

AN ABSTRACT OF THE THESIS OF

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Title PREPARATION AND REACTIONS OF 7-BICYCLO[3.3.1]-  
NONEN-2-ONE

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(Major professor) 

2-Carboxy-3(3-cyclohexen-1-yl)propionic acid, 3-(3-cyclohexen-1-yl)propionic acid and 3-(3-cyclohexen-1-yl)propionyl chloride were prepared in sequence from ethyl-2-carbethoxy-3-(3-cyclohexen-1-yl)propionate. Cyclization of 3-(3-cyclohexen-1-yl)propionic acid in polyphosphoric acid resulted in the formation of 4, 5, 6, 7-tetrahydroindanone which was identified by its ultraviolet spectrum and its physical properties.

7-Bicyclo[3.3.1] nonen-2-one was prepared by a Friedel-Crafts cyclization of 3-(3-cyclohexen-1-yl)-propionyl chloride. It was identified by its infrared spectrum and its physical properties.

3,3-Dimethyl-7-bicyclo[3.3.1] nonen-2-one was prepared by methylation of 7-bicyclo[3.3.1] nonen-2-one with potassium triphenylmethide and methyl iodide. It was characterized by its infrared spectrum, nuclear magnetic resonance spectrum and its carbon-hydrogen analysis.

The rate of deuterium exchange of 3,3-dimethyl-7-bicyclo-[3.3.1]nonen-2-one, studied at two base concentrations, was found to be much slower ( $k = 6.6 \times 10^{-3}$  liters/mole-hour) than that reported for the corresponding saturated ketone ( $k = 0.36$  liter/mole-hour). The slower exchange rate of the unsaturated ketone was ascribed to the strain caused by its carbon-carbon double bond.

PREPARATION AND REACTIONS OF  
7-BICYCLO[ 3. 3. 1] NONEN-2-ONE

by

KIRBY GRANT SALISBURY

A THESIS

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Date thesis is presented September 21, 1965

Typed by Opal Grossnicklaus

## TABLE OF CONTENTS

INTRODUCTION	1
HISTORICAL	4
Isolable Molecules with Bridgehead Double Bonds	4
Transient Intermediates with Bridgehead Double Bonds	6
DISCUSSION	13
EXPERIMENTAL	18
2-Carboxy-3-(3-cyclohexen-1-yl)propionic acid	18
3-(3-Cyclohexen-1-yl)propionic acid	18
3-(3-Cyclohexen-1-yl)propionyl chloride	19
7-Bicyclo[3.3.1]nonen-2-one	19
Cyclization of 3-(3-cyclohexen-1-yl)propionic acid	21
Methylation of 7-bicyclo[3.3.1]nonen-2-one	21
Potassium <i>tert</i> -butoxide catalyzed methylations	21
Procedure I	22
Procedure II	22
Sodium hydride catalyzed methylation	23
Potassium triphenylmethide catalyzed methylation	24
Deuterium exchange study of 3,3-dimethyl-7-bicyclo- [3.3.1]nonen-2-one	25
Series A	25
Series B	26
Quantitative infrared analyses	26
Infrared spectra	27
Nuclear magnetic resonance spectra	27
Vapor phase chromatography	27
Ultraviolet spectrum	28
Boiling points	28
Melting points	28
SUMMARY	29
BIBLIOGRAPHY	30

## LIST OF FIGURES

### Figure

- |   |  |    |
|---|--|----|
| 1 | Relation between free energy and rotation about the axis of the double bond. | 2  |
| 2 | Percent non-deuterated ketone versus time, hours.                            | 14 |

## LIST OF TABLES

### Table

- |   |                               |   |
|---|-------------------------------|---|
| 1 | Deuterium incorporation of XV | 9 |
|---|-------------------------------|---|

# PREPARATIONS AND REACTIONS OF 7-BICYCLO[3.3.1]NONEN-2-ONE

## INTRODUCTION

Many chemical properties of bridged ring molecules are of intrinsic interest in the study of the relation between geometry and chemical reactivity. Reactions which involve a bridgehead atom have evoked the greatest interest, principally because the ring geometry exerts its largest influence at that point. Bredt's rule (5), which states essentially that a double bond cannot be formed by a bridgehead atom, was derived from simple geometric considerations. As the discussion below will illustrate, the situation is more complex than this simple statement of Bredt's rule might imply.

