INFORMATION TO USERS

This dissertation was produced from a microfilm copy of the original document. While the most advanced technological means to photograph and reproduce this document have been used, the quality is heavily dependent upon the quality of the original submitted.

The following explanation of techniques is provided to help you understand markings or patterns which may appear on this reproduction.

1. The sign or "target" for pages apparently lacking from the document photographed is "Missing Page(s)". If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting thru an image and duplicating adjacent pages to insure you complete continuity.

2. When an image on the film is obliterated with a large round black mark, it is an indication that the photographer suspected that the copy may have moved during exposure and thus cause a blurred image. You will find a good image of the page in the adjacent frame.

3. When a map, drawing or chart, etc., was part of the material being photographed the photographer followed a definite method in "sectioning" the material. It is customary to begin photoing at the upper left hand corner of a large sheet and to continue photoing from left to right in equal sections with a small overlap. If necessary, sectioning is continued again — beginning below the first row and continuing on until complete.

4. The majority of users indicate that the textual content is of greatest value, however, a somewhat higher quality reproduction could be made from "photographs" if essential to the understanding of the dissertation. Silver prints of "photographs" may be ordered at additional charge by writing the Order Department, giving the catalog number, title, author and specific pages you wish reproduced.

University Microfilms

300 North Zeeb Road
Ann Arbor, Michigan 48106

A Xerox Education Company

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

73-6483

KO, Ming, 1946-
SUBSTITUENT EFFECT ON PHOTOCHEMICAL REARRANGEMENTS OF CROSS-CONJUGATED CYCLOHEXADIENONES RELATED TO INDANONE.

Georgia Institute of Technology, Ph.D., 1972
Chemistry, organic

University Microfilms, A XEROX Company, Ann Arbor, Michigan

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

SUBSTITUENT EFFECT ON PHOTOCHEMICAL REARRANGEMENTS OF CROSS-CONJUGATED CYCLOHEXADIENONES RELATED TO INDANONE

A THESIS

Presented to

The Faculty of the Graduate Division

by

Ming Ko

in Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

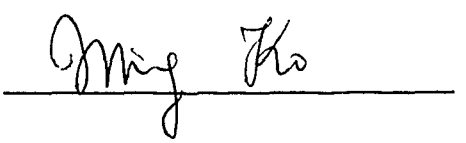
in the School of Chemistry

Georgia Institute of Technology

August, 1972

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

In presenting the dissertation as a partial fulfillment of the requirements for an advanced degree from the Georgia Institute of Technology, I agree that the Library of the Institute shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to copy from, or to publish from, this dissertation may be granted by the professor under whose direction it was written, or, in his absence, by the Dean of the Graduate Division when such copying or publication is solely for scholarly purposes and does not involve potential financial gain. It is understood that any copying from, or publication of, this dissertation which involves potential financial gain will not be allowed without written permission.



7/25/68

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

SUBSTITUENT EFFECT ON PHOTOCHEMICAL

REARRANGEMENTS OF CROSS-CONJUGATED CYCLOHEXADIENONES

RELATED TO INDANONE

Approved:

D. S. Caine, Chairman

Date approved by Chairman: September 1, 1972

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

PLEASE NOTE:

Some pages may have

indistinct print.

Filmed as received.

University Microfilms, A Xerox Education Company

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

ACKNOWLEDGMENTS

The author wishes to express his most sincere appreciation and gratitude to Professor D. S. Caine for his inspiring guidance step by step through the course of this research. His attitude and achievement in teaching and working provides an admirable figure of an educator and research worker for his students.

The author is indebted to Professors C. L. Liotta and J. C. Powers for their serving on the reading committee. He would like to thank Professor W. M. Spicer for the offer of a Graduate Teaching Assistantship for the first year of his study at the Georgia Institute of Technology.

Special thanks are due to Dr. Norman Tuller and Dr. Paul Ingwalson who provided technical assistance and helpful suggestions.

For their love and sacrifice the author is most deeply indebted to his parents abroad. Finally, the author would like to acknowledge the tireless assistance and constant encouragement of Miss Q. J. Hsieh. She not only helped to type the manuscripts several times, but also shared the sweetness and bitterness throughout this endeavor.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE OF CONTENTS

Page

ACKNOWLEDGMENTS ii

LIST OF CHARTS v

LIST OF TABLES vii

GLOSSARY OF ABBREVIATIONS viii

SUMMARY ix

Chapter

I INTRODUCTION 1

II INSTRUMENTATION AND EQUIPMENT 16

III EXPERIMENTAL 18

4,7a-Dimethyl-7,7a-dihydro-5(6H)-indanone(31b)
4,7a-Dimethyl-5(7aH)-indanone (28b)
Irradiation of 4,7a-Dimethyl-5(7aH)-indanone(28b) in Dioxane
Irradiation of 7,7a-Dimethyl-3a,7a-dihydro-3a,7cyclo-6(7H)-inadnone(29b)in Dioxane
Irradiation of 4,7a-Dimethyl-5(7aH)-indanone(28b)
Irradiation of 7,7a-dimethyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone(29b) in Absolute Ethanol
Irradiation of 28b in Absolute Ethanol
Irradiation of 4,4-dimethyl-5(4H)-indanone(32b) in Absolute Ethanol
Further Photolysis of 34 in Absolute Ethanol
1,4a-Dimethyl-3,4,5,6,7,8-hexadro-2(4aH)naphthalenone(38)
1,4a-Dimethyl-5,6,7,8-tetrahydro-2(4aH)naphthalenone(3b)
Irradiation of 1,4a-dimethyl-5,6,7,8-tetrahydro-2(4aH) naphthalenone(3b)in Dioxane
Irradiation of 1,8a-dimethyl-4a,5,6,7,8,8a-hexahydro-1,4a-cyclo-2(1H)naphthalenone(4b)
7,7a-Dihydro-7a-methyl-5(6H)-indanone(31a)
7a-Methyl-5(7aH)-indanone(28a)
Irradiation of 7a-methyl-5(7aH)-indanone(28a) in Dioxane at 2537 Å
Irradiation of 7a-Methyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone(29a)in Anhydrous Dioxane: Broad Spectrum Lamp

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE OF CONTENTS (Continued)

Page

Chapter

III EXPERIMENTAL (Continued)

Irradiation of 7a-Methyl-5(7aH)-indanone(28a) in Anhydrous Dioxane: Broad Spectrum Lamp
Irradiation of 7a-Methyl-5(7aH)-indanone in 45 Percent Methanolic Acetic Acid
Irradiation of 7a-Methyl-5(7aH)-indanone(28a)in Anhydrous Methanol, Broad Spectrum Lamp
Treatment of the 9-Methyl-5-methoxytricyclo-[4.3.$0^{2,9}$]-3-nonanone(42)with Lithium in Ammonia
Treatment of 7-Methyl-4a-methoxy-2-indanone(44)with Sodium Hydride
Preparation of 7a-Methyl-4-carbomethoxy-7,7a-dihydro-5(6H)-indanone(31j)
Attempted Dehydrogenation of 31j with DDQ
Attempted Dehydrogenation of 31j with Selenium Dioxide
7,7a-Dihydro-4-methoxy-7a-methyl-5(6H)-indanone(31d)
4-Methoxy-7a-methyl-5(7aH)-indanone(28d)
Irradiation of 4-Methoxy-7a-methyl-5(7aH)-indanone (28d) in Anhydrous Dioxane
4-Methoxy-7a-isopropyl-5(7aH)-indanone(28i)
Irradiation of 28i in Anhydrous Dioxane 2537 Å Light Source
Irradiation of 28i in Anhydrous Dioxane with Pyrex Filter
Preparation of 4-methoxy-10-methyl-$\Delta^{1,4}$-3-hexahydronaphthalenone(3d)
Irradiation of 3d in Anhydrous Dioxane
Preparation of 6-Acetoxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(55)
Saponification and Oxidation of 55; Attempted Preparation of 6-Methoxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(28e)
Attempted Preparation of 28e by Other Methods
Irradiation of 28e in Anhydrous Dioxane
Irradiation of 6-Methoxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(28e)in Methanol
Attempted Preparation of 6-Carboxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(28ℓ)
Preparation of Ethyl 2-(3'-oxobutyl)-cyclopentanone-2-carboxylate(60)
Cyclization of Ethyl 2-(3'-oxobutyl)-cyclopentanone-2-carboxylate(60)
Methyl 5-Oxo-5,6,7,8-tetrahydroindane-8-carboxylate (Alternate Method)
Dehydrogenation of 7,7a-dihydro-7a-carboethoxy-5(6H)-indanone 31h with DDQ

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

TABLE OF CONTENTS (Concluded)

Page

Chapter

III EXPERIMENTAL (Continued)

Irradiation of 28h (2537 Å Light Source) in Dioxane
Irradiation of 28h in Anhydrous Ethyl Alcohol
Irradiation of 28h in 45 Percent Aqueous Acetic Acid
Irradiation of 28h in Ethyl Alcohol, Broad Spectrum Lamp
Irradiation of 28h in Anhydrous Dioxane, Broad Spectrum Lamp
Irradiation of 28h in Anhydrous Ether
Irradiation of 28h in Anhydrous Ethyl Alcohol: Broad Spectrum Lamp with Quartz Flask
Irradiation of 28h in Anhydrous Dioxane: Broad Spectrum Lamp Without Pyrex Filter

IV DISCUSSION OF RESULTS 56

V CONCLUSIONS 89

VI RECOMMENDATIONS 91

APPENDIX 93

LITERATURE CITED 103

VITA 108

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

LIST OF CHARTS

Chart		Page
1.	Chart 1	2
2.	Chart 2	3
3.	Chart 3	4
4.	Chart 4	6
5.	Chart 5	7
6.	Chart 6	9
7.	Chart 7	11
8.	Chart 8	13
9.	Chart 9	15
10.	Chart 10	57
11.	Chart 11	64
12.	Chart 12	65
13.	Chart 13	76
14.	Chart 14	81
15.	Chart 15	87

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

LIST OF TABLES

Table		Page
1.	Irradiation of 7,7a-Dimethyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone	22
2.	Comparison of Light Absorption of Some Cyclic Dienones . . .	62
3.	Comparison of Spectral Properties of 42, 43 with 49, 50 . .	73
4.	Irradiation of 28h Under Various Conditions	85
5.	Comparison of nmr Spectra of 62 and 81	86

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

GLOSSARY OF ABBREVIATIONS

DDHQ	2,3-Dicyano-5,6-dichlorobenzohydroquinone
DDQ	2,3-Dicyano-5,6-dichlorobenzoquinone
DME	1,2-Dimethoxyethane
DMSO	Dimethylsulfoxide
glc	Gas Liquid Chromatography
Hz	Hertz
ir	Infrared
nm	Nanometer
nmr	Nuclear Magnetic Resonance
ppm	Parts per Million
SE-30	Silicone Gum Rubber (methyl)
TMS	Tetramethylsilane
uv	Ultraviolet

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

SUMMARY

The purpose of this research was to study the effects of substituent on the course of photochemical rearrangements of bicyclic cross-conjugated cyclohexadienones. The photochemical behavior of compounds having a five-membered B ring fused to the chromophore was particularly of interest.

The bicyclic 6/5-fused cyclohexadienones 28a, 28b and 1,4a-dimethyl-5,6,7,8-tetrahydro-2(4aH)naphthalenone 3b have been prepared and irradiated at 2537 Å in dry dioxane. The major product in each case was the corresponding bicyclo [3.1.0]hex-3-en-2-one 29a, 29b, and 4b together with some small amounts of linearly conjugated dienones 30a and 30b. Prolonged irradiation of these lumiproducts with light of wavelengths greater than 3000 Å in both dioxane and ethanol gave predominantly the starting cross-conjugated cyclohexadienones 28a and 28b, presumably via a bipolar mechanism. The bicyclo [3.1.0]hex-3-en-2-one 28b which has similar substitution to lumisantonin was irradiated with a 450-watt high pressure mercury lamp with a Pyrex filter in both dioxane and ethanol. In the former solvent it gave mainly the homoannular dienone 32b, while the latter it afforded the 5/6-fused ethoxy ketone 33. The homoannular dienone reacted photochemically with ethanol to provide the dienone ester 34 which was isomerized photochemically or thermally into its cis- and trans- conjugated esters, 35 and 36.

The 4-methoxy-7a-methyl-, and 4-methoxy-7a-isopropyl-5(7aH)-indanones were also synthesized and irradiated. Similar results of form-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

ing lumiproducts 29d, 29i and homoannular dienone 32i were also obtained.

From a mechanistic point of view, the formation of the tricyclic methoxy ketone 42 from the photochemical reaction of the unsubstituted dienone 28a in methanol or 45 percent acetic-methanol was particularly interesting. In order to elucidate the stereochemistry of the tricyclic compound 42, it was treated with lithium-liquid ammonia followed by sodium hydride to a product assigned the structure 45.

On irradiation compound 7a-carboethoxy-5(7aH)-indanone provides mainly one product, 7-carboethoxy-5,6-dihydro-2(4H)-indanone, whether the photoreaction was carried out in nucleophilic solvent (such as ethanol and aqueous-acetic acid) or non-nucleophilic media(such as dioxane and ether).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER I

INTRODUCTION

It has been well known (1) that photo-induced rearrangements of cross-conjugated cyclohexadienones give various products which are governed by such factors as the nature of the functional group attached to the chromophore, the nature of the solvent, and steric effects. Some of the mechanistic details of the reactions are still argumentative and inconsistent. However, the ionic bipolar intermediate mechanism has been widely approved. Theoretical calculations and emission data have been brought to bear on this proposal (2). The photochemical rearrangement of a cross-conjugated dienone into a lumiproduct can be rationalized as shown in Chart 1.

6/6-Fused bicyclic dienones undergo facile rearrangements into the corresponding bicyclo [3.1.0] hex-3-en-2-ones 4, termed lumiproduct, on photolysis at 2537 Å in inert solvents such as dioxane (Chart 2).

The bicyclo [3.1.0]hex-3-en-2-one skeleton, such as in compound 4, is itself subject to light-catalyzed rearrangement (1c). The compounds of type 4 are considered to give an intermediate such as 5, which may exhibit two modes of rearrangement:

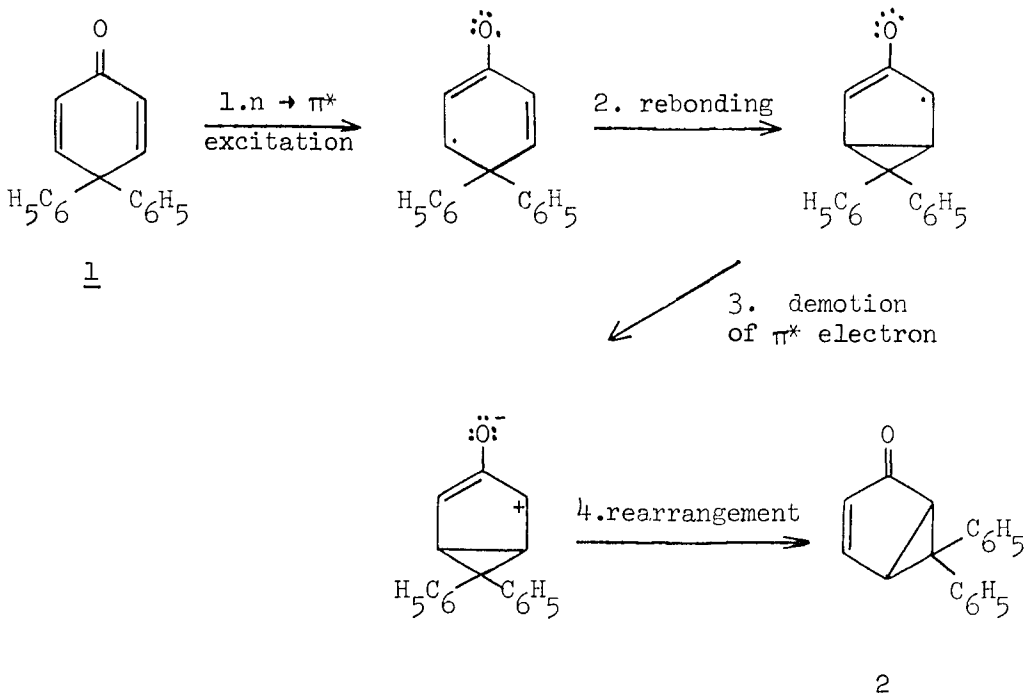
(A) 1,2-migration of the angular methyl substituent and

(B) rearrangement to a spiro dienone intermediate.

Type (A) migration is best illustrated by the light-induced isomerization of lumisantonin 9 (1), to give mazdasantonin 10 (3b) (Chart 3).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 1. Mechanism of the Photochemical Rearrangement of Cross-Conjugated Cyclohexadienone in Neutral Solvent.

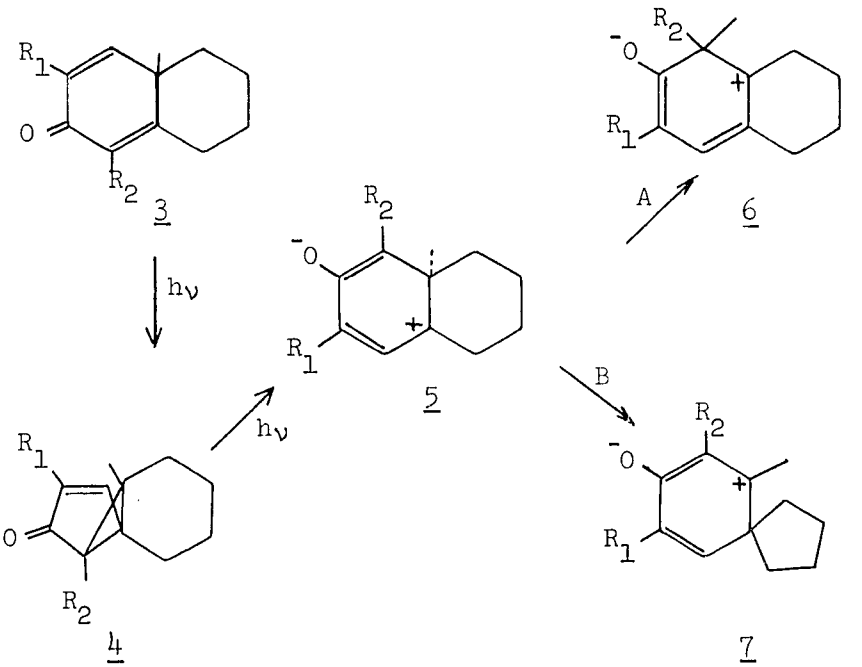


1

2

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 2



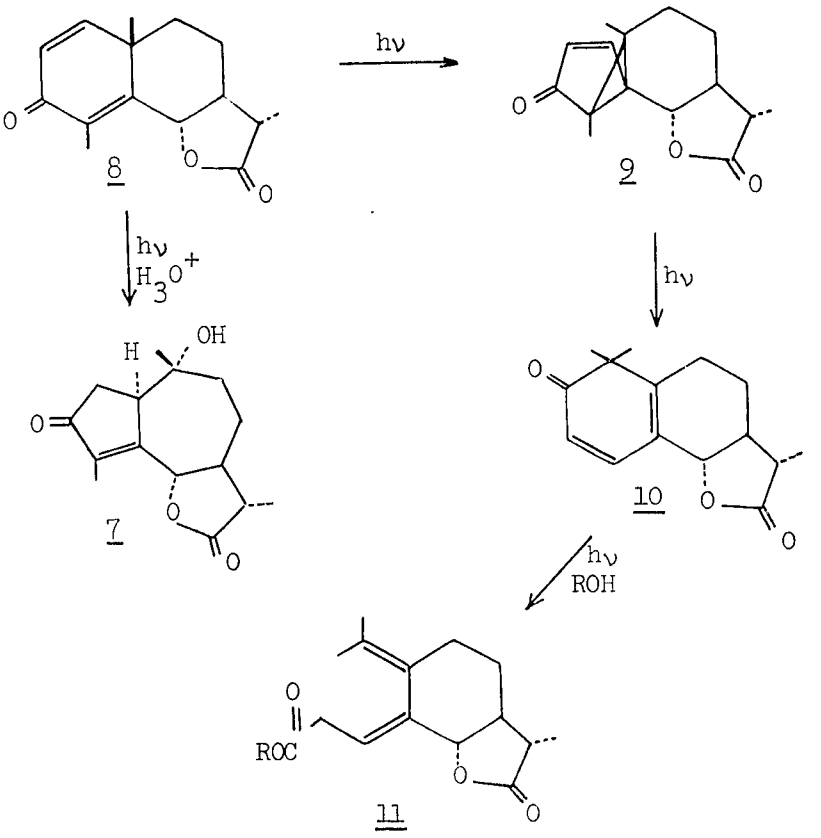
(a) $R_1 = R_2 = H$

(b) $R_1 = H$, $R_2 = CH_3$

(c) $R_1 = CH_3$, $R_2 = H$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 3



(a) R = Et

(b) R = H

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Rearrangement through a spiro intermediate is generally preferable, unless it is inhibited by the inductive or steric effects. This pathway usually leads to complicated mixtures of products owing to the fact that the spiro intermediates are photochemically labile and may undergo further rearrangement by several possible pathways (Chart 4).

The above results can be summarized as follows:

(1) conversions of 2,5-cyclohexadienones into bicyclo [3.1.0]hex-3-en-2-one,

(2) conversions of bicyclo [3.1.0]hex-3-en-2-one, depending on the respective positions of alkyl substituents, into either new 2,5-cyclohexadienones, 2,4-cyclohexadienones, or phenolic isomers,

(3) conversions of spirocyclic bicyclo [3.1.0]hex-3-en-2-one into spirocyclic 2,4-cyclohexadieones, and

(4) conversions of 2,4-cyclohexadienones into phenolic isomers.

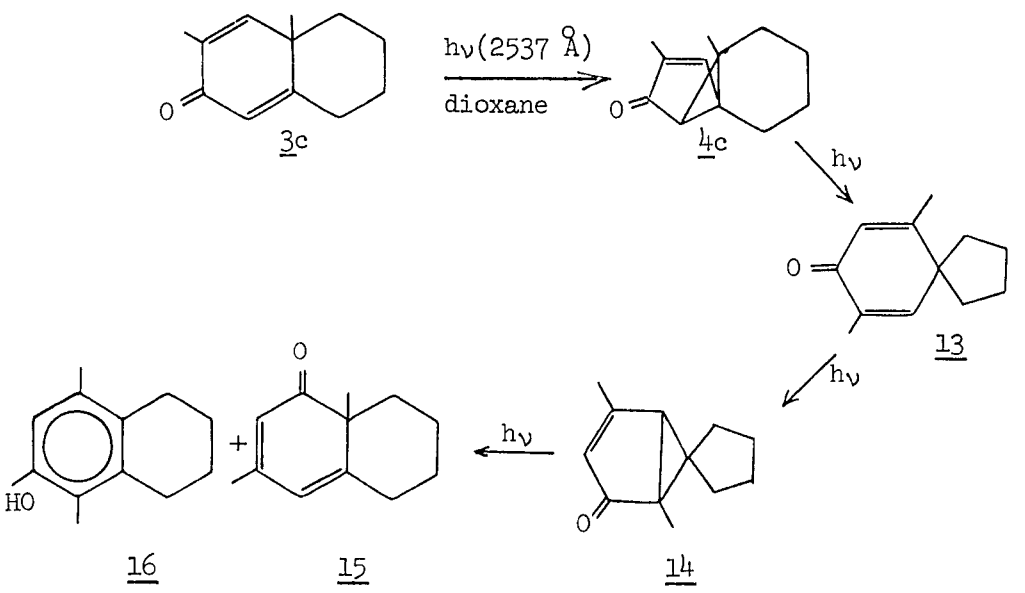
The nature of photolysis medium and length of irradiation period also play an important part in determining the course of cyclohexadienone rearrangements. For example, the photolysis of α-santonin 8 (1) gave lumisantonin 9 in dioxane, linearly conjugated dienone 10 in ether or benzene (3b), photosantonic acid 11b in water, and yielded the hydroxy ketone isophotosantonic lectone 12 in aqueous acid (1c,3a). (Chart 3).

Schuster (4) has also reported the observation of the solvent effects on the sterochemistry of the lumiketone rearrangements. This is illustrated in Chart 5.

From the point of view of synthetic usefulness, dienones are

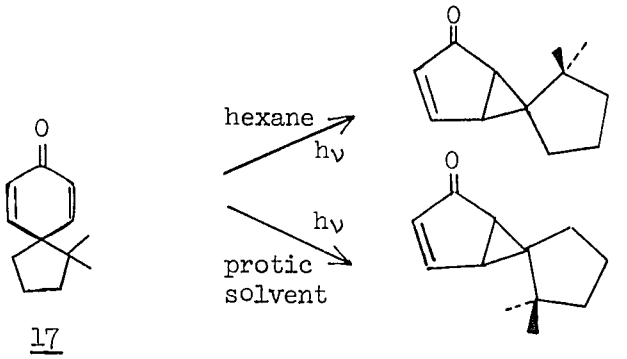
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 4



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 5



17

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

frequently photolyzed in protic nucleophilic solvents such as ethanol, aqueous acetic acid, etc.

