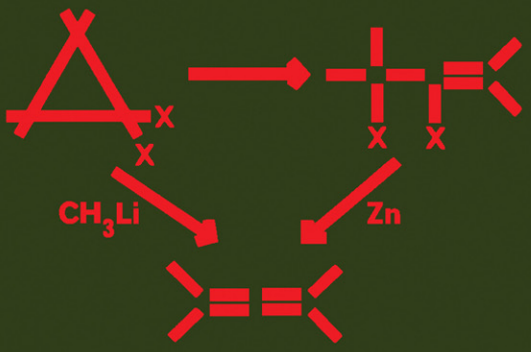


# ORGANIC FUNCTIONAL GROUP PREPARATIONS

By Stanley R. Sandler
and Wolf Karo

ORGANIC CHEMISTRY

A Series of Monographs

VOLUME 12-II

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# ORGANIC FUNCTIONAL GROUP PREPARATIONS

Volume II

This is Volume 12-II of
ORGANIC CHEMISTRY
A series of monographs
Edited by ALFRED T. BLOMQUIST, *Cornell University*

A complete list of the books in this series appears at the end of the volume.

# ORGANIC FUNCTIONAL GROUP PREPARATIONS

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## Chapter 16/ *C*-NITROSO COMPOUNDS



## Chapter 17/ *N*-NITROSO COMPOUNDS

# PREFACE

Volume II describes 17 additional functional groups and presents a critical review of their available methods of synthesis with preparative examples of each. Attention is especially paid to presenting specific laboratory directions for the many name reactions used in describing the synthesis of these functional groups.

The unique features of this work, as in Volume I, are that each chapter deals with the preparation of a given functional group by various reaction types (condensation, elimination, oxidation, reduction) and a variety of starting materials. In many cases the available data are summarized in tables to make them more useful to the reader. The literature has been checked up to 1970 and each chapter abounds with references.

The procedures for inclusion in this text, as in Volume I, had to meet the following requirements:

1. The laboratory operations should be safe and free from the danger of explosion.
2. The procedures should afford the highest yield possible of compounds of reliable structure.
3. The procedures should be relatively uncomplicated.
4. The procedures should be generally useful for a wide range of organic structures.

In several cases the preparations have been repeated in our laboratories, and supplementary information is given. As a general rule it is recommended that the purity of the products should be checked by gas chromatography especially if the procedure was originally described prior to 1960.

Some of the functional groups (ynamines, enamines, allenes, etc.) described in this volume have only of recent date been the subject of intensive investigation. For example, this volume contains the first preparative review of ynamines with synthesis procedures from the recent literature. In some chapters where reliable procedures for some compound types still do not exist, it is hoped that the reader will be stimulated to undertake research in these problem areas and report upon them.

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# ACKNOWLEDGMENTS

We would like to take this opportunity to thank Dr. Samuel Loshaek, Director of Research and Development of Borden Chemical, Division of Borden, Inc., Dr. Jack Dickstein, Manager of the Central Research Laboratories of Borden Chemical, Division of Borden, Inc., and also Dr. E. E. Rose, President, and Mr. H. K. Justi, Executive Vice President of Sartomer Resins, Inc. for encouragement and support in the preparation of this manuscript.

We express our gratitude to our wives and our families for their patience, understanding, and encouragement at all stages of the preparation of the manuscript.

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# ORGANIC FUNCTIONAL GROUP PREPARATIONS

Volume II

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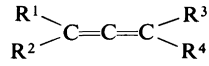
# CHAPTER 1 / ALLENES

## 1. INTRODUCTION

Reports on the synthesis of allenes by various methods have been increasing in the past few years. The synthesis of allenes involves some methods different from those described for the synthesis of olefins in Volume I, Chapter 2.

Allenes have the 1,2-diene structure (I), where $R^1$, $R^2$, $R^3$, $R^4$ = H, alkyl, aryl, halogen, heterocyclic, ether, etc. Since the terminal methylene groups lie



(I)

in mutually perpendicular planes, optical isomers are possible.

