Effects of Amine Structure and Base Strength on Acid-Base Cooperative Aldol Condensation

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Aldol condensation

- Reaction between two components with carbonyl groups (ketone/aldehyde)
- Important reaction to create new C-C bonds
  ➔ yield larger and more complex molecules

- Applications in the production of:
  - Vitamins and pharmaceutical compounds
  - Solvents
  - Plasticizers for polymers
  - Food preservatives
  - Dyes, flavors and fragrances
Sustainable society

Conversion of sugars into hydrocarbon fuels [1]

polyfructan → Dehydration → furfural → Aldol condensation →

Hydrogenation → Hydrodeoxygenation → alkanes

Industrial catalyst

In industry, mostly catalyzed using **homogeneous** (liquid) base catalysts such as KOH, Ca(OH)$_2$, NaOH or Na$_2$CO$_3$

Disadvantages:

(i) The necessity of energy intensive separation steps
(ii) A short catalyst life time
(iii) The low reusability
(iv) Important waste streams
(v) Intensive equipment corrosion

Develop new and optimize existing heterogeneous catalysts
Enzymatic catalysis


\[ \text{GOAL: incorporating these synergy effects into heterogeneous catalysis!} \]
Rational catalyst design

- Catalyst library
- Activity library
- Modelling
- Industrial application
- Insights in surface phenomena
- New concept
- Synthesis and characterization
- Performance testing
Outline

- Introduction
  - Aldol condensation
  - Rational catalyst design
- Catalyst synthesis and characterization
- Performance testing
  - Aldol condensation experiments
  - The promoting effect of silanols
  - Amine base strength
  - Amine structure
- Kinetic model based analysis
  - Kinetic model construction
  - Estimated values and parity diagrams
  - Base strength and steric hindrance
- Conclusions
Synthesis of the heterogeneous catalysts

Starting material: Silica gel 60
Specific BET surface: 497 m²/g
Total pore volume: 0.69 cm³/g
Average pore diameter: 5.6 nm

Concentration of precursor in the synthesis mixture determines the ratio of acid and base sites on the silica surface
The different catalysts

Type AB:
- APTES
- MAPTMS
- CAPTMS
- PAPTMS
- DEAPTMS

Type B:
- APTES
- MAPTMS
- CAPTMS
- PAPTMS
- DEAPTMS
Catalyst characterization

The presence of the amine groups and the removal of silanol groups is demonstrated via Diffuse Reflectance Infrared Fourier Transform (DRIFT) spectroscopy.

SILICA

APTES (AB & B)

MAPTMS (AB & B)

CAPTMS (AB & B)

PAPTMS (AB & B)

