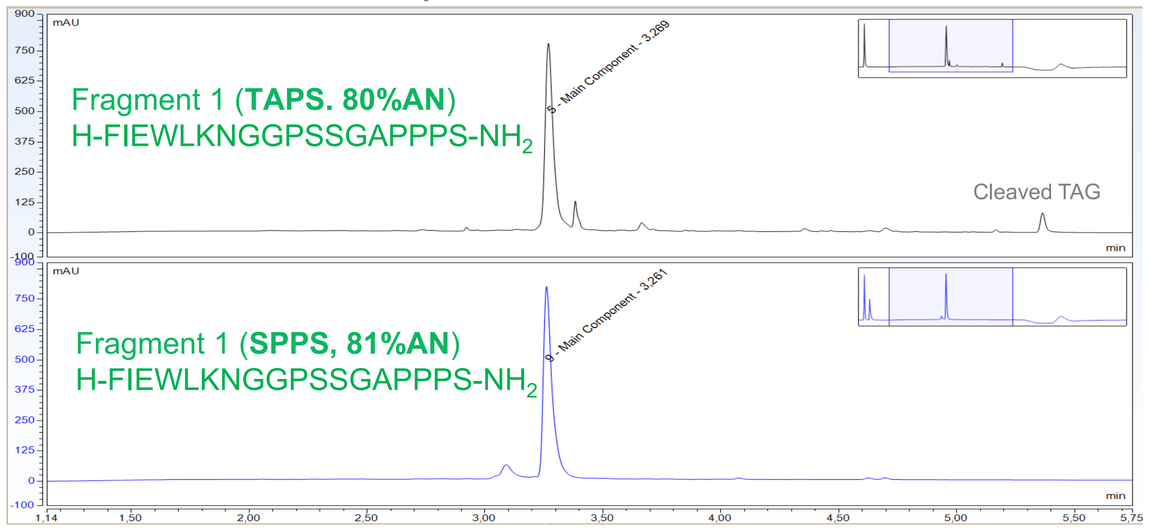

**Major Achievements:**

- Comparison TAPS fragment vs SPPS fragment synthesis
- → Same quality achieved
- Fragment condensation using **Peptidyl-TAG** fragment and **SPPS-fragment** to Exenatide „on-TAG“

### Condensation of Exenatide




### Comparison of TAPS vs. SPPS




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