

Modern Organic Synthesis

by Barry M. Trost and Edwin Vedejs



ACS Audio Courses

Modern Organic Synthesis

**by Barry M. Trost
and Edwin Vedejs**

**University
of Wisconsin**

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A WORD TO THE USER

ACS AUDIO COURSES are instructional units on subjects of significant interest that are suitable for both individual study and group use.

The ACS AUDIO COURSE on "Modern Organic Synthesis," by Professors Barry M. Trost and Edwin Vedejs of the University of Wisconsin, is intended for individuals who are concerned with putting organic molecules together. A survey of important modern synthetic techniques is presented within a context of several recent contributions in organic synthesis. Emphasis is placed on general methods. For maximum benefit the student is expected to have a background knowledge of basic organic chemistry as well as a familiarity with classical synthetic techniques.

This volume is the reference manual that is integrated with the audiotape of "Modern Organic Synthesis." The two together--the tape and manual--comprise the ACS AUDIO COURSE; neither is complete without the other. Because the lecturers refer constantly to the manual, each listener should have a copy of the manual as he listens, so he may follow these references.

The manual was not written to be a self-sufficient textbook. It was designed, rather, to be used as a workbook while listening to the tape. The listener is urged to take notes with the expectation that this activity will reinforce the learning process. The product is a personally annotated volume which should serve as an authoritative and up to date introduction to the subject.

Your comments and suggestions have proved to be exceptionally valuable guides for improving our educational programs. We hope you will continue to send them to us.

Department of Educational Activities
American Chemical Society

Contents

	Page	Tape Sides
Foreword	vii	
General Outline	1	
I. Synthesis of Cyclodecapentane (Trost)	3	1-3
II. Synthesis of a Degradation Product of Annotinine (Vedejs)	39	4-6
III. Synthesis of Helminthosporal (Trost)	65	7-8
IV. Synthesis of Cubane (Vedejs)	84	9-10
Bibliography	99	

* * * * *

Tape Side	Page
1	3
2	13
3	28
4	39
5	46
6	58
7	65
8	75
9	84
10	90

General Outline*

I. Planning a synthesis

- A. Synthetic goal -- definition of problem
- B. Consideration of properties of product
- C. Stereochemical relationships
- D. Recognition of structural types
- E. Correlation with simple building blocks
- F. Methods of structural alteration

II. Reaction types

A. Reductions

- 1. Catalytic hydrogenation
 - a. Heterogeneous catalysis
 - b. Homogeneous catalysis
- 2. Dissolving metals
 - a. Reduction of unsaturated systems
 - b. Replacement of halide by hydrogen
 - c. Olefin formation by reductive vicinal cleavage
- 3. Metal hydrides (aluminum, boron, and tin hydrides)
 - a. Carbonyl compounds
 - b. Halides

B. Oxidations

- 1. Cr(VI)
- 2. Permanganate
- 3. Lead tetraacetate and sodium metaperiodate
- 4. Osmium tetroxide
- 5. Ozonolysis
- 6. Selenium dioxide
- 7. Peracids
- 8. Halogenation
- 9. Peresters
- 10. Photosensitized oxidation

C. Carbon-carbon bond formation

- 1. Alkylations (including Michael reaction)
 - a. Activating and blocking groups
 - b. Specific enolate generation
 - (1) Enol acetate
 - (2) Enol silanes
 - (3) α,β -unsaturation
 - (4) Cleavage of α -substituents

c. Enolate derivatives

- (1) Enamines
- (2) Salts of Schiff bases

2. Condensations at the carbonyl group

- a. Aldol and related condensation
- b. Ylide reactions

- (1) Phosphorus ylides
- (2) Sulfur ylides

c. Claisen and related condensations

3. Cycloadditions

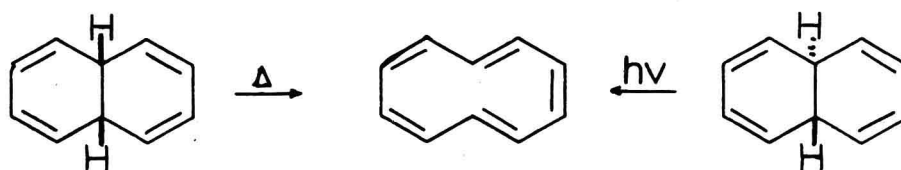
- a. Diels-Alder
- b. Carbenes
- c. Thermal and photolytic 2 + 2 additions
 - (1) Reactions of allenes and ketenes
 - (2) Reactions of activated olefins
 - (3) Enone cycloadditions

E. Rearrangements

- 1. Valence isomerizations
- 2. Rearrangements involving carbonium ions
- 3. Ring contractions; pinacol rearrangements

* Note: The course lectures do not follow the order of this outline.

