



Fragmentation of methylvinyl ketone dimer bicyclic acetals
by Roger Scott Bain

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in
Chemistry

Montana State University

© Copyright by Roger Scott Bain (1993)

Abstract:

Fragmentation of 5,7,7-trimethyl-6,8-dioxabicyclo[3.2.1]octane was investigated with different Lewis acids. The Lewis acids used in the study were: aluminum trichloride, tin tetrachloride, and titanium tetrachloride. The aluminum trichloride gives the most fragmentation products at room temperature. Tin tetrachloride produces the most products, at reflux. The 7-methyl-2,6-octadione was determined to be a reasonable intermediate for the fragmentation reaction. Two novel products were characterized from the fragmentation reaction.

FRAGMENTATION OF METHYL VINYL
KETONE DIMER BICYCLIC
ACETALS

By

Roger Scott Bain

A thesis submitted in partial fulfillment
of the requirements for the degree

of

Master of Science

in

Chemistry

MONTANA STATE UNIVERSITY
Bozeman, Montana

December 1993

APPROVAL

of a thesis submitted by

Roger Scott Bain

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

December 16, 1993
Date

Arnold C. Craig
Chairperson, Graduate
Committee

Approved for the Major Department

12/16/93
Date

David M. Swley
Head, Major Department

Approved for the College of Graduate Studies

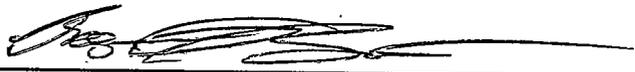
12/17/93
Date

Ed Brown
Graduate Dean

STATEMENT OF PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for a master's degree at Montana State University, I agree that the Library shall make it available to borrowers under rules of the Library.

If I have indicated my intention to copyright this thesis by including a copyright notice page, copying is allowable only for scholarly purposes, consistent with "fair use" as prescribed in the U.S. Copyright Law. Requests for permission for extended quotation from or reproduction of this thesis in whole or in parts may be granted only by the copyright holder.

Signature Date DEC. 16, 1993

To
The ladies in my life, with love

ACKNOWLEDGMENTS

This endeavor would have been impossible without help from a number of people. Special thanks go out to....

Dr. B.P. Mundy

Dr. A.C. Craig

Dr. M.S. Rees

Dr. T.S. Livinghouse

Dr. P.W. Jennings

Dr. E.C. Lund

Dr. S.R. Harring

Dr. P.L. McGrane

Mr. K.T. Hanson

Mr. R. Hughes

Mr. M. Morrison

Mr E. Adams

Dr. K. Strode

Ms. S.S. Siewert

Dr. J. Sears

all of my friends,

and Family

TABLE OF CONTENTS

	page
LIST OF TABLES.....	vii
LIST OF FIGURES.....	viii
ABSTRACT.....	ix
1. INTRODUCTION.....	1
2. RESULTS AND DISCUSSION.....	8
3. CONCLUSION.....	21
4. EXPERIMENTAL.....	22
REFERENCES.....	39

LIST OF TABLES

Table		Page
1.	Reaction of SnCl_4 with 7	11
2.	Reaction of TiCl_4 with 7.....	12
3.	Reaction of AlCl_3 with 7.....	13

LIST OF FIGURES

Figure	Page
1. Natural 6,8-Dioxabicyclo[3.2.1]octanes.....	1
2. Synthesis of (cis-6-methyltetrahydropyran-2-yl)acetic acid.....	2
3. Synthesis of natural products from AcI fragmentation.....	3
4. Bartelt fragmentation.....	4
5. Jun fragmentation.....	4
6. AlI_3 fragmentation.....	5
7. Synthesis of 7.....	6
8. Synthesis with (MVK) $_2$	7
9. $AlCl_3$ fragmentation products.....	8
10. Proposed Mechanism for Fragmentation.....	10
11. CH_2Cl_2 22°C.....	14
12. CH_2Cl_2 66°C.....	14
13. Reaction of Br_2 with 7.....	16
14. Proposed synthesis with 13.....	18
15. Proposed synthesis of Valerane backbone.....	19
16. Proposed synthesis of Eremophilone skeleton...	20

ABSTRACT

Fragmentation of 5,7,7-trimethyl-6,8-dioxabicyclo[3.2.1]octane was investigated with different Lewis acids. The Lewis acids used in the study were: aluminum trichloride, tin tetrachloride, and titanium tetrachloride. The aluminum trichloride gives the most fragmentation products at room temperature. Tin tetrachloride produces the most products at reflux. The 7-methyl-2,6-octadione was determined to be a reasonable intermediate for the fragmentation reaction. Two novel products were characterized from the fragmentation reaction.

