JOC YEAR IN REVIEW
1972
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THE BARAN GROUP MEETING
08/20/2003
The difficult decision

Some statistics

- Number of articles 1225!
- Full articles 480
- More than 25 total synthesis
- Isolation and characterization of 52 molecules
- Several novel methods
Total synthesis

- Prostaglandins
- (-)-Seychellene
- Mirestrol
- Guaiol
- (-)-Patchouli alcohol
- Dehydrojoubertiamine
- Cubane derivatives
- Cinobufacin
- Jasmone
Total Synthesis of cis-Jasmone

- Isolated from flower oils of Jasminum
- Indispensable in the reproduction of jasmine fragrance
- Several preparations have been reported
  - First synthesis at 1952 by Harper
  - Two total synthesis in 1972.

Two Efficient Methods for the Construction of cis-Jasmone


O

\[
\text{Et}_3\text{N, }0^\circ\text{C}
\]

hexanes

\[
\text{Zn, Acetic acid}
\]

\[
\text{H}_2\text{O}_2
\]

Acetic acid

\[
\text{DIBAL, Toluene, -78^\circ\text{C}}
\]

\[
\text{Ph}_3\text{P}=\text{CHCH}_2\text{CH}_3
\]

DMSO


Jasmone

515^\circ\text{C}

glass wool
-EtOH, CO

NaH

Benzene

cyclopropyloxopropanoate
Highlights

Baeyer-Villiger Ring Expansion

A Thermal Two Carbon Ring-Expansion
Total Synthesis of Patchouli Alcohol

- A tricyclic sesquiterpene isolated from patchouli oil
- An important raw material for the composition of perfumes
- First total synthesis by Buchi at 1956

A Synthetic Route to Racemic Patchouli Alcohol


[Diagram of the synthetic route]

(-)-Patchouli alcohol
Highlights

Proton attacks from the less hindered side

Base elimination

Both E and Z regioisomers

Assisted cleavage

Selective dehydration

Stereochemistry of the reduction
Synthesis Of Cubane Derivatives

- Interesting molecular structure
- Original work by Eaton et al. at 1964 reporting several derivatives of cubane skeleton
- First synthesis of homocubane from 2-cyclopentanone in less than 10% yield
A Facile Synthesis of Homocubane

First synthesis of cubane derivatives
Highlights

Spontaneous cyclization of bromo-cyclopentanones

An intermolecular Diels-Alder Reaction

Favorable intermediate

Favorskii type rearrangement
Total Synthesis of Prostaglandins F\textsubscript{1a} and E\textsubscript{1}

Prostaglandins are discovered by von Euler in 1932.

Carbocyclic oxygenated C-20 molecules are hormones that elicit an unusually diverse array of physiological response.

Several preparations have been reported.
A New Method for the Preparation of Prostaglandins


1. THP, TsOH
2. DIBAL -78°C

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1. CH₂N₂, ether
2. Ac₂O, pyridine 50°C
3. H₂, Pd/C 1 atm 5% Acetic acid Ethanol


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Synthesis of Corey’s lactone

1. NaH, THF, BnOCH₂Cl, -55°C

2. Cu(BF₄)₂, 0°C

3. KOH, H₂O, DMSO

4. mCPBA, NaHCO₃, H₂O, 0°C

5. 1. Ac₂O, pyr. 2. n-Bu₃SnH, AIBN, PhH

6. NaOH, H₂O, CO₂
Novel Methods

- Thallium chemistry in organic synthesis
- Novel etherification of alcohols
- Palladium-Catalyzed Vinylic Hydrogen Substitution (Heck reaction)
Novel Etherification of Alcohols

Dialkyl phosphites react with alcohols to give the corresponding ether in the presence of catalytic amount of acid.
Paladium-catalyzed Vinylic Hydrogen Substitution

Background before the discovery of Heck Reaction

\[ \text{RMX} + \text{H} \rightarrow \text{M'}X \rightarrow \text{R} + \text{HM'} \]

M: Hg, Sn, etc

\[ \text{example: HgOAc} \rightarrow \text{Pd(OAc)}_2 \rightarrow \text{Transmetation} \]

\[ \begin{align*}
 &\text{[PdOAc][HgOAc]} + \text{Pd(OAc)}_2 \\
 &\rightarrow \text{[PdOAc][HgOAc]} + \text{Hg(OAc)}_2
\end{align*} \]

Easy to isolate

\[ \begin{align*}
 &\text{[PdOAc][HgOAc]} + \text{[PdOAc][HgOAc]} \\
 &\rightarrow \text{[PdOAc][HgOAc]} + \text{[PdOAc][HgOAc]}
\end{align*} \]

\[ \text{β-elimination} \]

\[ \text{HPdOAc} \]

\[ \text{HPdOAc} \]

\[ \text{HPdOAc} \]
Disadvantages

- There is often a problem obtaining the organomercury, lead, or tin compounds.
- Thick slurries of salts difficult to manipulate if the reaction is carried out catalytically in palladium.
A New Method for the Arylation and Benzylation of Vinylic Hydrogen


Mechanism of Heck Reaction

RX + Pd $\rightleftharpoons$ [RPdX]

[RPdX] + H\_\_\_\_{\_} \rightleftharpoons \overset{H}{\overset{R}{\overset{\_\_\_\_\_\_}{\_\_\_\_\_\_}}}PdX

- Use of a base is essential in order to neutralize the hydrogen halide from the reaction
- Tolerate a number of functional groups
- Iodides react rapidly. Benzyl halides are less reactive
- Loss of stereochemistry. Both cis and trans products
Thalium Chemistry in Organic Synthesis

Background

- Thalium acetate was first described at 1903 by Meyer and Goldschmidt
- Among its applications are oxidative cleavage of cyclopropanes, the conversion of chalcones into isoflavones and the hydration of acetylenes

Year 1972

- Direct synthesis of allenic esters from β-ketoesters
- Oxidation of cyclohexanones to adipoinos
A New Synthesis of Allenic Esters

R₁, R₂, R₃=alkyl

Mechanism
Oxidation of Cyclohexane to Adipoins