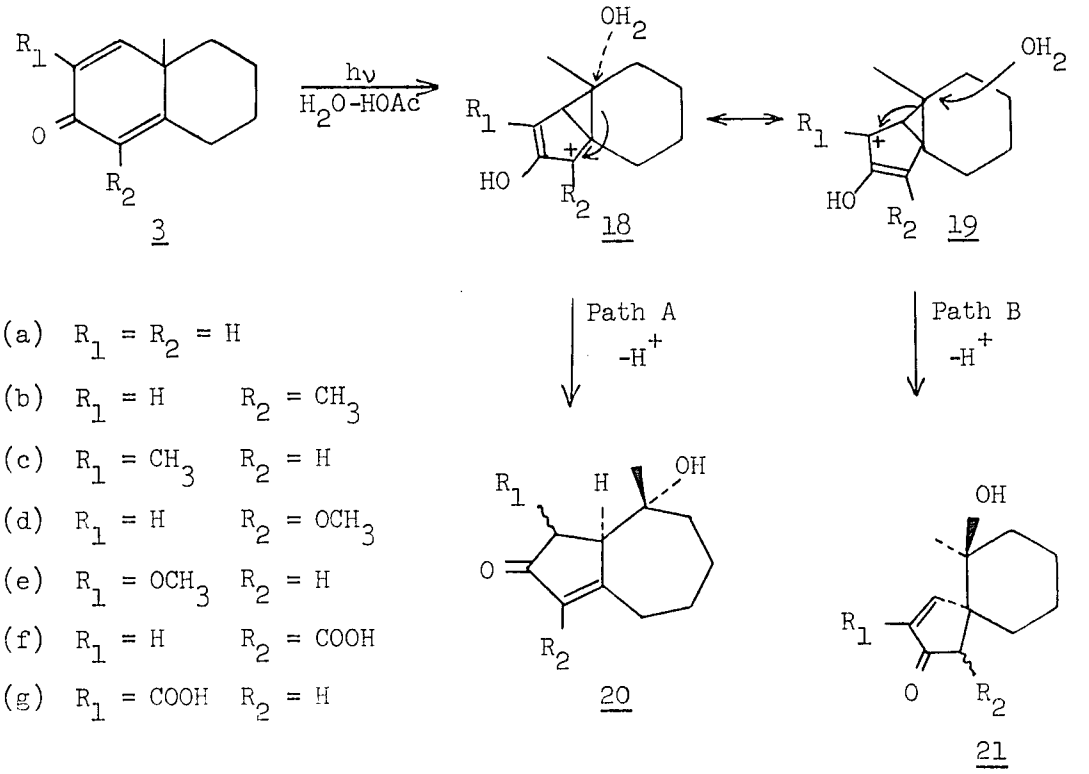
Chart 6 shows the reaction pathways considered to be involved in photochemical rearrangements of cross-conjugated cyclohexadienones such as 3 in aqueous acetic acid. The initially formed zwitterionic species is protonated to give the mesoionic species represented by 18 and 19. As expected on the basis of their inductive or hyperconjugative effects (5) methyl groups influence the course of solvolytic cleavage of such intermediates. For example, the 2-methyl dienone 3c gives mainly the spiro hydroxy ketone 21c (via path B), the 4-methyl dienone 3b gives mainly the 5/7 fused hydroxy ketone (via path A cleavage), and the ring A unsubstituted dienone 3a gives ca 15-20 percent each of 20a and 21a. In the latter case the two resonance forms 18 and 19 are of about equal energy and the possible cleavage pathways are competative. Phenolic products are also obtained in low yield from 3c and 3b, but the major product of irradiation of 3a is a phenol which arises via light induced reaction of the lumiproduct 4a.

The behavior of 3a indicates that generally speaking rearrangements of ring A unsubstituted dienones are of little synthetic value (6) (7).

Certain dienones having special structural features associated with ring B provide exceptions. For example, either a suitably disposed neighboring group, such as the acetexyl group in 22 (8) or steric factors, such as the C-6β methyl group in 23 (9) can influence the course of the rearrangement in the direction of 5/7-fused products.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 6. Mechanism of the Photochemical Rearrangement of Cross-Conjugated Cyclohexadienone in Aqueous-Acetic Acid.



(a) $R_1 = R_2 = H$

(b) $R_1 = H$ $R_2 = CH_3$

(c) $R_1 = CH_3$ $R_2 = H$

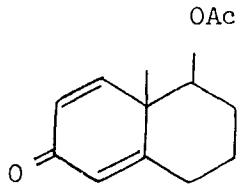
(d) $R_1 = H$ $R_2 = OCH_3$

(e) $R_1 = OCH_3$ $R_2 = H$

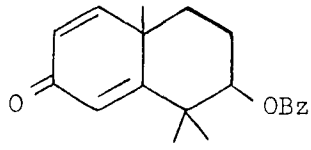
(f) $R_1 = H$ $R_2 = COOH$

(g) $R_1 = COOH$ $R_2 = H$

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



22



23

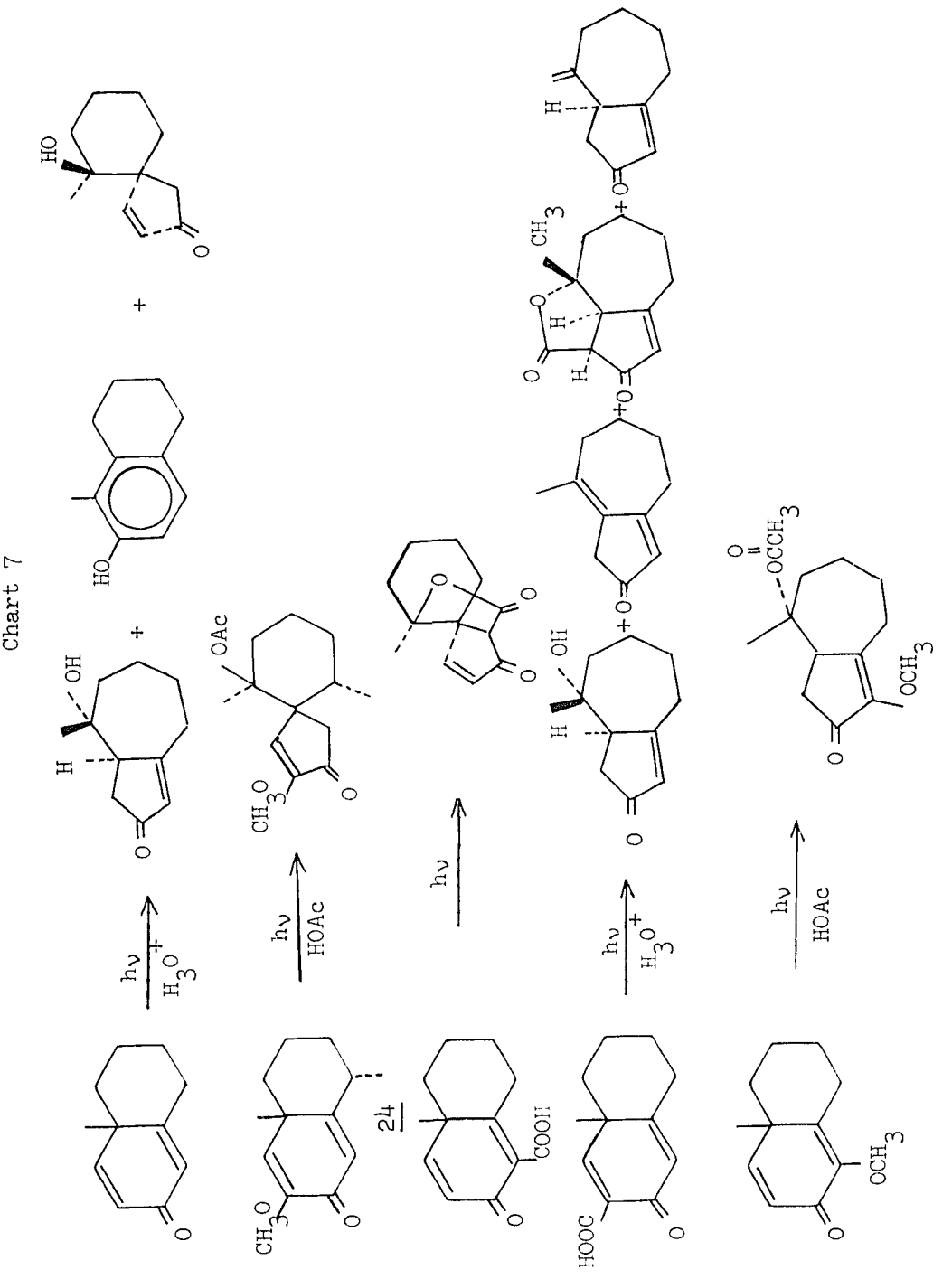
Caine and coworkers (10) have shown that substituents other than methyl groups may influence the course of rearrangement of dienone such as 3. For example, dienones having electron withdrawing substituents such as formyl, carboxyl, and carbomethoxyl located at C-2 give exclusively 5/7- fused products on irradiation in aqueous acetic acid (11), while the 4-carboxydienone gives exclusively spiro cyclic products (12). Methoxy substituted dienones exhibit similar behavior to the corresponding methyl substituted systems. The 2-methoxy compound gives exclusively a spiro-product (13), whereas the 4-methoxy compound gives exclusively 5/7-fused compound. These results are all consistent with the intervention of an intermediate represented by 18 or 19 in the reactions.

Several natural products such as opalopanone (14) and cyclochlorenone (15) have been sucessfully synthesized using transformation similar to those shown in chart 7. Related syntheses include α-bulnesene, aromadendrene and β-vetivone (16, 17).

Kropp has carried out a study of the photochemical behavior of the cyclohexadienone having an angular carbomethoxy group 3h (18), which initially gives rise to the lumiproduct 4h on irradiation in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 7

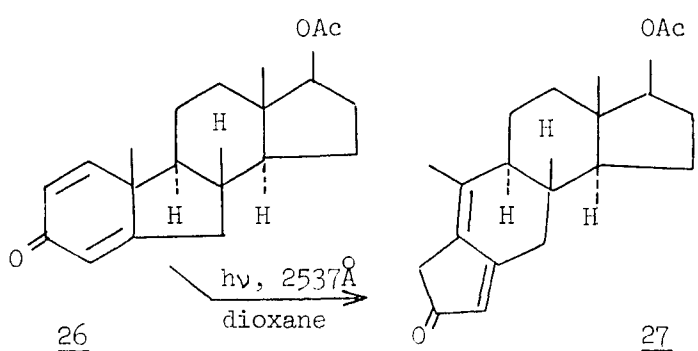


Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

dioxane. On further irradiation in either dioxane or acetic acid gave the phenol in 90 percent yield. The mechanism also can be rationalized in terms of a dipolar species analogous to 5. The electron withdrawing group at the angular position prohibits the formation of the spiro intermediate (Chart 8).

Although a great deal of effort has been devoted to studies on the photochemistry of monocyclic, 6/6-fused bicyclic, and steroidal cross-conjugated cyclohexadeinones, very little attention has been given to the behavior of compounds having a five membered ring fused to the chromophore. Jeger, Schaffner, and coworkers (19) have reported that B-nor-1-dehydrotestosterone 26 is converted directly into the linearly conjugated dieone 27 on irradiation in dioxane at 2537 Å.

Equation 1

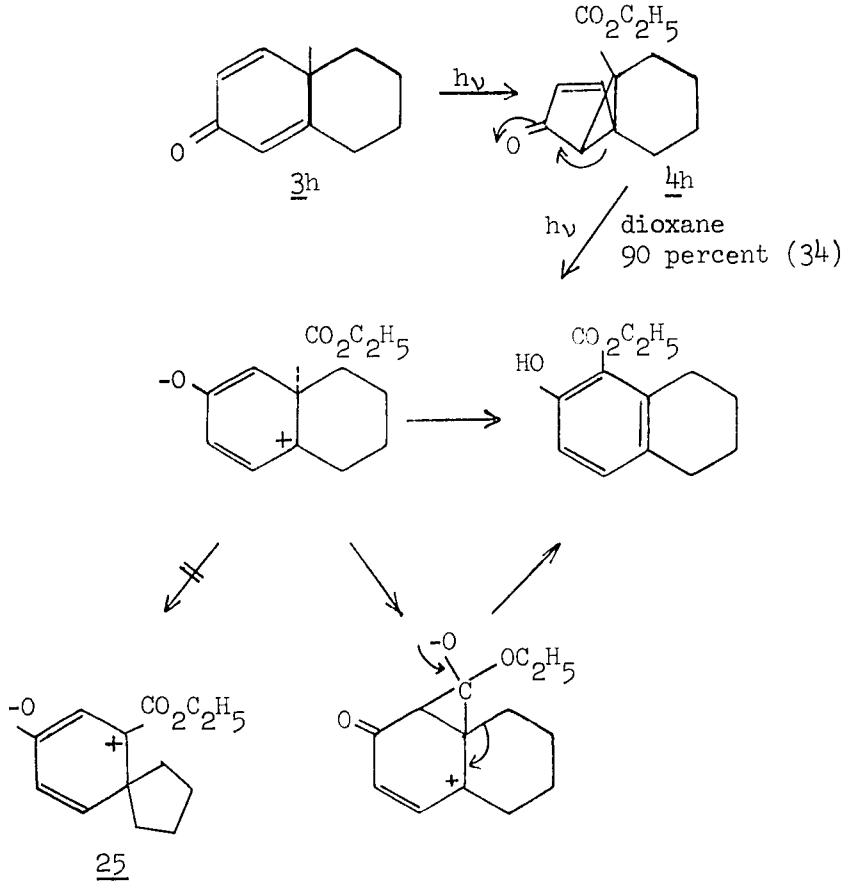


26 27

However, Caine and coworkers have found that bicyclic dienone 28a-c give in some cases small amounts of dienones related to 30a-c on irradiation in dioxone at 2537 Å, but the major products are bicyclo (3.1.0)hex-2-en-3-one derivatives such as 29a-c (20). Powers (20,21) and Gupton (22) have also carried out the photolysis of dienones 28a-c in nucleo-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 8

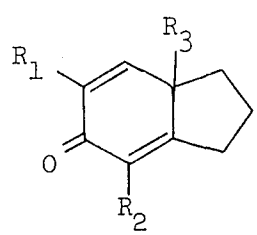


Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

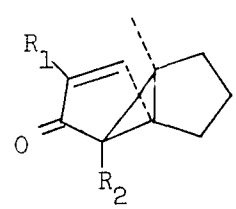
philic media and obtained the results shown in Chart 9.

The tricyclic product from 2-methyl and unsubstituted is of significant mechanistic interest.

It was the purpose of this research to obtain further proof for the structure assigned to some of photoproducts above (23), to study the photochemistry of the lumi-products such as 29a-c and compares their behavior with the related 6/6 fused systems (24), and synthesize and study the photochemistry of several new 6/5 fused cyclohexadienone having substituents other than methyl groups at the 2- and 4-position as well as the angular position.



28



29

For $R_3 = CH_3$ (a-g)

(a) $R_1 = R_2 = H$

(b) $R_1 = H$ $R_2 = CH_3$

(c) $R_1 = CH_3$ $R_2 = H$

(d) $R_1 = H$ $R_2 = OCH_3$

(e) $R_1 = OCH_3$ $R_2 = H$

(f) $R_1 = H$ $R_2 = COOH$

(g) $R_1 = COOH$ $R_2 = H$

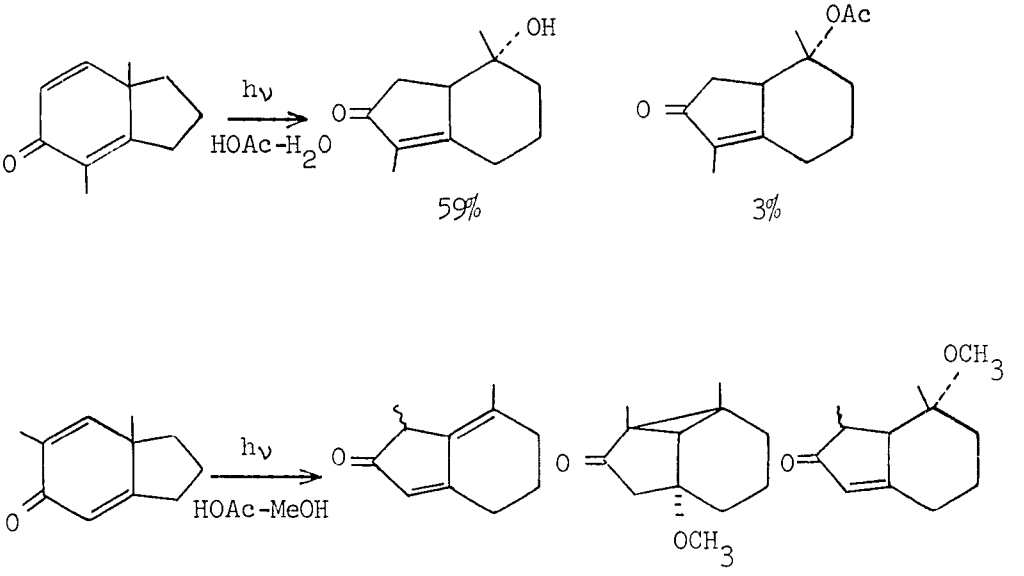
(h) $R_3 = COOEt$ $R_1 = R_2 = H$

(i) $R_1 = H$ $R_2 = OCH_3$

R_3 = isopropyl

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 9



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Melting points were determined on a Fisher Johns hot stage and are uncorrected. Carbon and hydrogen microanalyses were performed by Galbraith Laboratories, Incorporated, Knoxville, Tennessee or by Atlantic Microlab, Incorporated, Atlanta, Georgia. Ultraviolet spectra were recorded on a Cary Model 14 or a Beckman DBGT recording spectrophotometer using 1 cm balanced quarts cells with 95 percent ethanol as solvent. Infrared spectra were recorded on a Perkin-Elmer Model 137 or Perkin-Elmer Model 457 spectrophotometer using 0.2 mm sodium chloride cells. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 spectrometer using carbon tetrachloride (unless otherwise stated) as solvent. Positions of nmr absorptions are reported in ppm downfield from tetramethylsilane (TMS). The abbreviations s, d, t, q, and m refer respectively to singlet, doublet, triplet, quartet, and multiplet. Mass spectra were recorded on a Varian M-66 mass spectrometer. Solvents were removed with a commercial rotating evaporator unless otherwise stated. Gas liquid chromatographic analyses were performed on a Perkin-Elmer 881 Flame Ionization Gas Chromatograph and preparative gas liquid chromatography was performed on a Aerograph Model A-90P Manual Temperature Programmer Gas Chromatograph. Chromatography columns were prepared from commercial 80-200 mesh silica gel. Anhydrous magnesium sulfate or anhydrous sodium sulfate were used as drying agents in working up reactions. All inorganic chemicals used

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

in this research were reagent grade. Technical grade hydrocarbon solvents were used and were distilled prior to use. All solvents used in the photochemical work were purified according to the method of Fieser (25). Commercial anhydrous ether was stored over sodium metal ribbon and used without further purification. A Hanovia 450 watt high pressure mercury arc lamp, fitted with a Pyrex filter or used in all Pyrex apparatus similar to that described by Kropp and Erman (7,33) was employed in all irradiation experiments where long wavelength light was desired. A Hanau 7 watt low pressure mercury arc lamp, which furnishes greater than 90 percent emission at 2537 Å, was employed in other irradiation experiments. Solutions were deoxygenated prior to irradiation and agitated during irradiation with a stream of nitrogen.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER III

EXPERIMENTAL

4,7a-Dimethyl-7,7a-dihydro-5(6H)-indanone(31b)

The method employed by Powers (21) was followed. A 1000 ml three-necked round bottom flask equipped with a dropping funnel, magnetic stirrer bar, and thermometer was placed under positive nitrogen flow. Anhydrous ether, 400 ml, was added to the flask and a solution of 5.4 g (0.096 moles) of potassium hydroxide in 35 ml of absolute ethanol was added. The mixture was cooled, with stirring to -5°C by means of an ice-salt bath, and 62.4 g (0.64 moles) of 2-methylcyclopentanone was added. A solution of 24.6 g (0.293 moles) of ethyl vinyl ketone in ca. 150 ml of anhydrous ether was added dropwise at a rate sufficiently slow to maintain the temperature of the reaction at or below -5°C, then stirred for an additional hour with the cooling bath removed. The mixture was poured into 300 ml of 10 percent hydrochloric acid, and the layers were separated. The aqueous layer was extracted with two 50 ml portions of ether, and the combined organic layers were dried with magnesium sulfate. The solvents were removed in vacuo and the compound was distilled through a short path head at reduced pressure. Two-methylcyclopentanone, 31.0 g (49 percent recovery) b. p. 43-44°C/21 mm Hg was recovered, followed by 24.0 g of tractable material, boiling 99-113°C/1.0 mm Hg. The tractable material was dissolved in 300 ml 10 percent ethanolic potassium hydroxide and refluxed for 30 minutes in a nitrogen atmosphere. The mixture was cooled to room temperature,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

neutralized with glacial acetic acid, and the solvents were removed *in vacuo*. Water was added to dissolve the potassium acetate, the layers were separated, and the aqueous layer was extracted with two 25 ml portions of ether. The combined organic layers were dried with magnesium sulfate and the solvents were removed *in vacuo*. Distillation of the resulting yellow oil through a short path head gave 15.2 g (33 percent) of 31b, b.p. 87°C/0.85 mm Hg. Compound 31b had the same spectral properties as reported (21).

4,7a-Dimethyl-5(7aH)-indanone(28b)

Compound 31b was prepared by a modification of the method of Powers (21,30). A 1000 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirrer bar was placed under positive nitrogen flow. Freshly distilled anhydrous p-dioxane, 500 ml, was charged into the flask and 9.35 g (0.0413 moles) of 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) was added. The mixture was stirred until the DDQ dissolved, and 6.60 g (0.0403 moles) of 31b was added. The mixture was refluxed with stirring for 30 hours. The solution was cooled to room temperature, and the solid 2,3-dichloro-5,6-dicyano-phydroquinone (DDHQ) was collected by filtration with suction. The mixture was concentrated to *ca*. 50 ml by removal of solvents *in vacuo*. The mixture was cooled to room temperature and filtered with suction to remove the remaining DDHQ. It was then poured onto a loosely packed column of 70 g of alumina and eluted under pressure with 500 ml of benzene. The solvents were removed *in vacuo* and the resulting yellow oil was distilled through a short path head to give 3.92 g (60 percent) of 28b, b.p. 88C/0.5 mm Hg. Compound 28b gave the same spectral data

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

as reported (21).

Irradiation of 4,7a-Dimethyl-5(7aH)-indanone(28b) in Dioxane

The dienone 28b, 222 mg (0.0013 mole), was dissolved in freshly distilled dioxane and irradiated for 120 minutes using a Hanau NK 6/20 lamp. Using a stream of dry nitrogen, the solution was agitated constantly for 10 minutes prior to and during the irradiation period. After two hours irradiation analysis of the mixture by glc (26) showed the presence of starting material and two other volatile components in a ca. 2:7:1 ratio. The mixture was subjected to chromatography on silica gel. Elution with hexane (900 ml) gave 110 mg (50 percent) of 29b, b.p. 75-80°C (bath temperature)/0.2 mm, which showed: uv (95 percent EtOH) max 247 (ε 4,820) and 274 mμ (ε 2,900): ir ($CHCl_3$) 5.88 (C=O) and 6.36 μ (C=C): nmr (CCl_4) δ 7.28 (d, 1H, J_{AB} = 5.5Hz, C-7H), 5.74 (d, 1H, J_{AB} = 5.5Hz, C-6H), 1.56-2.80 (broad adsorption, 6H), 1.18 (s, 3H, C-4CH_3), and 1.08 (s, 3H, C-7aCH_3);

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.24; H, 8.40.

Further elution with 10 percent ether-hexane (200 ml) gave a small amount of starting material, and elution with more 10 percent ether-hexane gave ca. 12 mg (ca. 5 percent) of a solid material having an identical glc (26) relention time to the minor component of the photolysis mixture. This quantity of material was insufficient for complete characterization, but in a separate larger scale run, this component was collected directly by preparative glc (26). The product identified at 30b showed: m.p. 85-88°C; uv (95 percent EtOH) max 302 mμ

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(ϵ 14,000); ir (CCl_4) 5.99 (C = O) and 6.22μ (C = C); nmr ($CDCl_3$) δ 2.80 (s, 2H, C-3CH_2), 2.6 - 1.9 (broad adsorption, 6H), 1.80 (s, 3H, $ClCH_3$), and 1.72 (s, 3H, C-4CH_3);

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.28; H, 8.78.