CHAPTER 1

INTRODUCTION

Interest in the 6,8-dioxabicyclo[3.2.1]octane 1 skeleton is derived from the fact that there are a number of natural products with this structural feature. The numbering convention used in this paper, is shown in Figure 1.

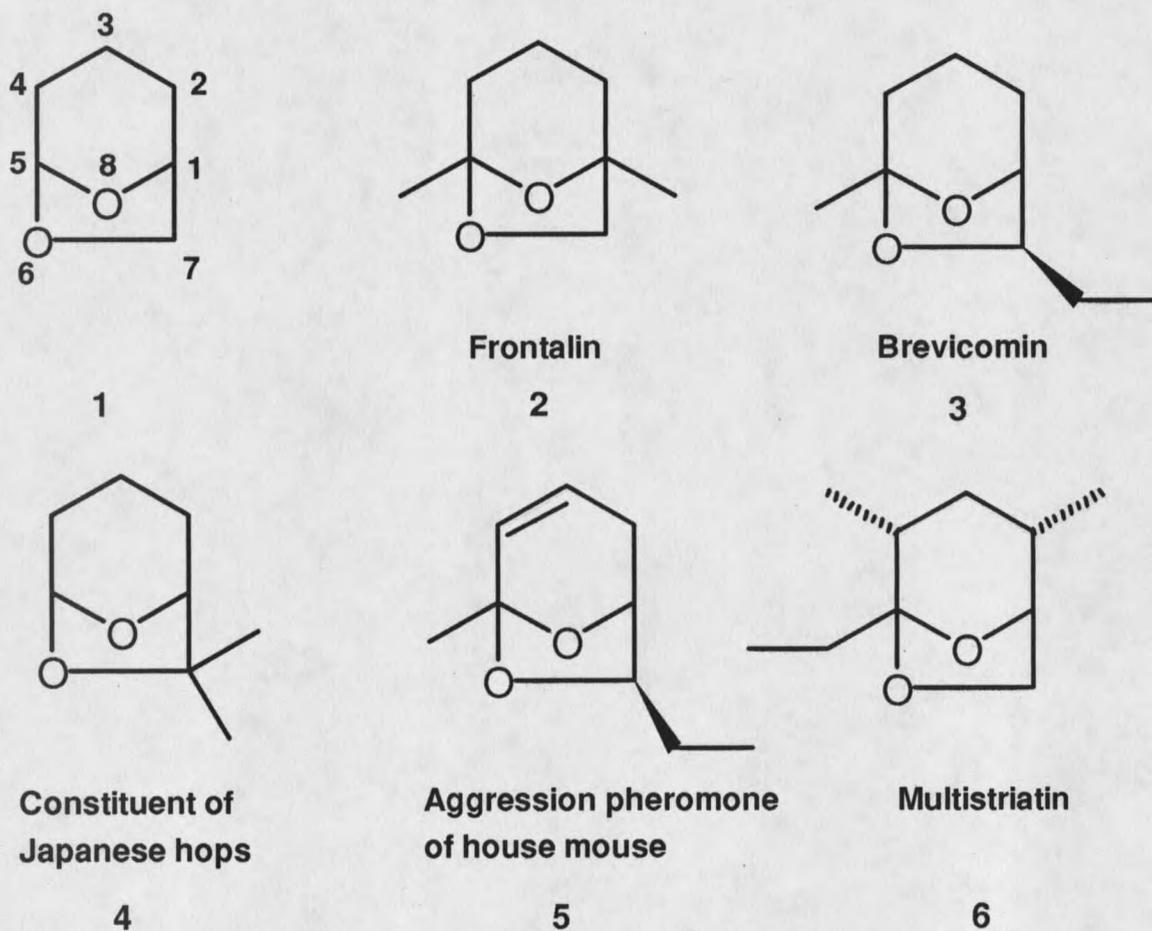
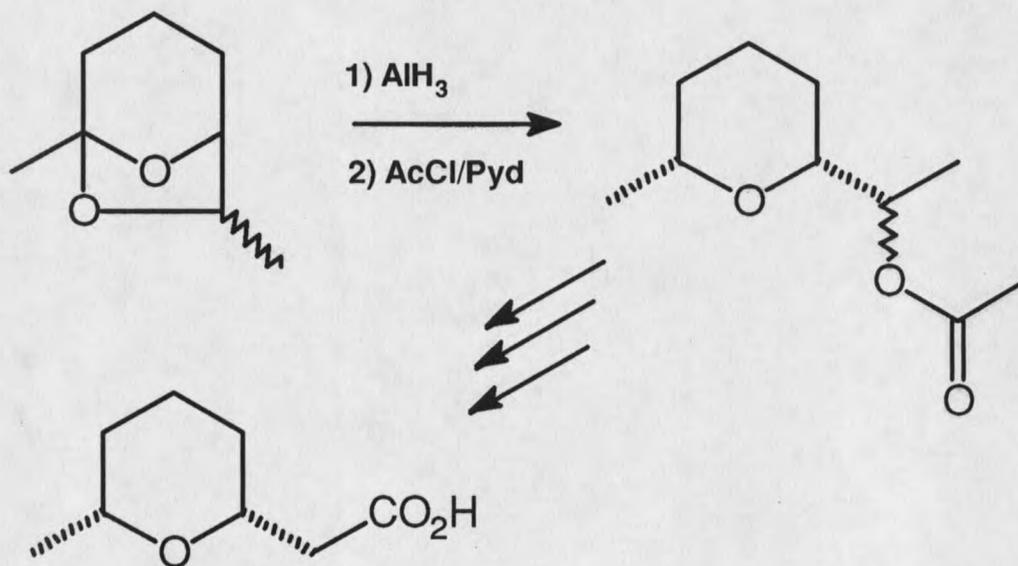


