

Journal of Organic Chemistry: 1974

A Brief Synopsis

-Mike DeMartino

-Group Meeting: 10-29-2003

Overview

- Some general observations
- The “prime-time-players”...what were they doing in JOC? (Thanks Dick Vitale, baby!)
- Some selected total syntheses

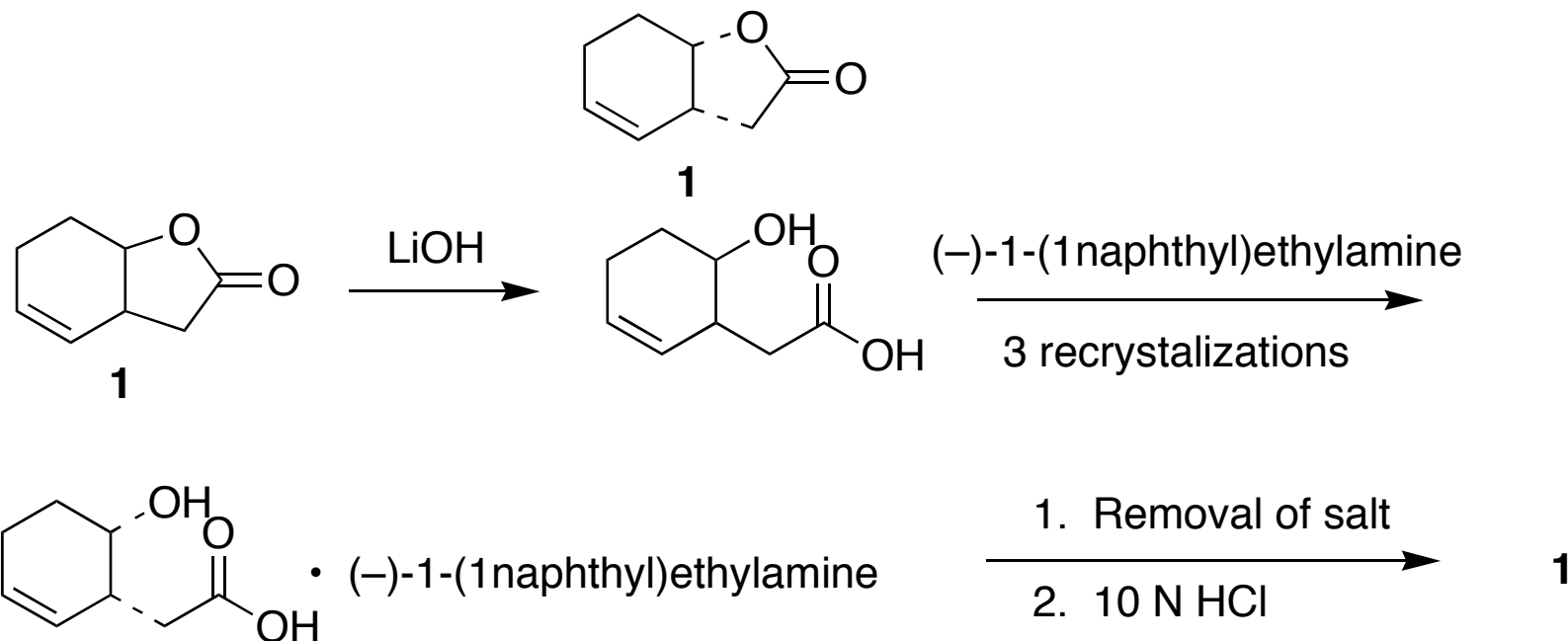
General Observations from Title Perusing

- Heterocyclic chemistry prevalent
- Surprisingly little Tin/Palladium chemistry
- Lots of Rearrangements:
 - Thermal
 - Photolytic
 - Acid Catalyzed
- ^{13}C spectroscopy a new thing in organic chemistry?!?
- Not many total syntheses, mostly steroids
- Sulfur chemistry very prevalent
- A lot of degradation chemistry

E.J. Corey (Harvard)

-Preparation of an optically active intermediate for the prostaglandins (p. 356)

-A racemic route had previously been developed from (+/-) **1** to (+/-)-11-deoxyprostaglandins

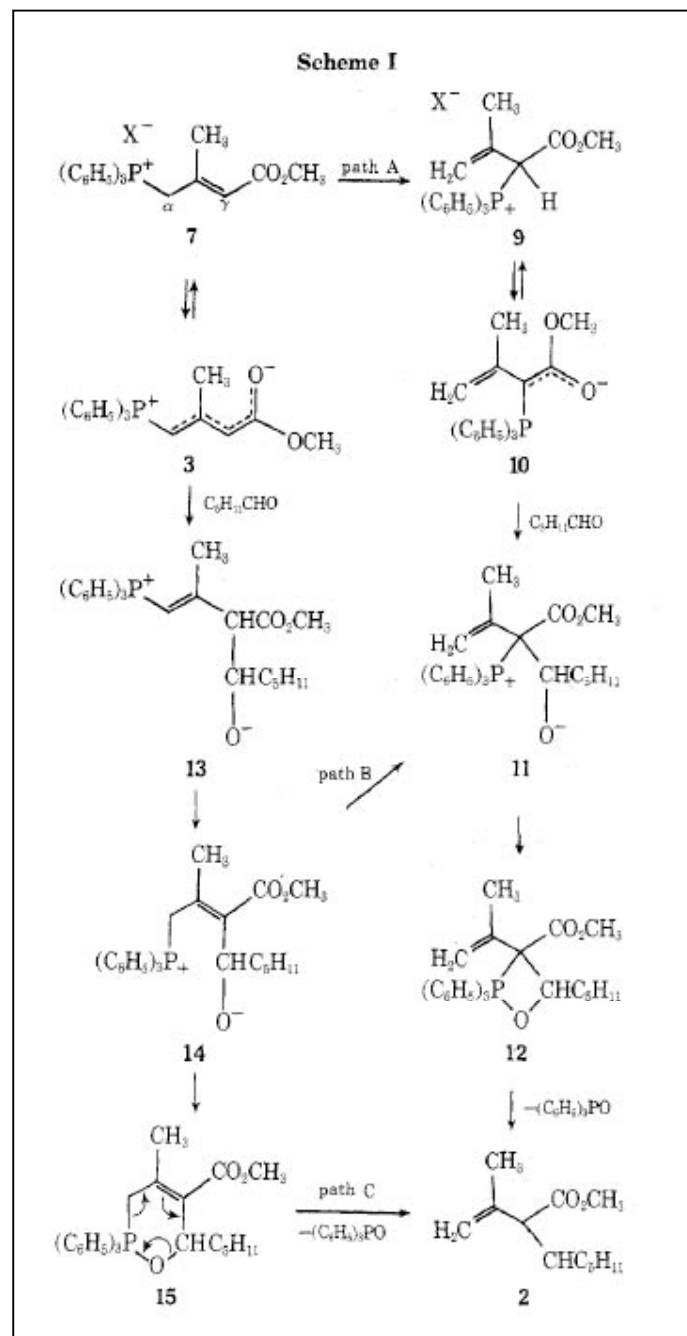
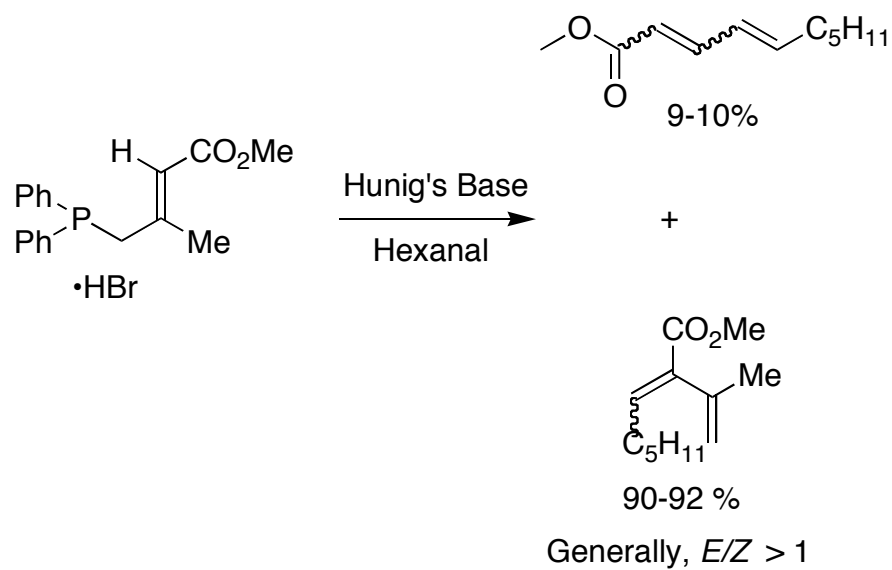


□□ Condensation of an allylic Phosponium Ylide (p. 821)

