Resins

Presented by
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Swollen cross-linked polymers (resins) represent the solvents for solid-phase organic reactions.
Resins - properties

- **Swelling:**
  - Most important property (necessary for diffusion and accessibility of active sites)
  - type of solvent depends on the sort of resin
  - higher swelling => higher loading
Resins - properties

- Size of the resin beads (80-200μm)
- Mesh size (70-170) (number of openings in a square inch)
- Mechanical and thermal stability
- Price
Resins –different types

- Cross-linked-polystyrene-resins
- Polyamine-resins
- Tentagel-resins
- Soluble resins
Cross-linked-polystyrene resins

- Most commonly used due to high availability, low cost and chemical stability

- styrene
- divinylbenzene
- polystyrene
- cross-linked polystyrene
Cross-linked-polystyrene resins

Merrifield resin
polymer beads 0.04-0.15 mm
co-polymer of styrene-divinyl benzene
with 1-2% cross-links
Cross-linked-polystyrene resins

Method to functionalize the resin

- Br₂, Tl(III)
- n-BuLi, TMEDA
  - more convenient
- n-BuLi
  - better p- vs o-regioselectivity
Cross-linked-polystyrene resins

Commercially available functional groups grafted onto PS resins

- Cl
- NH₂
- OH
- COOH
- CO
- Br
## Price

<table>
<thead>
<tr>
<th>Ordernumber</th>
<th>Product</th>
<th>capacity [mmol/g]</th>
<th>Price [□]</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>5g</td>
</tr>
<tr>
<td>H 400 00</td>
<td>Hydroxymethyl Polystyrene</td>
<td>0.8 - 1.5</td>
<td>40.--</td>
</tr>
<tr>
<td>H 400 01</td>
<td>Chloromethyl Polystyrene</td>
<td>0.8 - 1.2</td>
<td>---</td>
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<tr>
<td>H 400 02</td>
<td>Polystyrene AM - NH$_2$</td>
<td>0.8 - 1.4</td>
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<td>H 400 03</td>
<td>Polystyrene AM - COOH</td>
<td>0.8 - 1.2</td>
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<td>H 400 04</td>
<td>Polystyrene AM - SH</td>
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<td>H 400 04.1</td>
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<td>H 400 06</td>
<td>Polystyrene AM - CHO</td>
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<td>H 400 06.1</td>
<td>Polystyrene AM - CH(OEt)$_2$</td>
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<td>H 400 07</td>
<td>Formyl Polystyrene</td>
<td>0.6 - 0.9</td>
<td>82.--</td>
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<tr>
<td>H 400 08</td>
<td>Carboxy Polystyrene</td>
<td>1.0 - 1.8</td>
<td>82.--</td>
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<tr>
<td>H 400 09</td>
<td>Bromo Polystyrene</td>
<td>2 - 4</td>
<td>42.--</td>
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</tbody>
</table>
Solvent Compatibility

- Polystyrene resins swell in solvents of low to medium polarity (DMF, DCM, toluene)

- don’t swell in polar, protic solvents (alcohol and water)
Disadvantages of polystyrene-resins

- Only temperatures under 130°C
- No usage of very electrophilic reagents
Disadvantages for the synthesis of peptides:

- Not rigid enough => interactions between the reaction centers
- Resin hydrophobic, peptide hydrophilic => peptid-peptidchain-interactions
- Solvents that can be used are unfit for peptides
Polyamine-resins

- polyacrylamide polymers (most common) (Sheppard)

\[
\begin{align*}
\text{bulk monomer} & : \quad \text{80-90}\% \\
\text{cross-linking monomer} & : \quad \text{6-7}\% \\
\text{functionalized monomer} & : \quad \text{5-15}\% \\
A & = \text{CONMe}_2
\end{align*}
\]
Polyamine-resins

- Used for peptide synthesis
  mimic more closely the properties of the peptide chains

- Better swelling in polar, aprotic solvents
  (e.g. DMF, or N-methyl pyrrolidinone)
Tentagel-resins

- polyethylene glycol (PEG) (up to 70%) attached to cross-linked polystyrene through an ether link

Figure 1: Chemical architecture of TentaGel resins
| Order Number | Product       | Price in screenshot | |
|--------------|---------------|---------------------||
| S 30 900     | TentaGel S-OH | 41.-- 102.-- 383.-- 1010.-- | |
| S 30 901     | TentaGel S-Br | 41.-- 102.-- 383.-- 1010.-- | |
| S 30 902     | TentaGel S-NH₂| 41.-- 102.-- 383.-- 1010.-- | |
| S 30 903     | TentaGel S-COOH | 51.-- 115.-- 465.-- 1191.-- | |
| S 30 904     | TentaGel S-SH | 56.-- 128.-- 511.-- 1311.-- | |
| S 30 904.1   | TentaGel S-S-Trt | 51.-- 115.-- 465.-- 1191.-- | |
| S 30 016     | TentaGel S-FMP 0.2 - 0.25 mmol/g | 41.-- 102.-- 383.-- 1150.-- | |
Advantages of Tentagel-resins

- Swells in both protic and aprotic solvents
- Attached reacting groups project into solution rather than being anchored close to the polymer backbone

=> Conditions similar to solution phase chemistry
Disadvantages of Tentagel-resins

- Relatively low functional group loading compared with PS-resins
  (0.25 mmol/g compared to 0.5-1.2 mmol/g)
- Potential of PEG chains to complex Lewis acids
- Potential instability of PEG
Disadvantages of Tentagel-resins

- Presence of linear PEG impurities found after cleavage from the resin in the small molecule products
- Tendency for resins to become sticky and difficult to handle as the synthesis progress
Combinatorial synthesis in liquid phases

- Resin: MeO-PEG
  polyethylene glycol monomethyl ether

- Soluble in most solvents

  => Advantages:
  - homogeneous conditions
  - usage of catalysts
Combinatorial synthesis in liquid phases

- Crystallizes easily in diethyl ether
  => further handling like solid phase resins
There are 4 different main types of resins with specific variations available.

One needs to choose the resin carefully depending on the reaction conditions.

The resin equals the solvent in combinatorial chemistry.
Bibliography

- the script of professor König
- http://www.merckbiosiences.co.uk
- http://www.combichemistry.com
- http://www.uni-wuppertal.de
- http://www.rapp-polymere.com
- Terret, N.K., Kombinatorische Chemie
Thank you for your attention!