Electroreductive Synthesis of Cyclopropanes from 1,3-Dicarbonyl Compounds

1. LAH
2. MsCl, Et3N

- Methods at the time used less easily accessible 1,3 dihalides
- Slow addition of the substrate (till 3F/mol passed) to increase yield as substrate unstable in reaction condition
- Excellent yields observed (70-98%)

Cyclopropanation using Wittig reagent [one-step process]

- Isatin
  - (from Soxhlet)
  - Irregular reaction set up with Soxhlet apparatus to increase the yield

Organocopper Reagent Synthesis using Ultrasound chemistry [one-pot]

- Better yields than reported in the literature
- Cavitation effects responsible for reactivity
- Less polar solvent and low temp. to suppress polar byproducts

Fun Fact!
- Carried out in a modified ultrasound lab cleaner
Reductive Cyclization of 2-([2-Propynyl]oxy)ethyl Bromides by Cobaloxime (I) to Synthesize α-Methylene-γ-butyrolactones

\[
\begin{align*}
R_1 & \quad \text{NBS} \quad \text{OH} \quad \text{NaBH}_4 \quad \text{DCM} \\
& \quad \text{Br} \quad \text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \\
& \quad \text{cis stereochem observed in case of fused rings} \\
& \quad \text{benzylid proton decreases yield} \\
& \quad \text{oxidants that gave “complex mixtures”} \\
& \quad \text{SeO}_2/\text{EtOH} \quad \text{CrO}_3/\text{CH}_3\text{CO}_2\text{H} \quad \text{(ofBu)}_2\text{CrO}_2/\text{(CH}_3\text{CO)}_2\text{O} \\
& \quad \text{NaBH}_4 \\
& \quad \text{J. Org. Chem. 1982, 47, 1775-1777} \\
\end{align*}
\]

Photoisomerization of 2-Alkylindene to 2-Alkyldieneindanes

\[
\begin{align*}
& \quad \text{hv (254 nm)} \quad \text{CH}_3\text{CN/HCl} \quad \text{hexane} \\
& \quad \text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \\
& \quad [1,3] \text{ sigmatropic shift} \\
& \quad \text{inversion of stereochemistry} \\
& \quad \text{HCl} \quad \text{R}_1 = \text{H} \\
& \quad \text{J. Org. Chem. 1982, 47, 1051-1058} \\
& \quad \text{J. Org. Chem. 1982, 47, 1058-1063} \\
\end{align*}
\]

Reductive Cyclization of Mercurial Enones: An Early Report of a Giese Reaction

\[
\begin{align*}
& \quad \text{Hg(OAc)}_2 \quad \text{ROH} \quad \text{NaBH}_4 \\
& \quad \text{C-Hg bond not nucleophilic enough} \\
& \quad \text{Giese reaction} \\
& \quad \text{5 and 6 membered rings formed} \\
& \quad \text{J. Org. Chem. 1982, 47, 2231-2232} \\
\end{align*}
\]

Caution! reacts with strong E+ and e– acceptors

✔ approaches at the time required harsh conditions (eg. strong bases)

✔ present in a wide variety of sesquiterpenes

✔ important for biological activities
Electrooxidative Cleavage of Carbon-Carbon Linkages

\[
\text{R}_2 \text{O} \xrightarrow{\text{meOH-LiClO}_4-\text{Pt}} \text{R}_2 \text{CO}_2\text{Me}
\]

OR

\[
\begin{align*}
\text{R}_1 \text{O} & \rightarrow \text{R}_1 \text{OAc} \\
\text{MeOH-LiClO}_4-\text{Pt} & \text{MeOH-LiClO}_4-\text{Pt} \\
\text{R}_1 \text{O} & \rightarrow \text{R}_1 \text{OAc}
\end{align*}
\]

A

\[
\text{X} = \text{Ac, H, Me}
\]

Baran Group Meeting
02/22/24

Approach to Reversible Steroid-Diterpenoid Interconversion via [1,3] acyl shift

\[
\begin{align*}
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt} \\
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt}
\end{align*}
\]

Testosterone

\[
\begin{align*}
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt} \\
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt}
\end{align*}
\]

J. Org. Chem. 1982, 47, 47-52

Accessing Novel Steroid Skeletons using [1,3] acyl shift

\[
\begin{align*}
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt} \\
\text{MeOH-LiClO}_4-\text{Pt} & \rightarrow \text{MeOH-LiClO}_4-\text{Pt}
\end{align*}
\]

J. Org. Chem. 1982, 47, 4261-4264
**JOC Year in Review: 1982**

**Maithili S. Pokle**

**Baran Group Meeting**

**02/22/24**

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**An Approach to the Quadrone Skeleton via a Tamdem Aldol-Pinacol**

1. **LHMDS**
   - HMPA
   - **Cl**
   - **I**
   - $-78^\circ C$

2. **Hg(OAc)$_2$**
   - **HCOOH**
   - **10%aq. HCl**

**intramolecular silyl migration**

**syn stereochemical relationship important between enone and methyl ketone**

**Quadrone Skeleton**

- **40% overall yield**

**J. Org. Chem. 1982, 47, 2679-2681**

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**Electron-Transfer-Initiated Iminium Salt Photospirocyclization Methodologies**