I. Synthesis of Cyclodecapentaene



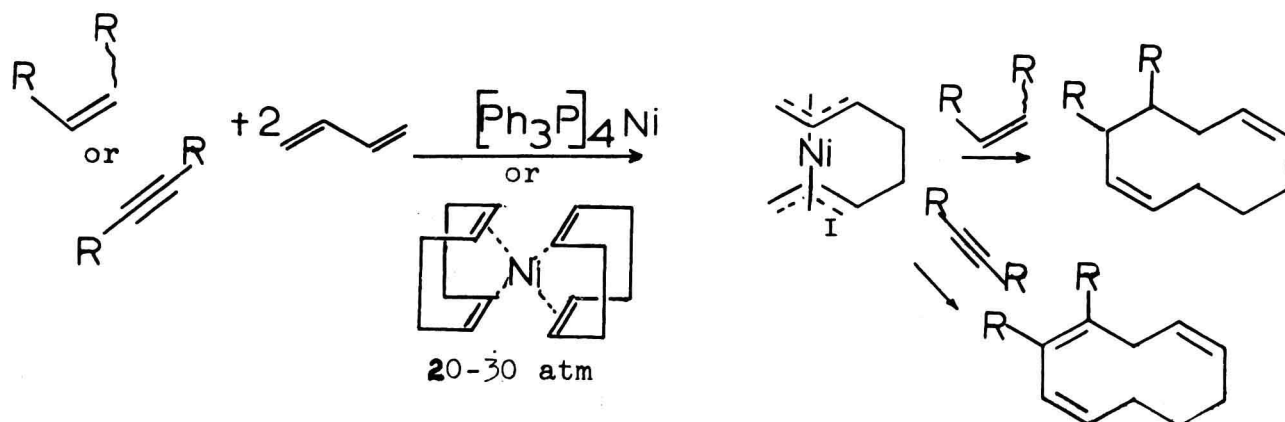
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S. Masamune and R. T. Seidner, Chem. Commun., 542 (1969).

E. E. van Tamelen and T. L. Burkoth, J. Amer. Chem. Soc., **89**, 151 (1963).

A. Synthesis of medium sized rings

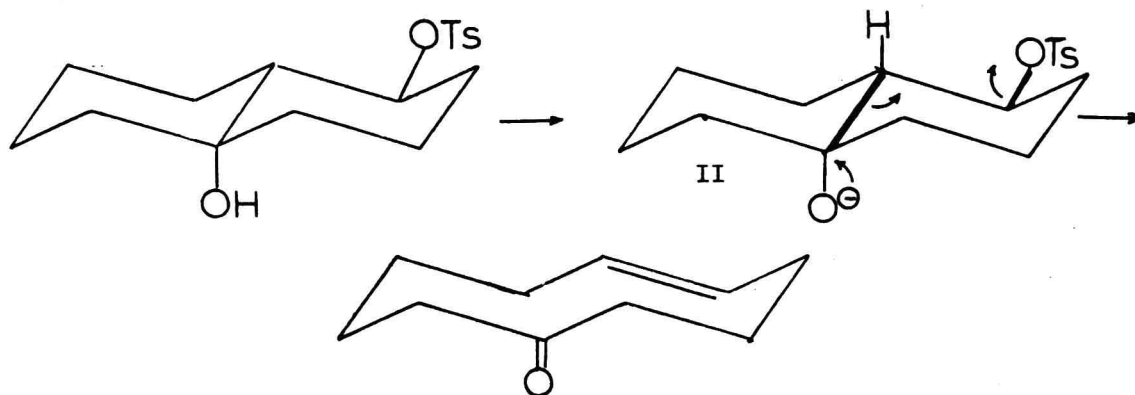
1. Transition metal catalyzed cycloadditions