Figure 1. Natural 6,8-Dioxabicyclo[3.2.1]octanes

The number of reported syntheses of frontalin¹, and brevicomin² in the past several years is high. The methodology is diverse; from radical¹ chemistry to fermentation² chemistry. The 6,8-dioxabicyclo[3.2.1]octane skeleton has a unique characteristic, it contains a bicyclic acetal. The term acetal is used, instead of ketal, to be consistent with what is now generally reported in the literature. It is noted that acetals are generally found in synthesis as protecting groups for ketones and aldehydes. Usually, when acetals are cleaved with acid, the resulting products are a diol and the ketone or aldehyde. So, when the acetal is part of a bicyclic ring system, the



Constituent of Civet

Figure 2. Synthesis of
(*cis*-6-methyltetrahydropyran-2-yl)acetic Acid

fragmentation of the ring system can lead to novel products. The 6,8-dioxabicyclo[3.2.1]octane frame is useful as synthetic intermediates^{3,4}, shown in Figures 2 and 3, for natural products. With this in mind, more modes of fragmentation were investigated.

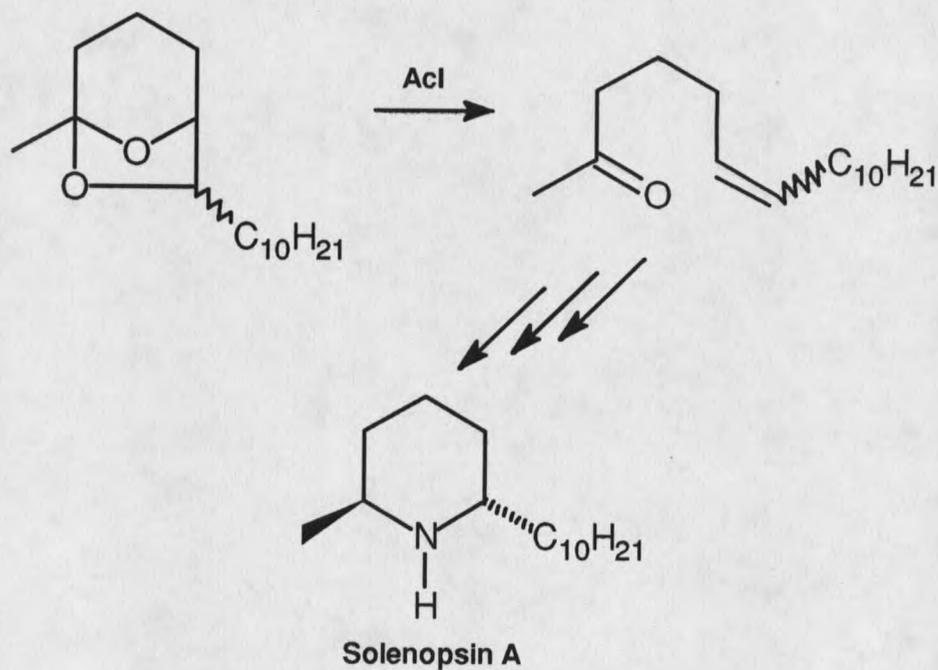
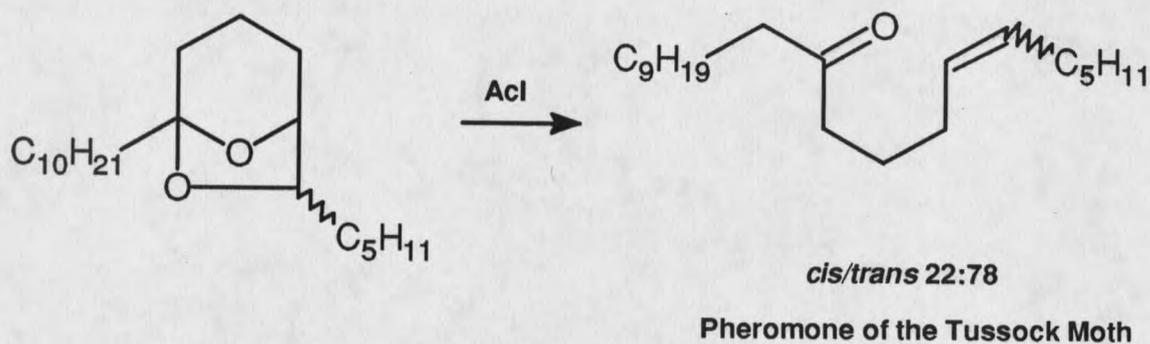


Figure 3. Synthesis of natural products from Acl fragmentation

Bartelt⁵ has demonstrated that when a bicyclic acetal is treated with trialkyl aluminum reagents; the product is an alcohol (Figure 4).

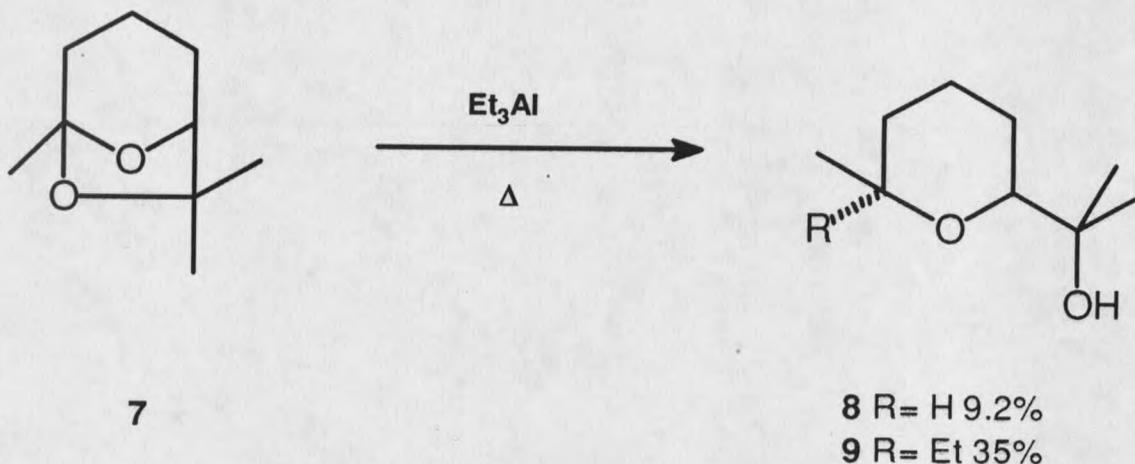


Figure 4. Bartelt fragmentation

More recently, Jun⁶ has reported the formation of a cyclopentane diol from a bicyclic acetal (Figure 5).