It is well known that the six atoms immediately around a double bond prefer to lie in a plane. According to the molecular orbital theory, this planar arrangement is preferred because maximum overlap of adjacent p-orbitals is required to form the strongest  $\pi$  bond. Rotation about the axis of the  $\sigma$  bond decreases the overlap until at the dihedral angle  $\theta = 90^\circ$  the p-orbitals are orthogonal and no  $\pi$  bond can exist. The relation between the angle of rotation and free energy of the system is illustrated in Figure 1. Geometric requirements for the construction of many bridged rings are quite severe, and deviation from these will again increase the

free energy of the system. As Bredt's rule suggests, the preferred geometries of the double bond and the bridged ring are often incompatible if the double bond is to be formed by the bridgehead atom.

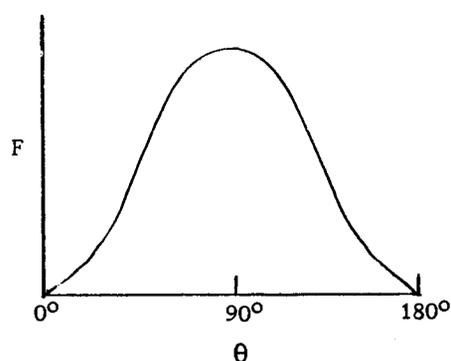


Figure 1. Relation between free energy and rotation about the axis of the double bond.

As the deviations from the preferred geometries for both the double bond and the ring system increase, the free energy of the molecule rises. When the necessary deviations raise the energy to such a level that the molecule can spontaneously isomerize or react to form a new substance, the molecule with a bridgehead double bond will no longer be isolable. However, species having even greater deviations, and hence higher free energies, may still play a role as transient intermediates in some reactions. A study of the rate of formation of such an intermediate is a convenient tool for determining relative stability and thus the extent of applicability of Bredt's rule.

Removal of a proton from the alpha carbon of a ketone generates an enolate ion which has the same geometric requirements for maximum stability as a carbon-carbon double bond. The rate of enolate ion formation can be easily determined by an exchange reaction. The synthesis of 3,3-dimethyl-7-bicyclo [ 3. 3. 1 ] nonen-2-one and the rate of its enolate formation will be described in this thesis.

## HISTORICAL

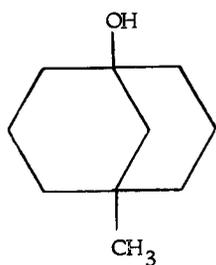
The first paper published by Bredt on the subject of bridgehead double bonds (4) did not state, in an explicit sense, the rule associated with his name. The ideas underlying the rule were developed over a period of time as the result of a series of investigations. According to Fawcett (9, p. 222), the rule may be stated as follows:

In polycyclic systems having atomic bridges, the existence of a compound having a carbon-carbon or carbon-nitrogen double bond at a bridgehead position is not possible, except when the rings are large, because of the strain which would be introduced in its formation by distortion of bond angles and/or distances. As a corollary, reactions which should lead to such compounds will be hindered or will give products having other structures.

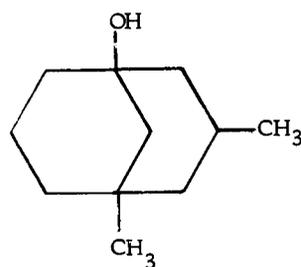
Isolable Molecules with Bridgehead Double Bonds