Reference

P. Heimbach and G. Wilke, Ann. Chem., **727**, 183, 194 (1969).

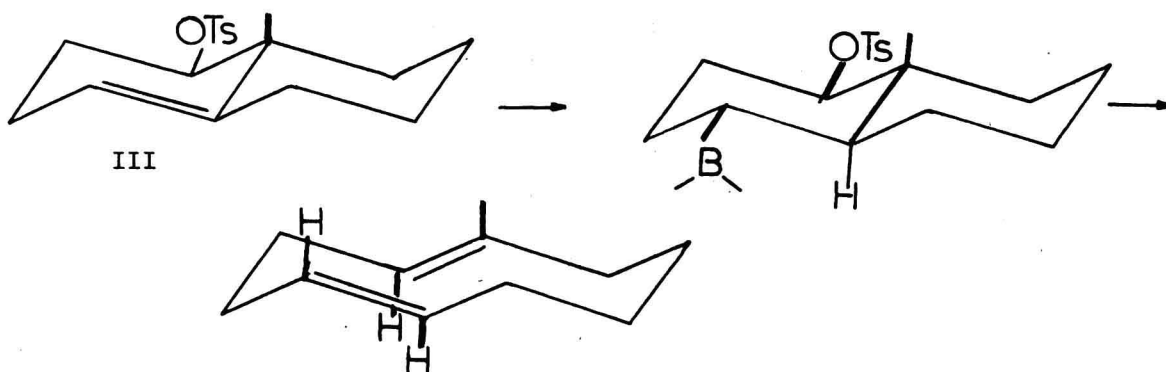
2. Four bond fragmentation



Reference

P. S. Wharton and G. A. Hiegel, J. Org. Chem., 30, 3254 (1965).

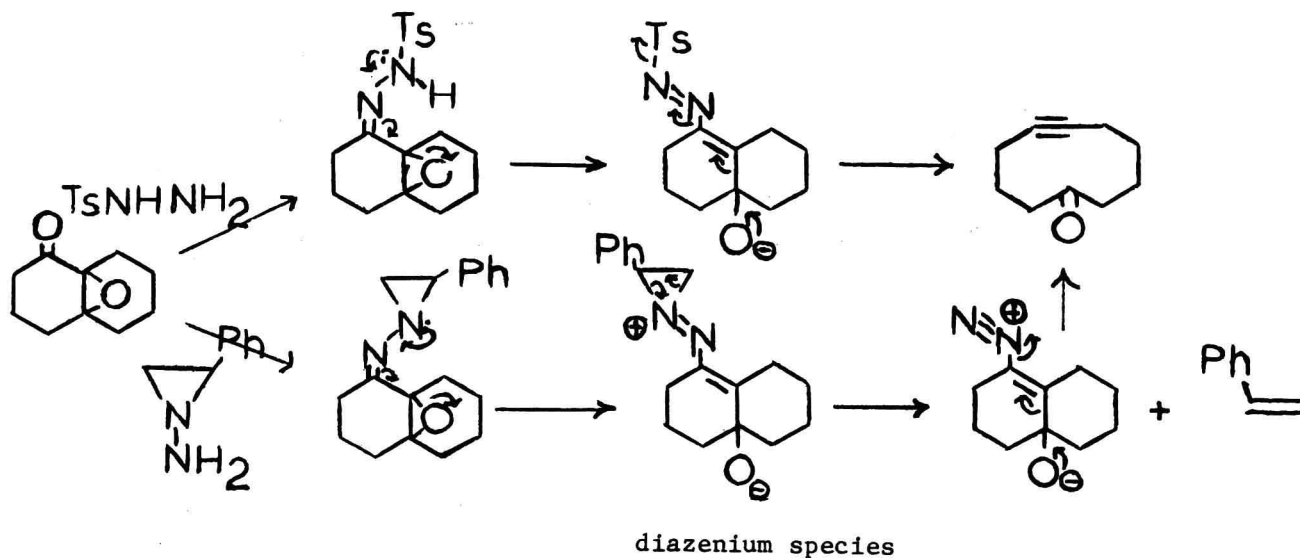
3. Five bond fragmentation



Reference

J. A. Marshall and G. L. Bundy, J. Amer. Chem. Soc., 88, 4291 (1966).

4. Hydrazine induced fragmentations of epoxyketones



Reference

A. Eschenmoser, et al., Helv. Chim. Acta , 51, 1461 (1968).

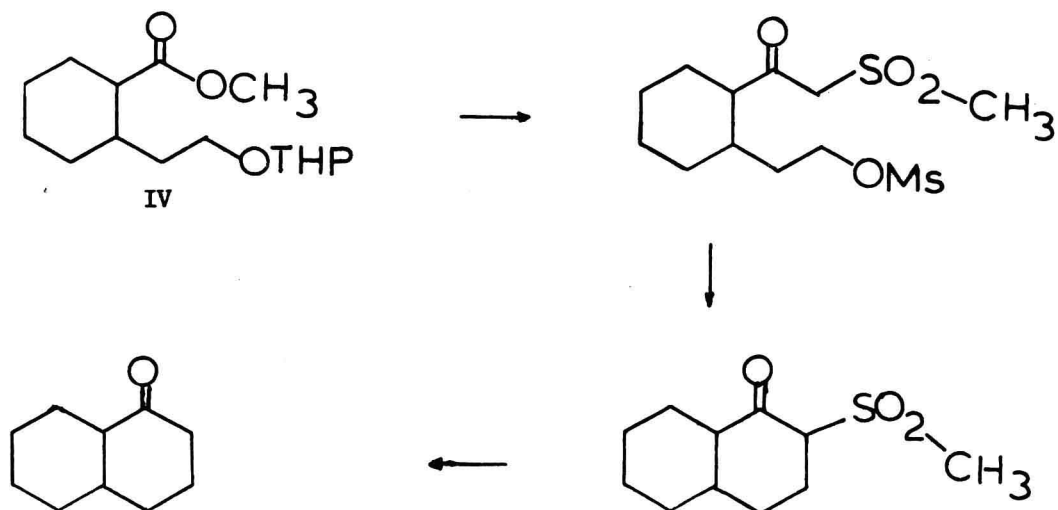
