Grüne Chemie in Österreich – Alternativen zur stofflichen Synthese

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Green Chemistry

12 Principles of Green Chemistry

- Prevent waste
- Design safer chemicals & products
- Design less hazardous chemical syntheses
- Use renewable feedstocks
- Use catalysts, not stoichiometric reagents
- Avoid chemical derivatives
- Maximize atom economy
- Use safer solvents & reaction conditions
- Increase energy efficiency
- Design chemicals & products to degrade after use
- Analyze in real time to prevent pollution
- Minimize the potential for accidents
Bioorganic Chemistry – The Chemistry-Biology Interface

Chemistry Utilizing Nature’s Resources

CO₂ Neutral Production Cycles
**Green & Sustainable Supply Chains**

**Feedstock**
- Flexible

**Conversion**
- Superior economics
- Fit with existing assets

**Green products**
- Favorable properties
- Processing fits with existing infrastructure

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**Sugar Conversion to Furans**

![Sugar Conversion Diagram]
Microwave Chemistry

Conventional vs. Microwave Heating

- Heat distribution by convection
- Direct absorption by solvent
- Local „Superheating”
- Immediate on/off of energy coupling

Towards Continuous HMF Production (DMSO)

Stopped-Flow Microwave

Fructose conversion

Levulinic acid yield

HMF yield

HMF selectivity

125°C & 2min $t_{\text{on}}$
FDCA as Renewable Monomer

HMF $\rightarrow$ FDCA

$\text{HMF} + \text{O}_2 \rightarrow \text{FDCA}$

Furan Derivatives as Fuel Additives
Biofuel Future …

We still have a "little" work to do!

However: by definition, perfect chemistry is ideally suited for continuous processing.
**Chemistry in Flow – Advantages**

**Mixing by Diffusion**

**Safe & Simple Pressurization**

**High Surface to Area Volume Ratio**
**Chemistry in Flow – Advantages**

**“On-the-fly” Analysis**

![Graph and equipment image for on-the-fly analysis](image)

**Integrated Chemical Processing**

1. Define the fluidics
2. Enter reaction conditions
3. Run experiment
4. View HPLC data

![Integrated chemical processing setup](image)
**Chemistry in Flow – Operational Modes**

**Rapid Reaction Optimization**
Samples experiencing different reaction conditions move through the flow reactor.

**Simple Reaction Scaling**
Utilize the benefits of flow chemistry to continuously synthesize g-lug overnight.

**Advanced Library Synthesis**
Different compounds in a library flow through the reactor separated by solvent.

**Flow vs. Batch**

<table>
<thead>
<tr>
<th>Continuous stirred tank reactor</th>
<th>Plug flow microreactor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Reactor volume</td>
<td></td>
</tr>
<tr>
<td>Residence time / s</td>
<td></td>
</tr>
<tr>
<td>Conversion / %</td>
<td></td>
</tr>
<tr>
<td>Reaction volume / cm$^3$</td>
<td></td>
</tr>
<tr>
<td>Space-time yield / h</td>
<td></td>
</tr>
<tr>
<td><strong>Industrial process</strong></td>
<td></td>
</tr>
<tr>
<td>Residence time / s</td>
<td>1760</td>
</tr>
<tr>
<td>Conversion / %</td>
<td>30-50 oscillating</td>
</tr>
<tr>
<td>Reaction volume / cm$^3$</td>
<td>2800</td>
</tr>
<tr>
<td>Space-time yield / h</td>
<td>0.7-2.0 oscillating</td>
</tr>
<tr>
<td><strong>Microreactor</strong></td>
<td></td>
</tr>
<tr>
<td>Residence time / s</td>
<td>3</td>
</tr>
<tr>
<td>Conversion / %</td>
<td>&gt;99</td>
</tr>
<tr>
<td>Reaction volume / cm$^3$</td>
<td>3</td>
</tr>
<tr>
<td>Space-time yield / h</td>
<td>500</td>
</tr>
</tbody>
</table>
Towards Continuous HMF Production (DMSO)

Continuous Flow Reactor

Flow Chemistry in Industry

Process Safety  
Reaction Control  
Parallel Operations  
Reactor Flexibility  
Simple Design  
Low Costs
Bioorganic Chemistry – The Chemistry-Biology Interface

Chemistry Utilizing Nature’s Properties

Catalytic Strategies in Synthesis

Enzyme Catalysis
- enantioselectivity
- chemoselectivity
- environmentally benign
- available
- inhibition

Organometal Catalysis
- enantiodivergence
- availability
- toxicity
- efficiency
- enantioselectivity

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[Diagram showing enzymatic processes and chemical structures]
**Perspectives for Enantioselective Synthesis**

![Perspectives for Enantioselective Synthesis](image)

Frost & Sullivan survey  
C&EN 2004

**Kinetic Resolutions towards Aroma Compounds**

- **Quercus & Aerangis lactones**
  - \( R = \text{C}_2-\text{C}_5 \)
  - \( n = 1,2 \)

- **Mango & Jasmin lactones**

- **Macrocyclic lactones of musk type**

![Kinetic Resolutions towards Aroma Compounds](image)
Aerangis Lactones

The Aerangis lactones

(5S, 6S)-cis lactone

fragrance of white orchids

Aerangis Lactones – Precursor Synthesis
Aerangis Lactones – Precursor Synthesis

\[
\text{Amberlyst 15} \quad \text{n-heptane}
\]

Aerangis Lactones – Resolutions prep

\[
\text{CPRMO Lb prep 4 h} \quad \text{>50% conv} \quad \text{74% yield} \quad \text{69% yield}
\]

\[
\text{CDMO Lb prep 4 h} \quad \text{30% conv} \quad \text{92% yield} \quad \text{47% yield}
\]
Aerangis Lactones – Single Operation Process

H₂ + Rh/C + Base
30 °C
0.5 M in n-heptane

>85 % cis
0.5 M sol.

>85 % trans
0.5 M sol.

>99 % cis
>99 % ee

>85 % trans
>99 % ee

0.5 M sol.

CPMO
CDMO

7 g / L
<25 min

Active Site of PAMO

FAD
R337
L443
**Improving Stability of BVMOs – Consensus Approach**

Structure Guided Consensus Concept
Application to CHMO<sub>Acidito</sub>

1. G 14 A
2. SLEI 74-77 EWSW
3. QG 83-84 TQ
4. F 136 Y
5. K 153 P (not possible)
6. A 209 P (never functional)
7. G 238 E
8. W 240 R
9. A 260 E
10. NM 290-291 DR
11. N 299 D
12. KG 302-303 RD (if more stable than I 295 E => salt bridge possible)
13. A 313 E
14. Q 316 R
15. N 336 E
16. E 346 V
17. EN 358-359 PR
18. EN 364-365 AD
19. RV 365-366 EH
20. KN 395-396 RE
21. M 412 L
22. Y 419 F
23. QYTV 451-454 KYAE
24. N 477 E (if this is advantageous than also Q 473 K/R => salt bridge possible)
24a. E477D in N477E/ Q473K
24b. E477D in N477E/ Q473R
25. KN 500-501 PR
26. N 519 E

Bommarius & Chaparro-Riggers <007ChemBioChem2295>

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**Directed Evolution of BVMOs**

- mutagenesis
- expression screening
- promotion
**Applied Biosynthetic Cell Factories**

**Flux within a Cell**
Towards Artificial Metabolic Pathways

Flux optimization

a) sub-optimal flux
   Input flux → E1 → E2 → E3 → Output flux

b) Spatially optimized and balanced flux
   Input flux → E1 → E2 → E3 → Output flux

Towards Artificial Metabolic Pathways