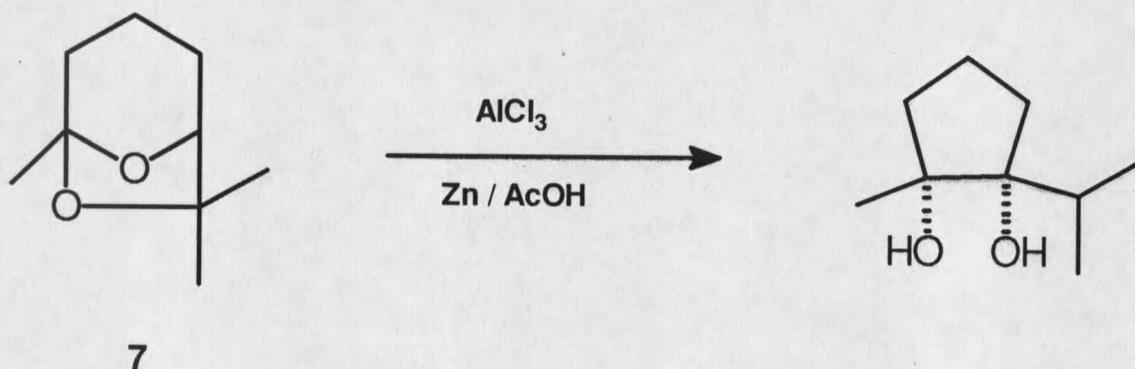


Figure 5. Jun fragmentation

During the search for new products of the fragmentation reaction, we decided to study the product ratios obtained with different Lewis acids; and to investigate how the solvent influences the reaction. What can be said about the mechanism of the reaction? What are the possible uses of the fragmentation product? The starting point of the investigation began with results reported by Jun⁷; the reaction of 7 with AlI_3 in refluxing acetonitrile; as shown in Figure 6.