B. Six-membered ring formation

1. Robinson annelation procedure

Reference

T. A. Spencer, H. S. Neel, D. C. Ward and K. L. Williamson,
J. Org. Chem., 31, 434 (1960).

2. Alkylation and/or acylation



References

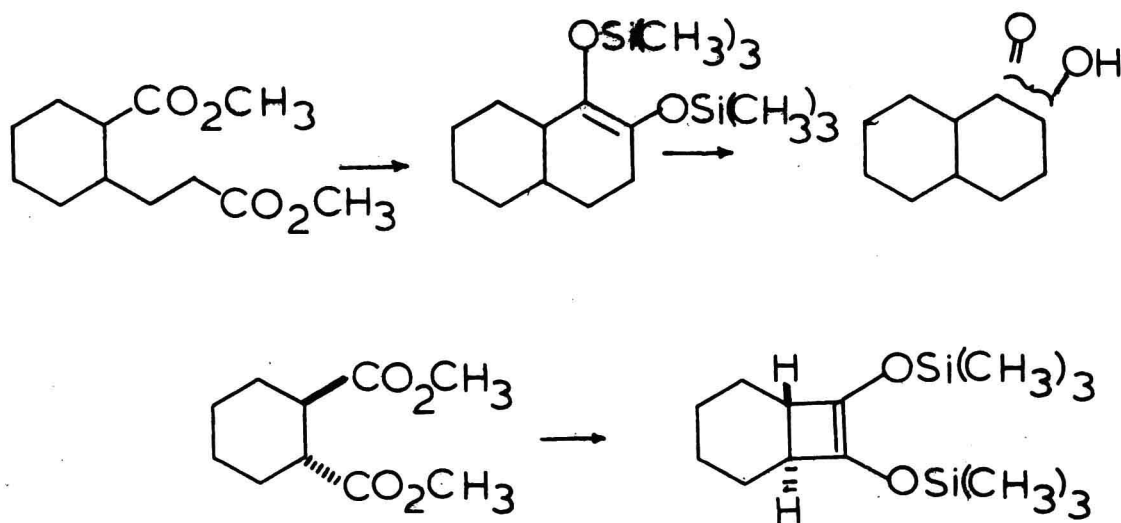
- P. G. Gassman and G. D. Richmond, J. Org. Chem., 31, 2355 (1966).
H. O. House and J. K. Larson, J. Org. Chem., 33, 61 (1968).

3. Dieckman or Thorpe Cyclizations

Reference

- C. R. Krüger and E. G. Rochow, Angew. Chem. Int. Ed. Eng., 2, 617 (1963).