-Generally, allylic phosphorous ylides condense on the □ carbon

-Many geometric isomers usually obtained

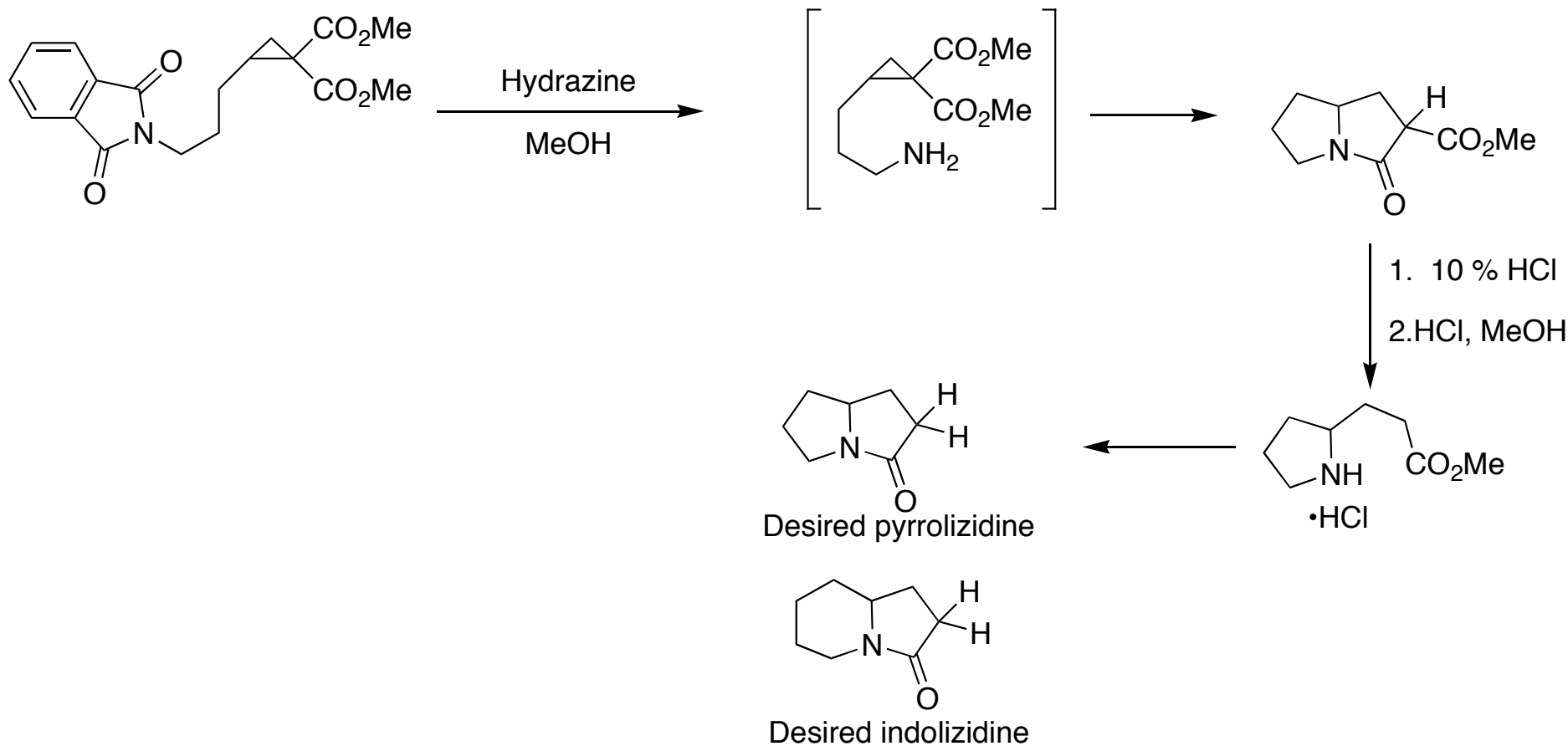
E. J. Corey (p. 256)



Samuel Danishefsky (Univ. of Pitt)

-A route to functionalized heterocycles by homoconjugate addition (p. 1979)

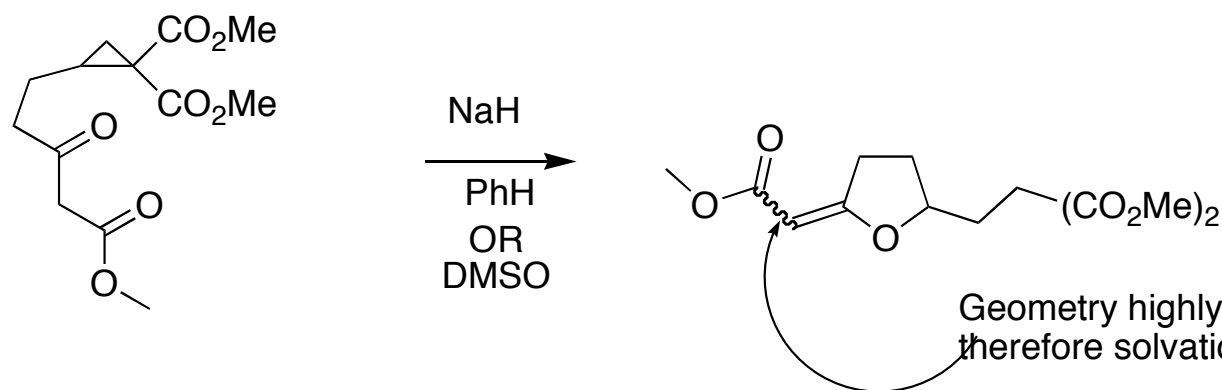
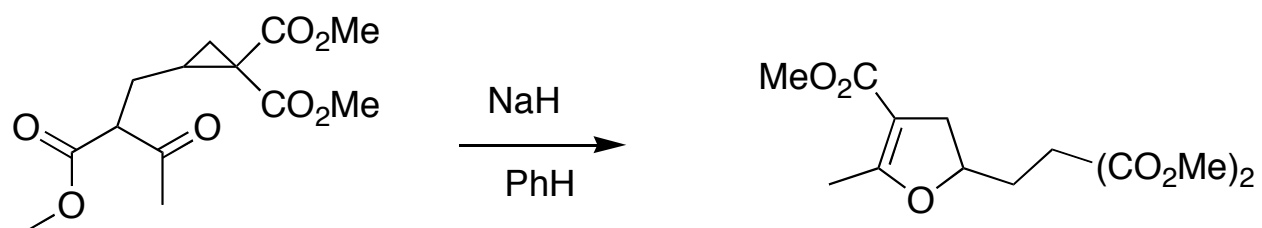
-The use of a highly substituted cyclopropane as an electrophile (generated by reacting the olefin with dimethyl diazomalonate in the presence of copper bronze)



-Showed in earlier work that mechanism goes through "Spiro-mode"

Samuel Danishefsky (Univ. of Pitt)

-Furanoid systems by intramolecular homoconjugate addition (p. 2658)



Geometry highly dependent on solvent and therefore solvation of reaction pathway

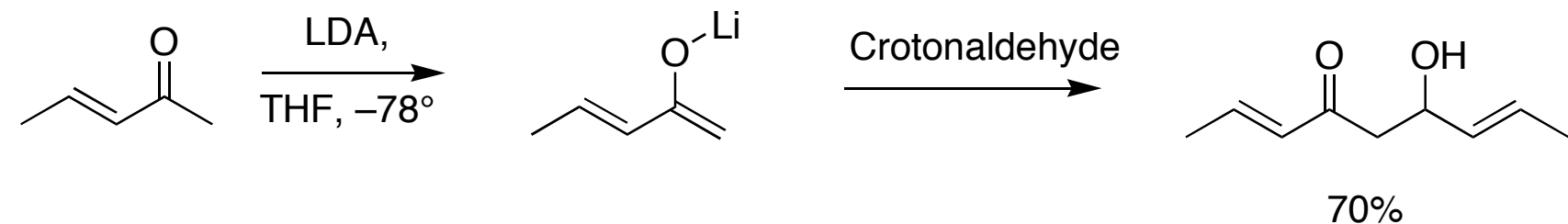
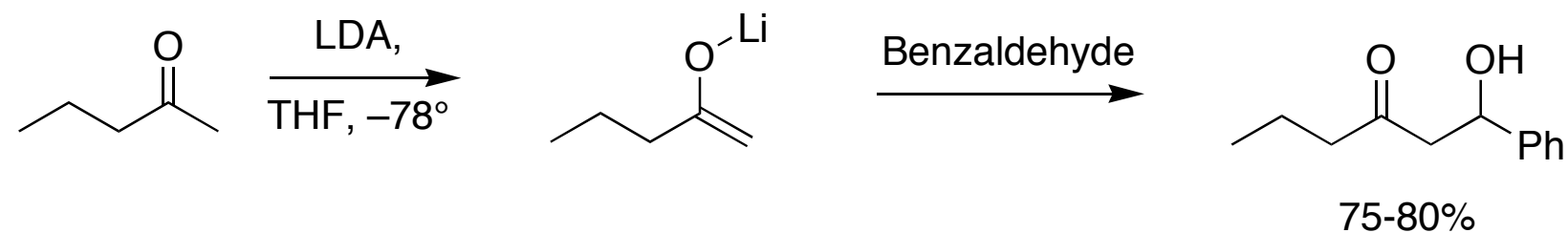
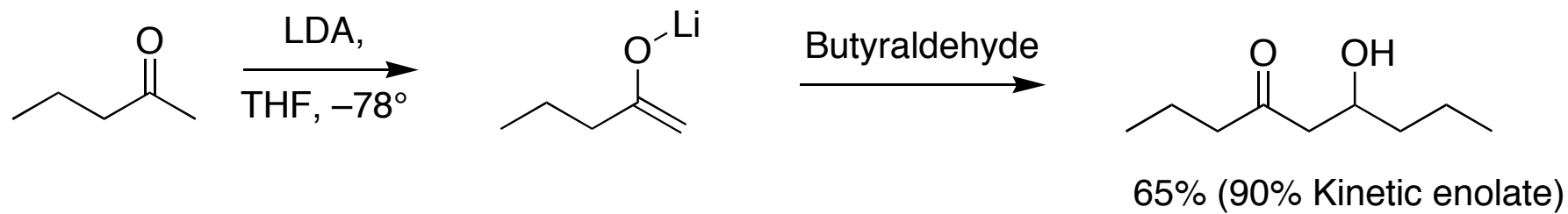
-O-Alkylation was dominant pathway in all systems they tried in this paper

Gilbert Stork (Columbia)

-Regiospecific Aldol condensations of the kinetic lithium enolates of methyl ketones (p. 3459)