Irradiation of 7,7a-Dimethyl-3a,7a-dihydro-3a,7cyclo-6(7H)-indanone(29b) in Dioxane

A solution prepared from 300 mg of the bicyclo[3.1.0]hex-3-en-2-one 29b in 200 ml anhydrous dioxane was irradiated for 90 minutes using a 450-watt Hanovia high pressure lamp fitted with a Pyrex filter. Using a stream of dry nitrogen the solution was constantly agitated for 15 minutes prior to and during the irradiation period. Removal of the solvent under reduced pressure yielded a mixture which by glc analysis (27) was shown to contain one major component and two minor components in an approximately 88:6:6 ratio. The retention time of one of the minor components was identical to that of the starting material. Chromatography of the mixture on silica gel using hexane as the eluting solvent led to the isolation of 151 mg (50 percent) of the major photoproduct,4,4-dimethyl-5(4H)-indanone 32b, as a light yellow oil. Compound 32b showed: uv (95 percent EtOH) max 335 mμ (ϵ 3,800); ir (CCl_4) 6.00 (C=O) and 6.12 μ (C=C); nmr (CCl_4) 6.86 (d, 1H, J_{AB} = 10 Hz), 5.79 (d, 1H, J_{AB} = 10Hz), 1.76-2.75 (broad absorption, 6H), and 1.16 (s,6H);

Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.52; H, 8.68.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

A solution of 102 mg 32b in 60 ml 95 percent ethanol was shaken with 17 mg of 10 percent palladium-on-carbon in a hydrogen atmosphere for 16 hours. Removal of the catalyst by filtration and removal of the solvent under reduced pressure gave the cis-fused tetrahydro derivative of 32b as a colorless oil, ir (CCl_4) 5.86 μ. This material was not purified, but was converted directly into its semicarbazone derivative, m.p. 203-206°C.

The second minor product showed a glc (27) retention time identical to that of 28b. In a run identical to that described above, 29b was irradiated at time intervals. The result was shown in Table 1.

Table 1. Irradiation of 29b.

Time of Irradiation (minutes)	Product Ratio		
	29b	32b	28b
15	3	2	1
30	2	2	1
60	2	3	1
90	1	10	?

Samples of 29b, 32b and 28b were collected by preparative glc (27) and showed spectral properties identical to those of authentic materials.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Irradiation of 4,7a-Dimethyl-5(7aH)-indanone(28b)

A solution of 650 mg of 28b was irradiated under identical conditions to those described for 29b. The reaction progress was monitored by glc analysis (27) of aliquots of the photolysis mixture taken at various time intervals. After a short irradiation time 29b was the major product, but on continued irradiation a peak corresponding to 32b began to develop. After a total irradiation period of 1.5 hours, 32b was the major volatile component in the photolysis mixture.

Irradiation of 7,7a-dimethyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone (29b) in Absolute Ethanol

A solution of 420 mg (0.0026 mole) of 32b in 250 ml absolute ethanol was irradiated for one hour using a 450-watt Hanovia high pressure mercury lamp in a Pyrex probe. During the photolysis the mixture was agitated with a stream of dry nitrogen. Removal of the solvents under reduced pressure and glc analysis (27) of the crude mixture showed the presence of the starting material and a major product in a ca. 23:77 ratio. Only traces of other volatile products were observed. Distillation of the mixture gave a fraction b.p. 75-85°C (bath temperature)/0.2 mm, which proved to be mainly starting material. A higher boiling fraction, b.p. 100-110°C (bath temperature)/0.2 mm, weighing 300 mg (55 percent) was collected. This fraction contained essentially one component which was identified as the 5/6-fused ethoxy ketone 33: uv (95 percent EtOH) max 242 mμ (ε 10,600), ir (CCl_4) 5.91 (C = O) and 6.08 μ (C=C); nmr (CCl_4) δ 3.45 (q, 2H, J_{AX} = 7Hz, O-$\underline{CH_2}$-CH_3), 2.9-1.6 (broad absorption, 9H), 1.63 (broad s,

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

3H,C-1CH_3), 1.10 (t,3H, J = 7Hz, O-CH_2-$\underline{CH_3}$), and 0.88 (s, 3H, C-4CH_3);

Anal. Calcd for $C_{13}H_2O_2$: C, 74.96; H, 9.68. Found: C, 74.72; H, 9.79.

Irradiation of 28b in Absolute Ethanol

A sample of 400 mg (0.0025) mole of 28b was irradiated under identical condition to those described above. The crude material was distilled. Compound 33 was the only photoproduct isolated.

Irradiation of 4,4-dimethyl-5(4H)-indanone 32b in Absolute Ethanol

Dienone 32b, 380 mg, in 250 ml absolute ethanol was irradiated under identical conditions to those described above for 29b. Removal of the solvent under reduced pressure gave 400 mg of crude liquid in the basis of its spectral properties appeared to be the diene ester 34. Attempted purification of the compound by preparative glc led to extensive isomerization to a mixture of 34 and the corresponding cis- and trans- conjugated diene 35 and 36. These products were collected by preparative glc and the amounts obtained were 95 mg and 115 mg, respectively. However, an analytical sample of 34 could be collected from the mixture. The sample showed uv (95 percent EtOH) λ max 280 nm (ε 830), 255 nm (ε 1650) ir (CCl_4) 5.74 (ester C=O), and 6.06 μ (conjugated diene); nmr (CCl_4) δ 5.42 (broaden t, J = 6Hz, 1H, vinyl H), 4.17 (q, J=7Hz, 2H, O$\underline{CH_2}$-CH_3), 2.97 (broadened d, J=6Hz, 2H, -$\overset{O}{\overset{\|}{C}}$-$\underline{CH_2}$-CH=), 1.70 (s, 3H, CH_3-C=), 1.65 (s, 3H, CH_3-C=) and 1.25 (t, 3H, O-CH_2-$\underline{CH_3}$); exact mass: 208.14668 (calcd: 208.14622).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.00;

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

H, 9.45.

In another run of the same reaction, different results were obtained. The pure dienone 32b, 0.25 g, dissolved in anhydrous ethanol and photolyzed for 30 minutes as before. Three peaks were observed in preparative glc (carbowax column) due to thermal isomerization through the blc column. Two of them were collected and identified as 35 and 36 with yields of 100 mg and 120 mg respectively. Attempt to isolate the unknown product was not successful, because it was converted to 36 in the glc column.

The spectral properties of 35 was following: ir (CCl_4) 5.78 and 5.83 μ; nmr (CCl_4) δ 6.60 (d, J=12Hz, 1H), 5.57 (d, J=12Hz, 1H), 4.05 (q, J=7Hz, 2H), 3.1 (m, 1H), 1.20 (t, J=7Hz, 3H), 1.00 (d, J=6.5Hz, 6H) and 1.7-2.7 (m, 6H); uv max (95 percent ethanol) 290 and 255 nm; exact mass 208.14610 (calcd 208.14622).

Compound 36 exhibited the following properties: ir (CCl_4) 5.83, 6.17 and 6.25 μ; nmr (CCl_4) δ 7.60 (d, J=15Hz, 1H), 5.60 (d, J=15Hz, 1H), 4.13 (q, J=7Hz, 2H), 3.10 (Septet, J=6.5Hz, 1H), 1.70-2.70 (m, 6H), 1.24 (t, J=6.5Hz, 3H), 1.00 (d, J=6.5Hz, 3H); uv max (95 percent ethanol) 296 and 255 nm; exact mass 208.14732 (Calcd 208.14622).

Further Photolysis of 34 in Absolute Ethanol

Compound 34, 50 mg, was dissolved in 10 ml absolute ethyl alcohol in a Pyrex test tube and attached to the outside wall of a Pyrex phototube. The photolysis was carried out as described above. After 30 minutes of irradiation, two new peaks with shorter retention times than the starting material were observed in a 1:1 ratio by glc. The photo-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

products exhibited the following spectral properties: ir (film) 5.70 and 5.78 μ, nmr showed two quartets at 4.4 and 4.2 δ, a doublet at 2.9δ, complicated bands 1.5-2.4 δ and two triplets at 1.3 and 1.4 δ. The spectral data showed the structure might be 73 together with some unchanged starting material 34.

The experiment was repeated two times. Inconsistent results and complicated products made the separation and identification difficult.

1,4a-Dimethyl-3,4,5,6,7,8-hexadro-2(4aH)naphthalenone(38)

Compound 38 was prepared by a method similar to that reported by Ross and Levine (28). A dried 500-ml three-necked round-bottom flask equipped with a thermometer, dropping funnel, and magnetic stirring bar was placed under positive nitrogen flow. Anhydrous ether, 200 ml, was added to the flask and a solution of 57g (0.10 mole) of potassium hydroxide in 20 ml of absolute ethanol was added. The mixture was cooled to -7°C with an ice-salt bath and 56.0g (0.50 mole) of 2-methylcyclohexanone was added. A solution of 21.5g (0.25 mole) of ethyl vinyl ketone in ca. 100 ml anhydrous ether was added at a rate sufficiently slow to keep the reaction temperature at or below -5°C. When the addition was complete, the mixture was stirred for 45 minutes at -5°C, then for 45 minutes with the ice-salt bath removed. The mixture was poured into 300 ml of 10 percent hydrochloric acid and the layers were separated. The aqueous layer was saturated with salt and extracted with two 100 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents were removed under reduced pressure. Distillation of the residue gave 15.0g of 2-methylcyclohexanone (26 percent recovery)

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(b.p. 70-73°C/55mm). The product 38 was distilled at 80-94°C/0.15mm with a yield of 20.8g (48 percent).

1,4a-Dimethyl-5,6,7,8-tetrahydro-2(4aH)naphthalenone(3b)

Compoune 3b was prepared by a modification of the method of Burn, Kirk and Petorw (30). A 1000-ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirring bar was placed under positive nitrogen flow. Freshly distilled anhydrous benzene 500 ml, and 25 ml glacial acetic acid were charged into the flask and 14.32g (0.0630 mole) of 2,3-dichloro-5,6-dicyano-p-venzoquinone (DDQ) was added. The mixture was stirred until the DDQ dissolved, and 10.25 (0.0629 mole) of 38 was added. The mixture was refluxed with stirring for 32 hours. The solution was cooled to room temperature, and the solid 2,3-dichloro-5,6-dicyanohydroquinone (DDHQ) was collected by filtration with suction. The mixture was concentrated to ca. 80 ml by removal of solvents under reduced pressure. The mixture was cooled to room temperature and filtered with suction to remove the remaining DDHQ. It was then poured onto a loosely packed column of 100g of alumina and eluted under pressure with 800 ml of benzene. The solvents were removed under reduced pressure and the resulting yellow oil was distilled through a short path head to give 8.3g (82 percent) of the dienone product. The detailed spectral data was the same as reported (29).

Irradiation of 1,4a-dimethyl-5,6,7,8-tetrahydro-2(4aH)naphthalenone (3b) in Dioxane

The dienone 3b, 972 mg (0.0055 mole), was dissolved in 120 ml anhydrous dioxane and irradiated with a Hanau NK 6/20 lamp for 3 hours.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Using a stream of dry nitrogen, the solution was agitated constantly for 15 minutes prior to and during the irradiation period. The reaction was monitored by glc (26) and 3b had been converted into a single volatile photoproduct after this time (90 percent conversion according to glc). The solvent was removed under reduced pressure, and the crude product was subjected to chromatography on silica gel. Elution of the column with hexane (275 ml) followed by 5 percent to 15 percent ether-hexane (2000 ml) have 680 mg (70 percent) of 1,8a-dimethyl-4a,5,6,7,8,8a-hexahydro-1,4a-cyclo-2(1H)naphthalenone 4b, b.p. 70-80°C(bath temperature)/0.2 mm. A sample was purified by preparative glc (26) and showed the same spectral properties as have been reported for 4b (29).

Irradiation of 1,8a-dimethyl-4a,5,6,7,8,8a -hexahydro-1,4a-cyclo-2(1H)naphthalenone(4b)

The lumi product 4b, 1.0g, (0.00567 mole), was dissolved in ca. 250 ml of anhydrous dioxane and irradiated for 2 hours with a 450 watt high pressure mercury arc source with Pyrex filter in room temperature. The solvent was removed in vacuo and the oily residue was analyzed by glc. The glc showed three major and seven minor peaks, besides the starting material. Attempts to separate pure compounds from the mixture by means of column chromatography and preparative glc were not successful. No products were isolated.

The progress of the photolysis reaction was monitored by examining aliquots of the reaction mixture at time intervals by glc. After 60 minutes a peak corresponding to the dienone 4b reached a maximum and began to disappear. The same result was obtained for the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

five-membered B ring analog of 4b, i.e. the initial product of irradiation of the lumiproduct was the cross-conjugated dienone.

7,7a-Dihydro-7a-methyl-5(6H)-indanone(31a)

Compound 31a was prepared by a method similar to that reported by Ross and Levine (28). A dried 2000 ml three-necked round-bottom flask equipped with a thermometer, dropping funnel, and magnetic stirring bar was placed under positive nitrogen flow. Anhydrous ether, 500 ml, was added to the flask and a solution of 44.8g (0.80 mole) of potassium hydroxide in 100 ml of absolute ethanol was added. The mixture was cooled to -7°C with an ice-salt bath and 98.14g (1.00 mole) of 2-methylcyclopentanone was added. A solution of 75.0g (1.07 moles) of methyl vinyl ketone in ca. 200 ml anhydrous ether was added at a rate sufficiently slow to keep the reaction temperature at or below -5°C. When the addition was complete, the mixture was stirred for 45 minutes at -5°C, then for 24 hours with the ice-bath removed. The mixture was poured into 500 ml of 10 percent hydrochloric acid and the layers were separated. The aqueous layer was saturated with salt and extracted with two 100 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents were removed in vacuo. Distillation at reduced pressure gave 120.30g of a tractable mixture b.p. 68-105°C/0.25 mm Hg which appeared, by infrared spectroscopy and vapor phase chromatography, to consist of 31a plus its precursor diketone and ketol. The tractable mixture was dissolved in 1600 ml 10 percent ethanolic potassium hydroxide and refluxed in a nitrogen atmosphere for 30 minutes. The mixture was cooled to room temperature and neutralized with glacial acetic acid. The solvents were removed in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

vacuo, water was added to dissolve the potassium acetate formed in the neutralization, and the layers were separated. The aqueous layer was extracted with two 300 ml portions of ether and the combined organic layers were dried over magnesium sulfate. The solvents were removed in vacuo and the product was distilled at reduced pressure through a short path distilling head giving 79.5g (55 percent) of 31a b.p. 65-67°C/0.30 mm Hg (lit. 112°C/4 mm Hg) (21).

7a-Methyl-5(7aH)-indanone(28a)

Compound 28a was prepared by the method of Bloom (31). A dried 1000 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirring bar was placed under positive nitrogen flow and 300 ml freshly distilled tert-butyl alcohol and two milliliters glacial acetic acid was charged into the flask. Freshly sublimed selenium dioxide, 2.3g (0.02 mole), was added and the misture was stirred until the selenium dioxide dissolved. Compound 31a, 3.3g (0.02 mole), was added and the mixture was refluxed, with stirring, for 64 hours. The mixture was concentrated to ca. 200 ml by distillation of solvents in a nitrogen atmosphere. The selenium metal formed was removed by several filtrations, with suction, and the remaining solvents were removed in vacuo. The resulting black viscous mass was taken up in 250 ml of ether and filtered with suction. The ethereal solution was washed with five 50 ml portions of 5 percent sodium hydroxide, dried with magnesium sulfate, and the solvents were removed in vacuo. Distillation through a short path head gave 0.76g (41 percent) of 28a b.p. 70-71°C/0.3 mm Hg (lit. 69-70°C/0.65 mm Hg) (31). The nmr spectrum of this compound

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

had not been previously reported. It showed absorptions at δ 7.02 (d, 1H, J_{AB} = 9.5 Hz), 5.99 (d of d, 1H, J_{AB} = 9.5 Hz, J_{BX} = 2.0 Hz), 5.89 (m, 1H) 1.32-3.08 (broad absorption, 6H), 1.21 (s, 3H).

Irradiation of 7a-methyl-5(7aH)-indanone (28a) in Dioxane at 2537Å

The dienone 28a, 570 mg (0.0038 mole), was dissolved in 300 ml anhydrous dioxane and irradiated with a Hanovia NK 6/20 lamp for 75 minutes. Using a stream of dry nitrogen, the solution was agitated constantly for 10 minutes prior to and during the irradiated period. The solvents were removed under reduced pressure, and the crude mixture was chromatographed on silica gel. Elution with 5 percent ether-hexane (1500 ml) gave 312mg (55 percent) of 7a-methyl-3,7a-dihydro-3a,7-cyclo-6(7aH)-indanone(29a)which was greater than 90 percent pure by glc (26). The analytical sample was collected by preparative glc and showed: uv max (95 percent EtOH) 236 (ε 6,300) and 271 mμ (ε 4,200); ir (CCl_4) 5.86 μ (C=O); nmr (CCl_4) δ 7.28 (d, 1H, J_{AB} = 5.5 Hz, C-7H), 5.77 (d of d, 1H, J_{AB} - 5.5Hz; J_{BX} = 0.8 Hz, C-6H), 1.47-2.27 (broad absorption, 7H), and 1.68 (s, 3H, C-7aCH_3):

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 80.99; H, 8.23.

Further elution with 10 percent ether-hexane (1000 ml) gave a small amount of starting material, and elution with ether (200 ml) gave 120 mg (21 percent) of the linearly conjugated dienone 30a which was greater than 90 percent one component by glc. The analytical sample was collected by preparative glc and showed: uv (95 percent EtOH) max 296 mμ (ε 19,000); ir (CCl_4) 5.86 (C=O), 5.97 (C=C) and 6.30 μ (C=C):

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

nmr (CCl_4) δ 5.69 (s, 1H, C-1H, 2.72 (s, 2H, C-$3H_2$), 1.53-2.90 (broad absorption, 6H), and 1.81 (s, 3H, C-$4CH_3$);

Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 80.71; H, 8.47.

Irradiation of 7a-Methyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone(29a)in Anhydrous Dioxane: Broad Spectrum Lamp

Compound 29a, 209 mg (0.00141 mole), was dissolved in ca. 250 ml of anhydrous dioxane and irradiated for 30 minutes with a 450 watt high pressure mercury arc source. The solvent was removed in vacuo, and the oily residue was placed on a silica gel column. Elution with hexane-ether mixtures gave no identifiable products. The expected phenolic product was not observed. The ir spectrum showed absorptions at 6.41 (m), 6.29 (m), 6.31 (s), 6.06 (s), 5.76 (m), and 5.59 μ (m). The acidic fraction extracted by 5 percent sodium hydroxide solution showed absorptions at 5.71, 5.88 and 6.25 μ. There was neither hydroxyl, nor aromatic characteristic absorption. The reaction was repeated with careful monitoring by glc after photolysis periods of 10, 20 and 30 minutes. The only product which developed was 7a-methyl-5(7aH)-indanone (28a) which reached its maximum yield at 20 minutes, and then decomposed on further photolysis.

Irradiation of 7a-Methyl-5(7aH)-indanone (28a) in Anhydrous Dioxane: Broad Spectrum Lamp

Compound 28a, 1.20g (0.0080 mole), was dissolved in ca. 250 ml of anhydrous dioxane and irradiated for 90 minutes with a 450 watt high pressure mercury arc source. The solvents were removed in vacuo. The

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

remaining resinous amber oil was placed on a silica gel column and eluted with hexane-ether mixtures. No identifiable products were isolated.

Irradiation of 7a-Methyl-5(7aH)-indanone in 45 Percent Methanolic Acetic Acid

Compound 28a, 1.34g (0.00926 mole), was dissolved in ca. 300 ml of 45 percent acetic acid in methanol solution and was irradiated with a 450 watt Hanovia high pressure arc source for 90 minutes. Solvents were then removed in vacuo leaving a brown oil. Vapor phase chromatographic analysis of the oil on a 10 foot column of SE-30 showed three major peaks in addition to starting material. The reaction mixture was then placed on a column of silica gel and eluted with hexane-ether mixtures. Compound 28a was eluted from the column with 10 percent ether-hexane. Elution with 25 percent ether-hexane yielded 0.43g (27 percent) of compound 42. Elution with 50 percent ether-hexane gave 0.422g (37 percent) of compound 43. Elution with 75 percent ether-hexane gave 0.32g (20 percent) of compound 30a.

Compound 42 exhibited the following properties: uv max (95 percent ethanol, 220 nm (ϵ = 3,500) and 298 nm (ϵ = 500); ir (CCl_4) 3.30, 3.40, 3.48, 3.53, and 5.78μ; nmr (CCl_4) δ 3.27 (s, 3H), 2.60 (d, J = 17 Hz, 1H), 2.20 (d, J = 17 Hz, 1H), 1.97 (d, J = 6 Hz, 1H), 2.62 (d, J = 6 Hz, 1H), 1.24 - 1.92 (broad absorption, 6H) and 1.10 (s, 3H).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.20; H, 9.07.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Compound 43 exhibited the following properties: ir (CCl_4) 3.37, 3.40, 3.52, 5.85 and 6.15 μ; uv max (95 percent ethanol) 230 mμ (ϵ = 12,800); nmr δ 5.75 (s, 1H), 3.20 (s, 3H), 1.15-3.08 (broad absorption, 9H) and 0.92 (s, 3H).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.14, H, 8.95.

Compound 30a exhibited the same spectral properties as have been reported (21).

Irradiation of 7a-Methyl-5(7aH)-indanone(28a) in Anhydrous Methanol, Broad Spectrum Lamp

Compound 28a, 5.50g was dissolved in ca. 250 ml of freshly distilled anhydrous methanol and irradiated with a 450 watt Hanovia high pressure arc. The reaction was followed by removing aliquots of the reaction mixture at regular intervals and analyzing these by glc with an Apiezon L column. After 140 minutes, the products ratio of 28a, 42, 43, 30a was 20 percent, 30 percent and 25 percent respectively. The crude mixture was chromatographed on a silica gel column. 1.4g (25 percent)of the desired product 42 was obtained.

Treatment of the 9-Methyl-5-methoxytricyclo-[4.3.$0^{2,9}$]-3-nonanone 42 with Lithium in Ammonia

Compound 42, 0.144g (0.000742 mole), was dissolved in 50 ml of anhydrous ether and added dropwise to ca. 250 ml of dry ammonia, with contained 0.036g of lithium metal, in a 500 ml three-necked round bottomed flask equipped with mechanical stirrer, acetone-dry ice condenser and dropping funnel (34). The mixture was stirred for one hour after which

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

excess ammonium chloride was added and the resulting reaction mixture was stirred for 30 minutes. The ammonia was then evaporated from the reaction mixture by allowing it to stand at room temperature overnight. To the ethereal solution remaining was added ca. 50 ml of water and the layers were separated. The water layer was extracted several times with ether and the combined organic layers were dried over sodium sulfate. The solvents were removed in vacuo leaving a brown oil. Infrared and nmr analysis showed the oil to consist of primarily compound 44 along with a small amount of compound 42. Vapor phase chromatographic analysis on a 10 foot column of SE-30, however, showed the presence of three compounds. One of the components was found to have the same retention time as compound 42. Preparative vapor phase chromatographic analysis of the reaction mixture on a 10 foot column of SE-30 allowed collection of the component which did not appear in the nmr and ir spectra of the crude mixture prior to glc studies. The ir spectrum of this component showed absorptions at 5.90 (C=O) and 6.19 μ (C=C) and it was assigned the structure 45. The reaction mixture was then distilled at reduced pressure yielding a colorless oil (compound 44), 0.12g, which exhibited the following properties: ir (film) 5.75 μ; nmr (CCl_4) δ 3.20 (s, 3H), 0.80-2.10 (m, 12H), and 1.21 (d, J = 7.0 Hz, 3H).

Treatment of 7-Methyl-4a-methoxy-2-indanone (44) with Sodium Hydride

Compound 44, 0.1227g (.000630 mole), was added to 0.0372g of sodium hydride in 25 ml of dimethoxyethane in a three necked round bottomed flask equipped with magnetic stirrer and condenser. The result-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

ing reaction mixture was placed under nitrogen flow and stirred for two hours after which time 30 ml of water and 50 ml of ether were added. The layers were separated and the water layer was extracted several times with ether. The combined organic layers were dried over sodium sulfate. The solvents were removed in vacuo leaving 0.092g of a yellow oil. Vapor phase chromatography showed the reaction mixture to consist of ca. 90 percent compound 45 and ca. 10 percent compound 44. The yellow oil was distilled at reduced pressure yielding a colorless oil which exhibited the following properties: ir (CCl_4) 5.92 and 6.19 μ; uv max (95 percent ethanol) 232 mμ (ϵ = 11,000) and 320 mμ (ϵ = 30); nmr (CCl_4) δ 5.77 (s, 1H), 2.27 (d, J = 4 Hz, 2H), 0.77 (d, J=7Hz, 3H), 1.5-2.9 (broad absorption, 8H).