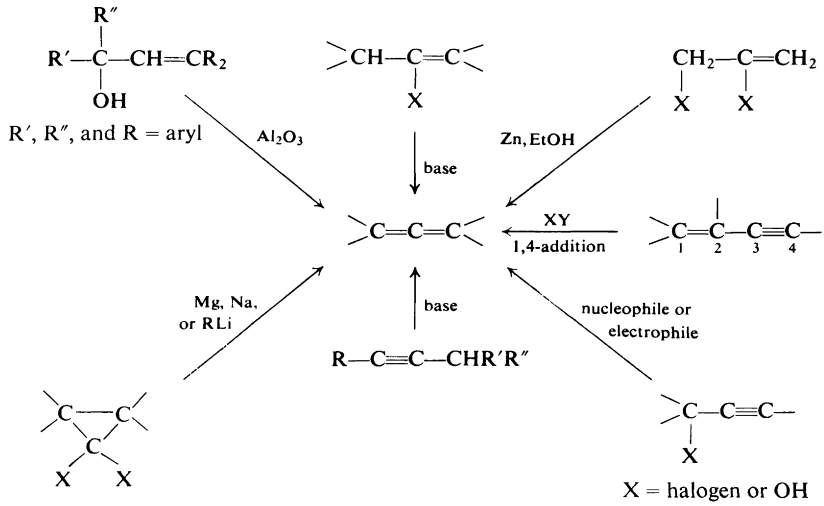
Allene is the generally accepted class name for all such compounds. However, the systematic name of 1,2-diene is also used as described for (II) and (III).

$CH_2{=}C{=}CH_2$
(II) Allene (Propadiene)

$CH_3{-}CH{=}C{=}CH{-}CH_3$
(III) 1,3-Dimethylallene (2,3-Pentadiene)

The first synthesis of allene was reported in 1887–1888 [1a–c]. Recently allenes have been screened for industrial applications in polymers [2,a b], antioxidants [3a, b], drugs [3a], dyes [3b], and fibers [4]. Allenes have also been

SCHEME 1

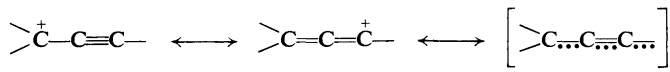


found to occur in the structure of compounds derived from natural organisms [5].

Allenes have been reviewed recently by Taylor [6], and earlier reviews [7a–e] are worth consulting.

Allenes are generally prepared by elimination of halogens, hydrogen halides, or water from adjacent carbon atoms, the dehalogenation of *gem*-dihalocyclopropanes, rearrangement of acetylenes, and the 1,4-addition to vinylacetylenes.

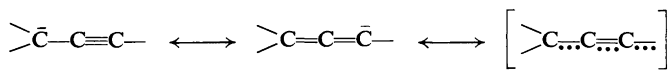
Richey [8], and then Pittman and Olah [9], observed the NMR spectra of acidic solutions of tertiary ethynyl carbinols, and their data support the idea that allenyl carbonium ions contribute significantly to the following ion structure:



(1)

Secondary ethynyl alcohols gave poor spectra because of the production of large amounts of by-products.

The structure of the propargyl-allenyl anion is still uncertain but by analogy to the carbonium ion above it may be that shown in Eq. (2).



(2)

## 2. ELIMINATION REACTIONS

The elimination reactions involving dehalogenation, dehydrohalogenation, and dehydration are often laborious compared to the more recent techniques involving dehalogenation of *gem*-dihalocyclopropanes [10a, b]. However, the availability of the starting materials is the deciding factor.

### A. Dehalogenation of *gem*-Dihalocyclopropanes

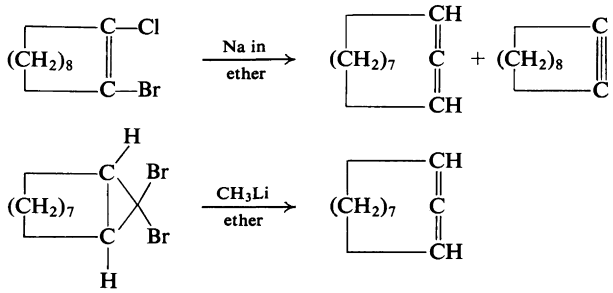
Doering and LaFlamme [10b] were the first to report that sodium and magnesium metal are capable of converting substituted *gem*-dibromocyclopropanes to allenes in varying yield. However, it was found that sodium reacts best in the form of a high surface dispersion on alumina. At a later date, Moore and Ward [11a] and then Skattebøl [12] reported that methyllithium or *n*-butyllithium reacts with *gem*-dibromocyclopropanes to give allenes in high yield. The related dichloro compounds were found to be inert to methyllithium but reacted slowly with *n*-butyllithium. Several examples of the preparation of allenes from *gem*-dibromocyclopropanes are shown in Table I.