-It had previously been difficult to trap the kinetic enolate with alkyl halides

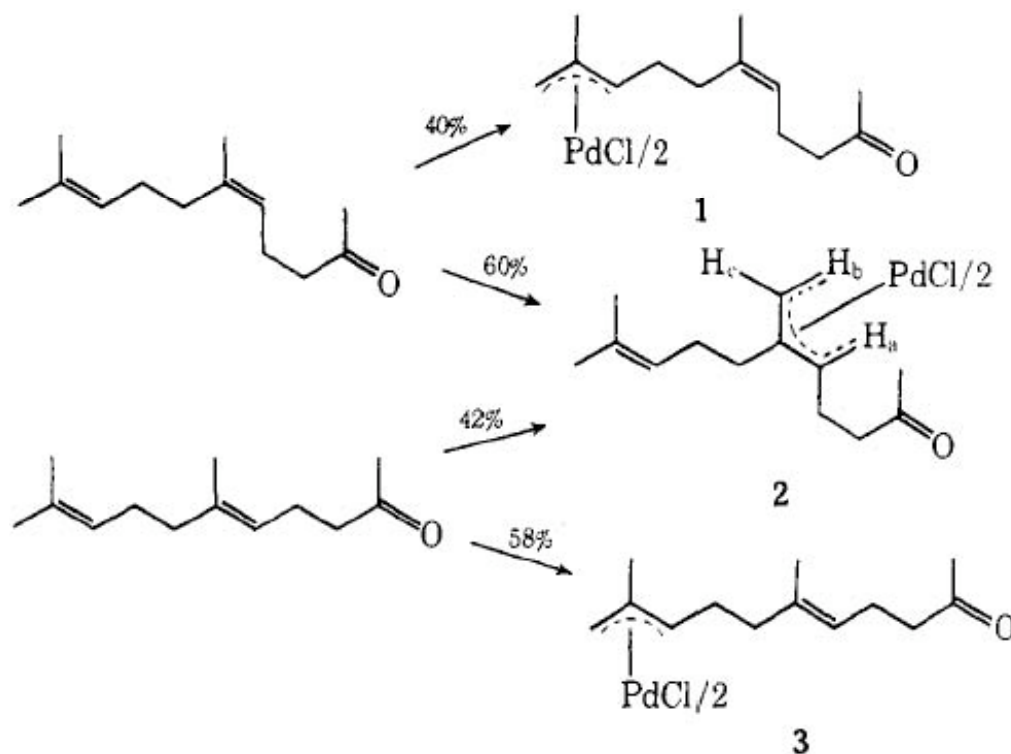
-So, used a more reactive electrophile to trap the enolate



Barry M. Trost (Wisconsin, Madison)

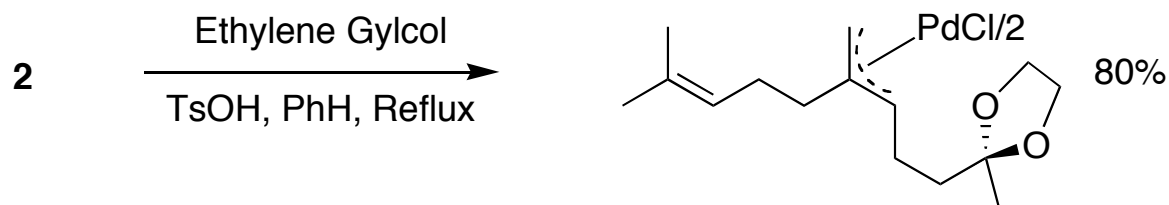
-Chemospecificity of allylic alkylations (p. 737)

-Use of cis and trans geranylacetone



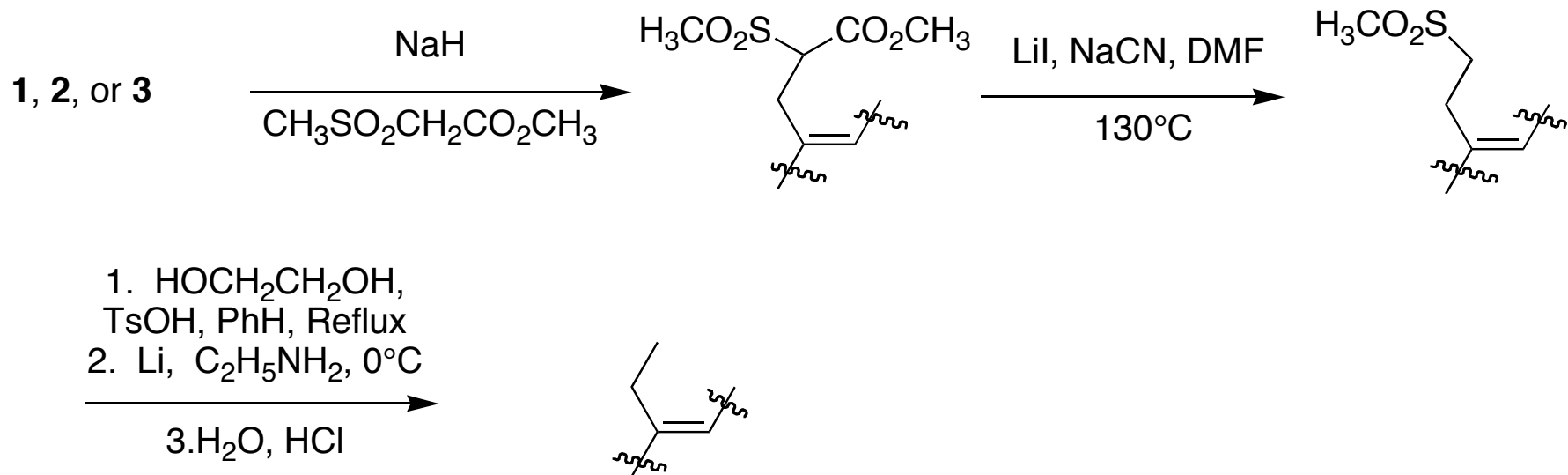
Conditions: PdCl₂, NaCl, CuCl, NaOAc
in AcOH

- η -allyl complexes are remarkably stable



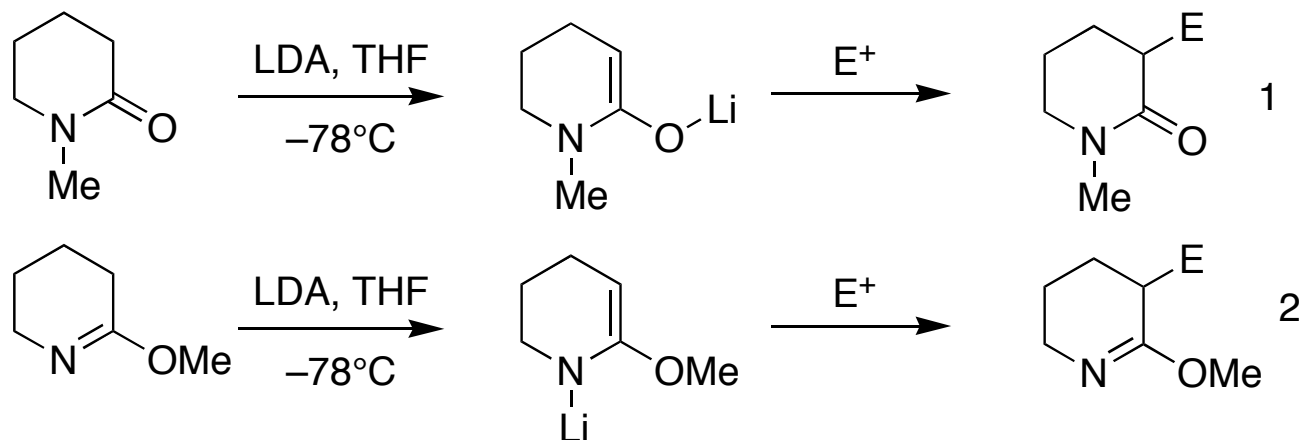
Barry M. Trost (Wisconsin, Madison)

Alkylations



Barry M. Trost (Wisconsin, Madison)

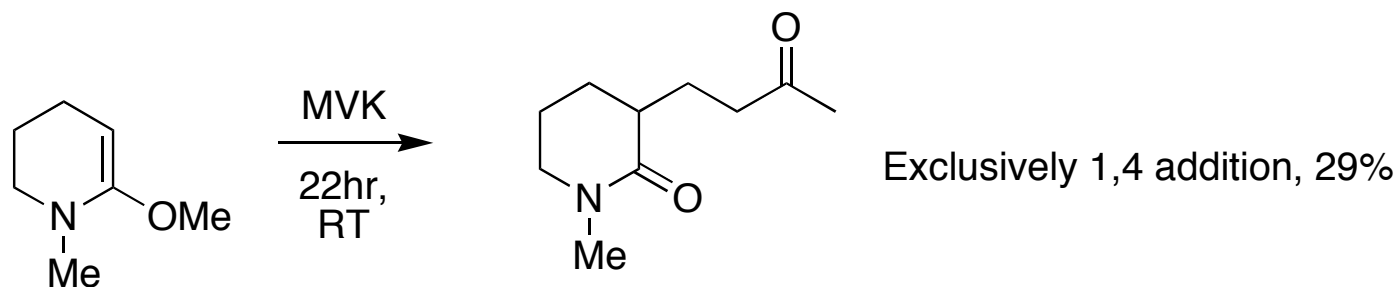
-Alkylation of Lactam Derivatives (p. 2475)



-Both of the above examples proceeded with C-alkylation exclusively with alkyl halides, chlorosilanes.

