Wednesday, June 6th, 2007

**Helvetica Chimica Acta:**
- Founded in 1918 by the Swiss Chemical Society as their premiere journal,
- Current publisher is the Verlag Helvetica Chimica Acta,
- Editing and print by Wiley, Weinheim,
- In its 90th year of publishing, it is one of the last national chemical journals.

**Current form:**
- Multidisciplinary journal (2004 spin-off -> Chemistry & Biodiversity),
- Publishes communications, full papers and reviews,
- Over 300 papers/year,
- 12 issues/year @ ~300 pages/issue.

**Statistics:**
- Over 20,500 papers published,
  - ~20,000 original research papers,
  - ~120 reviews,
- Approx 2/3 of the articles published in English,
- Impact:
  - Until the mid 1990’s between 2.0 - 2.5,
  - Since then declining,
- Importance:
  - From its inception to the 1990’s always among the leading national journals,
  - Always competing against Angewandte, Chem. Berichte, L. Annalen,
  - Authors come mainly from Switzerland followed by Germany and Austria.

Important papers selected according to the following criteria:
1. All papers ranked by # of citations,
2. Top 100 sorted according to main topic,
3. Organic chemistry papers screened for appearance in secondary literature.

It becomes evident, that the work of several select chemists has majorly contributed to HCA.
Systematic investigation of the chemistry of cumulenes, H. Staudinger et al., HCA 1919, 2, 554; ib. 4, 87; ib. 4, 103.

Nitrones could be synthesized in several ways; mostly by action of diazo compounds.

The preparation of the nitrones ultimately failed. Usually the products decomposed, or aziridines were obtained (realized by T.W. Taylor in the late 1920s).

Speculates on the possible stability of the triazine and on reactions with acetylenes. Does not follow up.

--> 1,3 dipolar character recognized but not employed.
Systematic investigation of the chemistry of pentavalent phosphorus. H. Staudinger et al., HCA, 2, 612; loc. cit. 619; loc: cit. 635; ib. 4, 861.

A. Eschenmoser et al., HCA 1967, 50, 708; Eine neuartige Fragmentierung cyclischer, α,β-ungesättigter Carboxylsysteme.

A. Eschenmoser et al., HCA 1972, 55, 1276; α,β-Epoxyketon -> Alkinon-Fragmentierung.

Studies to synthesize Exalton and Muscon required the development of new fragmentation pathways of unsaturated ketones (O-C-C-X fragmentation).

Using aminoaziridines instead of tosylhydrazine the scope of the reaction could be expanded, reaction time was lowered from days to hours.
A. Eschenmoser et al., *HCA* 1971, 54, 710; Sulfidkontraktion via alkyllative Kupplung.

Results from the efforts toward Vitamin B-12. A general approach to the synthesis of β-dicarbonyl type compounds.

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A. Eschenmoser et al., *HCA* 1971, 47, 2425; Claisen'sche Umlagerungen bei Allyl- und Benzylalkoholen mit Acetalen des N,N-Dimethylacetamids.

*Claisen*-type rearrangement with orthoamides.
Are endocyclic nucleophilic substitutions possible intramolecularly in 6-membered rings?

postulated intermediate: however:

\[
\begin{align*}
\text{O}_2 & \quad \text{SO}_3^- \\
\text{CH} & \quad \text{SO}_2 \\
\text{CH} & \quad \text{SO}_2
\end{align*}
\]

\[
\begin{align*}
\text{O}_2 & \quad \text{SO}_3^- \\
\text{CH}_3 & \quad \text{SO}_2 \\
\text{CH}_3 & \quad \text{SO}_2
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\end{align*}
\]

A. Eschenmoser et al., HCA 1970, 53, 2059; Endocyclische S-N-Reaktionen am gesättigten Kohlenstoffatom.

A. Eschenmoser et al., HCA 1955, 38, 1529; Über die relative Geschwindigkeit der Chlorsäureoxydation sekundärer, alicyclischer Alkohole.

A. Eschenmoser et al., HCA 1962, 45, 2254; Chlorsäureester als Zwischenprodukte bei der Oxydation von Alkoholen. Geschwindigkeitslimitierende Veresterung eines sterisch gehinderten Alkohols.

While the acylation of equatorial HO-groups proceeds faster than that of the corresponding epimers, the oxidation by Cr(VII) shows the opposing relationship. Mechanistic insights by skillful choice of substrates.

Reaction supposedly occurs via formation of chromic acid esters:

\[
\begin{align*}
\text{A} & \quad R_4\text{CHOH} + \text{HCrO}_4^- + \text{H}^+ \quad \rightarrow \quad R_4\text{CHOCrO}_3\text{H} + \text{H}_2\text{O} \\
\text{B} & \quad R_4\text{C}=\text{O} - \text{CrO}_4^- + \text{H}_2\text{O} \quad \rightarrow \quad R_4\text{C}=\text{O} + [\text{HCrO}_4^-] \\
\end{align*}
\]

Usually A equilibrates rapidly, B is rate determining \( \rightarrow k_{\text{obs}} \sim k_2 \). 

\( k_{\text{obs}} \) shows strong isotope effect. 

