Modular Microreactor Technology
Case Study: Alkylation of Phenylacetonitrile
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Hyderabad, February 2013
Agenda

- Introduction
- Microreactor Technology (MRT): Background
- Technical solutions
- Case study- Phenyl Acetonitrile aklylation
- Summary
Bayer Technology Services – a Bayer Group Company

Turnover worldwide(*) 460 Mio Euro
Employees worldwide(**) 3,080
(*)2011   (**)Dec 31, 2011

Client industries
- Health Care
- Crop Science
- Material Science/Polymers
- Chemicals

Offers services on external market
Portfolio

Product & Process Innovation

Process Optimization Troubleshooting

Engineering Procurement Construction
BTS India – Our focus

**BTS India for Bayer:**
1. Execute investment projects of Bayer in India
2. Sourcing of equipment & technical services from India for Bayer globally

**BTS India for Indian market:**
1. Project Management (Owner’s Engineering)
2. Process Optimization
3. Environmental Protection Technologies
4. Micro Reaction Systems
5. Technology Packages like BayQik (Technology for Sulphuric Acid Plants)

- Operations started in 2008
- Total group of approx 35 personnel
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Characteristics of Microreactors

Continuous flow

High surface-to-volume ratio

\[ \frac{A}{V} \quad [m^2 / m^3] \]

- Microreactor: 2,000 - 20,000
- Millireactor: 1,000 - 2,000
- Tubular reactor: 100 - 500
- Stirred vessel: 4 - 40

\( d < 10 \text{mm} \)
Batch Reactor Technology

→ Batch stirred tank principle:

The complete amount of fluid is processed same-time!

Issues:

→ heat management!

→ retention time distribution!

→ hot spots!

→ inhomogenity!

→ process safety!
Continuous Flow Technology

→ Continuous process principle:

A small amount of fluid is continuously processed!

Advantages:

→ better process control
→ reduced hazard potential
→ process modification possible
Micro-structured devices for chemical technology

- Efficient mixing
  - High reaction rates
  - Emulsions, dispersions
  - Solids producing processes (e.g. precipitations)

- Efficient heat transfer
  - Fast reaction
  - High exothermal reactions
  - Control of highly exothermic reaction
  - Simplified safety concepts

- Efficient mass transfer
  - Transfer limited separation processes

- Efficient radiation transport process
  - Photochemistry
  - Photo catalysis

MRT allows to operate in the optimal operation windows to achieve better processes and products!
Microreaction Technology

Benefits

- Higher selectivity, higher yield
- Control of exothermic reactions, increased safety
- Quick and reliable scale-up
- Compact reactors and plants

- Higher added value, simplified downstream processes
- New and intensified processes, new products
- Reduced time-to-market
- Flexibility and mobility

- Less development costs (labour, materials)
- Less risk (CAPEX, safety)
- High flexibility (products, output, location)
- High speed (project duration)
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Innovative Technology from Lab to Production

- Process development
- Material development
- Synthesis routes
- Small-scale production

- Production of fine & specialty chemicals
- Scalable to high throughput
- Multi-purpose

- Development of API's
- Simple scale-up
- Ready for GMP
- Production of API's

Modular MicroReaction System  Miprowa® Reactors  Lonza FlowPlate™
Modular Microreaction System (MMRS) - Toolbox for Process and Product Development

Varieties of more than 40 modules
Flexible concept
Easy process control and automation
Easy Scale-up

Pressure
0 - 100 bar
(other ranges on request)

Temperature
-100°C - 200 °C
(others ranges on request)

Materials
stainless steel
alloy
tantalum
(glass)
additional materials on request

single- and multi-step reactions

low temperature reactions

particle precipitation

heterogeneous reactions
Lonza FlowPlate™ Microreactors

**Laboratory System:**
- 1 – 50 mL/min
- Integrated in MMRS
- Process R&D
- Pre-clinical phase

**Small-scale Production:**
- A6: 30 – 150 mL/min
- A5: 100 – 300 mL/min
- Clinical phase 1, 2, 3

**Large-scale production:**
- 200 – 600 mL/min
- Production of commercial products
Miprowa® Reactors
From Lab to Production