Preparation of 7a-Methyl-4-carbomethoxy-7,7a-dihydro--5(6H)-indanone (31j)

A procedure similar to that employed by Wenkert (35) in another system was used. To a suspension of 1.12g (0.025 mole) of 53.4 percent sodium hydride-mineral oil dispersion in 50 ml of dry DME stirred under nitrogen was added 5g (0.03 mole) of 31a. The solution was stirred at room temperature overnight, heated to reflux, and the solvent removed by distillation until the volume remaining was approximately 20 ml. The reaction mixture was allowed to cool to room temperature and 100 ml of dry ether was added. Carbon dioxide which had been passed through a calcium chloride drying tube was then allowed to bubble into the solution for 1.25 hours while the temperature was maintained at 0°C by an ice bath. At the end of this time 50 ml of 10 percent sodium hydroxide was added to the cold reaction mixture and stirring was continued for an additional

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

15 minutes. The basic solution was then washed with three 50 ml portions of ether and acidified to pH 2-3 with dilute (3:1) hydrochloric acid at which time the solution became cloudy. The aqueous layer was then extracted with ether and the ether extracts were poured slowly into a stirred solution of diazomethane in ether (36). The cold reaction mixture was stirred for 0.5 hours after which the excess diazomethane was destroyed with aqueous hydrochloric acid. The layers were separated and the organic layer was washed twice with 50 ml portions of saturated sodium bicarbonate solution and once with saturated brine. The solution was then dried over anhydrous sodium sulfate, the drying agent removed by filtration, and the solvent removed in vacuo to leave 3.90g of a mixture, which according to the nmr spectrum appeared to contain 60 percent of 51 and 40 percent the desired enone 31j. The mixture was chromatographed on 60g silica gel column. Elution with 5 percent to 20 percent ether in hexane gave mainly 31j. Further elution with 30 percent to 50 percent ether in hexane gave mixtures of 51 and 52 observed by glc (26). The spectral properties were recorded as follows: Compound 31j: δ 3.75 (s, 3H), 2.35-2.75 (m, 2H), 1.68-2.15 (broad absorption,8H) and 1.23 (s, 3H). Compound 51: δ 5.87 (s, 1H), 3.77 (s, 3H), 2.35-2.75 (broad absorption, 3H), 1.67-2.16 (broad absorption, 6H) and 0.95 (s, 3H). Compound 52: δ 12.25 (s, 1H), 5.90 (s, 1H), 3.75 (s, 3h), 2.15 (broad absorption, 6H) and 1.24 (s, 3H).

Attempted Dehydrogenation of 31j with DDQ

A 100 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirrer bar was placed under positive nitrogen flow. Freshly distilled anhydrous dioxane, 50 ml, was charged into the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

flask and 0.37g DDQ was added. The mixture was stirred until the DDQ dissolved, and 0.35g of 31j was added. The mixture was refluxed with stirring for 24 hours. The solution was cooled to room temperature, and the solid DDHQ was collected by filtration with suction. The mixture was concentrated to ca. 50 ml by removal of solvents in vacuo. The mixture was cooled to room temperature and filtered with suction to remove the remaining DDHQ. It was then poured onto a loosely packed column of 70g of alumina and eluted under pressure with 500 ml of benzene. The solvents were removed in vacuo and the resulting yellow oil was distilled through a short path head to give a mixture which when analyzed by glc showed at least five peaks. Attempted isolation of the product by silica gel chromatography and by preparative glc was unsuccessful.

Attempted Dehydrogenation of 31j with Selenium Dioxide

A dried 100 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirring bar was placed under positive nitrogen flow and 40 ml freshly distilled tert-butyl alcohol and 0.14 ml glacial acetic acid was charged into the flask. Freshly sublimed selenium dioxide, 0.16g was added and the mixture was stirred until the selenium dioxide dissolved. Compound 31j, 0.2g (0.075 mole), was added and the mixture was refluxed, with stirring, for 46 hours. The mixture was concentrated by distillation of solvents in a nitrogen atmosphere. The selenium metal formed was removed by several filtrations, with suction, and the remaining solvents were removed in vacuo. The resulting black viscous mass was taken up in 30 ml of ether and filtered with suction. The solvents were evaporated in vacuo. Distillation

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

using a micro Hieckmann apparatus gave a 10 percent recovery of the starting material 31j as indicated by its nmr and ir spectra. No other products were recovered.

7,7a-Dihydro-4-methoxy-7a-methyl-5(6H)-indanone(31d)

Compound 31d was prepared by a method derived from that reported by Wendert (14,35). In a 500 ml three-neck flask equipped with a mechanical stirrer, dropping funnel, and Claisen head to allow having a thermometer inside the flask and a condenser with an inlet for nitrogen, which was established as the atmosphere, was placed 1.25g (0.7970 mole) of potassium and 9.35 ml of absolute ethanol were added dropwise with stirring. After the reaction was complete and the flask had cooled to room temperature, 900 ml of anhydrous ether were added, and the mixture cooled with an ice bath to 10°C. To this was added 16.7g (0.17 mole) of 2-methylcyclopentanone in 20 ml of anhydrous ether. A solution of 11.2g (0.085 mile) of 1,4-dimethoxy-2-butanone (37) in 120 ml of anhydrous ether was added dropwise with rapid stirring over about 2 hours, while a temperature of 8-10°C was maintained with an ice bath. After the addition was complete, the reaction mixture was stirred for 3 hours longer while being warmed to room temperature. An ethereal solution of glacial acetic acid (10 percent by volume) was added dropwise until the red color of the reaction mixture changed to yellow. The ether layer was decanted from the solid, washed with 50 ml each of water and saturated brine, dried (Na_2SO_4), concentrated, and distilled giving 9.46g (62 percent) of 31d as a colorless liquid: b.p. 38-88°C (0.51 mm). The spectral properties of 31d were in agreement with those reported by

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Tuller (14).

4-Methoxy-7a-methyl-5(7aH)-indanone(28d)

Compound 28d was prepared by a procedure similar to that employed by Burn, Kirk, and Petrow (30). A 1000 ml round-bottom flask equipped with a magnetic stirrer and reflux condenser and having a nitrogen atmosphere, was charged with 400 ml dioxane (freshly distilled over sodium), 4.6g (0.026 mole) of 31d and 5.97g (0.026 mole)of DDQ. The mixture was stirred until homogeneous and then stirred at reflux for 36 hours. After cooling to room temperature, the p-dioxane was removed in vacuo and the residue was dissolved in 100 ml of benzene and filtered to remove DDHQ. The filter cake was washed with 50 ml of benzene and the combined filtrates were concentrated. The residue was placed on a column of 50g of neutral alumina and rapidly eluted with 500 ml of benzene. Evaporation of the benzene gave 3.28g of a pale yellow oil which by glc analysis (Carbowax column) was shown to contain about equal amounts of 28d and the starting material, 31d. Chromatography on 100g of silica gel using hexane-ether as elutent afforded 1.57g of the enone 31d (20 percent ether in hexane) and 1.53g (51 percent) of the dienone 28d (40 percent ether in hexane), and 1.18g (15 percent) of the trienone 39d. The spectral properties of 28d were in agreement with those reported by Tuller (14).

Irradiation of 4-Methoxy-7a-methyl-5(7aH)-
Indanone (28d)in Anhydrous Dioxane

Compound 28d, 0.3g, was dissolved in ca. 250 ml of freshly distilled anhydrous dioxane and irradiated with a Hanau seven watt or

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

with a 450 watt high pressure mercury arc source with a Pyrex filter. The reaction was monitored by vapor phase chromatography. After 15 minutes irradiation, the starting material was gone and five new peaks had appeared. The solvents were removed in vacuo, and the crude oily product was placed on a column of 100g of silica gel. On elution of the column, no identifiable products were isolated.

4-Methoxy-7a-isopropyl-5(7aH)-indanone(28i)

Compound 28i was prepared by the same procedure as was described above for 28d. Using 75.7g (0.54 mole) of 2-isopropylcyclopentanone and 40g (0.30 mole) of 1,4-dimethoxy-2-butanone, 6.80g of the enone 31i was obtained. Dehydrogenation of this compound (10.0g) with selenium dioxide 20.0g, gave a volatile mixture of 7g, which was chromatographed on 250g silica gel using hexane-ether as the elutant afforded 5.43g of compound 28i (10-15 percent ether in hexane).

Compound 28i exhibited the following properties: ir (film) 5.76, 6.02, 6.06, 6.24 and 7.25 μ (gem dimethyl), nmr (CCl_4) δ 6.90 (d, J = 9.5 Hz, 1H), 6.15 (d, J = 9.5 Hz, 1H), 3.70 (s, 3H), 1.60-2.75 (broad absorption, 7H), 1.05 (d, J = 7Hz, 3H) and 0.64 (d, J = 7Hz, 3H). Exact mass: found 206.13101 (Calcd 206.13058).

Irradiation of 28i in Anhydrous Dioxane 2537 Å Light Source

Compound 28i, 0.3g was dissolved in ca. 250 ml of freshly distilled anhydrous dioxane and irradiated with a Hanau seven watt low pressure mercury arc source for 37 minutes (80 percent conversion). The solvents were removed in vacuo, and the crude oily product was analyzed by nmr. Two doublets at δ 7.23 and 6.05 ppm with a coupling

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

constant of 5.0 Hz which provided the evidence for the presence of the lumiproduct 29d. The crude mixture was placed on a column of 10 g of silica gel. Elution with 1 liter 7 percent ether-hexane gave mainly a new product 32i (0.12g, 40 percent). Compound 32i exhibited the following properties: uv max (95 percent EtOH) 313 mμ, 206 mμ; ir (film) 5.82, 5.92, 5.99, 6.10, 6.21, 6.39 and 7.27 μ (gem dimethyl); nmr (CCl_4) δ 6.87 (d, J = 5Hz, 1H), 5.82 (d, J = 5Hz, 1H), 3.96 (s, 3H), 1.75-2.75 (broad absorption, 7H), 0.87 (d, J = 5Hz, 6H). Exact mass: found 206.12558 (Calcd 206.13058).

Irradiation of 28i in Anhydrous Dioxane with Pyrex Filter

Compouns 28i, 0.4g, was dissolved in ca. 250 ml of anhydrous dioxane and irradiated for 45 minutes using a 450 watt lamp fitted with a Pyrex filter. The solvents were removed in vacuo, and the crude oily photoproduct was placed on a column of 15 g of silica gel. Elution with 7 percent ether-hexane gave 0.14 g (35 percent yield) of compound 32i. Further elution with 10 percent ether hexane recovered the starting dienone 28i.

Preparation of 4-Methoxy-10-methyl-$\Delta^{1,4}$-3-hexahydronaphthalenone(3d)

1,4-Dimethoxy-2-butanone 23.8g (0.18 mole) in 200 ml of dry ether was added over 2.5 hours to a mixture of 2-methylcyclohexanone 38.0 g (0.34 mole) and ethanolic potassium hydroxide (3.33 g KOH in 20 ml EtOH) in 220 ml of dry ether at 6-8°C under nitrogen atmosphere. After stirring for 3 hours while warming to room temperature the mixture (which had turned reddish brown) was approximately neutralized with a

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

solution of 4.5 g acetic acid 45 ml dry ether (acid added until mixture turned yellow). The ether layer was decanted and the residue washed with ether. The ether layers were dried, concentrated, and distilled. About 26 g of unreacted 2-methylcyclohexanone was collected at aspirator pressure at 58-65°C. Further distillation at a pressure of 0.07 mm gave the product 4-methoxy-10-methyl-Δ^4-3-octalone 2.93 g (0.015 mole) and DDQ 3.92 g (0.0172 mole) were dissolved in 160 ml of dry benzene and 5.4 ml of acetic acid was added. The mixture was refluxed under nitrogen atmosphere for 40 hours and was filtered to remove the DDHQ. It was then concentrated and poured onto a loosely packed column of 30g of alumina and eluted under pressure with 1 liter of benzene. The solvents were removed and the resulting brownish yellow oil was distilled through a short path head to give 1.40g of the product. ir (film) 6.03, 6.12, and 6.22 μ; uv max (95 percent EtOH) 242 nm (ϵ 10,500) and 270 nm (ϵ 6,000); nmr (CCl_4) δ 6.87 (d, 1H, J = 9.5 Hz), 6.13 (d, 1H, J= 9.5 Hz), 3.62 (s, 3H), 1.50-3.27 (broad absorption, 8H) and 1.27 (s, 3H).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.56; H, 8.39. Found: C, 74.52; H, 8.39.

Irradiation of 3d in Anhydrous Dioxane

Compound 3d, 0.12 g, was dissolved in ca. 200 ml of anhydrous dioxane and irradiated with a Hanau seven watt low pressure mercury arc source for 55 minutes (50 percent conversion by glc), and five peaks were observed. The solvents were removed in vacuo, and the crude oily photoproduct was placed on a column of 15 g of silica gel. No products

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

were isolated and identified.

Preparation of 6-Acetoxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(55)

The method of Seeback (38) was employed for the synthesis of 55. To a solution of 41 g (0.093 mole) of lead tetraacetate dissolved in 200 ml of glacial acetic acid and 200 ml of acetic anhydride was added 9.17 g (0.061 mole) of 55. The mixture was stirred under nitrogen at 70-80°C for 24 hours. Most of the solvent was removed by distillation at aspirator pressure, 100 ml of water was added, and the mixture was extracted thoroughly with ether. The ether extracts were cautiously neutralized with solid sodium bicarbonate and dried over anhydrous sodium sulfate. The drying agent was removed by filtration, and the ether was removed in vacuo. The dark brown oil which remained was subjected to vacuum distillation to give starting material and the corresponding $\Delta^{1,4}$-dienone boiling at 80-85°C/0.005 mm, followed by 6.25 g (50 percent) of the desired product 55 boiling at 100-130°C/0.005 mm. The following properties were observed for 55. The ultraviolet spectrum of 55 showed λ_{max}^{EtOH} 242 nm (ϵ 10,500); ir (CCl_4) 5.76, 5.94, 6.01, and 6.18 μ; nmr (CCl_4) δ 1.27 (s, 3H), 2.02 (s, 3H), 1.1-2.7 (broad absorption, 8H), 5.28-5.63 (m, 1H), and 5.68 (broad absorption, 1H).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.20; H, 7.74. Found: C, 69.26; H, 7.83.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Saponification and Oxidation of 55; Attempted Preparation of 6-Methoxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(28e)

The procedure of Rao and Axelrod (39) was employed for the oxidation of 55. A solution of 2.2 g (0.01 mole) of the keto-acetate 55 in 150 ml of methanol was treated with 1.2 g (0.022 mole) of potassium hydroxide dissolved in 10 ml of water. The resulting reaction mixture was stirred overnight at room temperature while a thin stream of oxygen was bubbled through the yellow solution using a fritted cylinder. The reaction mixture was then evaporated to near dryness, the residue was diluted with 50 ml of water, and the aqueous solution was washed with several 50 ml portions of ether. The aqueous layer was then acidified with dilute hydrochloric acid and extracted thoroughly with ether. The ether extracts were dried over anhydrous sodium sulfate, the drying agent was removed by filtration, and the solvent was removed *in vacuo* to leave a viscous yellow oil. The oil was not further purified, but was dissolved in 100 ml of day *t*-butyl alcohol stirred under nitrogen, and a solution of 0.45 g (0.115 gram-atoms) of potassium metal dissolved in 50 ml of dry *t*-butyl alcohol was added in a thin stream. The reaction mixture, which turned an orange-red, was stirred 0.5 hours at which time 4 g (0.028 mole) of methyl iodide was added in a thin stream. The reaction mixture was heated to reflux 20 minutes at which time approximately 3/4 of the *t*-butyl alcohol was removed by distillation. Fifty milli-liters of water was then added and the mixture was extracted with ether. The ether extracts were dried with anhydrous sodium sulfate. the drying agent was removed by filtration, and the ether was removed *in vacuo* to leave a yellow oil. Distillation gave

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

1.6 g material containing 20 percent of compound 28a, 70 percent of the unoxidized methoxy enone 31e and 10 percent of the desired product 28e. The mixture was placed on a column of 40 g of silica gel. Elution of 20 percent ether hexane gave a sample of pure 28e. It exhibited the following properties: uv (95 percent EtOH), ir (film) 5.75, 5.97, 6.10, and 6.19 μ, 246 nm (ε 10,300), nmr δ 5.90 (s, 1H), 5.77 (s, 1H), 3.57 (s, 3H) 1.40-2.80 (broad absorption, 6H), 1.22 (s, 3H).

Attempted Preparation of 28e by Other Methods

(a) The keto acetate 55, 6g, was dissolved in 300 ml of methanol and 6g of potassium bicarbonate (39) in 60 ml water was added. The mixture was refluxed under nitrogen atmosphere for 4 hours. It was then acidified with acetic acid. Most of the solvent was removed under reduced pressure. From the nmr spectrum of the crude product it appeared to be a 50:50 mixture of the hydroxy enone 31k and dienone 28k.

(b) To a solution made up of 5.4g of mixture of 28k and 31k (obtained from the previous method) in 20 ml of acetic acid was added 2.7g of bismuth trioxide (40). The mixture was heated at 100°C with stirring for 15 minutes. Another 2.7g of bismuth trioxide was added, and heating was continued for another 45 minutes. After the mixture was filtered, 200 ml of water and 200 ml of ethyl acetate were added to the filtrate. The organic layer was separated, washed with 150 ml of water, 75 ml of saturated aqueous sodium bicarbonate solution, dried over anhydrous sodium sulfate and concentrated. The oily residue

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

(4.5 g) was dissolved in DME (100 ml), 7 g of methyl iodide was added, 1 g of sodium hydride was added carefully in three portions. The mixture was stirred under nitrogen atmosphere at room temperature for 2 hours. Water was added and the organic materials were extracted by ether. Dried over anhydrous sodium sulfate. Solvents were evaporated in vacuo. The main product appeared to be 56 according to nmr spectrum.

(c) Compound 31k, 0.36 g, was mixed with 0.2 ml methanol, 1 g $Cu(OAc)_2 \cdot H_2O$ and 2.2 ml 50 percent water-acetic acid (41). The mixture was stirred and refluxed for one minute, then filtered. The filtrate was washed with saturated sodium chloride solution and then extracted with ether. The ether solution was washed with saturated sodium chloride solution, 5 percent sodium bicarbonate solution and again with saturated sodium chloride solution. Dried over magnesium sulfate, solvents were removed in vacuo. The recovered product proved to be only starting material. 31e: nmr (CCl_4) δ 6.45 (s, 1H), 3.58 (s, 3H), 0.85-2.65 (broad absorption, 9H) and 1.15 (s, 3H). 28k: nmr (CCl_4) δ 5.75 (s, 1H), 5.62 (t, J = 2Hz, 1H), 3.33 (s, 1H), 1.60-2.67 (broad absorption, 6H) and 1.14 (s, 3H). 31k: nmr (CCl_4) δ 5.75 (t, J = 2Hz, 1H), 3.34 (s, 1H), 4.35 (d, J = 6Hz, 1H), 1.60-2.67 (broad absorption, 8H) and 1.22 (s, 3H). 57: nmr (CCl_4) δ 6.45 (s, 1H), 2.58 (s, 2H), 1.45-2.42 (broad absorption, 6H) and 1.15 (s, 3H). 56: nmr (CCl_4) δ 6.14 (s, 1H), 5.62 (broad singlet, 1H), 3.62 (s, 3H), 2.46 (s, 1H), 2.42 (s, 1H), 1.55-2.00 (broad absorption, 4H) and 1.05 (s, 3H).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Irradiation of 28e in Anhydrous Dioxane

Compoune 28e 100 mg was dissolved in ca. 100 ml of freshly distilled anhydrous dioxane and irradiated with a Hanau seven watt low pressure mercury arc source. The reaction was monitored by glc; seven peaks all of about equal area were present after 60 minutes irradiation. The solvents were removed in vacuo, and the crude oily product was placed on a column of 8 g of silica gel. No identifiable products were isolated.

Irradiation of 6-Methoxy-7a-methyl-7, 7a-dihydro-5(6H)-indanone(28e) in Methanol

Compound 28e, 20 mg was dissolved in 10 ml of anhydrous methanol and irradiated for 60 minutes with a 450 watt high pressure mercury arc source. The solvents were removed in vacuo. The remaining resinous amber oil was placed on a silica gel column and eluted with hexane-ether mixture. No identifiable products were isolated. Glc analysis of the crude mixture showed that at least six components were present. The mixture was not investigated further.

Attempted Preparation of 6-Carboxy-7a-methyl-7,7a-dihydro-5(6H)-indanone(28f)

The method of Edwards et al. (42) was employed to a suspension of sodium hydride (1.86 g, .0775 mole) (3.48 g of 53.4 percent HaH in oil) in 100 ml dry benzene stirred under dry nitrogen was added dry methanol (1.67 g, 0.0522 mole). The suspension was heated to boiling for a few minutes, cooled to room temperature, and ethyl formate (5.735 g, 0.0775 mole) was added in a thin stream. The reaction mixture

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

was then stirred for 30 minutes; cooled in an ice bath, and the enone (31a) (5.0 g, 0.0310 mole) was added dropwise with stirring and cooling in 100 ml dry benzene. When addition was complete, the ice bath was removed and the mixture was allowed to stir 3.5 days. The suspension was acidified with 100 ml iced 5 percent sulfuric acid and stirred for 5 minutes. The layers were separated and the aqueous layer extracted three times with 50 percent benzene-ether. The combined organic layers were extracted with 250 ml of 2 percent aqueous potassium hydroxide. The basic extracts were washed once with ether and then acidified with dilute hydrochloric acid. The aqueous layer was than extracted several times with 50 percent benzene-ether, the organic layers were washed once with saturated sodium chloride solution and then dried over magnesium sulfate. Removal of the solvent gave 3.6 g dark yellow oil which distilled in vacuo. Spectral data indicated that 58 was present in the distillate. The distillate 2.33 g, was dissolved in 600 ml dioxane and 4g of DDQ was added. After 10 minutes, the reaction mixture was diluted with 1 liter of dichloromethane and filtered through a short column of alumina. The column was washed with 200 ml of dichloromethane, 2 liters of 10 percent ether in benzene and one liter ethanol. The solvent was evaporated and the residues were extracted with carbon tetrachloride and chloroform.

On chromatography of the oil on silica gel, a small quantity of a compound which appeared to be 28ℓ was obtained. It showed: nmr (CCl_4) δ 9.79 (s, 1H), 2.25 (s, 1H), 3.90 (broad singlet, 1H), 1.8-2.9 (broad absorption, 6H) and 1.36 (s, 3H). ir (film) 5.88, 6.01, 6.14 and 6.25 μ; uv max (95 percent EtOH) 220 and 236 nm.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

An insufficient quantity of material was available for further characterization.

Preparation of Ethyl 2-(3'-Oxobutyl)-cyclopentanone-2-carboxylate(60)

A solution of 49.6 g (0.318 mole) of ethyl cyclopentanon-2-carboxylate, 30.0 ml (25.5 g, 0.354 mole) of anhydrous methyl vinyl ketone, 12.0 ml of triethylamine and 200 ml of dry benzene was allowed to stand at room temperature for 7 days (43). The volatile components were then removed and the product was fractionally distilled, b.p. 140-142°C/2.5 mm, yield 66.3 g (92 percent).

Cyclization of Ethyl 2-(3'-Oxobutyl)-cyclopentanone-2-carboxylate(60)

In a 50 ml round-bottom flask fitted with a candenser and protected by a drying tube, a solution of 25 g ethyl 2-(3'-oxobutyl) cyclopentanone-2-carboxylate, 25 g of aluminum t-butoxide and 200 ml of dry benzene was added (44). The solution was stirred vigorously and refluxed for 48 hours. The mixture was poured into 600 ml of water and 30 ml of concentrated hydrochloric acid was added the mixture stirred vigorously until the layers separated. The benzene layer was separated and the aqueous layer extracted well with ether. The combined extracts were dried over anhydrous magnesium sulfate and the benzene and ether removed on the rotor-vaporator. Distilled at reduced pressure yield 11.0 g (47.8 percent), b.p. 108-110°C/0.3 mm.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Methyl 5-Oxo-5,6,7,8-tetrahydroindane-8-carboxylate (Alternate Method)

Methyl 5-pyrrolidine-2,6,7,8-tetrahydroidene-8-carboxylate (45a). A solution of dione ester 60 (42.5 g, 0.200 mole) and pyrrolidine (28.5 g, 0.401 mole) in anhydrous benzene (360 ml) was heated to reflux in an atmosphere of nitrogen under a Dean-Stark water separator. After 12 hours 6.9 ml (0.38 mole) of water had been collected. Evaporation of the solvent and excess pyrrolidine gave 45.2 g (91 percent) of a brownish liquid which proved to be the ester 61 ir (film) 5.81, 6.12 and 6.30 μ. Methyl 5-oxo-5,6,7,8-tetrahydroindane-8-carboxylate 31h. The crude enamine 61 was dissolved in benzene 360 ml and hydrolyzed by the procedure described by Stork (45b). A solution of sodium acetate (8.0 g) and acetic acid (16.2 ml) in water (16.2 ml) was added to the benzene solution of the enamine. The resulting mixture was heated to reflux under nitrogen for 4 hours. The mixture was then washed with water, 10 percent aqueous hydrochloric acid, saturated aqueous sodium bicarbonate solution, saturated sodium chloride solution, and dried. Evaporation of the solvent gave 33.0 g of a pale yellow oil. Distillation afforded 31.5 g (81 percent based on dienone ester 60) of a colorless liquid 31h. The spectral properties showed: ir (film) 5.82 and 6.02 μ, nmr (CCl_4) δ 5.77 (t, J = 1.9 Hz, 1H), 4.13 (q, J = 8.0 Hz, 2h), 1.55-2.75 (broad absorption, 10 H), and 1.22 (t, J = 8.0 Hz, 3H); exact mass 208.10998 (Calcd 208.10985).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Dehydrogenation of 7,7a-dihydro-7a-carboethoxy-5(6H)-indanone (31h) with DDQ

The enone 31h, 1.5 g, was refluxed with 1.7 g of DDQ in 100 ml of dioxane as before. On work up 0.88 g of crude oil was obtained. The nmr and glc analyses showed an approximately 60 percent conversion to the dienone, 30 percent of the recovery starting material, and 10 percent of the linearly conjugated dienone.