\( k_{\text{obs}} = \text{const} \frac{d[Cr\text{VI}]}{dt} \rightarrow k_{\text{rel}} = k_{\text{obs}} / k_{\text{ref}} \)

<table>
<thead>
<tr>
<th>( \beta )</th>
<th>( x )</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) 1-Oxy-cholestan ( ^2 )</td>
<td>k* ( \sim 9,7 )</td>
</tr>
<tr>
<td>b) 2-Oxy-cholestan</td>
<td>20</td>
</tr>
<tr>
<td>c) 3-Oxy-cholestan</td>
<td>( 1,0^* )</td>
</tr>
<tr>
<td>d) 4-Oxy-cholestan</td>
<td>35</td>
</tr>
<tr>
<td>e) 6-Oxy-cholestan</td>
<td>36</td>
</tr>
<tr>
<td>f) 7-Oxy-cholestan</td>
<td>3,3</td>
</tr>
<tr>
<td>g) 11-Oxy-allopregn-an-dion-(3,20)</td>
<td>&gt; 60</td>
</tr>
</tbody>
</table>

Used in control experiments to confirm rapid equilibration for cholestan.

Release of ringstrain, esp. 1,3-diaxial-interactions, on going from sp\(^2\) \( \rightarrow \) sp\(^3\) determines the reaction rate.
A. Eschenmoser et al., *HCA* 1955, 38, 1890; Eine Stereochemische Interpretation der biogenetischen Isopenregel bei den Triterpenen.

From a set of only four "arbitrary" assumptions not only the correct connectivities, but the relative stereochemistry of natural triterpenes were rationalized:

1) all -C=O-bonds in the squalen precursor shall be trans-configured,
2) the cyclization shall occur from a defined form of the squalen-chain,
3) the cyclization follows primarily antiparallel cationic additions;
   with shifts and elimination as secondary reaction principles,
4) the cyclization occurs as a cascade reaction.
D. Seebach *et al.*, *HCA* **1982**, 65, 365; Substitution of HMPT by the Cyclic Urea DMPU as a Cosolvent for Highly Reactive Nucleophiles and Bases.

Li-salts tend to aggregate heavily. This aggregation persists in aprotic solvents and thus often cosolvents are employed.

![Image of a chemical structure](image)

D. Seebach *et al.*, *HCA* **1988**, 71, 237; Note on the Preparation of 1,2-Diketones from Acetylenes.

The conversion of acetylenes into 1,2-diketones by the action of Ru(VIII) offers a mild variant of oxidizing carbons at late stages of synthesis (cf. the synthesis of ABCDEF-Ring System of Yessotoxin and Adriatoxin by Mori, *JOC* **2003**, 86, 9050).

![Image of chemical reactions](image)

HMPT was usually used as cosolvent, however, it is cancerogenic and substitutes were investigated. The cyclic dimethylpropyleneurea (DMPU) proves to be a suitable replacement.

- soluble even at low temperatures,
- does not get attacked by organolithium species (at low temp.),
- can be removed by extraction into water,
- breaks up the Li-aggregates well.

This happen, when you let a Swiss design a modell kit:

Requirements:
- accuracy in atom distances and bond angles, at the level of experimental exactitude,
- free rotation around bonds,
- easy view of geometric conformers,
- nuclei represented as points (to allow direct measurements by a ruler),
- no tools required for assembly,
- stability of the model,
- size should remain easy to handle,
- simple construction.

--> stick model fabricated from stainless steel.

desired precision: + 0.01 ang at a scale of 1 : 0.4 x 10^-8
--> + 0.02 cm tolerance in model


The first report on the chelating properties of Na₂EDTA, which has become the foundation for a number of qualitative analytical determinations.

\[
\begin{align*}
\text{HOOC} & - \text{CH}_2 & \text{CH} & - \text{COO}^- \\
\text{HN} & - \text{CH}_2 & - \text{NH} & - \text{COOH} \\
\text{HOOC} & - \text{CH}_2 & \text{NH} & - \text{COOH} \\
\end{align*}
\]

1) no metal ions present
2) xc Na⁺ present
3) xc Li⁺ present
4) xc Ba²⁺ present
5) xc Mg²⁺ present
6) eq Ca²⁺ present
7) xc Ca²⁺ present

\[
\begin{align*}
\text{K_k} & : \text{Gleichgewichtskonst. von: Me}^{+} + \text{HY}^- & \text{=} & \text{(MeHY)}^+ \\
\text{K_k1} & : \text{Gleichgewichtskonst. von: Me}^{+} + \text{Y}^{2-} & \text{=} & \text{(MeY)}^{2+} \\
\end{align*}
\]

\[
\begin{align*}
\text{Li}^+ & : \text{lg K_k}^2 = 2.79 \\
\text{Na}^+ & : \text{lg K_k}^2 = 1.66 \\
\text{Mg}^{2+} & : \text{lg K_k}^2 = 2.28 \quad \text{lg K_k}^3 = 8.69 \\
\text{Ca}^{2+} & : \text{lg K_k}^2 = 3.51 \quad \text{lg K_k}^3 = 10.59 \\
\text{Sr}^{2+} & : \text{lg K_k}^2 = 2.30 \quad \text{lg K_k}^3 = 8.63 \\
\text{Ba}^{2+} & : \text{lg K_k}^2 = 2.07 \quad \text{lg K_k}^3 = 7.76 \\
\end{align*}
\]