Sulfonation Chemistry – more sustainable approaches
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More sustainable sulfonations

Content

- Conventional sulfonation reactions
  - Where they are used, which products are manufactured, their benefits and disadvantages

- Alternative sulfonation reactions
  - What can be improved, what is more sustainable, benefits and disadvantages

- More sustainable sulfonation reactions
  - What they look like, their sustainable benefits
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Natural “sulfonations”

- Synthesis of thioles:
  - R-X + NaSH \( \rightarrow \) R-SH + NaX
  - Aryl-Grignard + sulfur
  - Diazonium salt + Na sulfide or Na xanthate

- Nature is not a model for sustainable sulfonations
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Conventional sulfonation

![Chemical reaction diagram]

**Difficulties:**
- Sulfuric acid: dilution effect due to formation of water: (large) excess of reagent necessary
- Sulfone formation as side reaction can be prevented by high excess of reagent
- Waste waters need to be neutralised (and oxidised due to dissolved organic residues)
- Sulfonic acids mainly easily soluble in water and reagent: difficult to isolate
- Sulfochlorination and subsequent hydrolysis: sulfonic acids better to isolate
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Conventional sulfonation

Conventional sulfonation:

- Benzene reacts with chlorosulfonic acid (-HCl) to form benzenesulfonic acid (SO₃H).
- Benzenesulfonic acid reacts with chlorosulfonic acid (-H₂SO₄) to form benzenesulfonyl chloride (SO₂Cl).

Bar chart showing the chlorosulfonation of benzene [kg]:

- Chlorosulfonic acid: -300 kg
- Benzenesulfonyl chloride: -200 kg
- Sulfuric acid/hydrochloric acid: 400 kg
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Challenges

- Paper chemistry: introduction of pure SO$_3$ would be the most efficient method
  - No waste
  - No dilution
  - Reactivity remains unchanged

- Problem:
  - Handling and availability: SO$_3$ is normally not available and highly reactive
  - Sophisticated solutions exist for dedicated sulfonation plants but no smart development for multi purpose environment

- Scale and type of process
  - Sulfonation in dedicated equipment: in general waste is not a «problem»
  - Problems are sulfonations in multi purpose equipment in «mid scale»

<table>
<thead>
<tr>
<th>Multi purpose</th>
<th>Dedicated / large volumes</th>
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<tbody>
<tr>
<td>API’s</td>
<td>Ion exchange resins</td>
</tr>
<tr>
<td>AI’s</td>
<td>Detergents</td>
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<tr>
<td>Dyes</td>
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<td>Polymers</td>
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Alternative sulfonation reactions

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth reaction conditions</td>
<td>Expensive</td>
</tr>
<tr>
<td>No aqueous, acidic waste</td>
<td>Not suitable for every sulfonation reaction</td>
</tr>
<tr>
<td>Liquid amines can be distilled off and re-used</td>
<td>Use of amines as «reaction aids»</td>
</tr>
<tr>
<td>Ideal for sensitive substrates</td>
<td>Hazardous reagents</td>
</tr>
<tr>
<td>Reactivity according to base strength of amines</td>
<td></td>
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Sulfur trioxide on a polymeric carrier

**Advantages** | **Disadvantages**
--- | ---
Moderated reactivity | Needs SO$_3$ source
«Rechargeable» | Liquid/dissolved substrates needed

Polyvinylpyridine SO$_3$ complex
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Sulfonation with PVPS

- Feasibility study:
  - Reaction of n-dodecanol with PVPS
  - Batch reaction
  - Feasibility confirmed: 80% conversion; no product isolation
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CABB’s Verbund and recycling system
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Sulfonation with SO$_3$ in a microreactor

- Commercially interesting reaction: sulfonation of an aromatic compound
- High reactivity, exothermic reaction: → microreactor
- Multi-purpose approach: → microreactor
- Challenges:
  - solid starting material
  - solid product
  - liquid range of SO$_3$ is between 18°C and 48°C
  - dosage of SO$_3$
  - quantitative analysis of SO$_3$ volume
  - analytical detection method of SO$_3$
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Sulfonation with SO$_3$ in a microreactor

- Fraunhofer successfully reacted liquid SO$_3$ with molten PNT to yield PNTS in a microreactor

Heated SO$_3$ dosage

N$_2$ dosage

Microreactor

Nitrotoluene addition
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Sulfonation with SO₃ in a microreactor: results and learnings

- p-Nitrotoluene (PNT) was successfully reacted with SO₃ to yield p-Nitrotoluenesulfonic acid (PNTS)
  - PNT is heated to 75°C to obtain a liquid starting material
  - Dosage of liquid SO₃ with a syringe pump, evaporation of SO₃ before reaction with PNT
  - Reaction is fast; selectivity and yield depend on temperature and concentration parameters
  - A continuous reaction of PNT with SO₃ was carried out and analytical results determined at steady state
- Multi product approach possible for all starting materials with “low” melting points, or in solution
  - such kind of aromatic compounds are difficult to handle in a microreactor without a solvent
  - inert solvent for SO₃ sulfonation is difficult to find
  - microreactor is not the most suitable equipment for this reaction
Continuous sulfonation with oleum/\(\text{SO}_3\) in CSTR reactors

- Cascade of four reactors: two for reaction, two for work-up
- Preparation of a solution of PNTS via sulfonation of PNT with sulfuric acid to start the reaction
- Water resp. mother liquor is added and temperature lowered to precipitate PNTS
- Continuous process with recycling of mother liquor up to 4 times
  - Yield 98.5%
  - Disadvantage: use of oleum and dilution with water results in waste sulfuric acid