A number of investigations have provided data leading to a rather clear-cut limitation on the types of bridged rings allowing isolation of unsaturated types with the double bond at the bridgehead. Ball-and-peg models indicate (9, p. 226) that in a bicyclo [ X. Y. Z. ] alkene ( $X \geq Y \geq Z \neq 0$ ), structures with a double bond at a bridgehead can be made without strain when  $X + Y + Z = S = 11$ . Many structures with a bridgehead double bond can be formed with little strain when  $S = 10$ , some with  $S = 9$ , but with  $S = 8$  the strain is quite large. Prelog and coworkers (19, 20, 21) have carried out studies concerning

double bonds at bridgehead positions in the bicyclo[ X. 3. 1] alkenone systems. They were able to isolate compounds which contained bridgehead double bonds in the [ 5. 3. 1] - as well as the [ 8. 3. 1]- alkenone systems. They concluded that X = 5 represents the smallest ring size where a bridgehead double bond could occur in an isolable compound. But in more recent work, Bond (3, p. 164, 182) has shown that [ 4. 4. 1] and [ 4. 3. 1] compounds with bridgehead double bonds can be isolated. A number of attempts have been made to isolate bicyclo [ 3. 3. 1] nonenes containing a double bond at the bridgehead position. Rabe (23) observed that I was extremely resistant to dehydration. In a later study (22) he found that II could



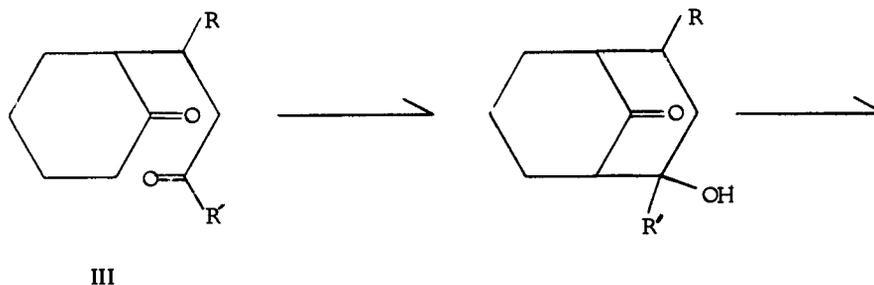
I



II

not be dehydrated even under drastic conditions. Stobbe and co-workers (28, 29) prepared several unsaturated bicyclo [ 3. 3. 1] ketones by the intramolecular aldol condensation of monocyclic 1, 5-diketones of the type III. They assumed that the double bond formed on dehydration of the intermediate aldols was at the bridgehead position. An investigation (6) of the ultraviolet spectra of some of those compounds has provided evidence that the double

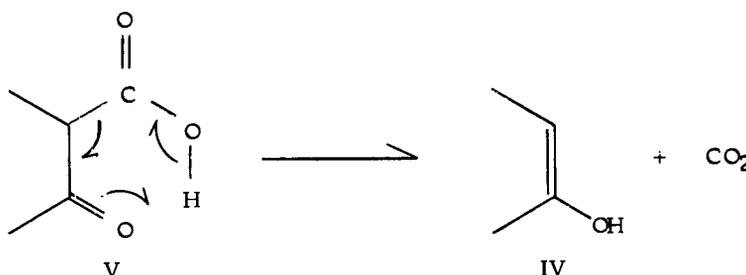
bond is not in the bridgehead position.



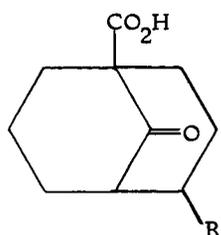
### Transient Intermediates with Bridgehead Double Bonds

The experimental evidence given above indicates that some systems are too strained to permit isolation of compounds containing bridgehead double bonds. However, the evidence does not rule out the possibility of existence of a transient reaction intermediate with a bridgehead double bond in these strained systems. The transient reaction intermediates of primary interest are the enol and the enolate forms of the bicyclic systems.

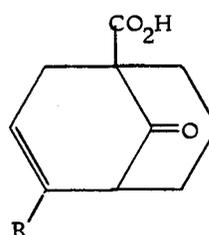
The most likely mechanism for decarboxylation of  $\beta$ -keto acids involves formation of an enol intermediate IV via a six-center transition state such as V (1). Decarboxylation reactions in which the



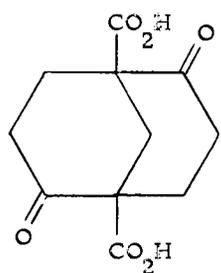
intermediate enol form must have a bridgehead double bond are of special interest. A number of [3.3.1] acids of the types VI (12, 13, 21) and VII (9, p. 245) have been shown to be stable to decarboxylation. In contrast, Meerwein (16) found that compound VIII was decarboxylated rapidly in water under relatively mild conditions for a compound of this structure. Later work by Ferris (10) on the similar  $\beta$ -keto acid IX showed that decarboxylation occurred rapidly at 145° C.



