Robert V. Stevens

**Biographical Information:**
- Born on March 24, 1941 in Mason City, Iowa
- Received B.S. degree in 1963 in Iowa State University
- Ph. D at Indiana University with Professor Ernest Winkert (1963-1966)
- Appointed to the faculty of Rice University (1966-1977)
- Professor of Chemistry in UCLA (1977-1984)
- Deceased on March 9, 1984

"Professor Stevens was a special kind of teacher. He would shuffle into an undergraduate class, clear his throat, and say, "Unhuh." The metamorphosis came when he picked up the chalk. No one who saw Professor Stevens work with chalk and the elegant structures he drew will forget the simple beauty of his lectures. He was a transformed man with chalk in his hands. His dry wit and diffident charm came through with clarity, and his sense of style and art pervaded the room"

- Professor Orville L. Chapman of UCLA

**Summary of research interests throughout Professor Stevens’s career:**
- Total synthesis of natural products
  - alkaloids
  - steroids
  - vitamins
- Development of chemical methods in synthesis
  - rearrangement of cyclopropylimines
  - stereocontrolled nucleophilic attack on immonium ions
  - nitroene additions

**Studies on total Syntheses of Alkaloids**

**Alkaloids synthesis by rearrangement of cyclopropylimines**

$$
\begin{array}{c}
\text{CN} \\
\text{HCl, cat.} \\
\text{H}^+, \text{100}^\circ \text{C} \\
\text{100-160}^\circ \text{C} \\
\text{HCl, cat.} \\
\text{TL, 1967, 5158} \\
\text{TL, 1968} \\
\end{array}
$$

**Synthesis of pyrrolizidine and indolizidine nucleus**

$$
\begin{array}{c}
\text{O} \\
\text{1. NH4Cl, reflux, xylene, 88\%} \\
\text{2. HCl, MeOH, 90\%} \\
\text{PhS} \\
\text{OMe} \\
\text{indolizidine} \\
\text{δ-coniceine} \\
\end{array}
$$

$$
\begin{array}{c}
\text{EtO} \\
\text{1. NH4Cl} \\
\text{2. HCl, MeOH} \\
\text{PhS} \\
\text{CHO} \\
\text{(-)-isoretrocanol} \\
\text{pyrrolizidine} \\
\end{array}
$$
Applications to complex nature product

Sceletium A-4

JOC, 1975, 3495

dl-Mesembrine

JACS, 90, 1968, 5580

Sceletium A-4

JOC, 1975, 3495

A formal synthesis of (±)-Aspidospermine

CC, 1971, 857

(±)-Aspidospermine

Acid catalysed rearrangement of cyclobutylimines

synthesis of tetrahydropyridines

JCS, CC, 1975, 682

30%-66%
Total synthesis of precocinelline and coccinelline with Robinson-Schopf reaction as the key step

Expeditious stereospecific total syntheses of (+)-Makomakine, (+)-Aristoteline and (+)-Hobartine

Stereorational total synthesis of (±)-porantherine

Use of nitriles as terminations of carbocation-olefin cyclization
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Synthesis of pyrrolobenzodiazepine nucleus of anthramycin

\[ \text{MeO}_2\text{C} - \text{NC} \xrightarrow{\text{CuO}} \text{MeO}_2\text{C} - \text{NH} - \text{C} = \text{O}_2\text{Me} \]

JCS, CC, 1975, 742

Expeditious total synthesis of Karachine

\[ \text{Cl}^- \text{N}^+ \text{O} \text{Me} \text{O} \text{Me} \xrightarrow{\text{DMSO, 100°C}} \text{OTMS Me} \]

Karachine

JCS, CC, 1983, 1425

Studies on benzocyclobutenones and total synthesis of (±)-taxodione

Total syntheses of vasicoline and vasicolinone

\[ \text{N} \text{O} \text{C} \xrightarrow{1. \text{AcNO}_2} \text{N} \text{O} \text{C} \xrightarrow{2. \text{H}_2/\text{PtO}_2} \text{N} \text{O} \text{C} \xrightarrow{3. \text{POCl}_3} \text{N} \text{O} \text{C} \]

Vasicoline

JOC, 1988, 1873

(±)-taxodione

JOC, 1982, 2393

JOC, 1982, 2396
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Studies on Spiro-Activated Cyclopropanes

1. synthesis of cyclopropane

2. Homoconjugated addition of Grignard

Studies on Quassinoids

(a)-Brefeldin A

JCS, CC, 1978, 754
JACS, 1978, 6479
JOC, 1980, 2780

Bruceantin

JOC, 1985, 4056
JOC, 1986, 4347
Total synthesis of steroids and vitamin D₃ using camphor as chiral intermediate

1. NaCH(CO₂CH₃)₂
2. NH₂OH

1. SO₂
2. NaBH₄
3. NBS

Studies on Sodium Hypochlorite "swimming pool chlorine"

1. Selective oxidation of secondary alcohol in the presence of primary alcohol

<table>
<thead>
<tr>
<th>ENTRY</th>
<th>DIOL</th>
<th>PRODUCT</th>
<th>% YIELD</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>2</td>
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</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>90</td>
</tr>
</tbody>
</table>

* All yields represent isolated pure products
* Isolated as the benzoate ester

2. Conversion of aldehyde to ester

<table>
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<tr>
<th>Reaction</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO NaOCl, TFA</td>
<td>CO₂Me</td>
</tr>
<tr>
<td>MeOH</td>
<td>MeOH</td>
</tr>
<tr>
<td>NaOCl, TFA</td>
<td></td>
</tr>
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</table>

JACS, 1977, 6105
JACS, 1983, 7713
T, 1985, 93

JOC, 1980, 2030, TL, 1982, 4647
Is oxazole synthesis and nucleophilic substitutions of 5-chloroisoxazoles

General Method for the nitrile oxide

Table II. Nucleophilic Substitution of 5-Chloroisoxazoles

---

a All isoxazoles were fully characterized spectroscopically.

b Yields represent chromatographically pure products. The isoxazoles were generated from the aldehyde and sodium metal, thiphenol and piperidine were deprotonated with n-BuLi at 0°C.
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Studies on Vitamine B₁₂ and Corrins

Vitamin B₁₂

Cobyril Acid

Synthetic Strategy

A → B → C → D

Total synthesis of Ni Octamethylcorphin

1. NBS, Et₃N, A
2. HCl
3. NH₂OH·HCl

89% 96%
90%
85%
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Studies towards vitamin B₁₂

Vitamin B₁₂ ↔ Cobyric acid

JACS, 1971, 6629
JACS, 1971, 6637
JACS, 1975, 5940

JACS, 1976, 6313
JACS, 1976, 6317
JACS, 1983, 7719
JACS, 1986, 1039