Lecture Combinatorial Chemistry
Polymer assisted solution-phase synthesis by flow-through

Reaction takes place in a microreactor which is filled with a special monolithic material

Reagents or catalysts are bound on a solid phase

Concept of flow-through reactors that contain a functionalized solid phase.
A: starting material
B: product
C: immobilized reagent or catalyst.
Advantages

- Convection instead of diffusion
- Full conversion of starting materials
- Process reliability (constant parameters)
- Less work up
- Use of immobilised reagents or catalysts
- Only the desired product is gained
- Safety and reproducibility
Setup of the flow system. PASSflow reactor Flow system:
1 microreactor, 2 oven, 3 pump, 4 valve unit, 5 chiller, 6 flask used for circulating the reaction components, 7 solvents/reagents, 8 reagent for loading the microreactor, 9 waste.
Microreactor

- A flow-through column filled with special monolithic material which contains small crosslinked polymer beads

Cross-sectional view through a PASSflow reactor

(PTFE=polytetrafluoroethylene)

Picture of a PASSflow reactor
Microreactor

Common dimensions:

- **Microreactor:**
  - 10 cm long
  - 5 mm in diameter
  - Polymer load: 1 mmol or 10 - 20 weight-%
  - Product: 1 mmol

- **Polymer:**
  - 1 - 5 µm in diameter
  - 2 - 20% crosslinking
Monoliths

- Consist of continuous substructures and regular or irregular channels

- High void volume
- Large geometric surface area

- Low pressure drop during the passage of a fluid
- Large contact area of reagents or catalysts with the fluid
Creation of novel monolithic materials

3 starts

- Copolymerisation of different monomers in the presence of porogens
- Polymerization of a monolithic polymeric phase wedged inside the microchannel pore system of an inert support (e.g. glass)
- Preparation of diblock polymers, in which a well-defined cylindrical and degradable polymer is embedded inside a second polymer
  - After removal of the second polymer: nanotubes
Use of PASSflow reactors for different synthetic demands
Use of PASSflow reactors for different synthetic demands 2
Combination of synthetic flow systems with purification and analytical steps

Purification by scavenger column or HPLC column:

Circular flow for adapting reaction times in multistep synthesis

= valve
Applications

Traditionally: enzyme-mediated transformations

 e.g. enzymatic preparation of UDP-galactose

Overall transformation

\[
\text{GalK} + \text{GalT} + \text{GalU} + \text{PpK} + \text{UMK} + \text{NDK} + \text{PPA} \rightarrow \text{UDP-galactose} + \text{Pi}
\]
Applications:

PASSflow synthesis with immobilized reagents
Applications: multistep synthesis

Three-step preparation of β-lactams in the flow-mode
Applications:

microwave-assisted synthesis
References