(In an alternative experiment, benzene was used as the solvent. In the case 0.60 g of crude material which contained ca. 50 percent of the desired dienone was obtained.)

The crude product, 0.98 g, was placed on a column of 30 g of silica gel. Elution with 15 percent to 17 percent ether in hexane gave mainly unreacted enone. Elution with 15 percent to 25 percent ether-hexane gave 0.52 g of 28h (yield 34 percent). Compound 28h was further purified by preparative glc and had the following properties. uv max (95 percent EtOH) 242 nm (ε 11,000); ir (film) 5.81 and 6.01 μ nmr (CCl_4) δ 7.02 (d, J = 9.5 Hz, 1H), 6.17 (d, J = 9.5, 1H), 6.07 (s, 1H), 4.15 (q, J = 7 Hz, 2H), 1.67-2.75 (broad absorption, 6H) and 1.20 (t, J = 7Hz, 3H).

Anal. Calcd for $C_{11}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 68.84; H, 7.06.

Further elution with 20 to 25 percent ether-hexane gave the linearly conjugated dienone 39h which exhibited the nmr spectral data as follows: nmr (CCl_4) δ 6.45 (s, 1H), 6.45 (q, J = 7Hz, 1H), 5.77 (s, 1H), 4.10 (broad absorption, 2H), 2.2-2.90 (broad absorption, 6H) and 1.15 (t, J = 7 Hz, 3H).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Irradiation of 28h (2537 Å Light Source) in Dioxane

Compound 28h, 0.27 g, was dissolved in ca. 100 ml of anhydrous dioxane and irradiated for 23 minutes (70 percent conversion by glc analysis of photolysis mixture). The solvents were removed in vacuo, and the crude oily photoproduct was placed on a column of 8 g of silica gel. Elution with 1 liter 3 percent ether in hexane gave a mixture of starting dienone 28h and a small amount of unidentified product. Further elution with 2 liter of 5-10 percent ether in hexane gave 70 mg of (65 percent yield) the dienone 62; b.p. 70-100°C (bath temperature)/0.5 mm; uv max (95 percent EtOH) 288 nm (ε 6,500) and 216 nm (ε 3,900); ir (film) 5.88, 6.11 and 6.29 μ; nmr (CCl_4) δ 6.02 (s, 1H), 4.19 (q, J = 6.5 Hz, 2H), 3.15 (s, 2H), 2.38-2.80 (broad absorption, 4H), 1.93 (t, J = 5Hz, 1H), and 1.33 (t, J = 6.5 Hz, 3H).

Anal. for $C_{11}H_{14}O_3$: Calcd: C, 69.88; H, 6.84. Found: C, 69.89; H, 6.90.

Irradiation of 28h in Anhydrous Ethyl Alcohol

Compound 28h, 0.14 g was dissolved in ca. 100 ml of freshly distilled anhydrous ethyl alcohol and irradiated with a Hanau seven watt low pressure mercury arc source. The reaction was monitored by vapor phase chromatography; starting material was converted to a single photoproduct after 15 minutes irradiation. The solvents were removed in vacuo, and the crude oily product was placed on a column of eight grams of silica gel. Elution with 2 liter 10 percent ether-hexane gave 0.082 g (60 percent yield) of pure compound 62.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Irradiation of 28h in 45 Percent Aqueous Acetic Acid

Compound 28h, 0.21 g was dissolved in ca. 250 ml of 45 percent aqueous acetic acid and irradiated for 25 minutes with a 450 watt Hanovia high pressure mercury arc source with a Pyrex filter. The solvents were removed in vacuo by azeotropic distillation with toluene and by freeze-dry. The crude oily photoproduct was placed on a column of 15 g of silica gel and eluted as before to give 0.15 g (65 percent yield) of 62.

Irradiation of 28h in Ethyl Alcohol, Broad Spectrum Lamp

Compound 28h, 0.24 g, was dissolved in ca. 250 ml of anhydrous ethyl alcohol and irradiated for 30 minutes (70 percent conversion by glc analysis). The solvents were removed in vacuo, and the crude oily photoproduct was placed on a column of 10 g of silica gel packed with 1:1 benzene-hexane. Elution with 2 liters, 3 percent ether in hexane gave a small amount of new product with a tentative structure of 29h. Elution with 6 percent to 10 percent ether in hexane recovered the starting dienone 28h. Further elution with 3 liters of ether-hexane gave 0.16 g, 65 percent yield, product 62. Continued elution with 2 liters of ether-hexane mixtures and 500 ml of ether gave 500 mg of a resinous material which appeared to be polymeric and was discarded.

Irradiation of 28h in Anhydrous Dioxane, Broad Spectrum Lamp

Compound 28h, 0.25 g, was irradiated in dioxane under the identical conditions as described above. After 30 minutes irradiation, compound

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

62 was isolated (0.12 g, 50 percent yield).

Irradiation of 28h in Anhydrous Ether

Compound 28h, 0.14 g was dissolved in ca. 100 ml of freshly distilled anhydrous ether and irradiated with a Hanau seven watt low pressure mercury arc source. The reaction was monitored by vapor phase chromatography; starting material was converted to one main photoproduct after 25 minutes irradiation. The solvents were removed in vacuo, and the crude oily product was distilled with a Hieckman tube. An isolation of 64 mg (46 percent yield) of 62 was obtained.

Irradiation of 28h in Anhydrous Ethyl Alcohol: Broad Spectrum Lamp with Quartz Flask

Compound 28h, 0.15 g, was dissolved in ca. 250 ml of anhydrous ethyl alcohol and irradiated for 12 minutes with a 450 watt high pressure mercury arc source without Pyrex filter. The solvents were removed in vacuo. The remaining resinous amber oil was placed on a silica gel column and eluted with hexane-ether mixtures. No identifiable products were isolated.

Irradiation of 28h in Anhydrous Dioxane: Broad Spectrum Lamp Without Pyrex Filter

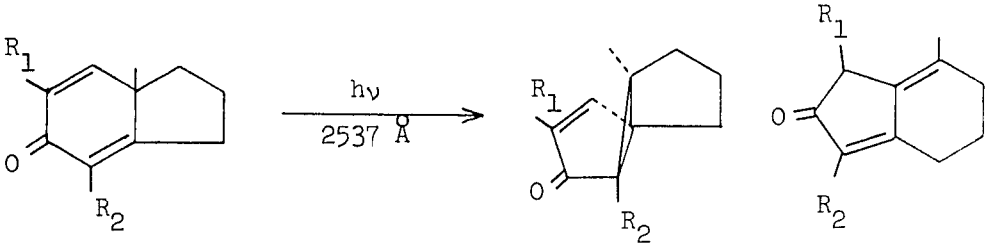
Compound 28h, 0.17 g, was dissolved in ca. 250 ml of anhydrous dioxane and irradiated for 90 minutes with a 450 watt high pressure mercury arc source. The solvents were removed in vacuo. The remaining resinous amber oil was placed on a silica gel column and eluted with hexane-ether mixtures. No identifiable products were isolated.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER IV

DISCUSSION OF RESULTS

As stated in Chapter I and III, this research was aimed to study the synthesis and photochemistry of cross-conjugated cyclohexadienone related to indanone. 6/5-Fused dienones such as 28 give lumiproducts 29 on irradiation in dioxane at 2537 Å. Compound 29b was prepared by the procedure of Powers (21), and its photochemical behavior was investigated in detail.



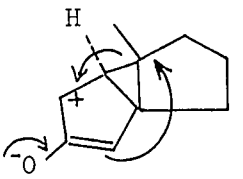
28 29 30

The formation of lumiproducts of the type 29 presumably occurs via 1,4-sigmatropic rearrangements (Path A) (Chart 10) in dipolar cyclopropyl intermediates of the type 18 generally accepted to be involved in dienone photolysis (1c). Jeger, Schaffner and coworkers (19a) have proposed that the formation of 27 from 26 involves the collapse of an intermediate analogous to 18 via Path B.

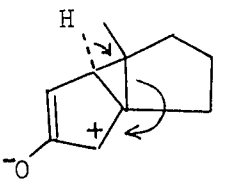
Because of the five-membered B ring an excessive amount of strain would be involved in the formation of a lumiproduct from 26; and that this accounts for the intervention of the new pathway. In

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 10



Path A → 29



Path B → 30

18'

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the case of the unsubstituted model dienone 28a, it appears that the two possible modes of rearrangement compete as indicated by the formation of both 29a and 30a in a 5:2 ratio. The exclusive reaction of 26 via a Path B type process must result from the added strain occurred by the trans fusion of the C ring to the five-membered B ring in the steroidal system (19).

The behavior of 28b and 28c indicates that alkyl substituents favor the Path A process. For 28c the lumiproduct was the only one observed. Methyl substituents would be expected to lower the energy of the intermediate relative to the unsubstituted case and they may also influence the stability of the tricyclic products relative to the bicyclic ones. Either of these factors or a combination of the two may account for product control in these cases.

Previous work has shown that lumiproducts such as 4b, and 9 undergo facile rearrangement on irradiation with light of wavelength greater than 3000 Å. Thus a dilute solution of 29b in dry dioxane was irradiated at room temperature for 90 minutes using a 450-watt Hanovia high pressure mercury lamp fitted with a Pyrex filter. Analysis of the photolysis mixture by glc (27) revealed the presence of one major produce comprising 88 percent of the volatile components and ca. 6 percent each of the starting material and a minor product. Chromatography of the mixture on silica gel led to the isolation of the major product, which was identified as the homoannular dienone 32b, in ca. 50 percent yield.

The ir and nmr spectral properties of 32b were consistent with the structure and it exhibited a uv absorption maximum at 355mμ in

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

95 percent ethanol. The uv maximum for 32b is close to the predicted value of 338mμ using the Woodward-Fieser rules. The related homoannular dienones derived from 9 and 6-epilumisantonin show uv absorption maxima at significantly shorter wavelengths (3b). Lack of planarity of the conjugated system and/or electron withdrawing effects associated with the presence of the lactone rings in the latter compounds may account for this.

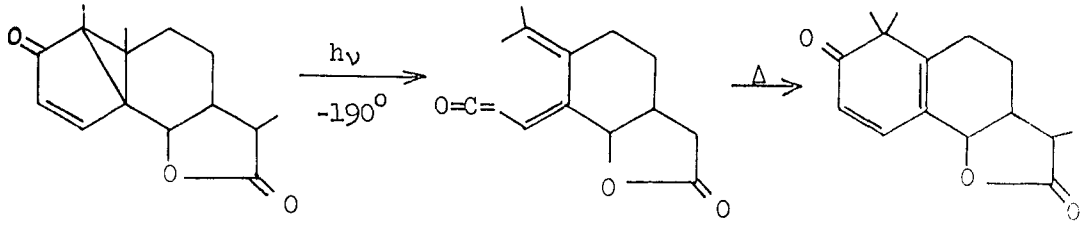
Catalytic hydrogenation of 32b using 10 percent palladium on carbon in 95 percent ethanol led to the isolation of its known tetrahydro derivative having a cis ring fusion (46).

The minor product of irradiation of 29b proved to be the dienone 28b. In a separate run, 29b was irradiated for 30 minutes and the photolysis mixture was analyzed by glc (27). The mixture was found to contain 29b, 32b, and 28b in an approximately 2:2:1 ratio. Direct irradiation of 28b under the same conditions as described for 29b also led to 32b. Monitoring of the reactions by glc (27) revealed that 29b was formed as an intermediate.

Lumisantonin 9 yields mainly a homoannular dienone 10 when irradiated at wavelengths greater than 3000 Å, and 29b having the same substitution on the bicyclo[3.1.0]hex-3-en-2-one moiety yields a similar product. Fisch and Richards (3b) have proposed that 10 is formed via a 1,2-methyl migration in the dipolar intermediate and have presented evidence for the intervention of such a species. However, using infrared spectroscopy Chapman and coworkers (3d) have observed that the ketene 63 is formed on irradiation of 9 at 77°K and that 63 is converted into 10 thermally. These workers have

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

suggested that the ketene pathway is likely to be involved to some degree in the photochemical conversion of 9 into 10 at room temperature.

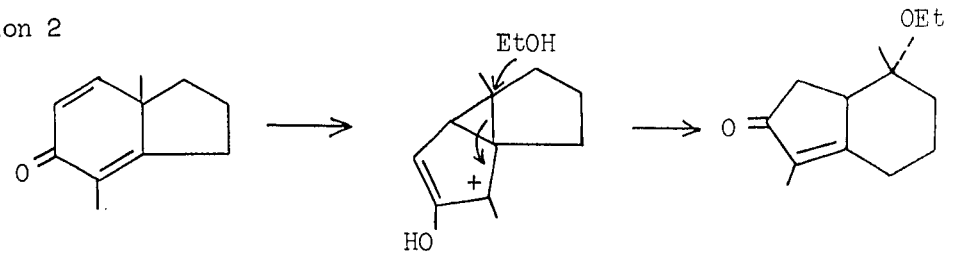


A ketene intermediate, presumably 64, has been observed by infrared spectroscopy when 29b was irradiated at 77°K (47). In view of this it appeared possible that 64 might be formed and trapped at room temperature if 29b were irradiated in a nucleophilic solvent such as ethanol. However, when 29b was irradiated under the conditions described above except substituting absolute ethanol for dioxane, the only photoproduct that could be isolated proved to the the ethoxy ketone 33 which was identified on the basis of its spectral properties. The ethanol adduct of the proposed ketene 64, i.e., 34, could not be detected in this run.

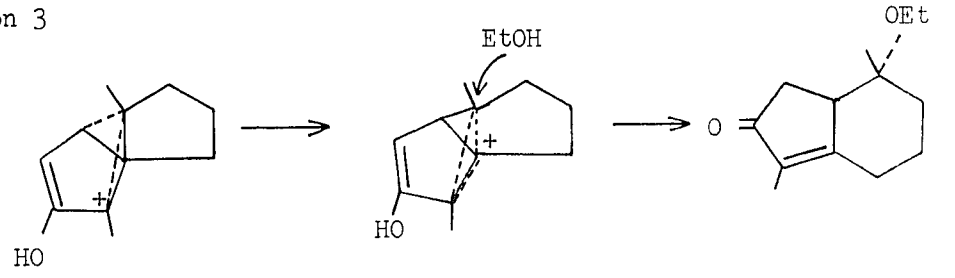
Compound 29b was primarily converted to the dieonone 28b and further irradiation gave a secondary compound 33. The possibility of direct conversion of 29b into 33 photochemically can not be excluded (equation 3).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 2

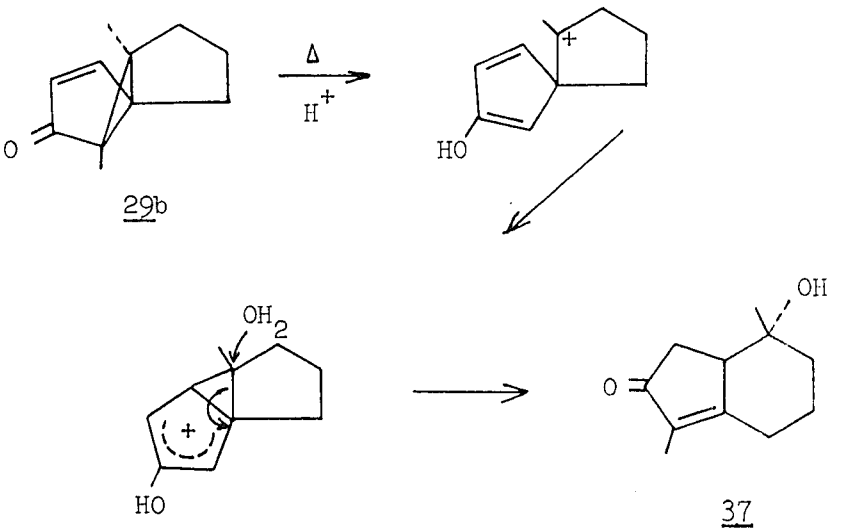


Equation 3



Photolysis of 29b is 45 percent aqueous acetic acid provided the hydroxy ketone (37). Thermal acid-catalyzed rearrangement gave the same product (equation 4).

Equation 4



29b

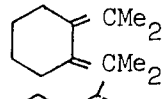
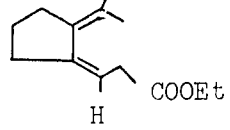
37

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

For reference purposes a sample of 34 was prepared by irradiation of 32b in absolute ethanol using the light source described above. The diene ester exhibited the expected nmr spectral properties which in the appropriate regions were very similar to those reported for photosantonic acid (48).

Despite the presence of a conjugated diene system, the photosantonic acid has no discernible absorptions in the usual ultraviolet region. Steric interference between the acetic acid moiety and one of the methyl groups of the isopropylidene residue is severe, and the two olefinic systems cannot be in the same plane. For compound 34 the two olefinic bonds, extending radially to the cyclopentane skeleton, and the inflexibility of the ring force the system to maintain plananity. The uv spectrum shows absorptions at 280 and 255 nm which suggests that the conjugated system is planar.

Table 2. Comparison of Light Absorption of Some Cyclic Dienones.

Compound	λ_{max}	ϵ_{max}	Ref.
	220	10,000	(49)
	260	750	(50)
	255	1,650	This Work

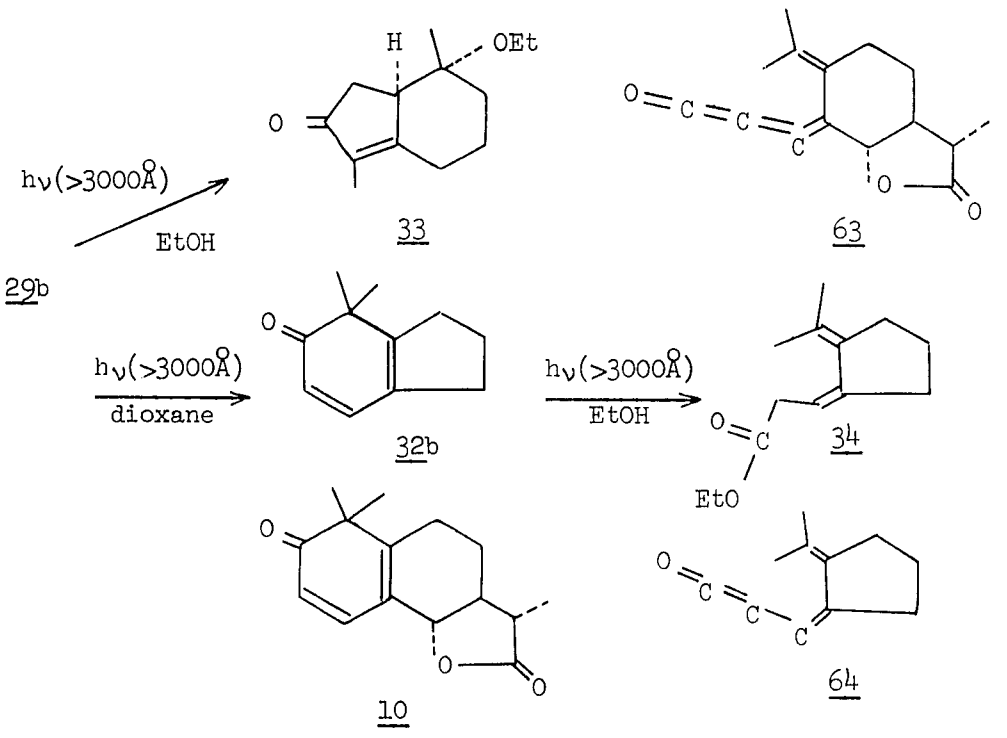
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Using molecular models constructed from Dreiding Stereomodels, it seems unlikely that the attached methylene group rotates freely without steric interference. Therefore, the observation of equal coupling of the two methylene hydrogens with the olefinic hydrogen can be explained if the magnetic coupling of the two methylene hydrogens with the olefinic hydrogen is not distinguishable in this case. Additional splitting of each of the lines indicates that long range coupling with hydrogens occurs.

The behavior observed for 29b in dioxane appears to be most readily explained by considering that light excitation leads to cleavage of the 4,5-bond to produce, after electron demotion, the dipolar species 65 (Chart 12). As pointed out above this type of pathway has been proposed in the conversion of 9 into 10 (3) and analogous pathways have invoked to explain the photochemistry of a number of bicyclo[3.1.0]hex-3-en-2-ones derived from fused ring cross-conjugated cyclohexadienones. In 65 (Chart 12) a 1,2-methyl shift from C-9 to C-4 (Path A) would give rise to 32b while a similar shift from C-9 to C-5 (Path B) would give 28b. A minor rearrangement product of 9 which could have arisen via a Path B type process has been tentatively identified (3b) (equation 5), and the exclusive formation of a cross-conjugated dienone, considered to arise by this type of pathway, has been reported for the irradiation of the lumi-product derived from 17β-hydroxy-1,4,9(11)-androstrien-3-one (equation 6).

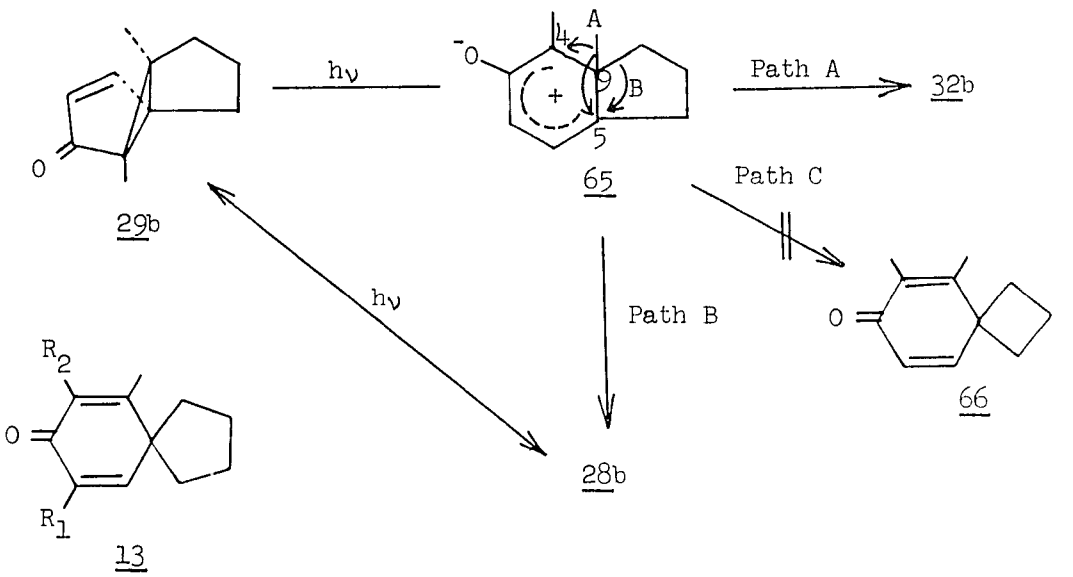
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 11



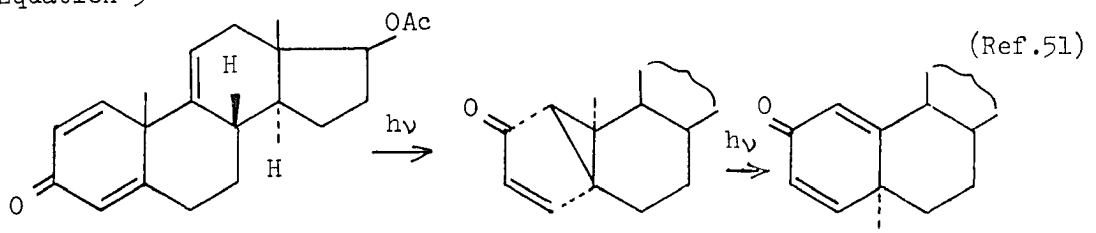
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 12



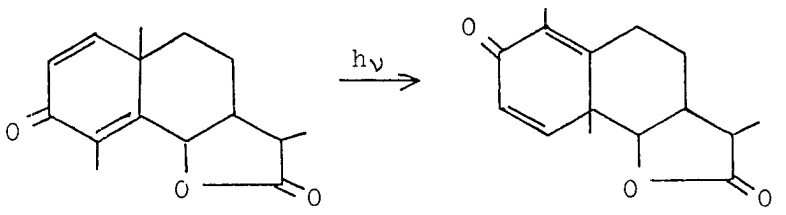
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 5



(Ref.51)

Equation 6



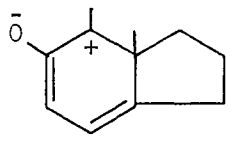
(Ref.36)

The results after short irradiation time can be explained by considering that the Path A and Path B modes of reaction of 65 compete with the former being somewhat favored. On extended irradiation 32b greatly predominates since 28b is photochemical labile being reconverted into 29b.