<table>
<thead>
<tr>
<th>Advantages</th>
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</thead>
<tbody>
<tr>
<td>High yield</td>
<td>Needs (\text{SO}_3) source</td>
</tr>
<tr>
<td>Continuous process for large volumes</td>
<td>No real multi purpose approach</td>
</tr>
<tr>
<td></td>
<td>Formation of waste</td>
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\[
\begin{align*}
\text{O}_2\text{N} & \quad \xrightarrow{\text{SO}_3 / \text{H}_2\text{SO}_4} \quad \text{115°C} \quad \text{O}_2\text{N} \quad \text{SO}_3\text{H} \\
\end{align*}
\]
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Batch sulfonation with SO$_3$ in liquid SO$_2$

- Reaction in heterogeneous phase
- Suspension of PNT in liquid SO$_2$
- Exothermic reaction upon addition of SO$_3$ and SO$_2$ under reflux
- Distillation of SO$_2$ lets PNTS precipitate
- 98.6% yield with >99% purity

<table>
<thead>
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<tbody>
<tr>
<td>No waste!</td>
<td>Needs SO$_3$ source</td>
</tr>
<tr>
<td>Multi-purpose approach</td>
<td>Needs SO$_2$ liquid</td>
</tr>
<tr>
<td>High yield and high purity</td>
<td></td>
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<tr>
<td>Recycling of SO$_2$</td>
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Calculation of PNT sulfonetion processes

- Calculation of material and waste efficiency shows similar results of both processes
- Cost calculation of the two different processes shows surprisingly very similar process costs
- Better multi purpose approach: sulfonation in liquid SO$_2$ with SO$_3$ as reagent

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<thead>
<tr>
<th></th>
<th>Continuous / oleum</th>
<th>Batch / SO$_2$ / SO$_3$</th>
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<tbody>
<tr>
<td>Process Mass Intensity (PMI)</td>
<td>1.78</td>
<td>1.03</td>
</tr>
<tr>
<td>E-factor</td>
<td>0.78</td>
<td>0.03</td>
</tr>
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Sulfonation of polymers with SO$_3$ in SO$_2$

- Sulfonation of a polymer: pre- or postpolymerisation, homogeneous or heterogeneous
- Degree of sulfonation (dS) determines hydrophilicity
- Conventional process: solution of polymer in concentrated sulfuric acid
  - Precipitation into water, extended washing: very large amounts of waste water
- Alternative sulfonation process: SO$_3$ in liquid SO$_2$

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<thead>
<tr>
<th></th>
<th>Conventional (sulfuric acid)</th>
<th>SO$_3$ in SO$_2$</th>
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<tbody>
<tr>
<td><strong>Benefits</strong></td>
<td>Polymer partially soluble in SE</td>
<td>Heterogeneous reaction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Better control of dS</td>
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<tr>
<td></td>
<td></td>
<td>No chain cleavage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No discoloration</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Cleavage of polymer, discoloration</td>
<td>Low solubility of polymer</td>
</tr>
<tr>
<td></td>
<td>Large volumes of waste water</td>
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<td></td>
<td>Long washing process</td>
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Sulfonamide: conventional sulfonation with CI(III)SO₃H

Original process:

- Reaction of the aromatic compound with CI(III)SO₃H in dichloromethane at -5°C
- Subsequent reaction of intermediately formed sulfonic acid with CI(III)SO₃H to yield sulfonyl chloride
- Reaction of sulfonyl chloride with aqueous ammonia solution to yield sulfonamide

- HCl and H₂SO₄ are removed as aqueous waste
- Dichloromethane and toluene are completely recycled
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Sulfonamide: improved sulfonation with $\text{SO}_3/\text{SO}_2$

**CABB's improved process**

- Reaction of aromatic compound with $\text{SO}_3$ in liquid $\text{SO}_2$ at -20°C
- Reaction of sulfonic acid with thionyl chloride
- Reaction mixture is heated to 25°C which leads to evaporation of $\text{SO}_2$
- Reaction of sulfonyl chloride with aqueous ammonia solution in toluene
- $\text{SO}_2$ evaporates and is completely recycled
- HCl is converted into hydrochloric acid as commercial sales product
- One pot synthesis
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Sulfonamide: comparison of process efficiency

- No chlorinated nor other solvent necessary
- Sulfur dioxide comes out of the pipeline and is evaporated back into the Verbund system
- Different sulfonation technology: advantage of direct sulfonation with liquid sulfur trioxide
- Most efficient use of reagents (no loss of one molecule ClSO3H as sulfuric and hydrochloric acid)

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<thead>
<tr>
<th></th>
<th>CH₃Cl / ClSO₃H</th>
<th>SO₂ / SO₃ / SOCl₂</th>
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</thead>
<tbody>
<tr>
<td>Waste water</td>
<td>13 kg per kg product</td>
<td>5.9 kg per kg product</td>
</tr>
<tr>
<td>PMI</td>
<td>20.2</td>
<td>12.7</td>
</tr>
<tr>
<td>E-factor</td>
<td>19.2</td>
<td>11.7</td>
</tr>
<tr>
<td>Atom efficiency</td>
<td>44%</td>
<td>51%</td>
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Conclusion

- Creation of waste in sulfonation reactions can be avoided using SO$_3$ as reagent
- Nearly no waste is formed using SO$_3$ in liquid SO$_2$ (E-factor almost zero)
- Sulfonations with SO$_3$ can be best controlled in continuous reactions (reactivity, exothermicity) or in liquid SO$_2$ (reactivity moderator) at low temperatures
- Sulfonations with SO$_3$ in SO$_2$ leads to better atom efficiency, lower PMI and lower E-factor values compared to other sulfonations (provided that the SO$_2$ is recycled)
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