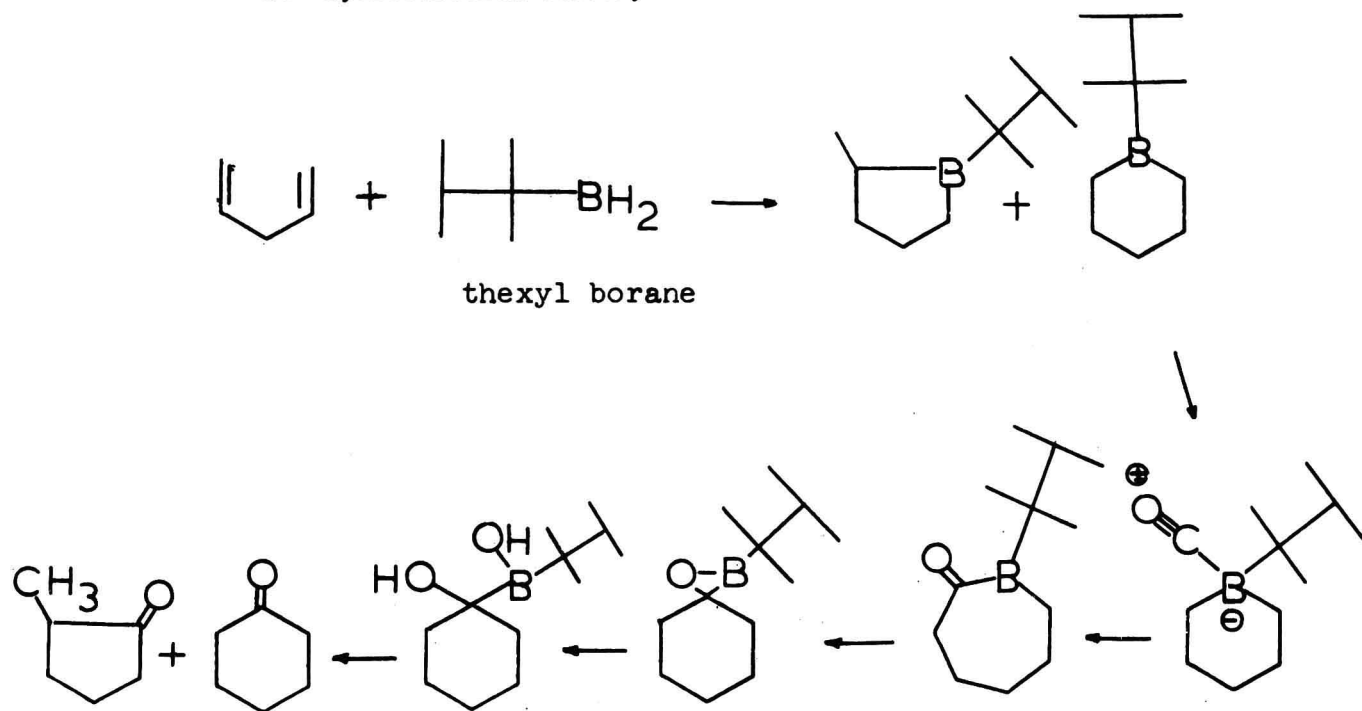
4. Acyloin condensation



Reference

J. J. Bloomfield, J. R. S. Irelan and A. P. Marchand,
Tetrahedron Lett., 5647 (1968).

5. Hydroboration-carbonylation

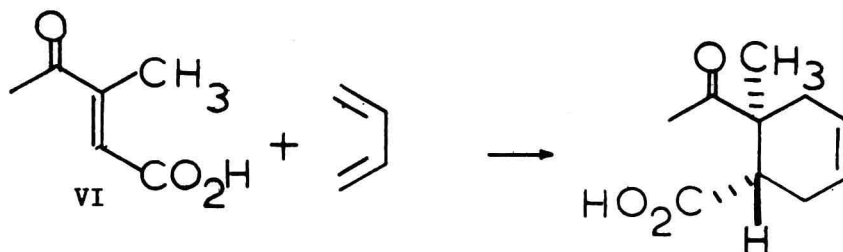
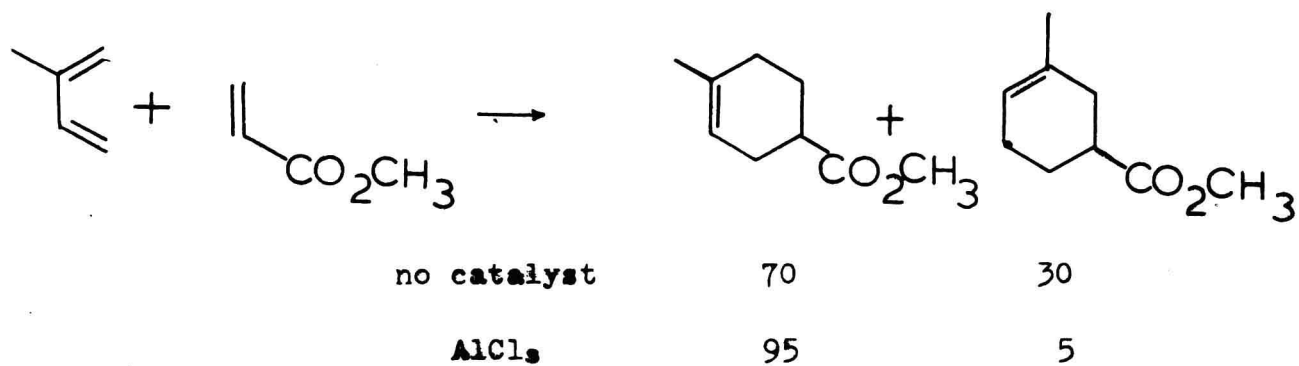


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H. C. Brown and E. Negishi, J. Amer. Chem. Soc., **89**, 5258, 5477 (1967).

6. Ylides

7. Cycloadditions



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- G. A. Berchtold, J. Ciabattini and A. A. Tunick, J. Org. Chem., **30**, 3679 (1969).
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C. Olefin formation

1. Dehydration

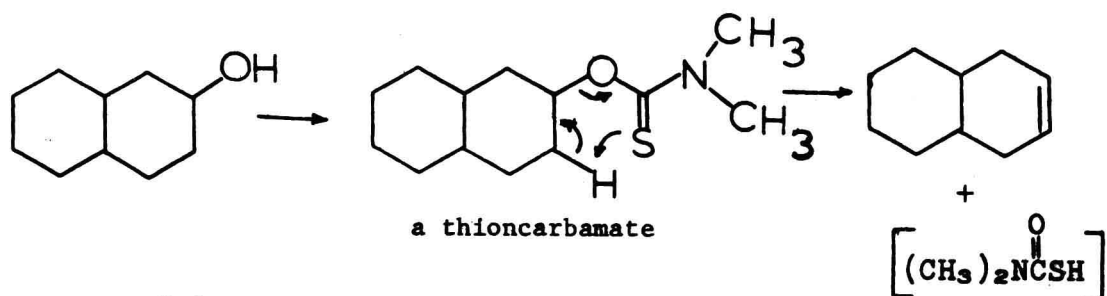
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V. J. Traynelis, W. L. Hergenrother, H. T. Hanson and J. A. Valicenti, J. Org. Chem., 29, 123 (1964).