DEAPTMS (AB & B)
Catalyst characterization

The active site concentrations are determined from CHNS elemental analysis

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Amine(^{[a]}) [mmol g(^{-1})]</th>
<th>Silanol(^{[b]}) [mmol g(^{-1})]</th>
<th>Silanol/amine(^{[c]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTES 1</td>
<td>0.29</td>
<td>0.67</td>
<td>2.33 ± 0.13</td>
</tr>
<tr>
<td>APTES 2</td>
<td>0.32</td>
<td>0.69</td>
<td>2.15 ± 0.11</td>
</tr>
<tr>
<td>APTES 3</td>
<td>0.33</td>
<td>0.67</td>
<td>2.07 ± 0.11</td>
</tr>
<tr>
<td>APTES 4</td>
<td>0.35</td>
<td>0.61</td>
<td>1.73 ± 0.09</td>
</tr>
<tr>
<td>APTES 5</td>
<td>0.40</td>
<td>0.56</td>
<td>1.39 ± 0.07</td>
</tr>
<tr>
<td>APTES 6</td>
<td>0.49</td>
<td>0.50</td>
<td>1.03 ± 0.04</td>
</tr>
<tr>
<td>APTES 7</td>
<td>0.59</td>
<td>0.45</td>
<td>0.77 ± 0.04</td>
</tr>
<tr>
<td>APTES 8</td>
<td>0.65</td>
<td>0.27</td>
<td>0.42 ± 0.03</td>
</tr>
<tr>
<td>MAPTMS 1</td>
<td>0.34</td>
<td>0.67</td>
<td>1.96 ± 0.10</td>
</tr>
<tr>
<td>MAPTMS 2</td>
<td>0.35</td>
<td>0.67</td>
<td>1.90 ± 0.10</td>
</tr>
<tr>
<td>MAPTMS 3</td>
<td>0.41</td>
<td>0.66</td>
<td>1.60 ± 0.08</td>
</tr>
<tr>
<td>MAPTMS 4</td>
<td>0.47</td>
<td>0.51</td>
<td>1.09 ± 0.05</td>
</tr>
<tr>
<td>MAPTMS 5</td>
<td>0.61</td>
<td>0.35</td>
<td>0.57 ± 0.03</td>
</tr>
<tr>
<td>MAPTMS 6</td>
<td>0.70</td>
<td>0.31</td>
<td>0.44 ± 0.02</td>
</tr>
<tr>
<td>MAPTMS 7</td>
<td>0.80</td>
<td>0.13</td>
<td>0.17 ± 0.02</td>
</tr>
<tr>
<td>CAPTMS 1</td>
<td>0.30</td>
<td>0.67</td>
<td>2.20 ± 0.14</td>
</tr>
<tr>
<td>CAPTMS 2</td>
<td>0.43</td>
<td>0.60</td>
<td>1.40 ± 0.06</td>
</tr>
<tr>
<td>CAPTMS 3</td>
<td>0.56</td>
<td>0.40</td>
<td>0.72 ± 0.04</td>
</tr>
<tr>
<td>CAPTMS 4</td>
<td>0.74</td>
<td>0.25</td>
<td>0.35 ± 0.03</td>
</tr>
<tr>
<td>PAPTMS 1</td>
<td>0.29</td>
<td>0.66</td>
<td>2.23 ± 0.16</td>
</tr>
<tr>
<td>PAPTMS 2</td>
<td>0.58</td>
<td>0.37</td>
<td>0.63 ± 0.04</td>
</tr>
<tr>
<td>DEAPTMS 1</td>
<td>0.33</td>
<td>0.66</td>
<td>2.03 ± 0.12</td>
</tr>
<tr>
<td>DEAPTMS 2</td>
<td>0.52</td>
<td>0.48</td>
<td>0.93 ± 0.04</td>
</tr>
<tr>
<td>DEAPTMS 3</td>
<td>0.55</td>
<td>0.42</td>
<td>0.77 ± 0.04</td>
</tr>
<tr>
<td>DEAPTMS 4</td>
<td>0.60</td>
<td>0.45</td>
<td>0.76 ± 0.04</td>
</tr>
</tbody>
</table>

\(^{[a]}\) The amine concentration on the cooperative acid-base (Type AB) and the corresponding base (Type B) catalysts is identical. The error on this measurement is for all samples ±0.01 mmolg\(^{-1}\). \(^{[b]}\) The reported silanol concentration is only valid for cooperative acid-base catalysts (type AB). The error on this measurement amounts to ±0.01 mmolg\(^{-1}\) for all samples. \(^{[c]}\) The ratio of silanols to amines given in the table is only valid for cooperative acid-base catalysts (type AB).
• Introduction
  • Aldol condensation
  • Rational catalyst design
• Catalyst synthesis and characterization
• Performance testing
  • Aldol condensation experiments
  • The promoting effect of silanols
  • Amine base strength
  • Amine structure
• Kinetic model based analysis
  • Kinetic model construction
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• Conclusions
Performance testing

Operating conditions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Purpose</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amine groups</td>
<td>Active site</td>
<td>1 mmol/l</td>
</tr>
<tr>
<td>Silanol groups</td>
<td>Active site promotion</td>
<td>0 – 2.6 mmol/l</td>
</tr>
<tr>
<td>4-nitrobenzaldehyde</td>
<td>Reactant 1</td>
<td>15 – 177 mmol/l</td>
</tr>
<tr>
<td>Acetone</td>
<td>Reactant 2</td>
<td>1.4 – 7.0 mol/l</td>
</tr>
<tr>
<td>Methyl 4-nitrobenzoate</td>
<td>Internal standard</td>
<td>13 mmol/l</td>
</tr>
<tr>
<td>n-hexane</td>
<td>Solvent</td>
<td>3.7 – 6.4 mol/l</td>
</tr>
<tr>
<td>Temperature</td>
<td></td>
<td>15 – 55°C</td>
</tr>
</tbody>
</table>