The *gem*-dibromocyclopropanes are treated with an etheral solution of either methyllithium or *n*-butyllithium at 0° to −80°C. Methyllithium is preferable to *n*-butyllithium because occasionally difficulties are encountered in completely separating the *n*-butyl bromide from the allene product.

TABLE I
PREPARATION OF ALLENES FROM *gem*-DIBROMOCYCLOPROPANES

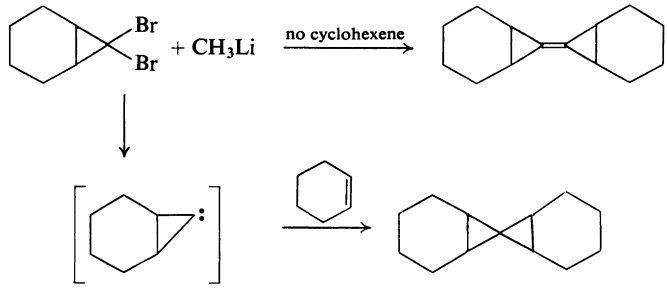
| Starting olefin | Product allene | Dehalogenating reagent | Yield (%) | Ref. |
|---|---|---|---|---|
| *trans*-2-Butene | 2,3-Pentadiene | Na–alumina | 44 | 10 |
| 1-Pentene | 1,2-Hexadiene | Na–alumina | 64 | 10 |
| 2-Methyl-2-butene | 2-Methyl-2,3-pentadiene | Mg | 34 | 10 |
| | | $CH_3Li$ | 69 | 12 |
| Isobutylene | 3-Methyl-1,2-butadiene | $CH_3Li$ | 92 | 12 |
| 1-Ethoxy-2-methyl-2-propene | 1-Ethoxy-3-methyl-1,2-butadiene | $CH_3Li$ | 71 | 12 |
| 1-Pentene | 1,2-Hexadiene | Mg | 45 | 10 |
| 2-Hexene | 2,3-Heptadiene | $CH_3Li$ | 88 | 11 |
| | | $C_4H_9Li$ | 83 | 11 |
| 1-Octene | 1,2-Nonadiene | $CH_3Li$ | 81 | 11 |
| | | $C_4H_9Li$ | 49 | 11 |
| 1-Decene | 1,2-Undecadiene | $CH_3Li$ | 68 | 11 |
| | | $C_4H_9Li$ | 43 | 11 |
| *cis*-Cyclooctene | 1,2-Cyclononadiene | $CH_3Li$ | 81 | 11 |
| *cis*-Cyclononene | 1,2-Cyclodecadiene | $C_4H_9Li$ | 78 | 11 |
| *cis*-Cyclodecene | 1,2-Cycloundecadiene | $C_4H_9Li$ | 89 | 11 |
| Styrene | 1-Phenylpropadiene | $CH_3Li$ | 82 | 12 |
| 1,1-Diphenylethylene | 1,1-Diphenylpropadiene | $CH_3Li$ | 43 | 12 |
| Cycloocta-1,5-diene | 1,2,6-Cyclononatriene | $CH_3Li$ | 80 | 12 |

The $C_8$–$C_{11}$ cyclic allenes [11a, b] which have been synthesized by this route are obtained only with difficulty by other methods [13] as mixtures with the corresponding acetylenic isomer (Eqs. 3).




(3)

Smaller cyclic olefins react with dibromocarbene to give the *gem*-dibromobicyclic systems, but these have not been reported to give allenes on reaction with methyl- or *n*-butyllithium. One possible reason may be the severe ring strain of cyclic allenes with less than seven carbon atoms. For example, Moore and Ward [14] found that 7,7-dibromobicyclo[4.1.0]heptane reacts with methyllithium to give bicyclic carbene intermediates which can be trapped with olefins (Eq. 4).