2. Ester pyrolysis



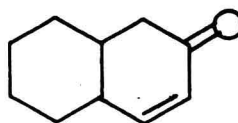
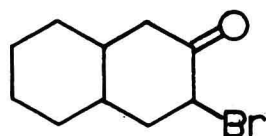
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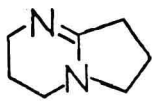
W. S. Briggs and C. Djerassi, J. Org. Chem., 33, 1625 (1968).

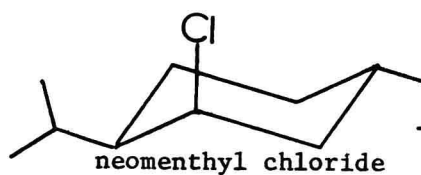
G. J. Karabatsos and K. L. Krumel, J. Amer. Chem. Soc., 91, 3324 (1969).

M. S. Newman and F. W. Hetzel, J. Org. Chem., 34, 3604 (1969).

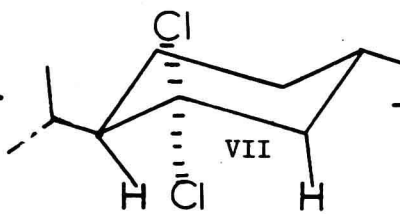
3. Dehydrohalogenation




1,5-diazabicyclo
[4.3.0.]non-5-ene



neomenthyl chloride



VII



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R. Hanna, Tetrahedron Lett., 2105 (1968).

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