Batch reactor (Parr)

Reversed-phase high-performance liquid chromatograph (Agilent)
The promoting effect of silanols

Turnover frequency: \[ TOF = \frac{dX_{\text{benz}}/dt|_{t=0}}{c_{\text{amines}} c_{\text{benz},t=0}} \]
Effect of the amine base strength

Experimentally obtained turnover frequencies

<table>
<thead>
<tr>
<th>Amine active site</th>
<th>$\text{TOF}_{\text{unprom}}$ (s$^{-1}$)[a]</th>
<th>$\text{TOF}_{\text{prom}}$ (s$^{-1}$) [b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminopropane</td>
<td>2.0 $10^{-4}$</td>
<td>7.8 $10^{-4}$</td>
</tr>
<tr>
<td>Methylaminopropane</td>
<td>1.0 $10^{-3}$</td>
<td>3.3 $10^{-3}$</td>
</tr>
<tr>
<td>Cyclohexylaminopropane</td>
<td>9.6 $10^{-6}$</td>
<td>3.1 $10^{-5}$</td>
</tr>
<tr>
<td>Phenylaminopropane</td>
<td>-</td>
<td>7.0 $10^{-6}$</td>
</tr>
<tr>
<td>Diethylaminopropane</td>
<td>1.2 $10^{-5}$</td>
<td>3.9 $10^{-5}$</td>
</tr>
</tbody>
</table>

[a] Turnover frequencies calculated by averaging the TOF’s obtained using the unpromoted base catalysts (samples B); [b] Turnover frequencies calculated by extrapolating the TOF’s obtained using the cooperative acid-base catalysts (samples AB) towards a molar silanol-to-amine ratio of infinity.

$\Delta H^\circ$, $\Delta S^\circ$ and corresponding $pK_{a,298K}$ values for deprotonation [1]

<table>
<thead>
<tr>
<th>Amine active site</th>
<th>$\Delta H^\circ$ (kJ. mol$^{-1}$)</th>
<th>$\Delta S^\circ$ (J. mol$^{-1}$.K$^{-1}$)</th>
<th>$pK_{a,298K}$ of the ammonium ion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminopropane</td>
<td>57.91</td>
<td>-8.37</td>
<td>10.58</td>
</tr>
<tr>
<td>Methylaminopropane</td>
<td>52.59</td>
<td>-30.12</td>
<td>10.79</td>
</tr>
<tr>
<td>Cyclohexylaminopropane</td>
<td>57.49</td>
<td>-17.15</td>
<td>10.97</td>
</tr>
<tr>
<td>Phenylaminopropane</td>
<td>33.39</td>
<td>3.56</td>
<td>5.66</td>
</tr>
<tr>
<td>Diethylaminopropane</td>
<td>43.43</td>
<td>-60.67</td>
<td>10.78</td>
</tr>
</tbody>
</table>

Amine structure effects

\[ \text{Aldol condensation} \]

\[ \text{Steric hindrance} \]

\[ \text{Salt formation} \]
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Proposed reaction mechanism
The primary amine is considered to be the reference active site.

In all other cases, the equilibrium coefficient $K_{im}$ equals zero.

Changing the amine affects all reaction steps occurring on the amine itself, i.e. $k_1$, $k_3$, $k_4$ and $k_{-4}$, by a change in activation entropy $\Delta S_{amine}$ and activation energy $\Delta E_{amine}$.