-For 1 (Stronger enolate), reaction with methyl vinyl ketone proceeds with 1,2 addition; for 2, (weaker reagent), reaction to MVK proceeded with conjugate addition

This selectivity is due to the less reactive reagent having its charge more delocalized in the transition state. To test this hypothesis, a control experiment:



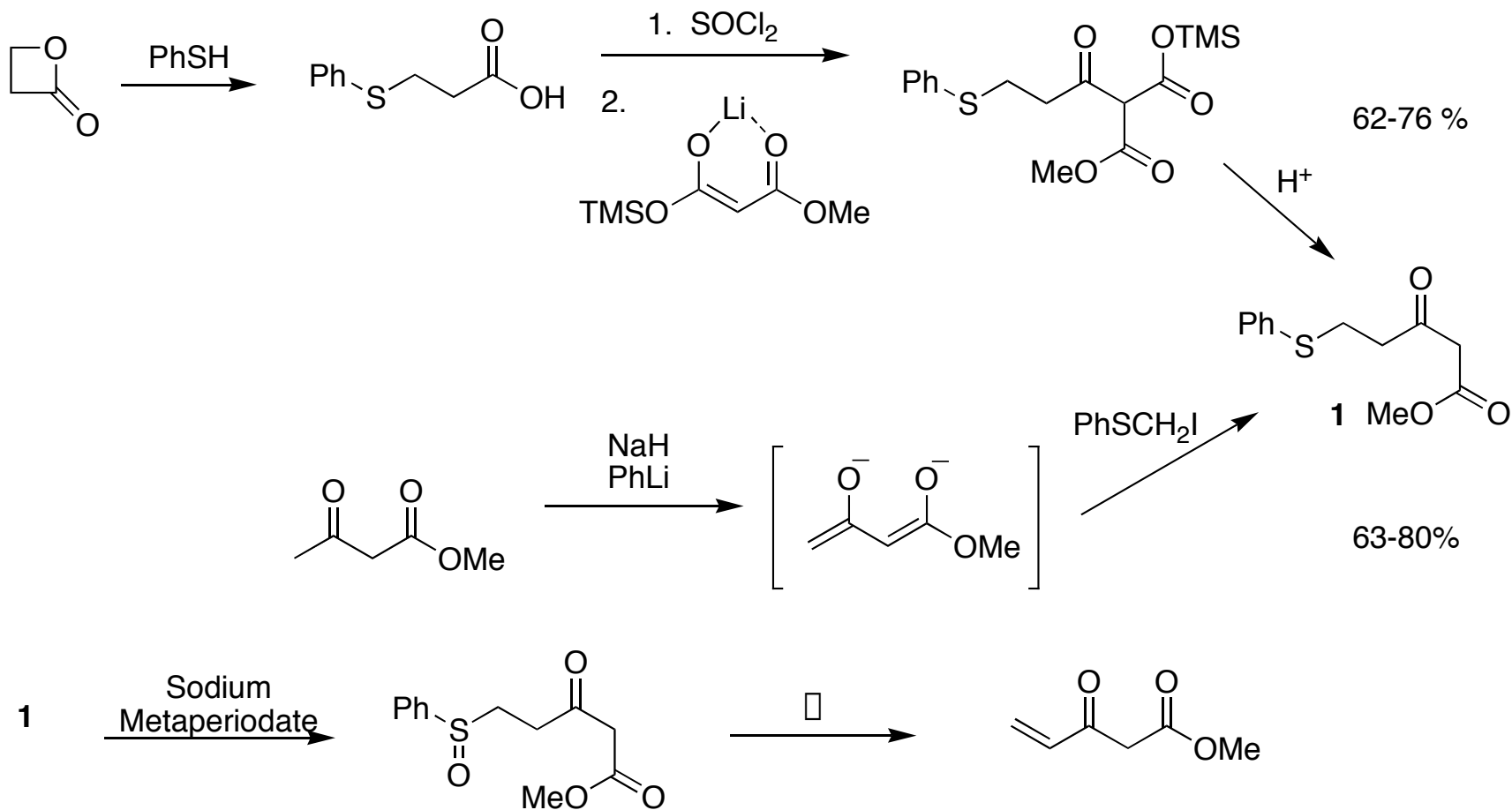
Barry M. Trost (Wisconsin, Madison)

-A convenient approach to Methyl 3-oxo-4-pentenoate (p. 2648)

-Not easily synthesized

-The two main previous methods either ended with a final step of 7-12% (acid catalyzed elimination), or was based on a retro-Diels-Alder step (great yield, but requires special high-temp pyrolysis apparatus).

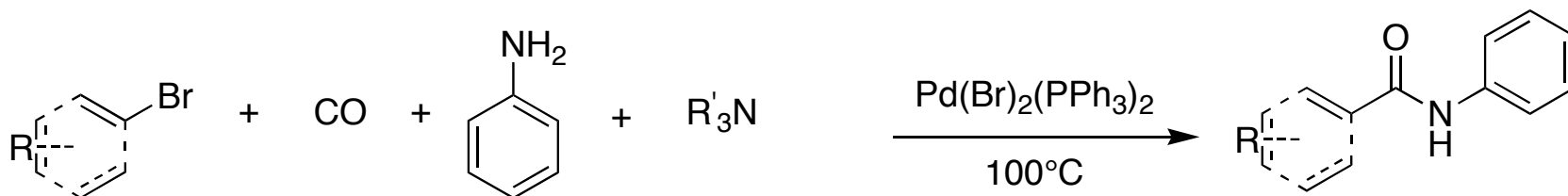
-Utility seen as an "annelating agent" in the synthesis of terpenes and alkaloids



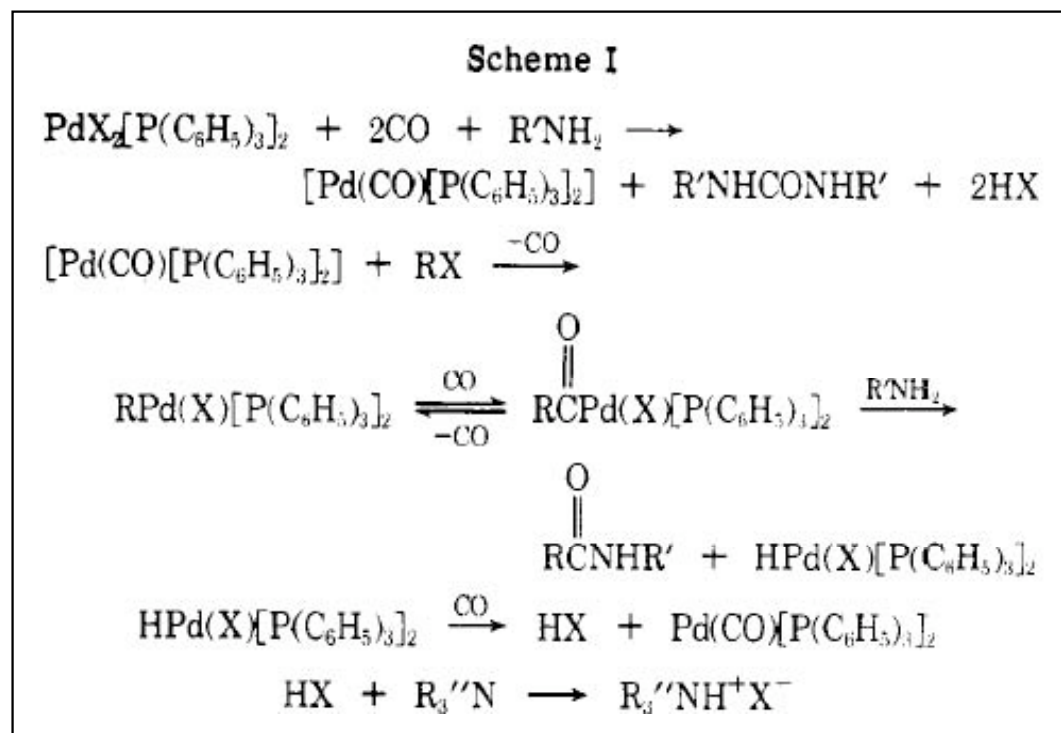
Summary: 3-step route, 60-76% overall; 5-step route, 60-72% overall

R. F. Heck (Univ. of Delaware :-)

-Palladium catalyzed Amidation of aryl, heterocyclic, and vinylic halides (p. 3327)

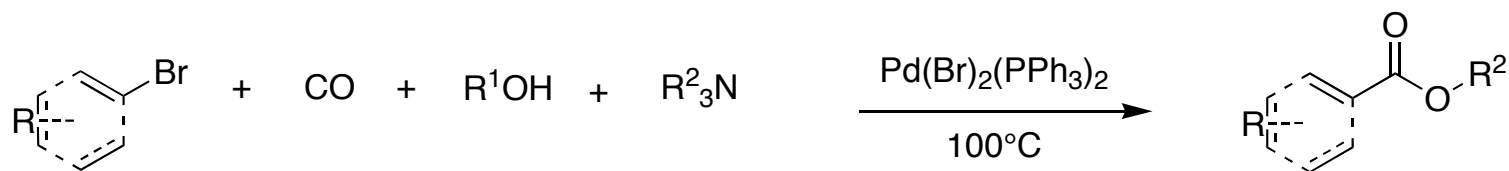


Possible Mechanism:

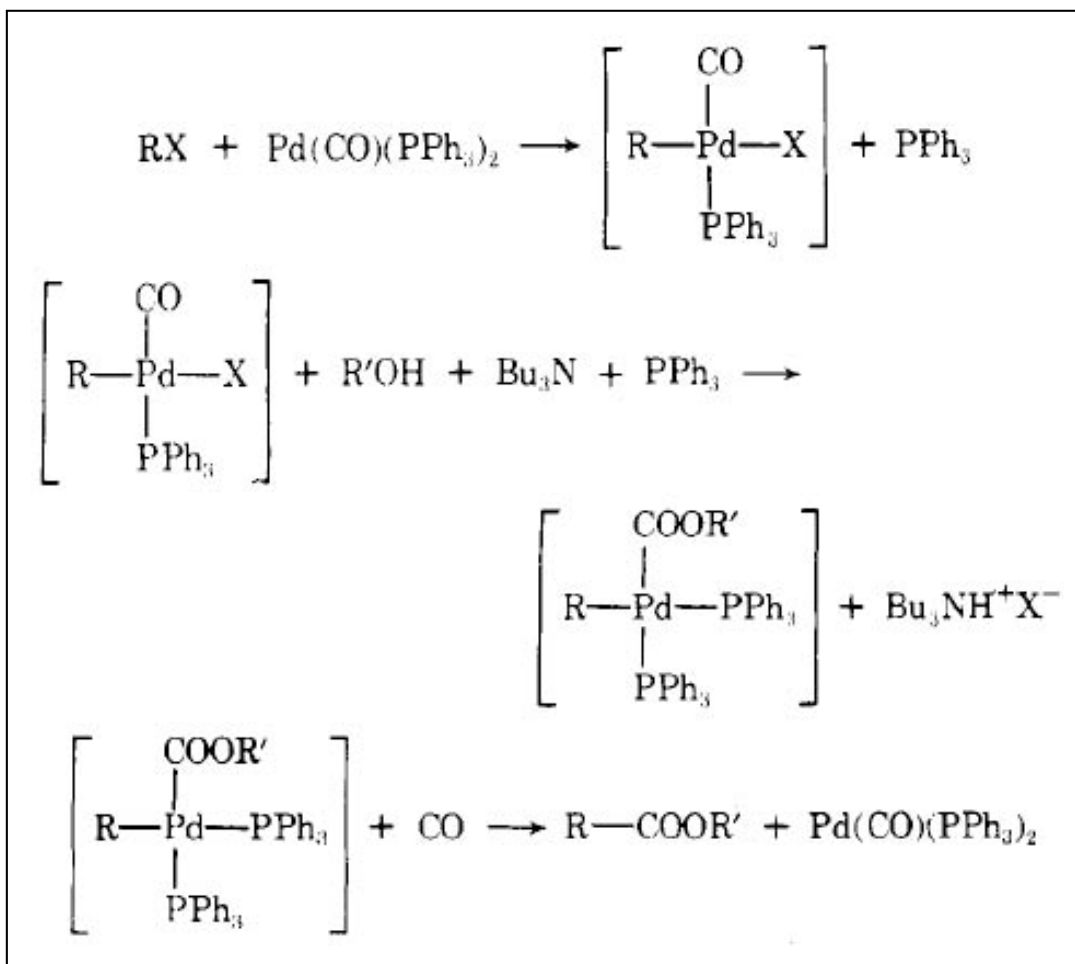


R. F. Heck (Univ. of Delaware :-)

-Palladium catalyzed carboalkoxylation of aryl, benzyl, and vinylic halides (p. 3318)



Possible Mechanism:

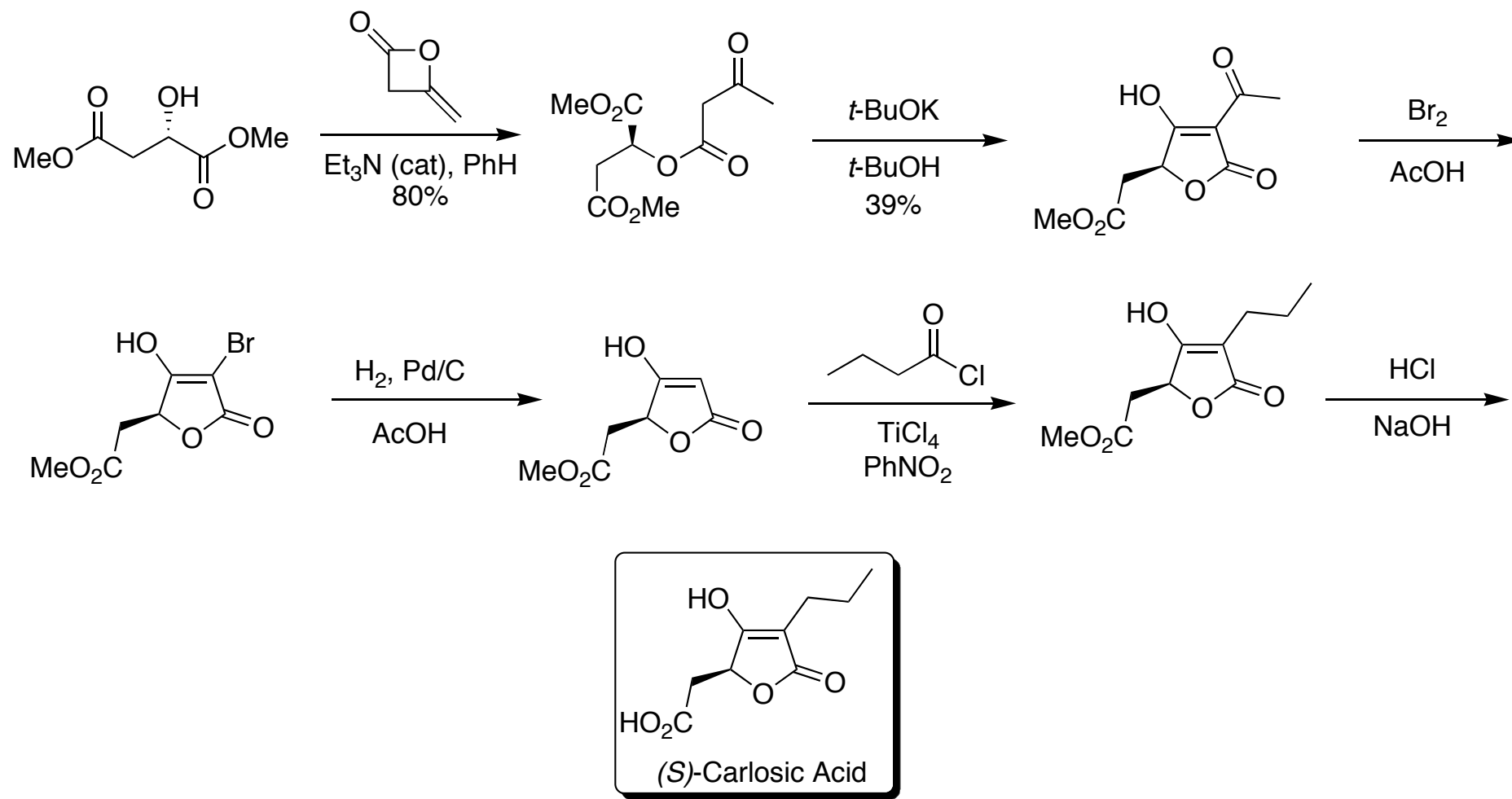


- The following people did wonderful chemistry in JOC, '74, but time constraints cause their omission:
 - David Evans (UCLA)
 - Useful Prostaglandin Intermediate (p. 3176)
 - Applications of trimethylsilyl cyanide (p. 914)
 - Herbert C. Brown
 - New organoborane structures via alpha-bromination of borapolycyclanes (p. 861)
 - Synthesis of olefins: alpha-elimination of alpha-chloroboronic esters (p. 2817)
 - Synthesis of terminal acetylenes via treatment of lithium ethynyltrialkylborates with Iodine (p. 731)
 - Herbert House
 - Chemistry of Carbanions (p. 3102)
 - Electron transfer reactions: reduction of enones with Cr(II) compounds (p. 1173), and of nonconjugated acetylenes (p. 747)
 - Robert E. Ireland
 - Claisen rearrangement of *N*-Allylketene *O,N*-Acetals (p. 421)
 - And of course, many others...

(S)-Carlosic Acid

Blommer and Kappler, p. 113

Temple University



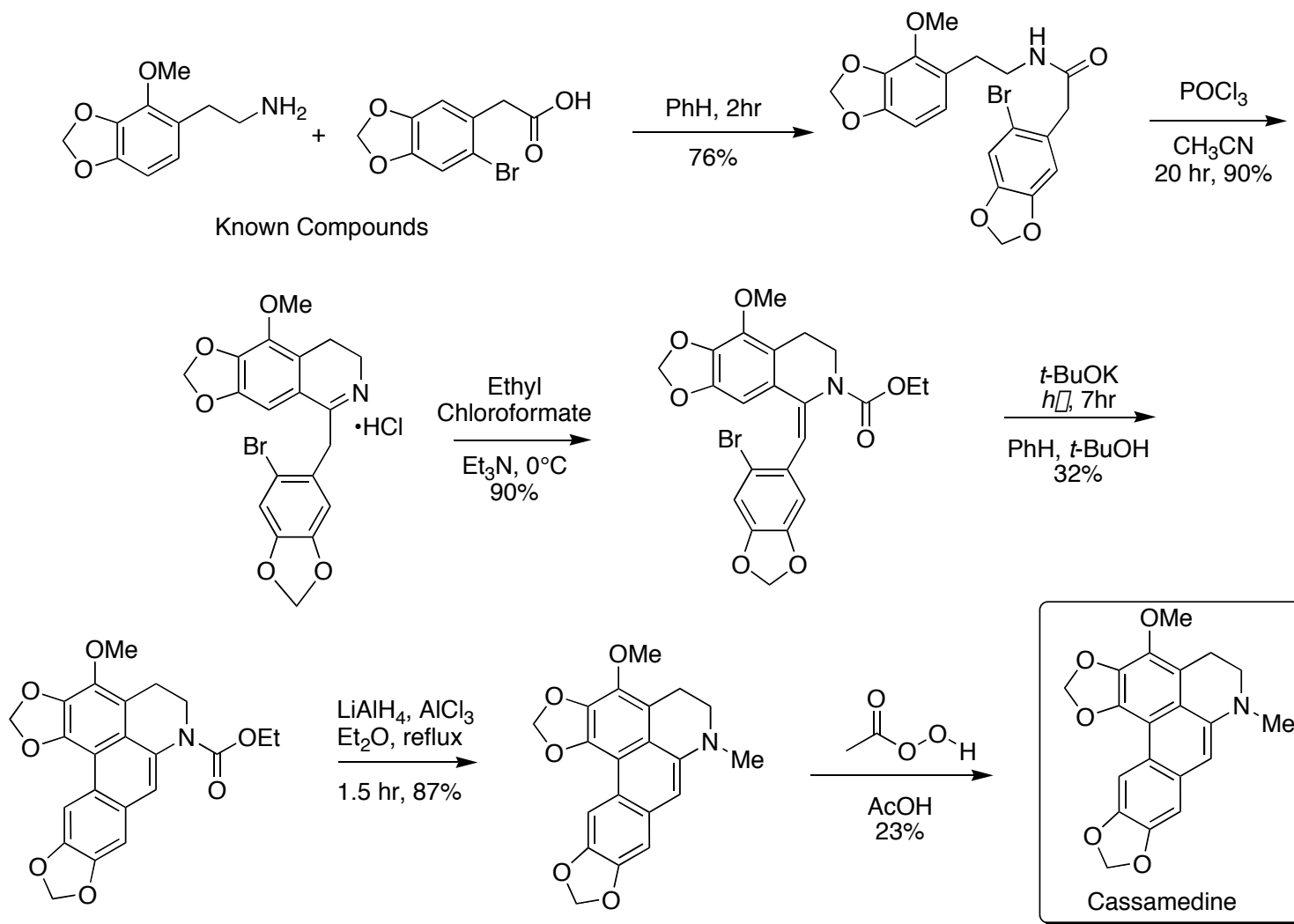
Note: all yields in the synthesis were 70-80%, except the "key step," the cyclization