The behavior of 29b in ethanol also can be explained in terms of 65, if one consideres that in going from the aprotic solvent dioxane to the protic one Path B becomes greatly favored. Some rather striking solvent effects have been observed in other lumiporduct rearrangements (1c). For example, in dioxane 14 is converted to the homoannular dienone 15 as the major product. In acidic media, however, two products 15 and 16 are formed in approximately equal yield (18b).

Thus it appears that the resonance structure of 65 having the smallest amount of charge separation is important in the reaction carried out in nonpolar solvent such as dioxane.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



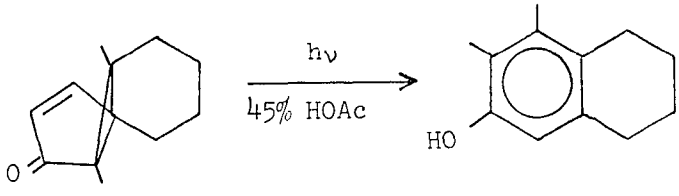
65

Irradiation of the dienone 3b in the neutral media, such as dioxane, produced the lumiproduct 4b as usual. This compound was further irradiated with a 450-watt mercury lamp with a Pyrex filter. The course of the reaction was monitored by removing aliquots of the photolysis mixture and analyzing them by glc. The dienone was found to be the major product (Path B) after short period of irradiation a result just as the same as its five-membered B ring analog.

On prolonged irradiation a mixture which by glc analysis was shown to contain more than ten peaks. Attempts to isolate pure products from the mixture were not successful.

Kropp (7) has reported that irradiation of lumiporudcts 4b in various media leads to photoproducts which are presumably formed by way of spirodienones 13a (equation 7).

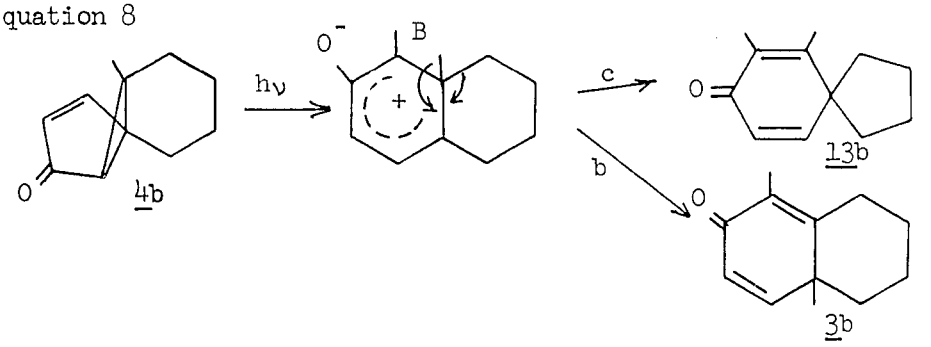
Equation 7



The formation of intermediate 3b can be explained, just like its five membered B ring analog, by a 1,2-shift of the angular methyl group. It is not understood whether the complicated mixture was derived from the lumiproduct 4b or the cyclohexadienone 3b (equation 8).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

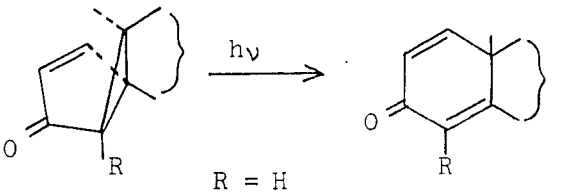
Equation 8



Irradiation of lumiproduct 29a again, gave the starting dienone which reached its maximum at 20 minutes. Several other products were also formed in this run but these could not be isolated. The expected phenol type products was not detected by spectral analysis. The photolysis of 28a with a 450 watt high pressure mercury lamp gave a similarly complicated mixture.

The conversion of bicyco[3.1.0]hex-2-en-3-ones into cross-conjugated dienones can be explained if migration of the angular methyl group of the zwitterionic intermediate to the other angular position (Path B) occurs irrespective of the size of the B ring.

Equation 9



R = H

R = CH_3

In 65 Path A rearrangement may be favored in dioxane because in the nonpolar solvent charge separation must be minimized in the dipolar species. However, in ethanol 65 may be protonated on oxygen giving a mesoionic species in which other factors could favor Path B

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

rearrangement.

No significant amounts of products which could be considered to be derived from 1,2-methylene migration (Path C) in 65 were observed. A Path C type rearrangement in a species analogous to 65 would lead to 66. However, Path C products are apparently completely eliminated as the size of the ring attached to the bicyclo[3.1.0]hex-3-en-2-one moiety is reduced from six to five members. Kropp (7) has suggested that a methylene shift does not take place in the rearrangement of 9, because a spirodienone having two trans fused five-membered rings would be highly strained. The work of Schuster and Fabian (53) which showed that Path A and Path C products arise on irradiation of 6-epilumisantonin supports this suggestion. A spiro[5.3]nonane derivative such as 66 would be expected to be much more strained than 13. Thus the photochemical behavior of 29b appears to provide excellent additional support for Kropp's hypothesis.

Although the above explanation which suggests that the common intermediate 65 gives rise to both 28b and 32b is consistent with the observed data, the fact that a ketene arises when irradiation of 29b is conducted at 77°K indicates that the room temperature reaction may be quite complicated. Indeed, our evidence does not allow the possibility to be ruled out that 32b arises in part or wholly via ketene 63 in dioxane. Also, the possibility exists that a cyclopropanone (54) precursor to 65 intervenes, although the irradiation at 77°K did not provide evidence on this point (47).

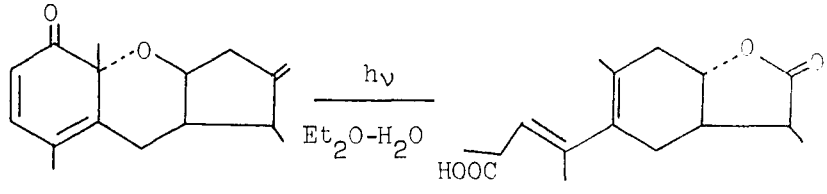
Besides compound 34 irradiation of homoannular dienone 32 in ethyl alcohol with a 450 watt high pressure lamp with a Pyrex filter

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

produced two more minor products, compound 35 and 36, the cis and trans conjugated esters. The crude mixture was purified by collection through a preparative glc column and it was found that compound 36 was the main product isolated. The observation indicated that compound 34 was transformed into 35 and 36, either by a thermal rearrangement or by a photo-induced isomerization. The former process is a suprafacial sigmatropic shift and the latter is an antrafacil (1,5) sigmatropic migration (55) of a methylene hydrogen of 34. In addition, compound 35, the cis conjugated ester, was isomerized in the glc column to give a more stable trans conjugated ester 36.

Both the cis and trans conjugated ester, 35 and 36, are considered to possess planarity character for the cisoid conjugated butadiene ester system, because of the electronic absorption at 250 and 290 nm for the cis 250 and 296 nm for the trans isomer, respectively.

Equation 10

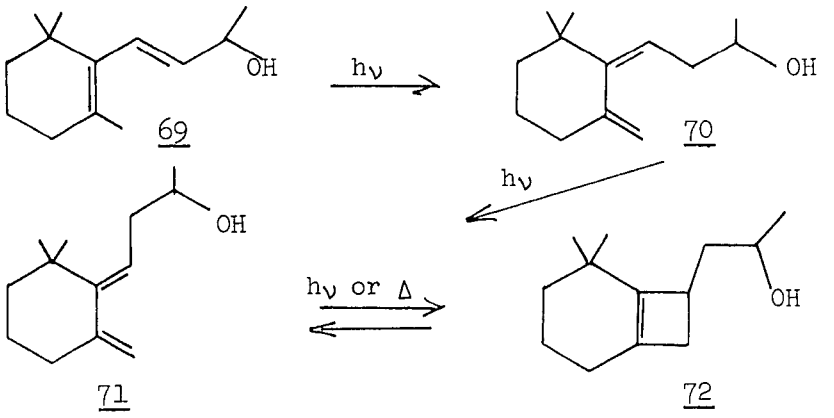


However, according to Dauben (56) the diene system of the product of irradiation of a homoannular dienone derived from Ψ-santonin in aqueous ethanol is not planar.

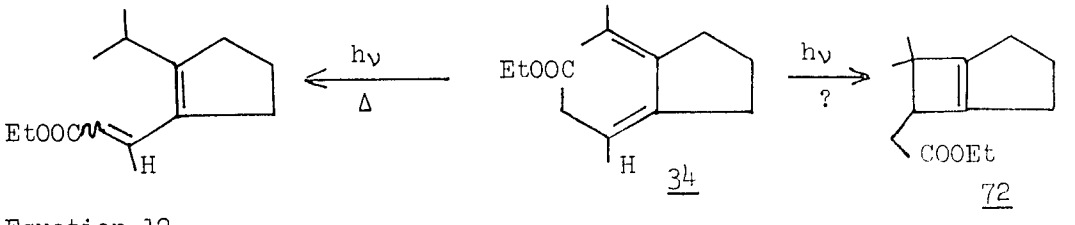
Upon photolysis of β-ionol 69, Roof et al. (57) observed the appearance of 70. Further irradiation of the compound led to the formation of 71. Prolonged irradiation of the original reaction mixture, as well as photolysis of pure 71, produced a compound to which the bicyclooctene structure 72 was assigned.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 11



The above results are analogous to the observation of the compound 34, 35 and 36 involving a (1,5) sigmatropic migration. However, the last step of cyclization of butadiene system probably not occurred for 34. The ring closure in 71 was facile probably because of release of steric interference between the α-methylene of the side chain and the two geminal methylene group. On contrast, the cis-butadiene system of 34 is too hindered to allow the ring closed to form a cyclobutene ring.

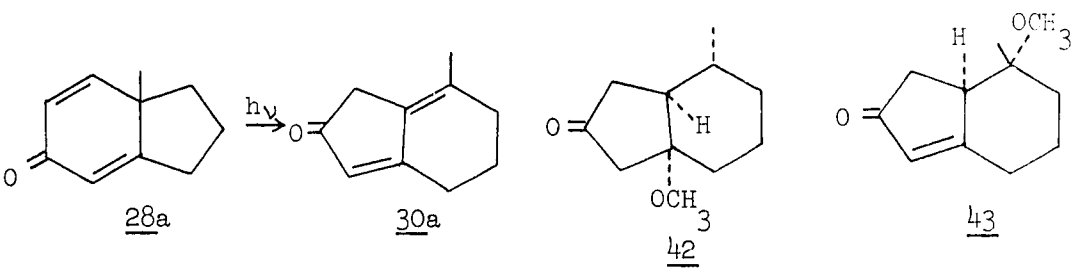


Equation 12

The unsubstituted cross-conjugated dienone 28a was irradiated either in 45 percent methanolic-acetic acid or anhydrous methanol. Vapor phase chromatographic analysis of the crude reaction mixture showed the presence of three compounds in addition to the starting material. Isolation of the compounds by applying liquid chromatography on silica gel gave 30a, 42 and 43.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 12



28a 30a 42 43

45% HOAc-MeOH	20%	27%	27%
MeOH	18%	25%	40%

The use of methanol gave the better results, because of the milder reaction conditions and the product was more easily worked up.

Compounds 42 and 43 were found to have silimar spectral properties to its analog 49 and 50 (22), respectively (Table 3).

In order to obtain additional evidence for the structural assignment of 42, reductive cleavage of the cyclopropane ring with lithium in liquid ammonium was carried out (58). It was reported that cyclopropane rings which are conjugated with carbonyl groups can be cleavaged stereospecifically by reduction with lithium in liquid ammonia. The stereospecificity of the reduction is based on the fact that the bond of the three membered ring, most nearly in the plane of the pi framework, is the one which is broken.

Taking advantage of the results of Caine (59) and Piers (60) that the dissolving metal reduction of compound 74 occurs with a high degree (> 90 percent) of inversion at the β carbon atom, it was considered that a similar stereospecific protonation at the β position might be involved in the ring opening of 42.

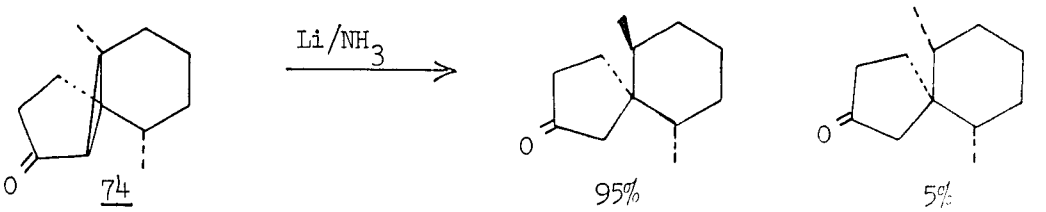
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Table 3. Comparison of Spectral Properties of 42, 43 with 49, 50.

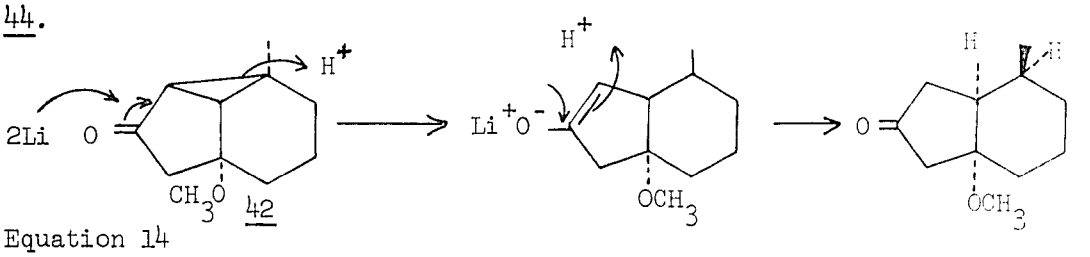
Compound	ir(μ)	uv(mμ)	nmr(δ)
49	5.80(C=O)	223 (ε=2,900) 297 (ε=1,500)	3.24(s, 3H), 2.55(d, 1H, J=18Hz), 2.24 (d, 1H, J=18Hz), 1.50-1.94 (broad absorption, 7H), 1.22 (s, 3H), 1.18 (s, 3H).
42	5.78(C=O)	220 (ε=3,500) 298 (ε=500)	3.27 (s, 3H), 2.60 (d, 1H, J = 17Hz), 2.20 (d, 1H, J = 17 Hz), 1.97 (d, 1H, J = 6 Hz), 1.24-1.92 (broad absorption, 6H), 1.10 (s, 3H).
50	5.87(C=O) 6.16(C=C)	233 (ε=14,500)	5.72 (m, 1H), 3.22 (s, 3H), 1.24-3.12 (broad absorption, 8H), 1.11 (d, 3H, J = 7Hz), 0.98 (s, 3H).
43	5.85(C=O) 6.15(C=C)	230 (ε=12,800)	5.75 (s, 1H), 3.20 (s, 3H), 1.15-3.08 (broad absorption, 9H), 0.92 (s, 3H).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 13



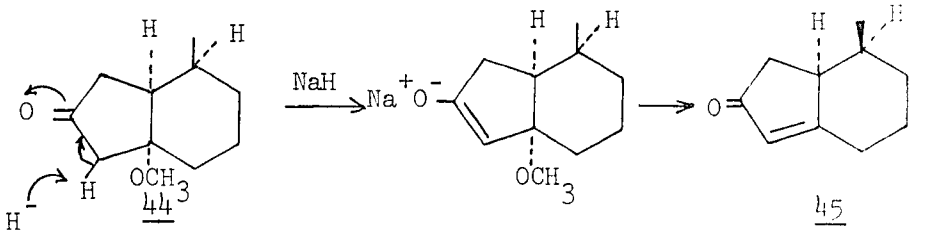
Reduction of 42 with excess lithium in liquid ammonia at -78° afforded predominantly one product, which we believe has the structure 44.



Equation 14

Compound 44 was further reacted with sodium hydride in 1,2-dimethoxyethane in which case the pentenone 45 was produced (equation 15).

Eqn. 15



Careful examination of the nmr spectrum of compound 45 shows that the chemical shift of the methyl group shifted 0.44 δ up-field, compared to the methoxy ketone 44. This is due to the shielding effect of the pi electron at the cyclopentenone ring. The coupling constant of the doublet of the methyl is 7.0 Hz, which is the same with the axial methyl in a methyl cyclohexanone analog (61). Owing to the stereo-specific ring cleavage of 42 by lithium-ammonia reaction, the back-side attack of proton caused the C-9 methyl group to be axial. This

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

result is consistent with the assumption, that the tricyclic compound 42 has the indicated structure in which the three and six membered rings are cis fused.

We suggest that the tricyclic ketone 42 may be formed by either thermal or photochemical addition of solvent to the tricyclic enone 47. The presence of the three-membered ring forces the five and six membered rings to be almost perpendicular the each other so that the double bond of 47 is highly strained. If the reaction does involve 47 it seems unlikely that it is formed from a zwitterionic ground state intermediate such as 18'. According to orbital symmetry rules (55), 18' would undergo a 1,4-sigmatropic rearrangement with inversion at C-9 to give 84 having a transfused 3/6 system or it would rearrange to the lumiproduct 29a by the usual route.

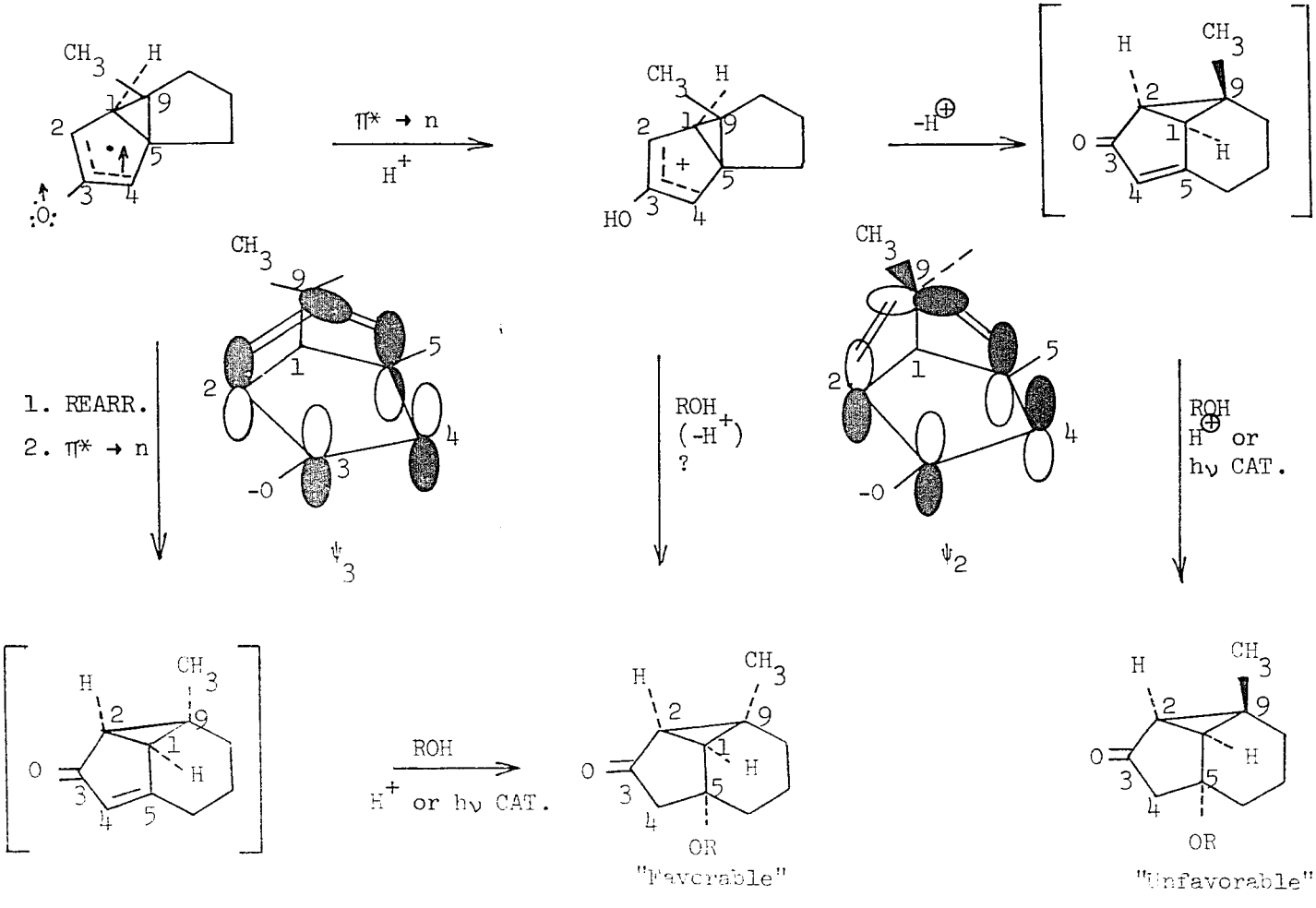
A possible mechanism for the formation of 47 which can give 42 by addition of methanol is shown in Chart 13. A 1,4-sigmatropic rearrangement of the diradical species can take place with retention of configuration at C-9 because in this excited state species Ψ_3 would be the highest occupied MO of the oxobutadiene system involved in the migration.

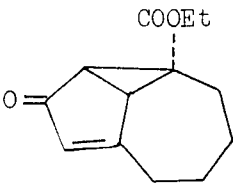
The formation of 49 from 28c reported by Gupton (22) appears to be analogous to the formation of 42. Some recent reports have indicated that other cross-conjugated cyclohexadienones may undergo rearrangements involving diradical intermediates. For example, Kropp has reported that a small amount of the enone ester 82 is formed on irradiation of the angular carbacthoxy dienone 3h.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

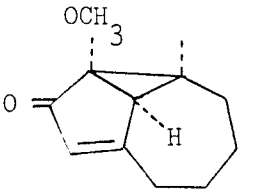
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 13



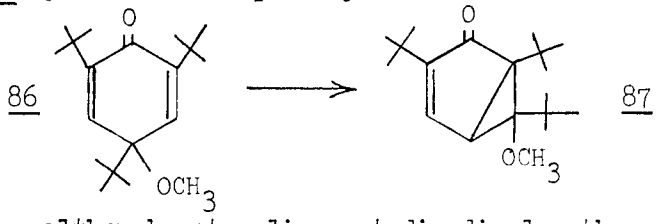


82



83

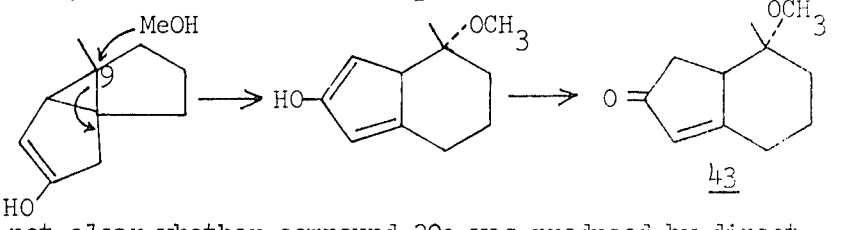
Caine and Chao have found that in addition to the normal lumiproduct 4e a tricyclic compound assigned structure 83 was obtained on irradiation of the methoxy dienone 3e in dioxane (59). Ogura and Matsuura (62) have suggested that the lumiketone 87 is formed form the dienone 86 by a diradical pathways.



However, although not ruling out diradical pathways in dienone rearrangements Schuster and coworkers (63) have questioned the latter results.

The formation of 43 can be easily rationalized by the attack of methanol at C-9 of the zwitterionic species.

Equation 16

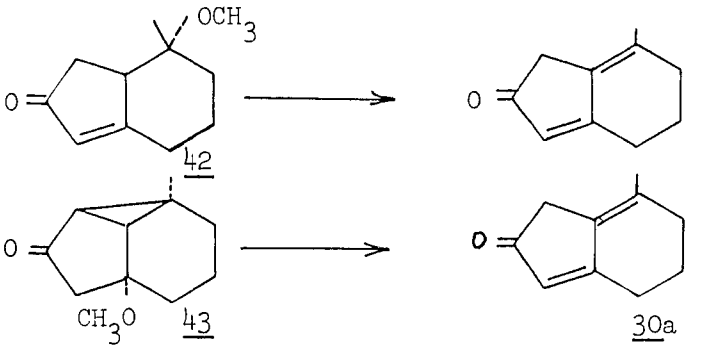


43

It is not clear whether compound 30a was produced by direct photolysis of the starting dienone 28a, or derived from the thermal rearrangement of 42 and 43. During the purification of compounds 42 and 43 by collecting through a preparation glc, conversion to compound 30a was observed.