The presence of silanol groups induces a change in the reaction entropy $\Delta S_{OH'}$ and reaction energy $\Delta E_{OH'}$.

\[
R_{prom} = k_1' K_{ads,1} C_{0, prom} a_{ace} + k_1 C_{0, prom} a_{ace} - k_2 C_{1, prom} - k_2' K_{ads,2} C_{1, prom} a_{benz}
\]

\[
k_1 = A_{1, ref} e^{-\frac{\Delta S_{amine}}{R} - \frac{(E_1 + \Delta E_{amine})}{R} \left(\frac{1}{T} - \frac{1}{T_{ref}}\right)}
\]

\[
k_1' K_{ads,1} = k_1 e^{-\frac{\Delta S_{OH'}}{R} - \frac{\Delta E_{OH'}}{R} \left(\frac{1}{T} - \frac{1}{T_{ref}}\right)}
\]
Parity diagrams

◊ APTES catalysts, □ MAPTMS catalysts and Δ CAPTMS catalysts
### Estimated values for the kinetic descriptors with their 95% confidence intervals

<table>
<thead>
<tr>
<th>Pre-exponential factor</th>
<th>Activation energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_1$</td>
<td>$5.04 \times 10^{-5} \pm 0.23 \times 10^{-5}$ l/(mol.s)</td>
</tr>
<tr>
<td>$k_2$</td>
<td>$5.81 \times 10^{-2} \pm 0.14 \times 10^{-2}$ l/(mol.s)</td>
</tr>
<tr>
<td>$k_3$</td>
<td>$20.4 \pm 9.6$ l/(mol.s)</td>
</tr>
<tr>
<td>$k_4$</td>
<td>$2.02 \times 10^{-2} \pm 0.37 \times 10^{-2}$ l/(mol.s)</td>
</tr>
<tr>
<td>$k_{-4}$</td>
<td>$4.60 \pm 1.12$ l²/(mol².s)</td>
</tr>
</tbody>
</table>

$^a$ Value determined using the Jobac method. $^b$ Non-significantly estimated parameter.

### Estimated values for the catalyst descriptors with their 95% confidence intervals

<table>
<thead>
<tr>
<th>Entropic difference</th>
<th>Reaction enthalpy / Activation energy difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Promotional effect of silanols</td>
</tr>
<tr>
<td>$\Delta S_{OH^i}$</td>
<td>$-8.25 \pm 0.16$ J/(mol.K)</td>
</tr>
<tr>
<td>$\Delta E_{OH^i}$</td>
<td>$8.7 \pm 1.8$ kJ/mol</td>
</tr>
<tr>
<td></td>
<td>Nature of the amine sites</td>
</tr>
<tr>
<td>$\Delta S_{im}$</td>
<td>$13.5$ J/(mol.K) $^a$</td>
</tr>
<tr>
<td>$\Delta S_{MAPTMS}$</td>
<td>$-46.4 \pm 2.6$ J/(mol.K)</td>
</tr>
<tr>
<td>$\Delta S_{CAPTMS}$</td>
<td>$-23.7 \pm 5.0$ J/(mol.K)</td>
</tr>
<tr>
<td>$\Delta H_{im}$</td>
<td>$43.8$ kJ/mol $^a$</td>
</tr>
<tr>
<td>$\Delta E_{MAPTMS}$</td>
<td>$10.4 \pm 1.0$ kJ/mol</td>
</tr>
<tr>
<td>$\Delta E_{CAPTMS}$</td>
<td>$17.6 \pm 3.2$ kJ/mol</td>
</tr>
</tbody>
</table>

$^a$ Value determined using the Jobac method.
Base strength & Steric hindrance

![Graphs showing relationship between base strength and steric hindrance](image-url)
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Conclusions
Conclusions

- **Acid-base synergetic effects** were successfully incorporated in heterogeneous catalysts using the silanol groups of the support as promoting sites.

- The **turnover frequency** increases with increasing silanol-to-amine ratio until an upper limit is reached at a silanol-to-amine ratio of 1.7.

- Distinct **differences in turnover frequency** (TOF) were obtained using different amines:
  - Primary amines exhibit a reasonable TOF.
  - The TOF of secondary amines depends on the substituent.
  - Tertiary amines exhibit an extremely low TOF.

- **Basicity effects** are quantified via differences in activation entropies and energies.

- A cyclohexyl substituted on the amine results in an increase in activation energy of about 17 kJ/mol due to steric hindrance.

- A **secondary amine with a small substituent avoiding steric hindrance** seems to be the optimal amine type to catalyze the aldol condensation.
Thank you for your kind attention!