Cassamedine

Cava and Libsch, p. 577

UPenn

-An alkaloid isolated from *Cassytha americana*



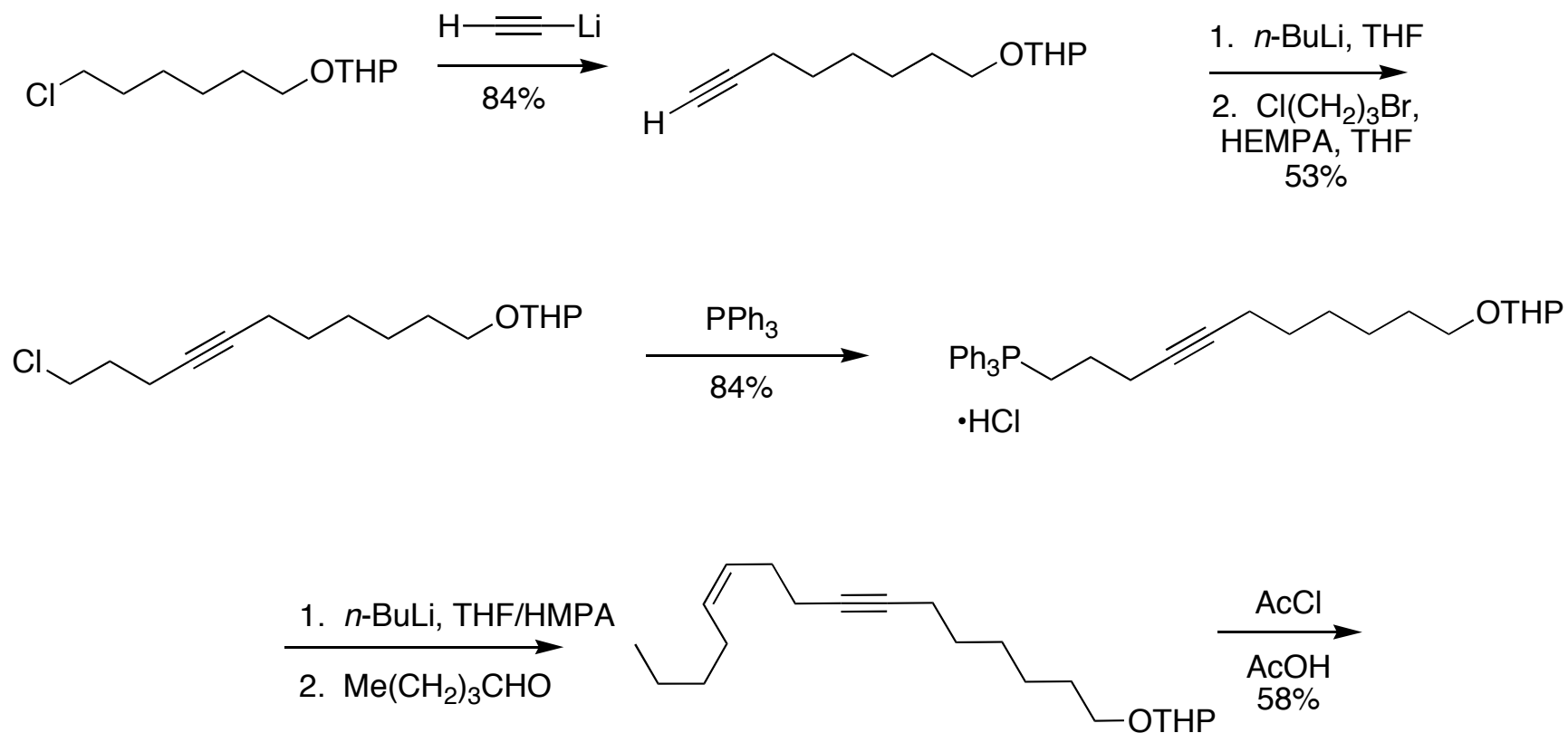
The Sex Pheromone of the Pink Bollworm

Phillip E. Sonnet, p. 3793

U.S. Dept. of Agriculture, Maryland

-Isolated from the *Pectinophora gossypiella*, the pink bollworm moth

-Isolated as 1:1 mixture of geometric isomers

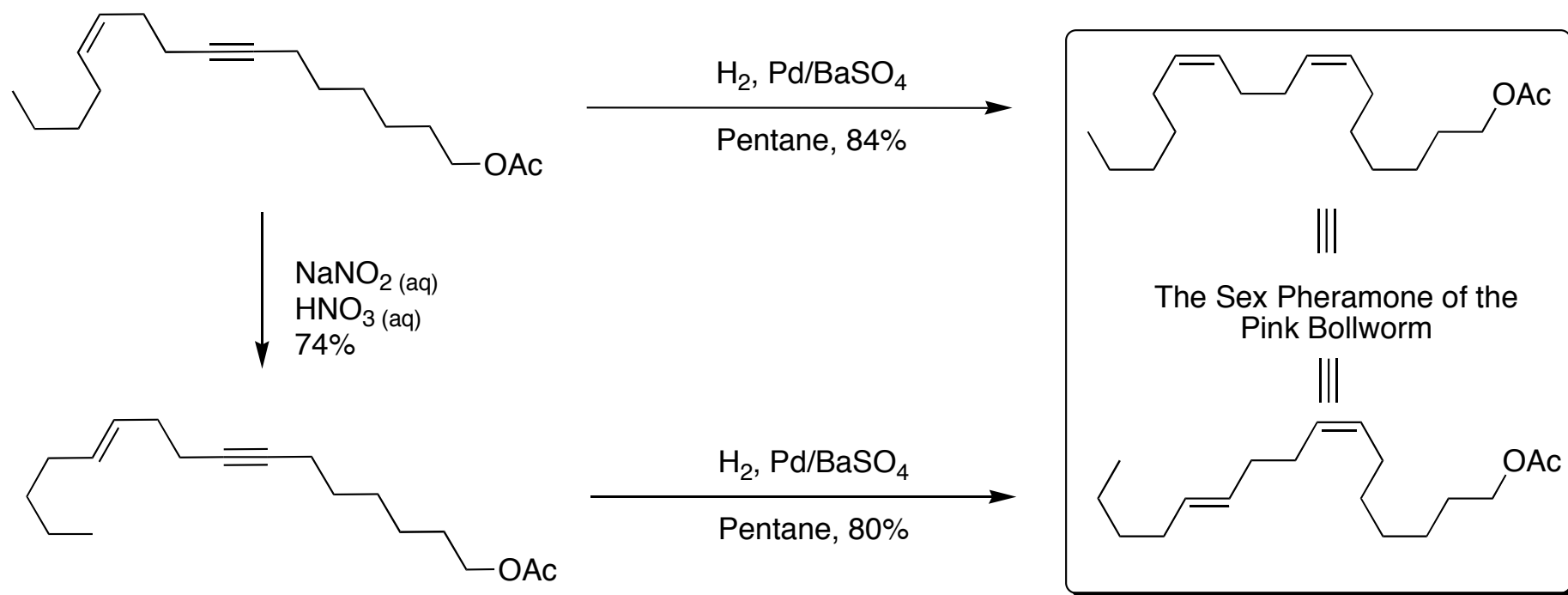


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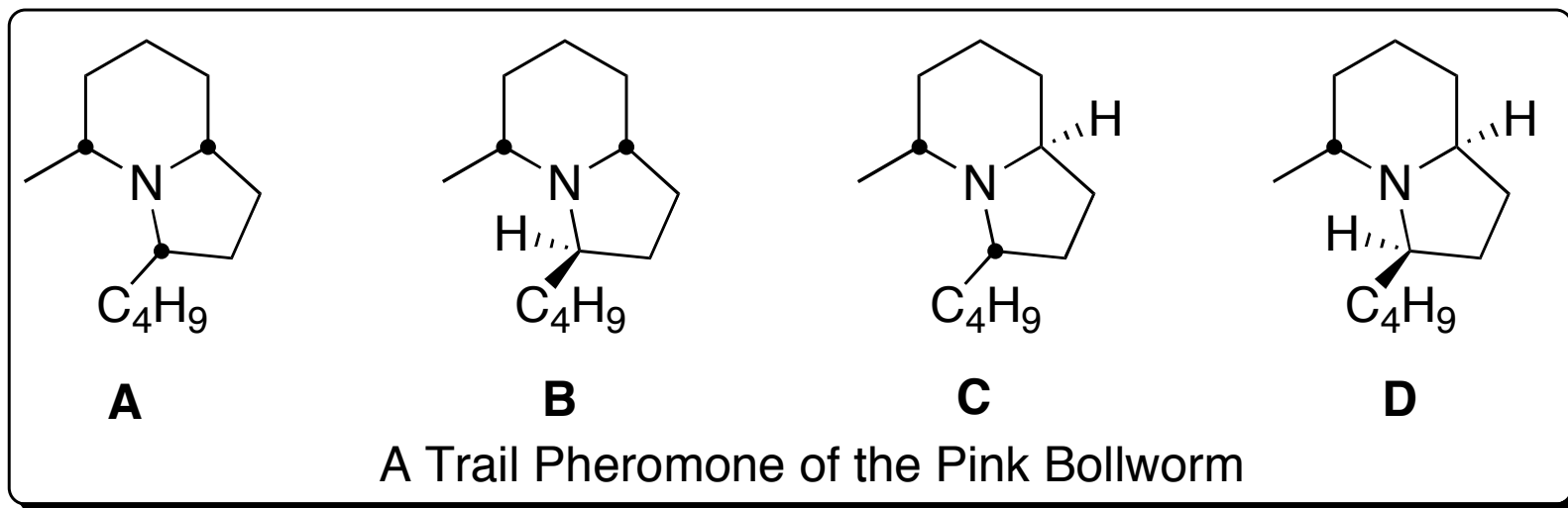


