The issue (December 2015, Volume 98, Issue 11-12) of Helvetica Chimica Acta is dedicated to Albert Eschenmoser and his art of Organic Synthesis.

"Corrin Syntheses – Part I – VI" had been originally planned to be submitted to Helvetica Chimica Acta around 1975, as 'full paper' in the conventional sense with the intention of covering in full detail the work carried out at the ETH from early 1960 up to the time of the writing.

The series was not intended to include the work on the synthesis of vitamin B_{12} itself: "The work done at the ETH on the synthesis of vitamin B_{12} is not to be a part of this series, since it will be subject of a joint publication of the Harvard and the ETH groups, covering the B_{12} work done at Harvard as well as at the ETH."

Influence and assistance of corrin model studies on the B_{12} syntheses:
- information on preparative procedures and the scope of the C,C-coupling by imido ester/enamine condensation
- spectroscopic and chemical properties of hemicorrinoids and corrinoids
- complexation and decomplexation procedures
- introduction of Me groups in meso-positions
- the 'targeted discovery' of the photochemical A/D-seccorrin-corrin cycloisomerization
The earliest exploratory experiments aimed at the synthesis of the B/C component

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Route A

\[ \text{OH} \rightarrow \text{CO}_2H, 170 ^\circ \text{C} \rightarrow \text{NH}_3, 130 ^\circ \text{C} \rightarrow \text{AgNO}_3 \rightarrow \text{EtO}_2 \text{N} \rightarrow \text{CO}_2 \text{Me} \rightarrow \text{NH}_3, \text{MeOH} \rightarrow 290 ^\circ \text{C} (30\%) \text{ or hv (254 nm)} \rightarrow \text{Cyclohexane (40-50\%)} \]  
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Route B

\[ \text{1. AgNO}_3 \rightarrow \text{2. i-PrI} \rightarrow \text{NC} \rightarrow \text{CO}_2(t-\text{Bu}) \rightarrow \text{HN} \rightarrow \text{CN} \rightarrow 170 ^\circ \text{C} \]  
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Route C

\[ \text{KCN} \rightarrow \text{NC} \rightarrow \text{P}_4\text{S}_10 \rightarrow \text{NC} \rightarrow \text{NH}_3 \rightarrow (\text{PhCOO})_2 \]  
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"Responsible for these failures are not the (highly reactive) imido-ester components, but rather the nucleophilic partners which are not enamines but enamides or vinylogous enamides."

The most remarkable property of monocyclic ene-lactam

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\[ \text{O} \rightarrow \text{HN} \rightarrow \text{TsOH/DCM 40 ^\circ \text{C}} \rightarrow \text{A} \rightarrow \text{NH} \rightarrow \text{B} \rightarrow \text{C} \rightarrow \text{D} \rightarrow \text{Et-N+HCl, 185 ^\circ \text{C} (>90\%)} \rightarrow \text{quasi-A/D component} \]  
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Synthesis of Corrin Complexes via A-B Ring Closure. Preparation of A/D Components

Original plan for the synthesis of the A/D component

Route A (rather long, though instructive)

Route A (cont.) Expectations vs. observations on the way to aziridine

Route A (cont.) A safe method for converting imido-ester groups into the corresponding amide groups

Route A (cont.) A general method for the determination of the relative configuration of substituted aziridines

Route A (cont.) mixture immediate Pd/H₂

Quasi-A/D Components: all four peripheral rings would be derived from one single precursor.

"Dream corrin synthesis": all four peripheral rings would be derived from one single precursor.

Route B (short, though inefficient)

Route C (the efficient route to the A/D component)
Ni\textsuperscript{II} complexes of corrin in the pentamethyl series

\begin{align*}
\text{Ni}^{II} \text{complexes of corrin in the pentamethyl series} \\
\text{Ni}^{II} \text{complexes of corrin in the pentamethyl series}
\end{align*}

Co\textsuperscript{II} complexes of corrin in the pentamethyl series

Coupling of hemicorrinoid A/D and B/C components to corrin by thioimido-ester enamine condensations

Coupling of quasi-A/D and B/C components

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Baran Group Meeting 04/16/2016
Coupling of quasi-A/D and B/C components (cont.)

\[
\text{hv} \quad 145^\circ C
\]

Preparation of Metal-Free Corrin Derivatives via A-B Ring Closure

1. \((\text{PhCOO})_2\) TFA DCM, r.t
2. MeOH

Methods for the introduction of Me groups in the meso-positions of the corrin chromophore

\[
\begin{align*}
\text{Ph-S-CH}_2\text{Cl} & \quad \text{AgBF}_4 \quad \text{DIPEA} \quad \text{MeCN} \\
\text{(CH}_3)_2\text{N}^+=\text{CH}_3^- & \quad \text{Raney-Ni} \quad \text{PdH}_2 \\
\text{CH}_2\text{SPh} & \\
\text{Co}^{\text{III}} & \\
\text{Ni}^{\text{II}} & \\
\text{Pd}^{\text{II}} & \\
\text{Cu}^{\text{II}} & \\
\text{Be}^{\text{II}} & \\
\text{Cd}^{\text{II}} & \\
\text{Zn}^{\text{II}} & \\
\text{Li}^{\text{II}} &
\end{align*}
\]

\[
\text{Li}^{\text{II}}, \text{Zn}^{\text{II}}, \text{Cd}^{\text{II}}, \text{Be}^{\text{II}}, \text{Co}^{\text{III}}, \text{Rh}^{\text{III}}, \text{Cu}^{\text{II}}, \text{Ni}^{\text{II}}, \text{Pd}^{\text{II}}
\]

\[
\begin{align*}
\text{t-BuOD, D}_2\text{O, N}_2 & \\
\text{5,10 mono- or dideuteration} \quad \frac{\text{HC}5}{\text{HC}10} = 0.6 \quad \frac{k(\text{H} \rightarrow \text{D})\text{C}5}{k(\text{H} \rightarrow \text{D})\text{C}10} = 2.1
\end{align*}
\]

Strategy of a corrin synthesis via the photochemical A-D ring closure

Synthesis of metal complexes of A/D-secocorrinate (cont.)

Improvement by alkylation coupling

Synthesis of by the A/D-secocorrinate BC+D+A strategy

The first experiments testing the existence of the A/D-secocorrin-corrin cycloisomerization

Corphin

Dependence of cycloisomerization from the nature of the coordinating metal ion