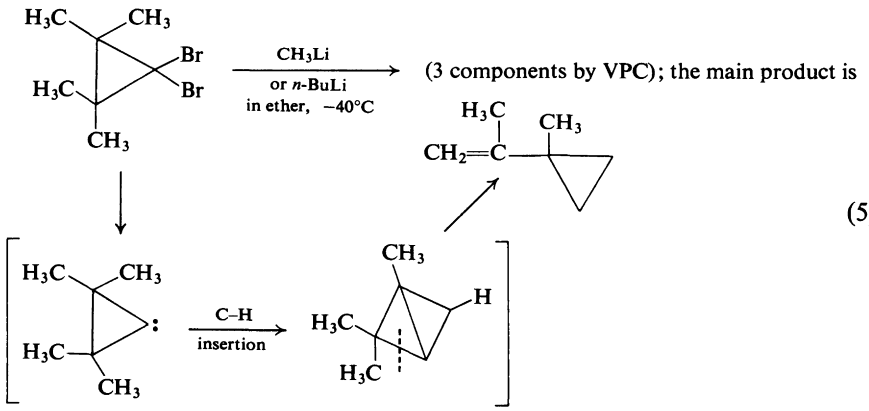



(4)

Skattebøl [12], on the other hand, could not detect such carbene intermediates by their addition product (spiropentanes) to olefins using *gem*-dibromocyclopropanes derived from noncyclic olefins.

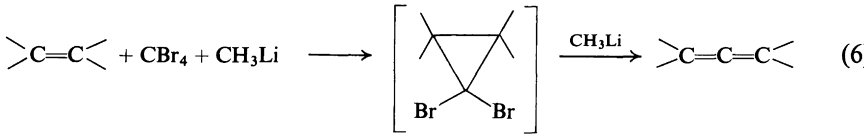
In a few cases, allenes are not always the sole product. For example, 1,1-dibromotetramethylcyclopropane does not give tetramethylallene but a mixture of products which is mainly 1-methyl-1-isopropenylcyclopropane [12] (Eq. 5).

The preparation and dehalogenation of *gem*-dibromocyclopropanes to give allenes can be carried out in one step by the reaction an excess of olefins with




(5)

carbon tetrabromide and 2 equivalents of methyllithium in ether at –65°C [15]. Using *n*-butyllithium in hexane gives reduced yields, as in the two-step process [11, 12] (Eq. 6). (Table II lists a few cyclic allenes prepared by this one-step process.)

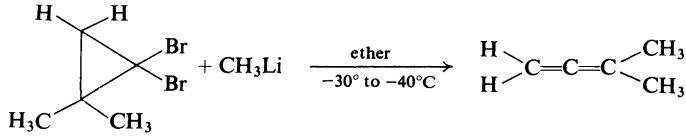



(6)

TABLE II
ONE-STEP OLEFIN-TO-ALLENE CONVERSION USING CARBON TETRABROMIDE–OLEFIN–LITHIUM ALKYL

| Olefin | R–Li | Temp. (°C) | Allene | Yield (%) |
|---|---|---|---|---|
| *cis*-Cyclooctene | $CH_3$ | –65 | 1,2-Cyclononadiene | 74 |
| 1,5-Cyclooctadiene | $CH_3$ | –65 | 1,2,6-Cyclononatriene | 64–71 |
| | $C_4H_9$ | –65 | 1,2,6-Cyclononatriene | 37 |

### 2-1. *Preparation of 3-Methyl-1,2-butadiene* [12]

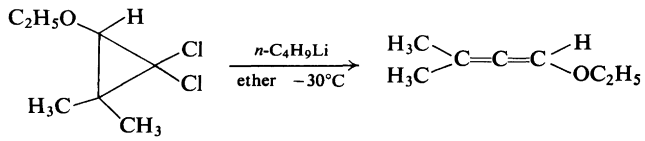



(7)

To a flask cooled with Dry Ice–acetone (–30° to –40°C) and containing 22.8 gm (0.10 mole) of 1,1-dibromo-2,2-dimethylcyclopropane and 25 ml of dry ether is added 2.2 gm (0.10 mole) of methyllithium in 80 ml of ether over a ½ hr period. The reaction mixture is stirred for ½ hr, hydrolyzed with water, the ether separated, washed with water, dried, and distilled to afford 6.2 gm (92%), b.p. 40°C, $n_D^{24}$ 1.4152.