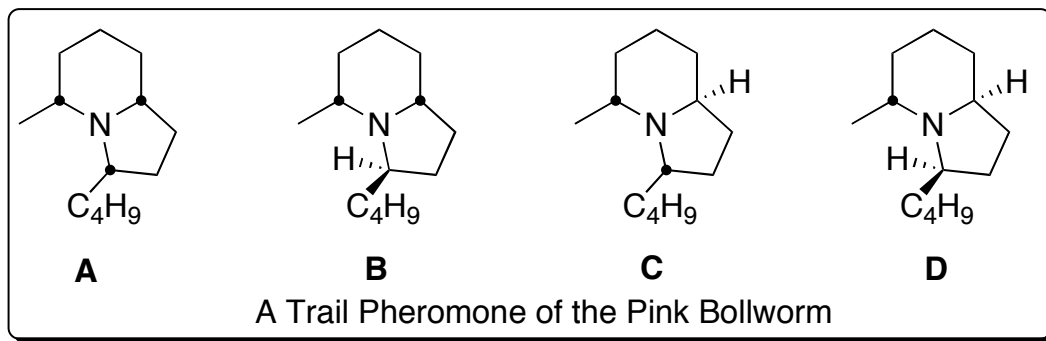
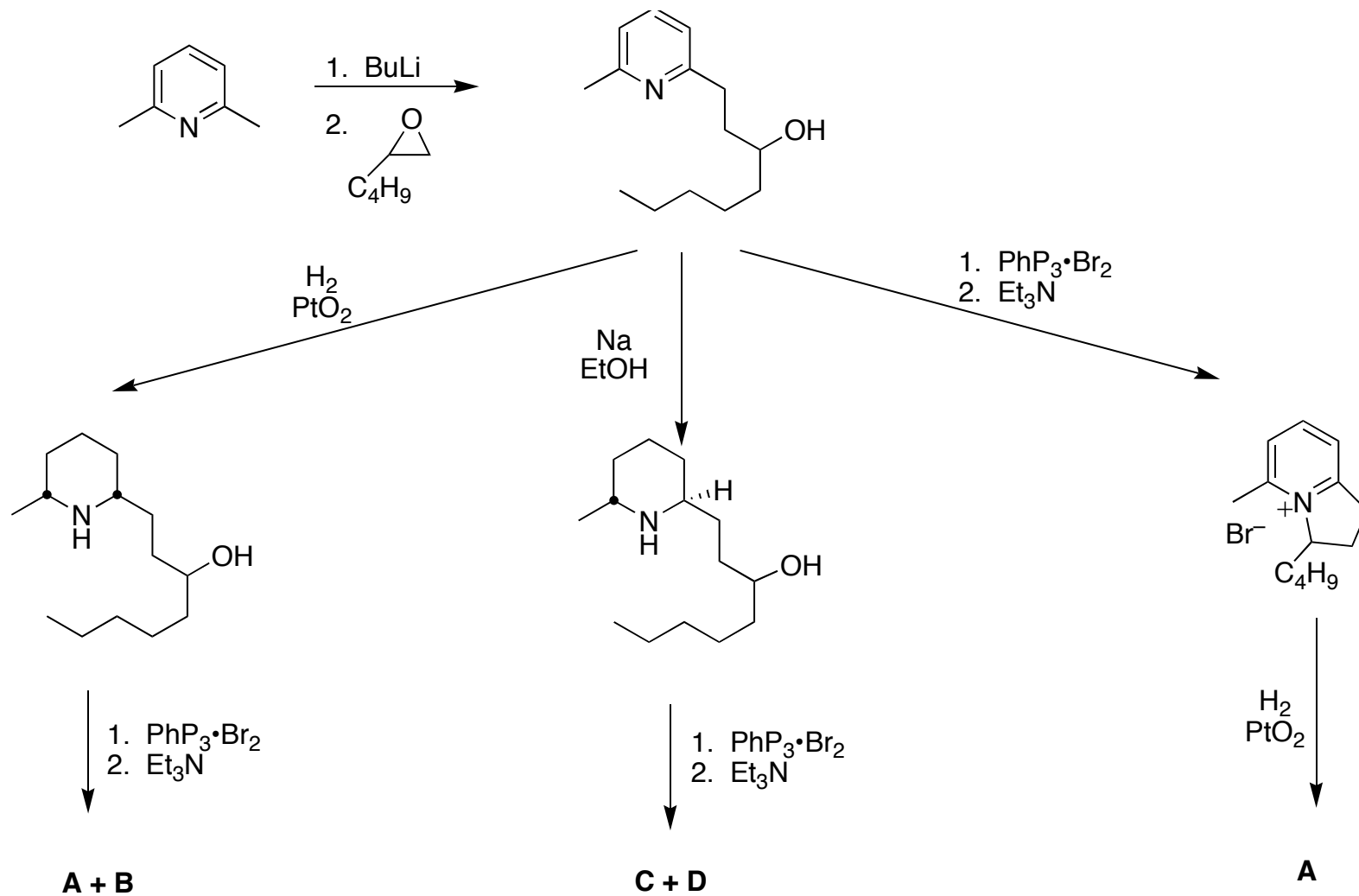
A Trail Pheromone of the Pharaoh Ant

Sonnet, Oliver, p. 2663

U.S. Dept. of Agriculture, Maryland

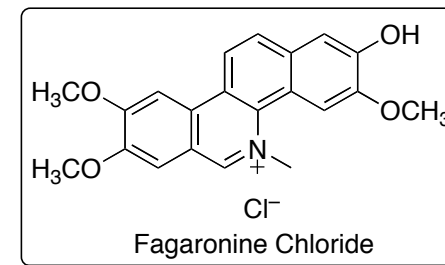
- Isolated from the *Monomorium pharaonis*, the Pharaoh Ant
- It was known that the pheromone had the general structure of 3-butyl-5-methoctahydroindolizine, but absolute stereochemistry of *active* pheromone was not elucidated
- Synthesized all four stereoisomers because they were interested in the pheromone's utility as a pest control agent





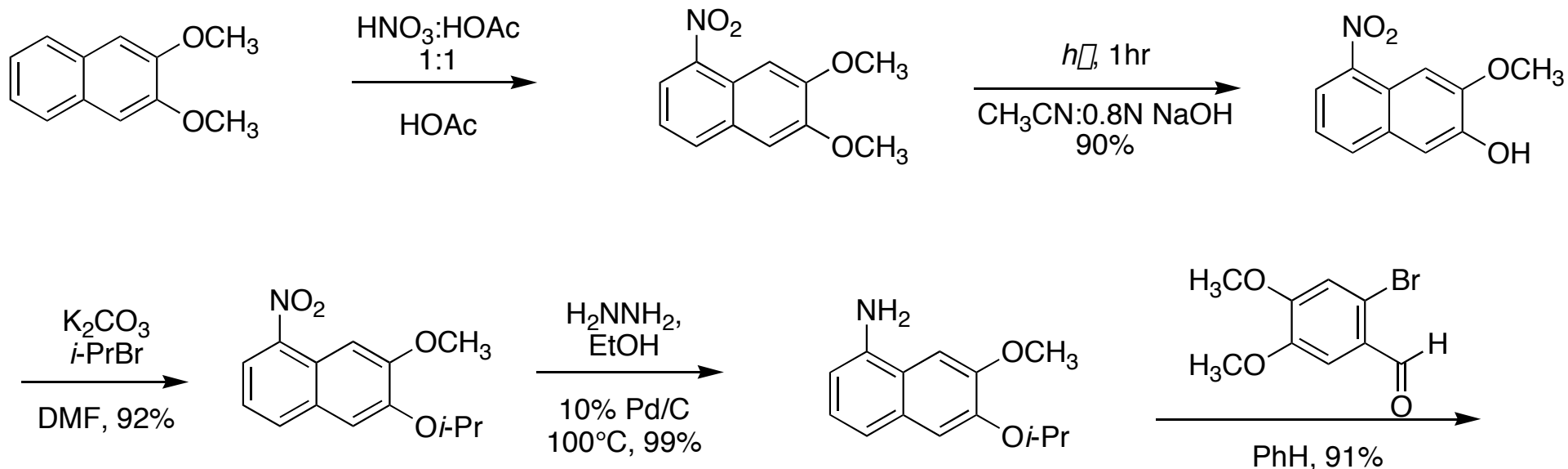
Fagaronine Chloride

Stermitz, p. 3239



Colorado St. Univ., Fort Collins

- Extremely active antileukemic alkaloid
- Isolated from *Faraga zanthoxyloides*
- Note: synthesis also proved structure