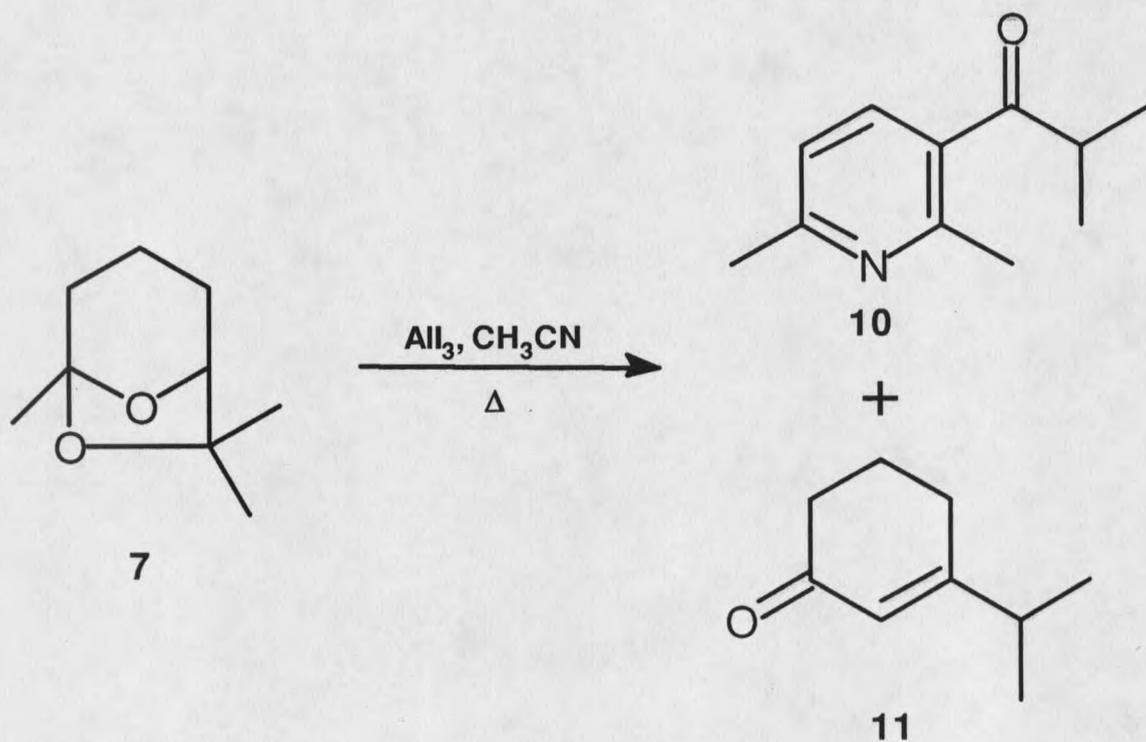


Figure 6. AlI_3 fragmentation

As shown in Figure 7, compound 7 was synthesized from methyl vinyl ketone (MVK). The intermediate of the reaction sequence is MVK dimer (MVK)2.

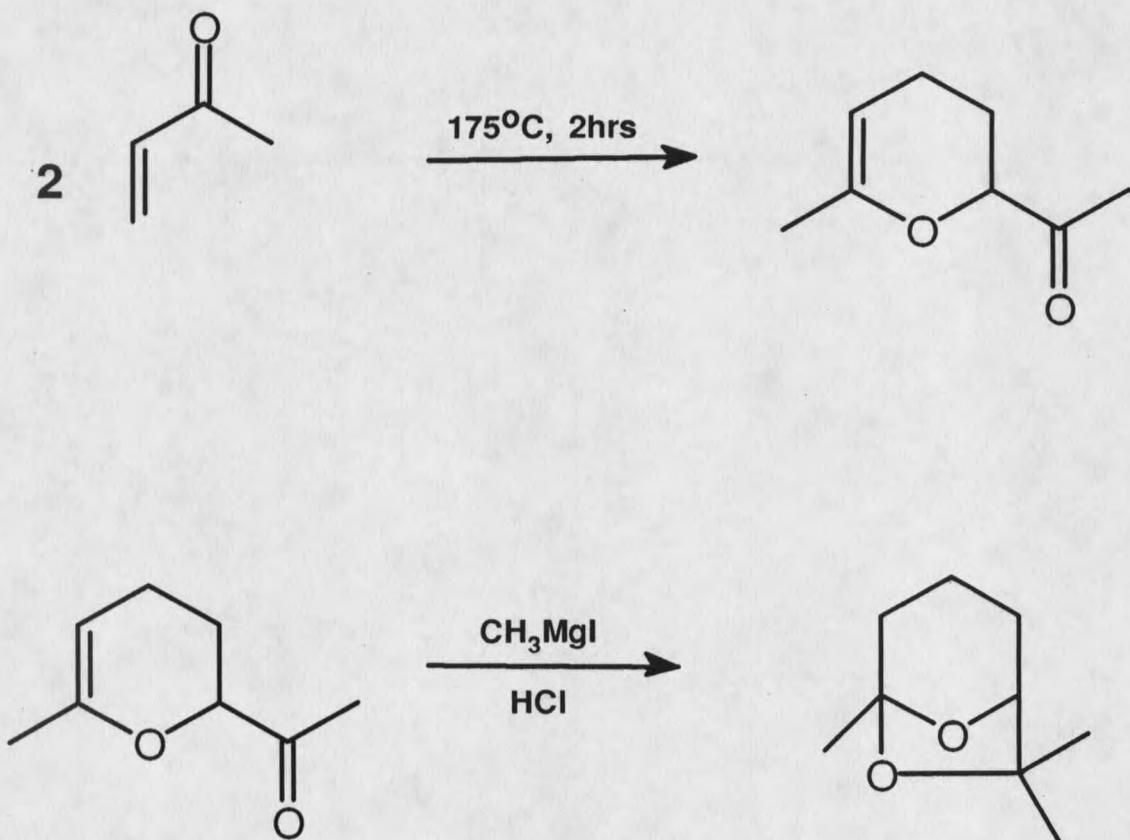


Figure 7. Synthesis of 7

(MVK)2 was thought to be a useful building block for 7-acetyl-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3H)-naphthalenone as shown in Figure 8. We desired to determine if acetal 7, could be further functionalized after treatment with bromine. If so, it would add to the diverse uses of bicyclic acetals in synthesis.