1-Phenyl-1,2-propadiene, b.p. 64°–65°C (11 mm), $n_D^{24}$ 1.5809, is obtained in a similar manner in 82% yield by the reaction of 1,1-dibromo-2-phenylcyclopropane with methyllithium at –60°C.

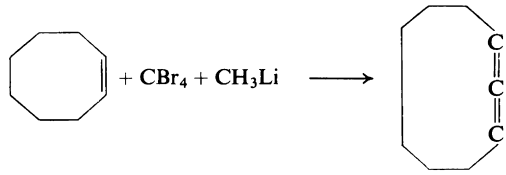
### 2-2. *Preparation of 1-Ethoxy-3-methyl-1,2-butadiene* [16]




(8)

To a flask cooled to −30° to −40°C and containing 20.0 gm (0.11 mole) of 1,1-dichloro-2-ethoxy-3,3-dimethylcyclopropane in 30 ml of dry ether is added dropwise 100 ml of a 1.3 *M* ethereal *n*-butyllithium solution (0.13 mole) over a 1 hr period. The reaction mixture is then stirred for an additional ½ hr while it is warmed to room temperature. Water is added, the ether is separated, washed with water, dried over sodium carbonate, and then fractionally distilled to afford 7.3 gm (59%) of impure allene, b.p. 55°–57°C (65 mm), $n_D^{25}$ 1.4344. Redistillation gives a pure product, b.p. 51°C (60 mm), $n_D^{20}$ 1.4400.

***2-3. One-Step Olefin-to-Allene Conversion of cis-Cyclooctene to 1,2-Cyclononadiene*** [16]

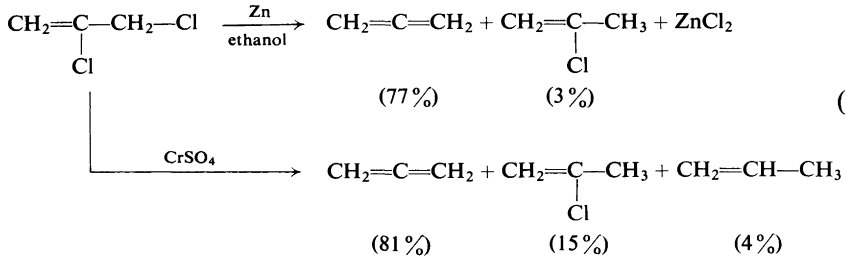



(9)

To a stirred reaction mixture consisting of 55.0 gm (0.50 mole) of *cis*-cyclooctene and 41.5 gm (0.125 mole) of carbon tetrabromide cooled to −65°C is added 74.0 ml (0.125 mole) of methyllithium in ether (Foote Mineral Co.) over a 45 min period. After stirring at −65° to −68°C for an additional ½ hr, another 80.5 ml (0.135 mole) of methyllithium is added over a ½-hour period. The reaction mixture is stirred for another ½ hr at −68°C, warmed to 0°C, water added, the ether separated, washed with water until neutral, dried over sodium sulfate, and then fractionally distilled to afford 11.3 gm (74%), b.p. 62°–63°C (16 mm), $n_D^{20}$ 1.5060.

## B. Dehalogenation of Vicinal Dihalo Compounds

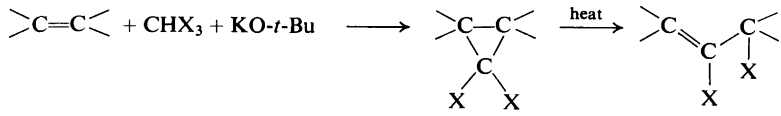
The use of zinc in ethanol to dehalogenate haloallyl halides to allenes was reported earlier by Gustavson and Demjanoff [17a, b]. This method is still a useful one and has been applied when the starting dihalides are available. Recently chromous sulfate has also been shown to be an effective reagent at room temperature [17c] (Eq. 10).




(10)

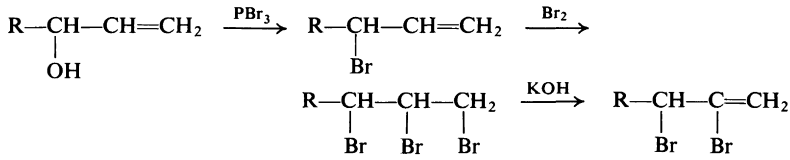
The main drawback to the dehalogenation method is that the haloallyl halides are usually difficult to obtain. Some of the available methods of synthesis of haloallyl halides are the following.