- **1 – 10 L/h**
  - For use with MMRS
  - Process development & intensification
  - Small-scale production

- **10 – 100 L/h**
  - Process development & intensification
  - Small-scale production

- **100 – 10,000 L/h**
  - Quick scale-up
  - Robust & easy to maintain
  - Production

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**Miprowa® Lab**

**Miprowa® Standard**

**Miprowa® Production**

- Dr. Frank Schael • Modular Micro reactor technology • February 2012

Ehrfeld Mikrotechnik BTS
Scale-up Strategy

R&D and kilo lab
0.05 – 10 L/h

Pilot scale
10 L/h – 100 L/h

Production Scale
40 L/h – 10,000 L/h
Cascade Micromixer

chaotic advection mixing

Inlet

dividing the fluid continuum and shifting sideways

recombining in different order

compressing into original shape

dividing

recombining
CFD Simulation of mass transport in a cascade micromixer
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Case Study: PTC Alkylation

Research details

- Research carried by St. Petersburg State university of Technology and Institute of Industrial Chemistry, Dresden
- Reaction: Alkylation of Phenyl Acetonitrile by Phase Transfer Catalysis
- Reaction product is an important Pharma Intermediate
- Reaction is conventionally carried out with metal hydrides with use of solvents like benzene
- Purpose: Compare performance with batch reactor and optimise parameters for microreactor

Paper Publishers

- University of Petersburg: E.S. Borovinskaya, V.M. Uvarov
- Institute of Industrial design: L. Mammitzsch, W. Reschetilowski
- Ehrfeld Microtechnik: Frank Schael
Alkylation of Phenylacetonitrile: Reaction Scheme

Figure 1. Reaction scheme of alkylation of phenylacetonitrile.
Case Study: Reaction Mechanism

$$C_2H_5X + [PhCHCN]^{-}TEBA^+ \rightarrow TEBA^+X^- + PhCH(C_2H_5)CN$$

**Organic phase**

$$TEBA^+OH^- + PhCH_2CN \rightarrow [PhChCN]^{-}TEBA^+ + H_2O$$

**Interfacial region**

$$TEBA^+OH^- + NaX \leftrightarrow NaOH + TEBA^+X^-$$

**Aqueous phase**

- $NaX$
- $NaOH$
Case Study: Comparison of schemes

Batch Reactor
- Reaction in Round bottom flask with mechanical/magnetic stirrer with reflux cooler
- Ethyl bromide added dropwise to reaction mixture
- Reaction product is extracted by ethyl acetate and analyzed by GC

Microreactor Setup
- Microreactor chosen with 70 μm channels. Reynolds number varied in the range 10-100
- Reactants were preheated using thermostat and pumped
- Product collected in flask containing ethyl acetate and analyzed by GC.
Phenylacetonitrile alkylation: Microreactor Setup

Ethyl bromide
TEBA
Phenylacetonitrile

24 mm

NaOH (45%)

Phenylbutyronitrile
Results: Reaction time

- Conversion, yield, %
- Time on stream, min

- Microreactor
- Batch reactor with mechanic stirrer 1200 rpm
- Batch reactor with magnetic stirrer
Results: Reaction performance

![Graph showing reaction performance with Phase ratio on the x-axis and Range, % on the y-axis. The graph includes three lines: Conversion (black circles), Yield (gray circles), and Selectivity (black squares).]
Results: Phase ratio/ Catalyst loading

![Graph showing conversion vs. time on stream for different phase ratios and catalyst loadings.](image-url)
We had a small problem with the scale-up out of the laboratory.

**RESULTS**

- Reaction was appreciably faster in microreactor compared to batch reactor
- Lower organic ratio leading to lower recovery cost
- Lower catalyst loading leading to lower operating cost
- Multiple options evaluated within a short time

**NEXT STEPS**

- Scale up of lab setup
- Conversion of upstream/downstream processes to continuous.

We had a small problem with the scale-up out of the laboratory....
Thank you!

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