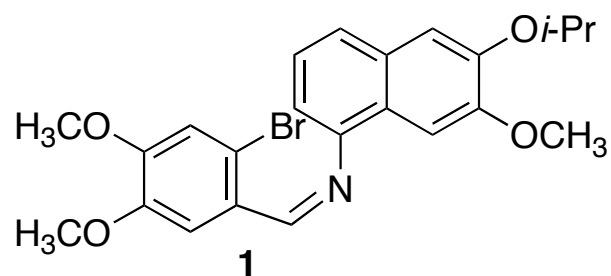


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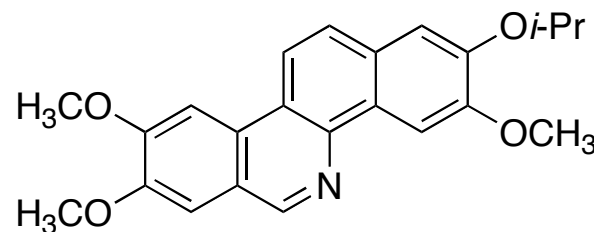
Stermitz, p. 3239

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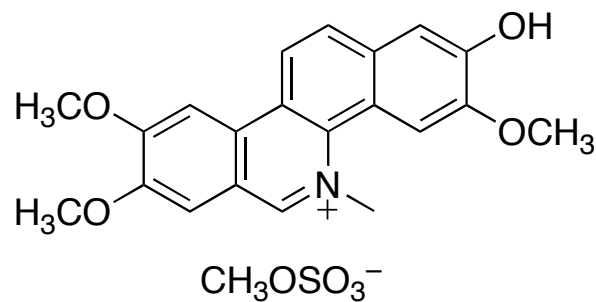
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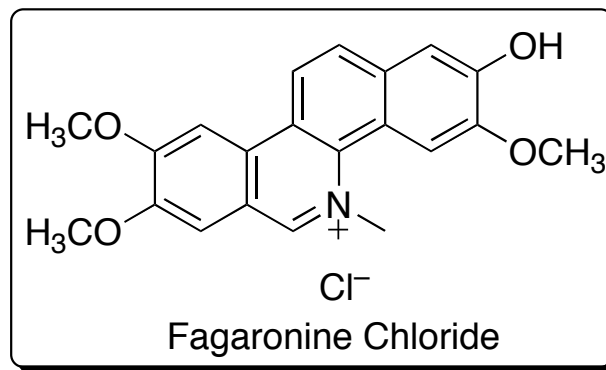
1. Na, NH₃(liq)
2. 1
3. NH₄Cl, 24%



Dimethyl Sulfate,
PhNO₂/Xylene
180°C



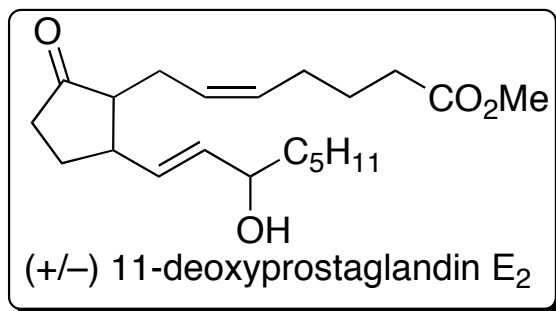
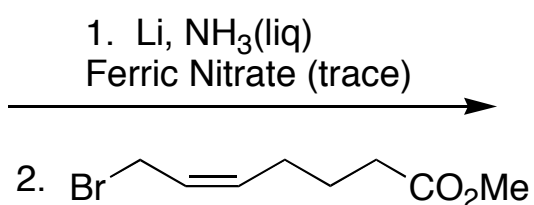
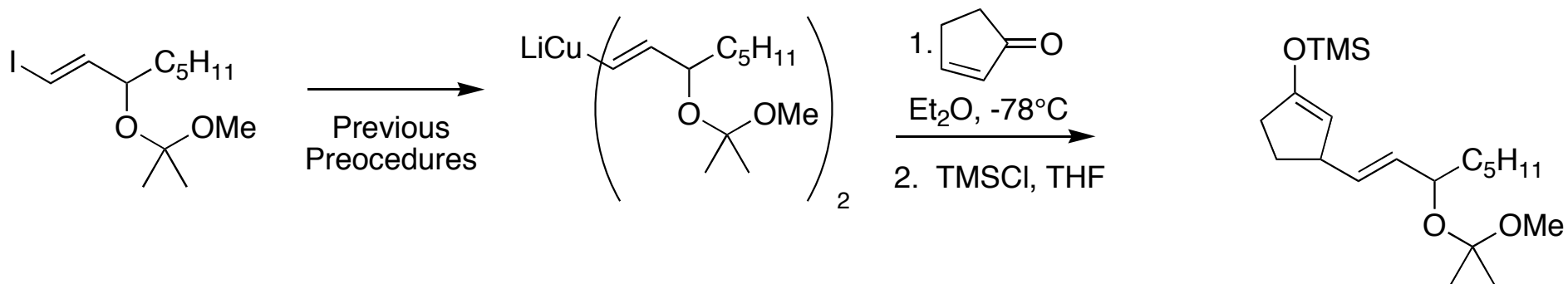
8% NaCl_(aq)
88%



(+/-) 11-deoxyprostaglandin E₂

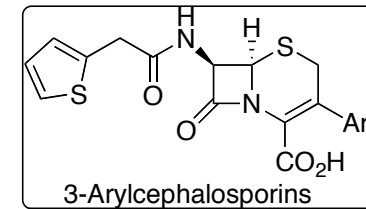
Jonh Petterson, John Fried, p. 2506

Syntex, California



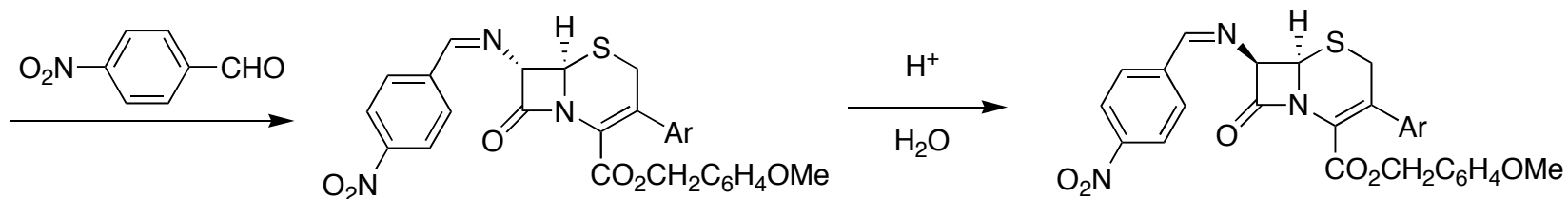
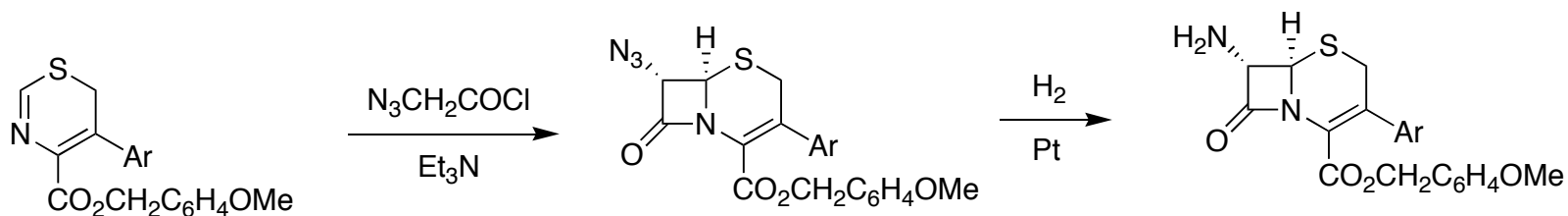
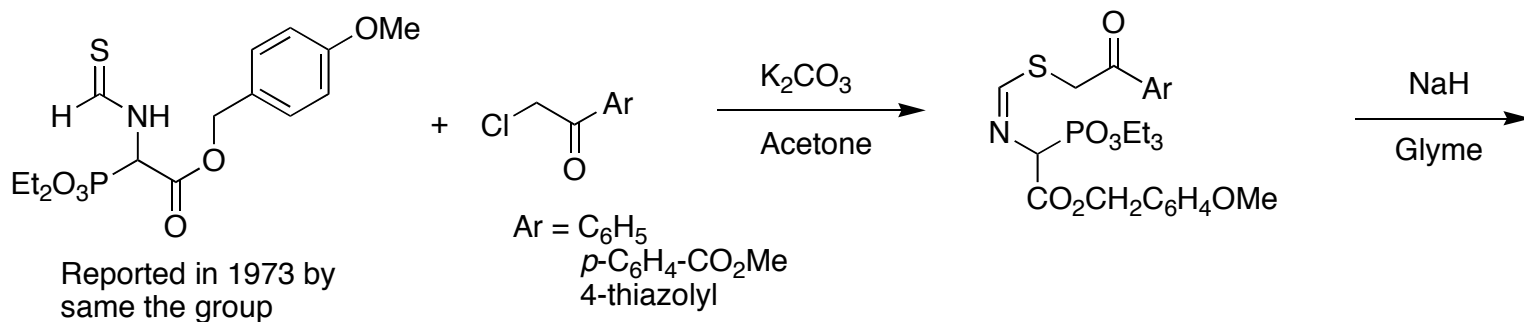
3-Arylcephalosporins

Firestone, Maciejewicz, Christensen, p. 3384



Merck Sharp and Dohme Research, New Jersey

- Semisynthetic β -Lactam Antibiotics
- High potency, acid stable, high degree of tolerance by man
- Many modifications prior to this work



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