(1) Thermal rearrangement of *gem*-dihalocyclopropanes [17d]:



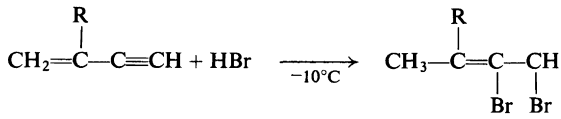
(11)

(2) Reaction of allyl alcohols [7a]:



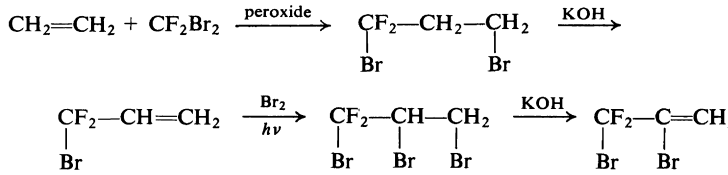
(12)

(3) Reaction of vinylacetylene with HBr [18]:



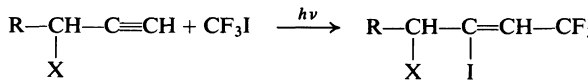
(13)

(4) Free radical reaction of alkenes with tetrahalomethanes [19]:



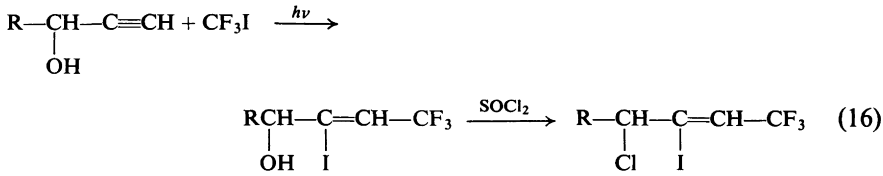
(14)

(5) Free radical addition of trifluoroiodomethane with propargyl halides [20]:



(15)

(6) Free radical addition of trifluoroiodomethane with propargyl alcohols [20]:



(16)

### 2-4. *Preparation of 1,1-Difluoroallene* [19]



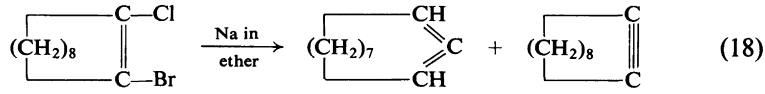
(17)

To a flask equipped with stirrer, condenser, and dropping funnel is added 40.0 gm (0.61 gm-atom) of zinc dust in 40 ml of absolute ethanol. After the condenser outlet is connected to a series of Dry Ice–acetone traps cooled to −80° to −70°C, the mixture is heated to gentle reflux while 20.3 gm (0.0852 mole) of 1,2-dibromo-1,1-difluoropropene in 30 ml of 95% ethanol is added dropwise over a 2 hr period. The reaction mixture is heated for an additional hour, and then the gaseous products which are condensed in the Dry Ice traps are purified by several vaporization distillations to afford 3.6 gm (56%) b.p. −21° to −20°C (thermocouple immersion), ir 4.95 μ $\left(\rangle C{=}C{=}C\langle\right)$ and no absorption at 4.6 μ (—C≡C—). The addition of bromine at −80°C yields the starting material. At room temperature under pressure in the absence of oxygen the product allene slowly polymerizes to a water-white viscous liquid.

Allene has been prepared recently [17b] in a similar manner by adding 260 gm (2.34 moles) of 2,3-dichloropropene dropwise over a 2–3 hr period to a refluxing mixture of 400 ml of 95% ethanol, 80 ml of water, and 300 gm (4.6 gm-atoms) of zinc dust. The allene is trapped and purified in a manner similar to 1,1-difluoroallene.

Sodium metal in ether has also been used to dehalogenate cyclic 1,2-dihaloalkenes to cyclic allenes with some cyclic alkyne as a by-product [13].

### 2-5. *Preparation of 1,2-Cyclodecadiene* [13]



(18)