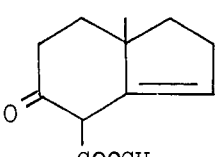
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 17

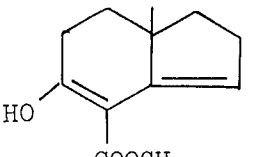


In view of the interesting effects of substituents on the course of photochemical rearrangements of 6/6 fused dienones such as 3a-g, the preparation and a study of the photochemistry of several ring A substituted dienones of the type 28a-i was undertaken. The synthesis of the C-4 carboxy dienone 28f was attempted first. It was hoped that this compound could be prepared by a procedure similar to that used by Brake (12) for the synthesis of 3f. Thus the enone 31a was treated with sodium hydride in DME to form the conjugated enolate and the latter was treated with carbon dioxide followed by acidification and addition of diazomethane. The nmr spectrum of the material which was isolated from this sequence indicated that it was a mixture of the desired β-keto ester 31j and the isomer 51 having the double bond deconjugated. Chromatography of the mixture on silica gel allowed the isolation of a very low yield of crude 31j; the major product isolated after column chromatography appeared to be the enol 52. The conversion of 31j into 28j using DDQ and selenium dioxide under various conditions failed to produce the desired product; using DDQ a very complicated mixture of products was obtained whereas attempted oxidation with selenium dioxide led to complete decomposition of the starting material.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



51



52

The synthesis of the 2-carboxy dienone 28g was also attempted. The enone was treated with ethyl formate in benzene in the presence of sodium methoxide to prepare the 2-hydroxy methylene derivative. Dehydrogenation of this material with DDQ using a method similar to that employed by Edwards et al.(42) for related steroidal compounds gave a complex mixture of products. The nmr spectrum of this mixture indicated that it contained only ca. 10 percent of the expected 2-formyl dienone 28ℓ.

This material could not purified sufficiently for further oxidation to 28g.

A procedure similar to that reported by Dawson (13) for the synthesis of 31e was followed in an effort to prepared 28e. The enone 31a was heated with excess lead tetracetate at 70-80° for 24 hours. This reaction lead to the formation of the 2-acetoxy enone 55 along with some of the dienone derived from β-elimination of acetic acid.

Attempted conversion of 55 into 28e by hydrolysis of acetate with aqueous methanolic potassium hydroxide followed by air oxidation of the hydroxy ketone intermediate and methylation with methyl iodide gave a very poor yield (5-10 percent).

Other modification of this procedure are described in the

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

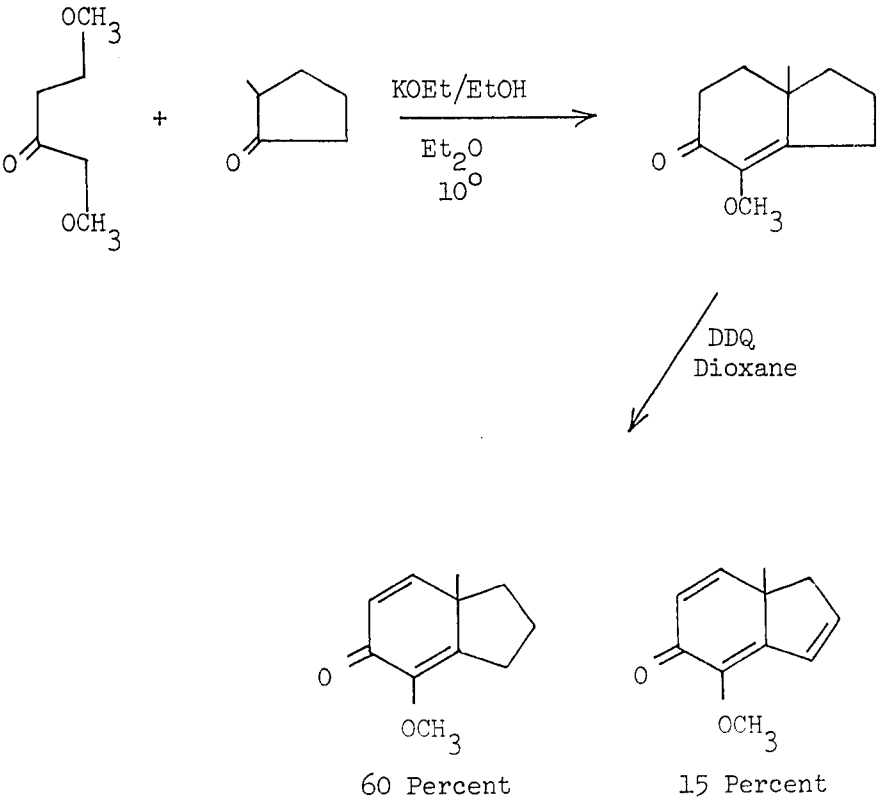
Experimental (Chapter III). In all cases poor yields were obtained.

We also wished to determine the influence of methoxy groups on the photochemistry of 6/5-fused dienones. For this purpose the 4-methoxy compounds 28d and 28i as well as the related 6/6-fused 4-methoxy compound 3d were prepared. The 2-methoxy compound 28e was also synthesized but the yield of product was too low for a thorough investigation of its photochemistry to be made. Compound 28d was obtained by the method of Caine and Tuller (64) by oxidation of the methoxy enone 31d with DDQ in dioxane. It was found that in addition to the desired dienone the trienone 39d was produced in 15 percent yield in the reaction. The dienone and the trienone were separated by column chromatography. Using selenium dioxide for dehydrogenation of 31d the desired dienone was produced in only 35 percent yield.

Compound 28d was irradiated in dioxane both with a 2537 Å light source and a broad spectrum lamp (with a Pyrex filter). Although doublets at δ 7.23 and δ6.05 ppm with a coupling constant of 5.0 Hz which are characteristic of lumiproducts such as 29a were present in the nmr spectrum of the photolysis mixture. Attempts to isolate pure photoproducts proved futile. Glc analysis indicated that several volatile products were produced. It seems possible that 29d may have been formed but rearranged rapidly to other products, such as 32d which might also be photolabile (equation 18).

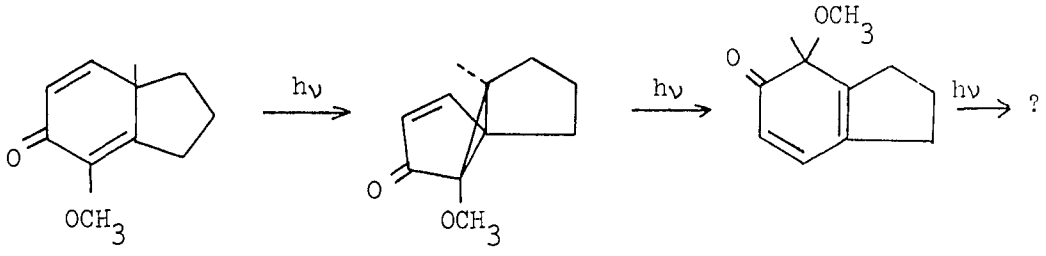
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 14



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 18

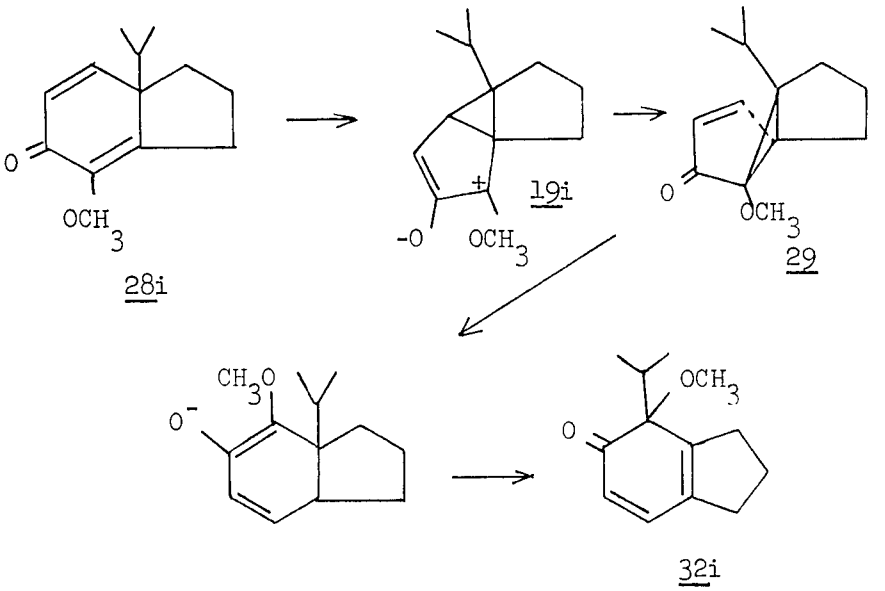


Following the same scheme as above, the dienone 28i was prepared. 2-Isopropyl cyclopentanone was condensed with 1,4-dimethoxy-2-butanone and the resulting enone was oxidized with DDQ. Purification of the product by silica gel chromatography gave a satisfactory sample of the material.

Compound 28i was irradiated in dioxane both with a 2537 Å light source and a broad spectrum lamp with a Pyrex filter. Glc analysis indicated that three new compounds were formed. The nmr spectrum suggested that the lumiproduct 28i and the homoannular dienone 32i were presented in the photomixture. However, chromatography of the reaction mixture on silica gel only allowed the isolation of 32i and no pure 29i could be obtained. On irradiation, compound 28i disappears more slowly than its methyl analog, and it also appears somewhat more stable photochemically compared to 29d. Perhaps the isopropyl group retards the formation of 29i which presumably arises from the dipolar intermediate 19i while further rearrangement of 29i via the dipolar species 68i may also be retarded.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Equation 19

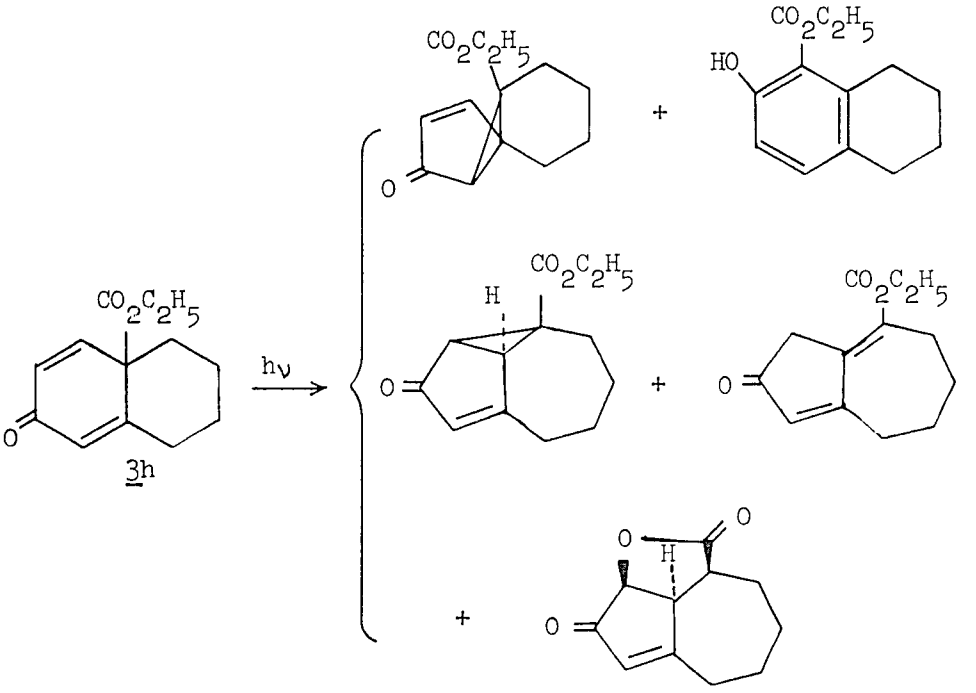


As noted earlier, 6/5-fused dienones such as 28a and 28c gave tricyclic ketones such as 42 and 49, considered to arise by addition of solvent to the corresponding enones, on irradiation in acetic acid-methanol. Kropp (18, 65) has found that irradiation of the 6/6-fused angular carboethoxy dienones, 3h in aqueous acetic acid gave mainly the lumiproduct 29h, but, along with other products (equation 18), the tricyclic enone 82 was also produced in low yield. He also pointed out (18b, 65) that hydroxy ketones which were expected to be obtained in this reaction were not isolated. Although the stereochemistry of this compound was not specified by Kropp, we propose that the angular carboethoxy group is in the α configuration and therefore the mode of formation of this product may be similar to that involved in the formation of 47. Thus it appeared of interest to study the photochemical behavior of 28h. A compound having both

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

features, the angular carboethoxy group and the five membered B ring which give rise to novel tricyclic photoproducts, incorporated in the same molecule.

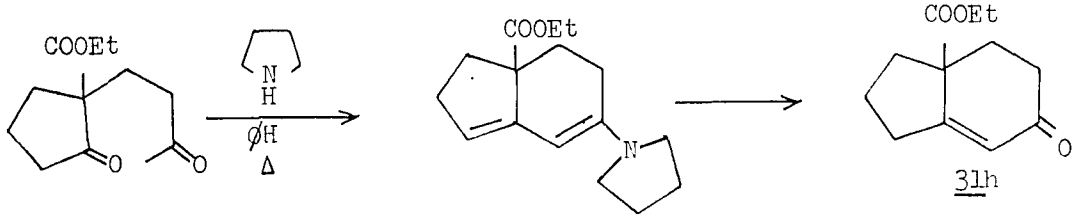
Equation 18:



The synthetic route to 28h involved oxidation of the enone 31h. Dauben (44) had prepared the latter compound earlier by cyclization of the diketone 60, readily available by Michael addition of 2-carboethoxy cyclophentanone to MVK (methyl vinyl ketone) with aluminum t-butoxide (conventional methods of cyclization of 60 lead to opening of the five membered ring). Although this method could be used for

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

the synthesis of 31h, in our honds it gave a low yield and was time consuming. The method recently reported by Scanio and Hill (45) proved a better way of preparing 31h. This involved heating of 60 with pyrolidine in benzene using a Dean-Stark apparatus to remove water. This procedure probably involves an enamine intermediate and gives as high as a 91 percent yield.



Dehydrogenation of 31h with DDQ gave 28h in 60 percent yield. Chromatography on silica gel gave the pure product; attempted chromatography of 28h on alumina led to its decomposition.

Dienone 28h was irradiated under various conditions as indicated in Table 4.

Table 4. Irradiation of 28h Under Various Conditions.

Solvent	Irradiation Time (min)	Light Source	Yield of 62(%)
Dioxane	23	2537 Å	65
Dioxane	30	450 watt	50
EtOH	15	2537 Å	60
EtOH	30	450 watt	65
45% HOAc-H_2O	25	450 watt	65
Ether	25	2537 Å	46

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

We were surprised to find that under all conditions, the only product isolated was the homoannular linearly conjugated dienone 62. The spectral properties of 62 are similar to those of 81 which is also a minor product of irradiation of 3h. It showed infrared absorption at 5.96 μ (for the cyclopentenone and conjugated ester grouping superimposed) and at 6.11 and 6.31 μ indicative of conjugated carbon-carbon double bonds. The ultraviolet spectrum of 62 showed a maximum at 288 mμ (ε 6,500) indicative of the conjugated systems (66). The nmr spectrum of 62 was also indicative of the structure (Table 5).

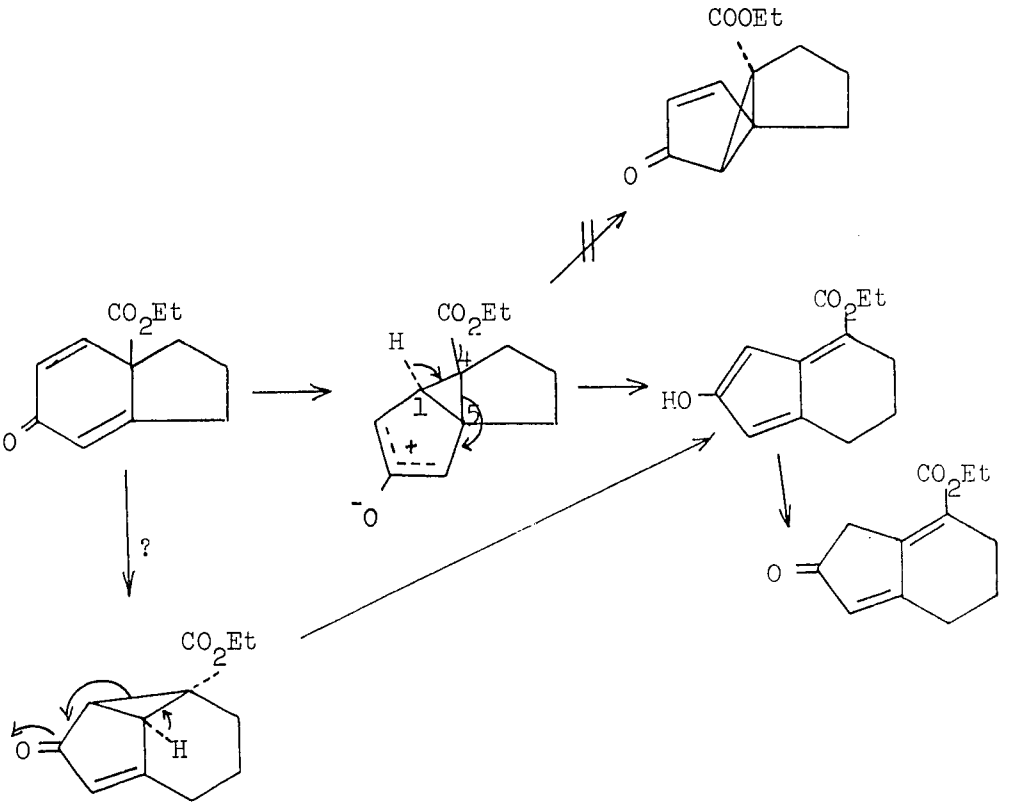
Table 5. Comparison of nmr Spectra of 62 and 81

62 (δ)	6.02 (s, 1H), 4.19 (q, 2H), 3.15 (s, 2H), 2.38-2.80 (broad absorption, 4H), 1.93 (t, 1H), and 1.33 (t, 3H)
81(δ)	6.24 (s, 1H), 4.26 (q, 2H), 3.36 (s, 2H), 2.8 (m, 4H), 1.88 (m, 4H), and 1.36 (t, 3H)

Thus the major product of irradiation 28h is a dienone related to a minor product of irradiation 3h. It is possible that this product is formed directly from a dipolar intermediate such as 79 in a manner similar to that considered to be involved in the formation of related dienones such as 28a-c. It is also possible that the tri-

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

Chart 15



Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

cyclic product 88 may be formed in this case but rearranged to product by a thermal reaction. However, if such a species were produced in the nucleophilic solvents employed it would be expected to have undergone 1,4-addition of the solvent by a process similar to that suggested for conversion of 47 to 42.

It is of interest that no lumiproduct related to 29h was produced from irradiation of 28h. This process would require a 1,4-sigmatropic rearrangement involving breaking of the 1,9-bond and formation of the 4,9-bond in the dipolar intermediate. It appears that the strain resulting from the presence of the five membered B ring causes the 5,9-bond to be more susceptible to cleavage than the 1,9-bond so that path A (Chart 6) is favored.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER V

CONCLUSIONS

In the work reported in this thesis, it was found that the title class of compounds — the cross-conjugated cyclohexadienones such as 28a, 28g and 3b all rearranged to their lumiproducts 29a, 29b, and 4b in a short time interval of irradiation.

The lumiproducts were photolabile and converted back into the corresponding dienones by irradiation with a 450-watt high pressure mercury lamp fitted with Pyrex filter. The formation of the lumiproducts apparently involved intervention of a zwitterionic cyclopropyl intermediate while a zwitterionic species is also likely to be involved in the conversion of lumiproducts to dienones. Prolonged photolysis of the lumiproduct 29b caused a 1,3-shift of the angular methyl group in the dipolar intermediate and furnished the homoannular dienone 32b which was further reacted with ethanol photochemically.

The photochemical conversion of the unsubstituted dienone 28a into the tricyclic product 42 on irradiation in methanol or in 45 percent acetic acid-methanol appears to be best explained in terms of the rearrangement occuring at the stage of a diradical rather a zwitterionic intermediate. This postulate was supported by the evidence concerning the sterochemistry of the product, as well as the indifference of the reaction to the properties of the solvents (both anhydrous methanol and acetic acid-methanol gave nearly the same results).

The preparation of 28e,f,g was unsuccessful. This was probably

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

due to the fact that deconjugation of the double bond into the five-membered B ring was a very favorable process.

The photochemistry of the carbethoxy dienone 28h was instructive and useful. This compound having the electron withdrawing carbethoxy substituent gave only 7-carbethoxy-5,6-dihydro-2(4H)-indenone (62) on irradiation in several solvents. This provided strong evidence for the contention that a polar intermediate having a positive character distributed through the conjugated system of the carbon skeleton is involved in the rearrangement. The relatively high conversion of the 6/5-fused dienone into a 5/6-fused system was particularly of synthetic interest.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

CHAPTER VI

RECOMMENDATIONS

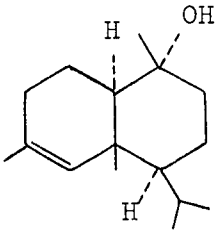
A thorough study of the synthesis and photochemistry of 6-methoxy-, 4-carboxy-, and 6-carboxy-, 7a-methyl-5(7aH)- indanone should be attempted.

The use of the new method of 4-carboxylation of 7a-alkyl-7,7a-dihydro-5(6H)-indanones reported by Micheli (67) might be useful for obtaining the enone 31f which might be converted into the corresponding dienone by the procedure of bromination and then dehydrobromination (13). The photochemical behavior of 28f might show interesting differences from that of 3f owing to the presence of five-membered B ring in the former case.

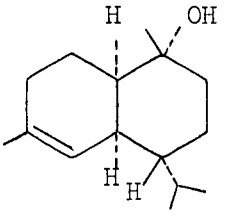
It should be also of interest to synthesize 28g by another method (11). Condensation of ethyl acetoacetate with 2-formyl-2-methyl-cyclopentanone, and then base-catalyzed cyclization might provide the desired product 28g. The investigation and the results of the irradiation of this compound compared with that of compound 3g should furnish better understanding for the mechanism of photochemical rearrangements of cross-conjugated cyclohexadienones.