- **N-prenyl side chain incorporated into the system to guarantee efficient electron transfer**

- **$E_{1/2}(-) = -1.5 \text{ eV} \text{ (iminium salt)}$**
  - **$E_{1/2}(+) \text{ of olefin has to be below +2.0 eV}$**

- **$h\nu (>240 \text{ nm})$**
  - **MeOH**

- **low yield reasons**
  1. heterolytic cleavage in competition with Nu attack
  2. formation of the 2 consecutive quaternary carbons

- **drawbacks!**
  1. need alkyl substitution to control oxidation potential
  2. diradical formation regiochemistry

- **easy to make**
  - **useful method for the construction of pyrrolidine-ring containing heterocycle and aza-spiro ring system**

- **from R1**
  - **either $R_1 = \text{SiR}_3 \text{ OR}$**
  - **$R_2 = \text{CH}_2\text{SiR}_3$**

- **rapid Nu$^-$ induced deallylation of the diradical**

- **enhance electron transfer efficiency**

- **(84-95%)**

**Harrington alkaloids**

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**J. Org. Chem. 1982, 47, 3360-3362**

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Semisynthesis towards Vinca Alkaloids from Catharanthine using Polonovski-“Potier” reaction

1. mCPBA
2. TFAA; R
3. NaBH₄
4. H₂/Pd-C
5. AgBF₄

J. Org. Chem. 1982, 47, 4261-4264

Pierre Potier
(1934-2006)
A pharmacist turned natural-product chemist!! known for developing a lot of anti-cancer drugs in the market today like docetaxel (Taxotere), Vinorelbine (Navelbine), and Paclitaxel (Taxol) (the first large-scale synthesis)

Fun fact
2g of Vincristine from 1000 kg of Cantharathine 0.0002% yield. Very much in need of a synthetic route

J. Nat. Prod. 1980, 43, 72

Portier Approach

- 70°C frozen conformation at -70°C

kinetic attack

thermodynamic conformation

R = vindoline

abundantly available!!

abundantly available!!

Catharanthine major alkaloidal constituent of Catharanthus roseus

R' = 10-vindolyl
Serendipitous discovery of Navelbine (noranhydrovinblastine)

J. Nat. Prod. 1980, 43, 72

}\n
Synthesis of Novel Phosphorus Heterocycles: 1,3-Dihydro-2,1-Benzoxaphosphole 1-Oxides

J. Org. Chem. 1982, 47, 1677-1682

\n
Synthesis of Strained Heterobicycles from Alkynes and Heterocumulenes


Carbodiimide

Dewar Pyridones

N-Sulfinylaniline

very temperature dependent

\n
Synthesis of Navelbine (noranhydrovinblastine)

X = OCOCF₃

noranhydrovinblastine

unexpected extrusion of one carbon atom

orally active less neurotoxic than natural vinca alkaloids

JOC Year in Review: 1982

Baran Group Meeting 02/22/24

Me

Me

R

AlCl₃

or

Al₂Br₆

DCM

Me

Me

Me

AlCl₃

Me

Me

Me

AlCl₃

OR

Me

Me

Me

Al₃Br₆

H

B

MeN

C

S

Me

Me

Me

Me

AlCl₃

3

Me

Me

Me

Me

H

S

AlCl₃

Me

Me

Me

Me

N

S

Me

Me

Me

Me

NH

S

O

–80°C

A

Me

Me

Me

Me

NH

S

O

–60°C

A

Me

Me

Me

Me

N

S

O
JOC Year in Review: 1982

**Nobel Prizes in 1982**

**Chemistry** - Aaron Klug for “his development of crystallographic electron microscopy and his structural elucidation of biologically important nucleic acid-protein complexes.”


**J. Org. Chem. Statistics**

- **1,359 articles**
- **Top Publishing Authors:**
  1. H.C. Brown (21)
  2. J.F. Blount (11)
  3. W. Herz (8)
  4. Leo A. Paquette (8)
  5. H. Kwart (7)

**Most Cited Papers**


**Things around the world**

- **Blockbuster movies**
- **Star-studded births**
- **Legendary rivalries**
- **Great music**

**1982: A year of ....**

- **Blockbuster movies**
  - [Blade Runner](#)
  - [Star Trek II: The Wrath of Khan](#)
  - [Grease](#)

- **Star-studded births**
  - [Keke Rosberg](#), the first Finnish driver to win the F1 driver’s championship with Williams

- **Great music**
  - [Diet Coke Hits the Shelves](#)

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    5. H. Kwart (7)

- **Most Cited Papers**

**Things around the world**

- **Sony launches the first consumer compact disc (CD) player**
- **Keke Rosberg, the first Finnish driver to win the F1 driver’s championship with Williams**
- **The first computer virus, the Elk Cloner, written by 15-year-old Rich Skrenta is found**
- **Time magazine’s person of the Year: The computer**
- **The birth of emoji**
- **Diet Coke Hits the Shelves**
- **The first episode of Late Night with David Letterman debuts on NBC**
- **Doctors were able to successfully implant an artificial heart in a human body**