Finally, the compound 3-isopropyl-7a-methyl-5(7aH)-indanone should be prepared and its photochemistry should be studied. Photochemical rearrangement of this compound appears to provide possible synthetic routes to sesquiterpenes such as a α-cadinol and T-murrolol (68).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



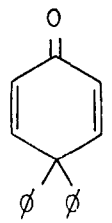
α-cadinol



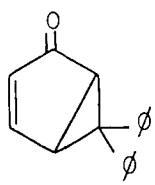
T-murrolol

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

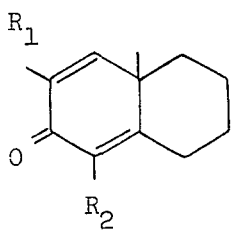
APPENDIX



1



2



3

(a) $R_1 = R_2 = H$

(b) $R_1 = H$, $R_2 = CH_3$

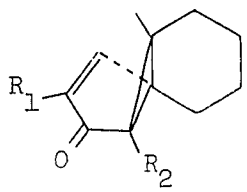
(c) $R_1 = CH_3$, $R_2 = H$

(d) $R_1 = H$, $R_2 = OCH_3$

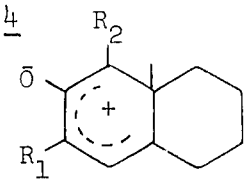
(e) $R_1 = OCH_3$, $R_2 = H$

(f) $R_1 = H$, $R_2 = COOH$

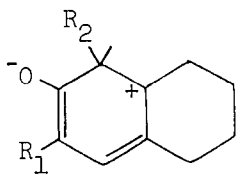
(g) $R_1 = COOH$, $R_2 = H$



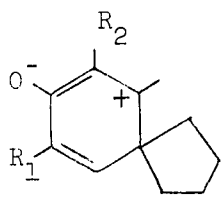
4



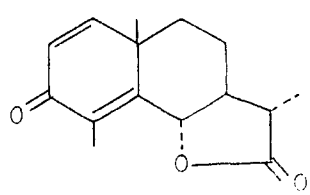
5



6

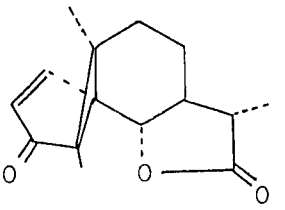


7

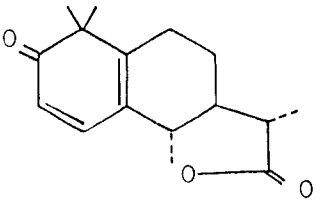


8

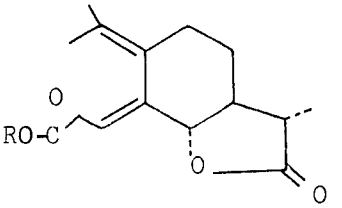
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



9



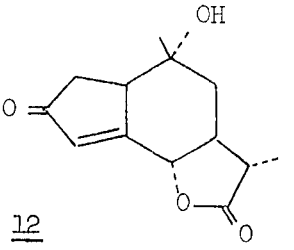
10



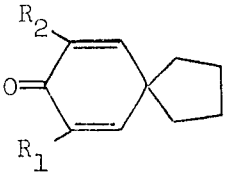
11

(a) R = C_2H_5

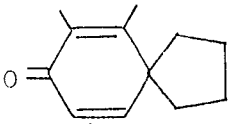
(b) R = H



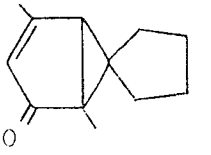
12



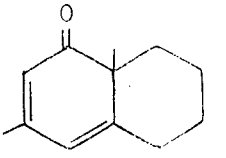
13



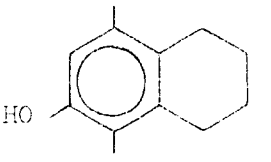
13b



14

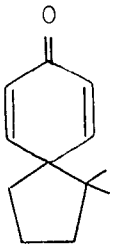


15

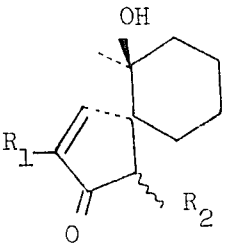


16

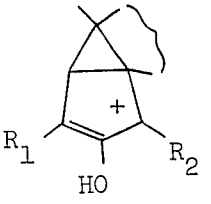
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



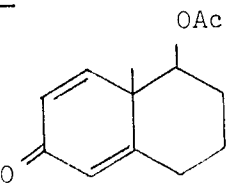
17



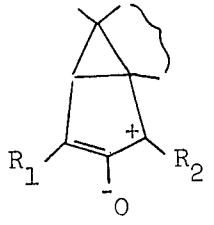
21



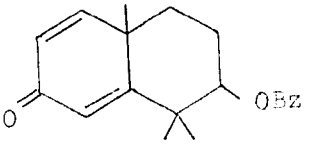
18



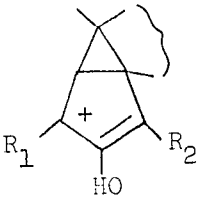
22



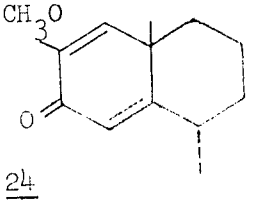
18'



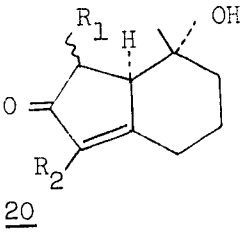
23



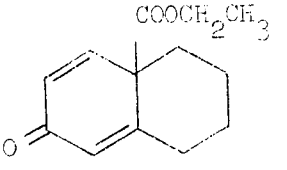
19



24

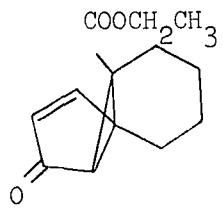


20

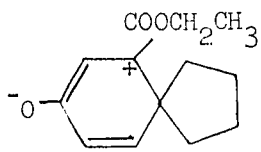


3h

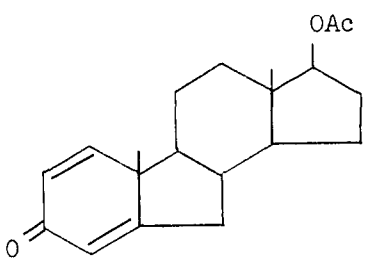
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



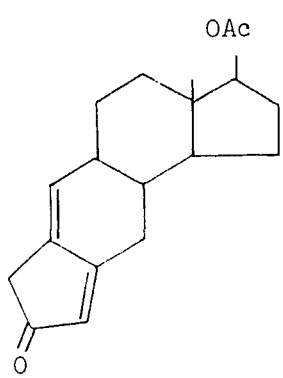
4h



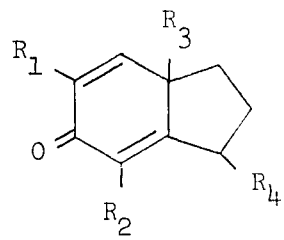
25



26



27



28

For $R_3 = CH_3$, $R_4 = H$

(a) $R_1 = R_2 = H$

(b) $R_1 = H$, $R_2 = H$

(c) $R_1 = CH_3$, $R_2 = H$

(d) $R_1 = H$, $R_2 = OCH_3$

(e) $R_1 = OCH_3$, $R_2 = H$

(f) $R_1 = H$, $R_2 = COOH$

(g) $R_1 = COOH$, $R_2 = H$

For $R_4 = H$

(h) $R_3 = COOEt$, $R_1 = R_2 = H$

(i) $R_1 = H$, $R_2 = COH_3$,
R_3 = isopropyl

(j) $R_1 = H$, $R_2 = COOCH_3$
$R_3 = CH_3$

(k) $R_1 = OH$, $R_2 = H$, $R_3 = CH_3$

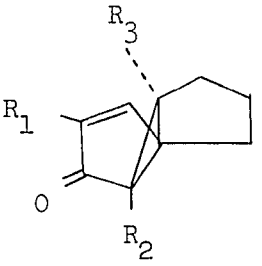
(l) $R_1 = CHO$, $R_2 = H$, $R_3 = CH_3$

For $R_1 = H$, $R_3 = CH_3$

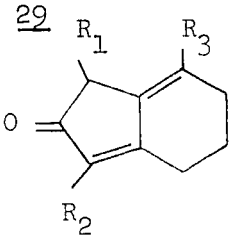
(m) R_4 = α-isopropyl

(n) R_4 = β-isopropyl

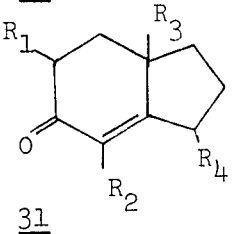
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



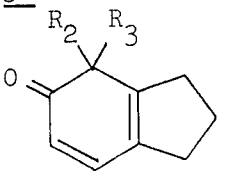
29



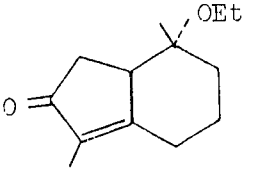
30



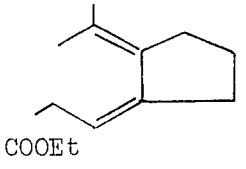
31



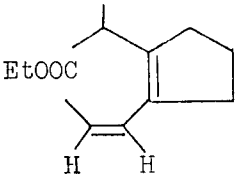
32



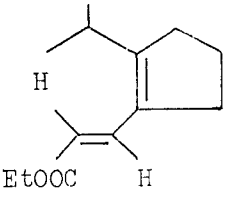
33



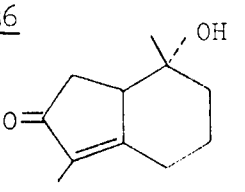
34



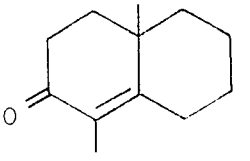
35



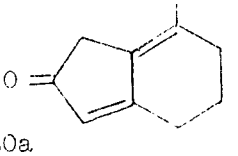
36



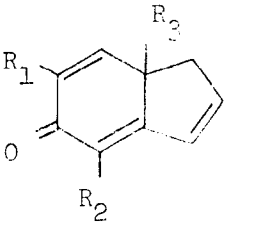
37



38

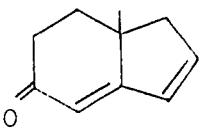


30a

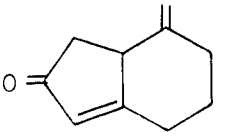


39

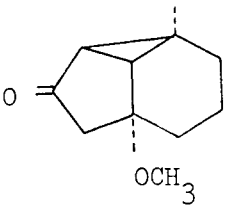
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



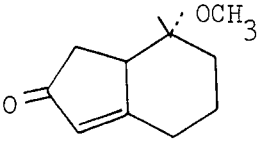
40



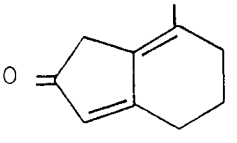
41



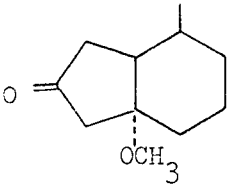
42



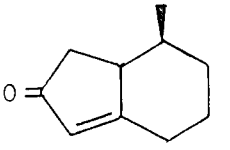
43



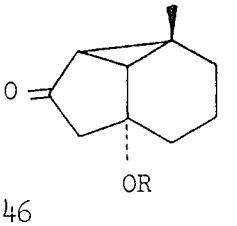
30a



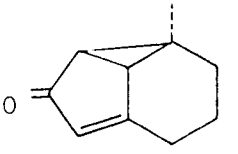
44



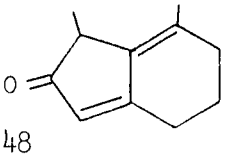
45



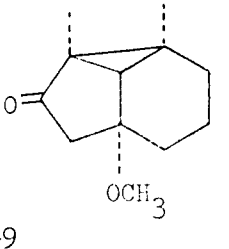
46



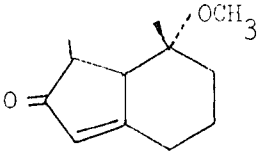
47



48

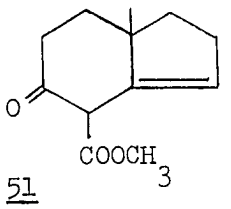


49

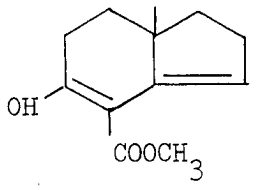


50

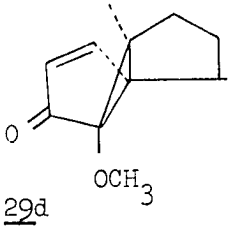
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



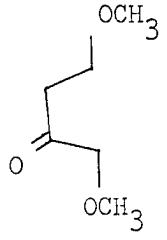
51



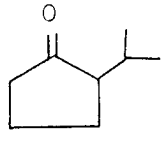
52



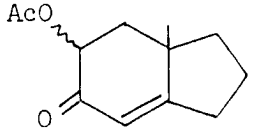
29d



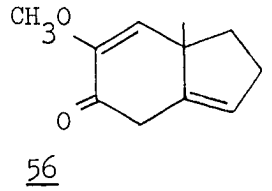
53



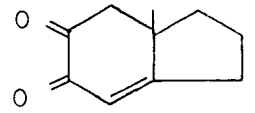
54



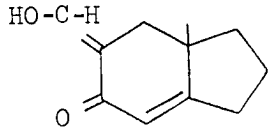
55



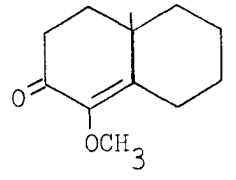
56



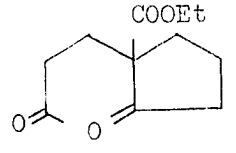
57



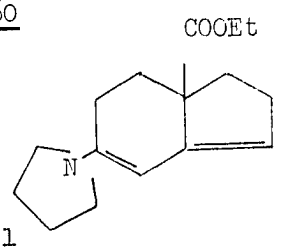
58



59

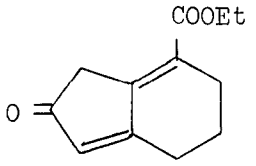


60

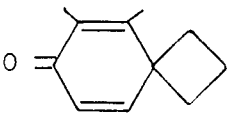


61

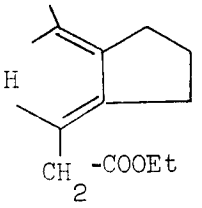
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



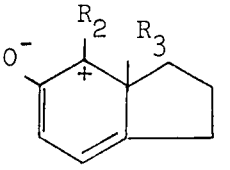
62



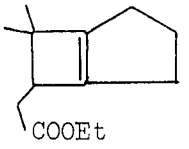
66



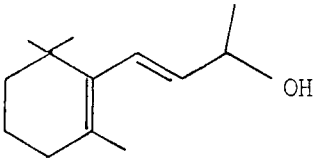
67



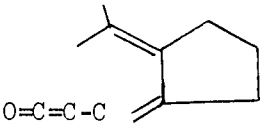
68



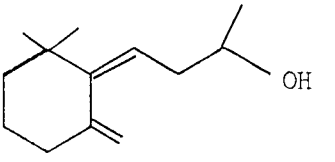
73



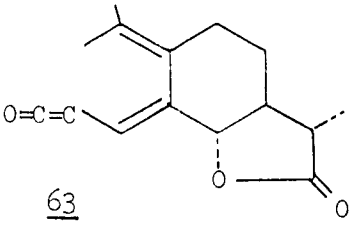
69



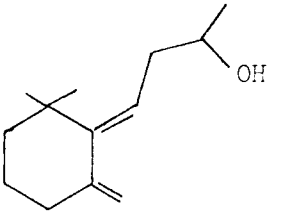
64



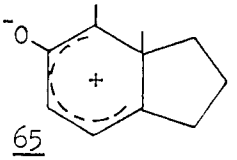
70



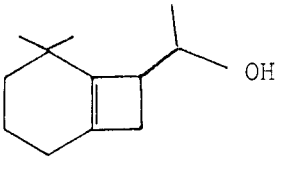
63



71

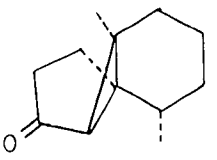


65

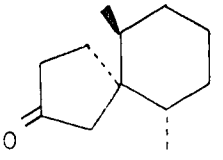


72

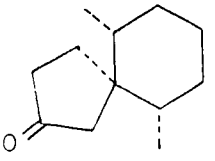
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



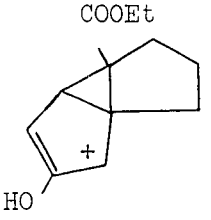
74



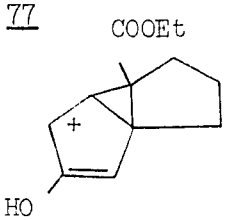
75



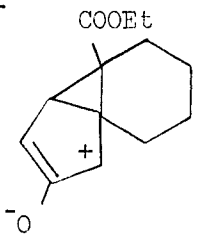
76



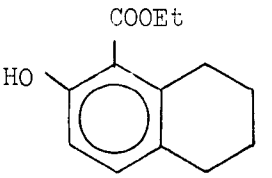
77



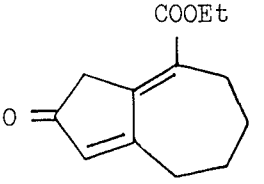
78



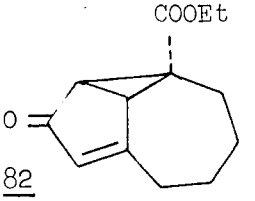
79



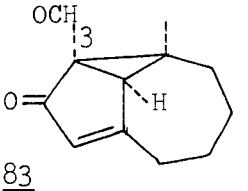
80



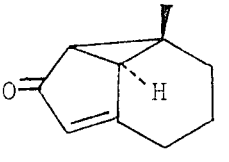
81



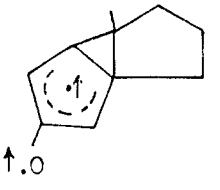
82



83

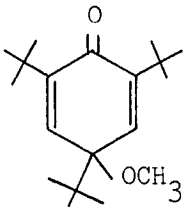


84

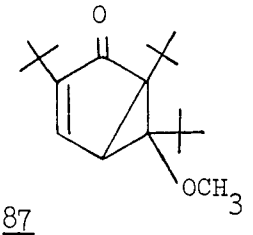


85

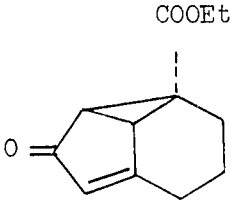
Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.



86



87



88

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

LITERATURE CITED*

1. a) H. E. Zimmerman, Angew. Chem. Int. Ed. Engl. 8 1 (1969)

   b) N. J. Turro, et al., Annual Survey of Photochemistry, vol. 1-3, Wiley-Interscience, New York, 1969-1971.

   c) P. J. Kropp, "Organic Photochemistry," O. L. Chapman, editor, vol. 1, Marcel Dekker, Inc., New York, 1967, p. 1.

2. a) H. E. Zimmerman and J. O. Grunewald, J. Amer. Chem. Soc., 89, 5163 (1967).

   b) H. E. Zimmerman, R. W. Brinkley, J. J. McCollough, and G. Zimmerman, J. Amer. Chem. Soc., 89 6589 (1967).

   c) H. E. Zimmerman and D. I. Schuster, J. Amer. Soc.,84, 4527, (1962).

   d) H. E. Zimmerman, Chem. Comm., 176 (1968).

   e) O. L. Chapman, "Advances in Photochemistry," W. A. Noyes, Jr., G. S. Hammond and J. N. Pitts, Jr., eds., vol. 1, Wiley-Interscience, New York (1936).

   f) G. A. Taylor, Chem. Comm., 896, (1967).

3. a) D. H. R. Barton, Helv. Chim. Acta., No. 279, 2611 (1959).

   b) M. H. Fisch and J. H. Richard, J. Amer. Chem. Soc., 90. 1547 1553 (1968); 85, 3029 (1963).

   c) O. L. Chapman and L. F. Englert, ibid., 85, 3028 (1963).

   d) L. Barber, O. L. Chapman and J. D. Lassila, ibid., 90, 5933 (1968).

4. D. I. Schuster and W. V. Curran, J. Org. Chem., 25, No. 12, 4192 (1970).

5. a) P. J. Kropp, J. Amer. Chem. Soc., 86, 4053 (1964).

   b) P. J. Kropp, ibid, 85, 3779 (1963).

* For the complete title of all journals referred to, see Chemical Abstracts, Vol. 55, p. 1J(1961), and supplements thereafter.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

6. D. Caine and J. F. DeBardeleben, Jr., Tetrahedron Letters, 4585 (1965).

7. P. J. Kropp and W. F. Erman, J. Amer. Chem. Soc., 85, 2456 (1963).

8. D. Caine and F. N. Tuller, Unpublished Work.

9. P. J. Kropp, J. Org. Chem., 29, 3110 (1964).

10. D. Caine, J. F. DeBardeleben, Jr., and J. B. Dawson, ibid., 3627 (1966).

11. J. F. DeBardeleben, Jr., Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia 1967.

12. B. F. Brake, M. S. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1972.

13. J. B. Dawson, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1969.

14. F. N. Tuller, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1971.

15. P. F. Inwalgson, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1972.

16. D. H. R. Barton, J. T. Pinhey, and R. J. Wells, J. Chem. Soc., 2518 (1964).

17. a) P. G. Sammes, Quart. Rev., Chem. Soc., 1970, 24(1).

    b) P. G. Sammes, Synthesis, 1970(2).

18. a) P. J. Kropp, Tetrahedron Letters, 3647 (1964).

    b) P. J. Kropp, Tetrahedron, 21, 2183 (1965).

19. a) G. Bozzato, H. P. Throndsen, K. Schaffner, and O. Jeger, J. Amer. Chem. Soc., 86, 2073 (1964).

    b) J. Frei, C. Ganter, D. Kaji, K. Kocsis, M. Miljkovic, A. Sienwinski, R. Wenger, K. Schaffner and O. Jeger, Helv. Chim. Acta., Vol. 49, 1049 (1966).

20. A preliminary account of this work has been published. See D. Caine, W. J. Powers, III, and A. M. Alejandre, Tetrahedron Letters, 6071 (1968).

21. W. J. Powers, III, Ph.D. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1968.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

22. J. T. Gupton, III, M. S. Thesis, Georgia Institute of Technology, Atlanta, Georgia, 1969.

23. D. Caine, J. T. Gupton and Ko Ming, Unpublished results.

24. D. Caine, Ana M. Alejande, Ko Ming, and W. J. Powers, III, J. Org. Chem., 37, 706 (1972).

25. L. F. Fieser, Experiments in Organic Chemistry, 3rd ed., D. C. Heath and Company, Boston.

26. A. 10 ft. x 1/4 in. column containing 15 percent silicone SE-30 on Chromosorb W was employed.

27. A 10 ft. x 1/4 in. column containing Carbowax K-20M on Chromosorb W was employed.

28. N. C. Ross and R. Levine, J. Org. Chem., 29, 2341 (1964).

29. P. J. Kropp, J. Amer. Chem. Soc., 87, 3914 (1965).

30. D. Burn, R. Kirk and V. Petrow, Proc. Chem. Soc., 14(1960).

31. S. M. Bloom, J. Amer. Chem. Soc., 81, 4728 (1961).

32. E. C. DeFeu, F. J. McQuillin and R. Robinson, J. Chem. Soc., 53 (1937).

33. R. Srinivasan, ed., Organic Photochemical Syntheses, Vol. 1, Wiley-Interscience, 1971.

34. A. Smith, B. J. L. Huff, W. J. Powers, and D. Caine, J. Org. Chem., 32, 2851 (1967).

35. E. Wenkert and G. Jackson, J. Amer. Chem. Soc., 81 5601 (1959).

36. J. A. Moore and D. E. Reed, Org. Syn., 41, 16(1961).

37. G. F. Hennion and F. P. Kupiecki, J. Org. Chem., 1601 (1953).

38. E. Seeback and T. Reichstein, Helv. Chim. Acta., 27, 948 (1944).

39. P. N. Rao and L. R. Axelord, J. Amer. Chem. Soc., 82, 2830 (1960).

40. J. S. Baran, J. Amer. Chem. Soc., 80, 1687 (1958).

41. Bloomquist, et al., Organic Syntheses, Coll. Vol. 4, 838 (1963).

42. J. A. Edwards, M. C. Calzada, L. C. Ibanez, M. E. Calzas, J. Org. Chem., 29, 3481 (1964).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

43. W. G. Dauben and J. W. McFarland, J. Amer. Chem. Soc., 82, 4245 (1960).

44. W. G. Dauben, J. W. McFarland, and J. B. Rogan, J. Org. Chem., 26, 297 (1961).

45. C. J. V. Scanino and L. P. Hill, Synthesis, 1, 651 (1970).

46. J. A. Marshall, N. H. Andersen, and P. C. Johnson, J. Amer. Chem. Soc., 89, 2748 (1967).

47. O. L. Chapman, Private communication.

48. E. E. Van Tamelen, S. H. Levin, G. Brenner, J. Wolinsky, and P. E. Aldrich, J. Amer. Chem. Soc., 81, 1666 (1959).

49. W. J. Bailey and H. R. Golden, J. Amer. Chem. Soc., 75, 4780 (1953).

50. W. J. Bailey and W. B. Lawson, J. Amer. Chem. Soc., 79, 1444 (1957).

51. Lj. Lorenc, M. Miljkovic, K. Schaffner, and O. Jeger, Helv. Chim. Acta., 49, 1183 (1966).

52. P. J. Kropp, Private communication.

53. D. I. Schuster and A. C. Fabian, Tetrahedron Letters, 4093 (1966).

54. L. Barber, O. L. Chapman, and J. P. Lassila, J. Amer. Chem. Soc., 91, 3664 (1969).

55. R. B. Woodward and R. Hoffmann, The Conservation of Orbital Symmetry, Academic Press, Inc., 1970.

56. W. G. Dauben, A. Lightner and W. K. Hayes, J. Org. Chem., 27, 1897 (1962).

57. A. A. M. Roof, A. van Wageningen, C. Kruk and H. Cerfontain, Tetrahedron Letters, 367 (1972).

58. a) Y. Noel, Bull. Soc. Chim. France, 4321 (1968).

b) Fraisse-Julien, et al., Bull. Soc. Chim. France, 4444 (1968).

59. D. Caine and T. I. Chao, Unpublished results.

60. E. Piers and P. M. Worster, J. Amer. Chem. Soc., 94, 2895 (1972).

61. F. Johnson, N. A. Strarkovsky, and W. D. Gurowitz, J. Amer. Chem. Soc., 87, 3492 (1965).

62. a) T. Matsuura and K. Ogura, J. Amer. Chem. Soc., 89, 3846 (1967).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

62. b) T. Matsuura and K. Ogura, J. Amer. Chem. Soc., 98, 3850(1967).

c) H. E. Zimmerman and J. S. Sweton, J. Amer. Chem. Soc., 89, 906 (1967).

63. D. I. Schuster, K. Vasanth Probler, S. Adcock, J. VanderVeen, and H. Fijiwara, J. Amer. Chem. Soc., 93, 1557 (1971).

64. D. Caine and F. N. Tuller, J. Amer. Chem. Soc., 93, 6311 (1971).

65. P. J. Kropp, Private communication.

66. A. T. Nielson, J. Org. Chem., 22, 1539 (1957).

67. R. A. Micheli, Ger. Offen. 2, 033, 644 (Cl. C07c); CA 74 124990v (1971).

68. a) Y. T. Lin, Y. S. Cheng, and Y.H. Kuo, Tetrahedron Letters, 3881 (1969).

b) Y. H. Kuo, Y. S. Cheng and Y. T. Lin, ibid., 2375 (1969).

c) Y. S. Cheng, Y. H. Kuo and Y. T. Lin, Chem. Commun., 565 (1967).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.

VITA

Ming Ko was born in Nan-Nin, Kwangsi, China, in 1946. He received his B. S. in chemistry from National Taiwan University, Taipei, Taiwan in June 1968.

The author came to the Georgia Institute of Technology with an award of Graduate Teaching Assistantship in September 1968. He started the research work under the supervision of Professor D. S. Caine at that year.

After his graduation, the author has planned to work for Professor Szwarc at The College of Forestry at Syracuse University in the field of polymer chemistry.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.