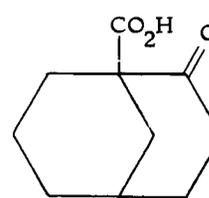
VI



VII



VIII



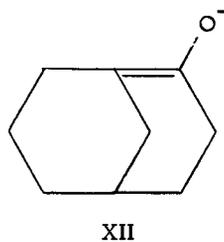
IX

The stable acids VI and VII would have had to form an intermediate enol of the type X, had decarboxylation occurred. On the other hand, the acids VIII and IX which were decarboxylated, presumably passed through the enol XI during the course of the reaction. The expectation that enol X should be appreciably more strained

than enol XI is readily verified by using Dreiding molecular models to measure the distances which separate atoms prior to forming the last bond in these two systems (12). The experimental results of decarboxylation reactions can thus be rationalized. It would appear then, that a transient double bond can exist at a bridgehead in some bicyclo[3.3.1] nonenes.

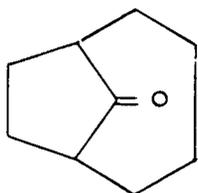


The bridgehead enolate ion like the enol, is another transient reaction intermediate that has been studied in strained systems. Removal of a bridgehead proton from bicyclo[3.3.1] nonan-2-one leads to the formation of an enolate ion of the type XII. The enolate ion may be formed by base catalysis in a deuterated solvent. Deuterium incorporation at a position  $\alpha$  to the carbonyl group testifies

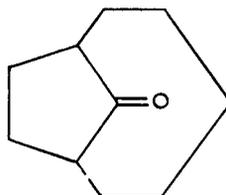


to the formation of the enolate ion. Biemann (2) found that the bicyclic[5.2.1] ketone XIII completely exchanged both bridgehead

hydrogen atoms when treated with sodium methoxide and deuterated methanol for one hour at room temperature. Under these conditions, compound XIV, in which  $S = 7$  as in the [3.3.1] system, did not incorporate any deuterium. However, when the reaction was carried out at reflux temperature, incorporation of deuterium did occur as is shown in Table 1.



XIV



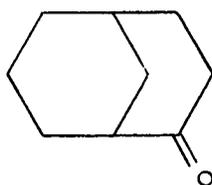
XIII

Table 1. Deuterium incorporation of XV

Time (hours)	Percent containing deuterium		
	non	mono	di
24	84	15	1
48	41	47	13

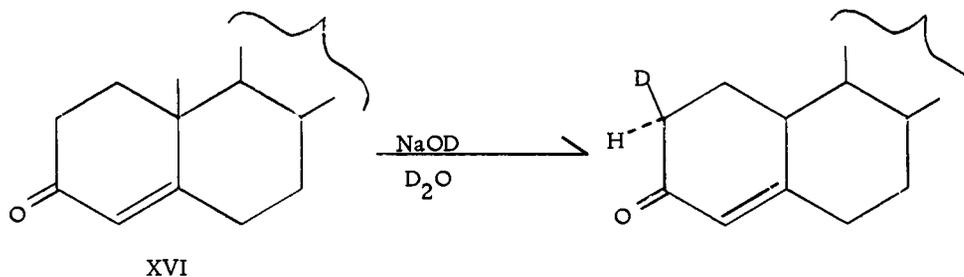
Schaefer (27) found that bicyclo[3.3.1]nonan-2-one (XV) incorporated an average of 2.46 deuterium atoms per molecule when heated for six days at 95° C in deuterium oxide which was one-tenth molar in sodium deuterioxide. The NMR spectrum showed that only hydrogens adjacent to the carbonyl group had undergone exchange and therefore

that the bridgehead enol had indeed been formed. Cope and co-workers (7), in a similar study of the same compound (XV) in deuterated methanol containing sodium methoxide, isolated a product mixture after 22 hours at room temperature, which contained 36%, 40%, 22%, and 2%, respectively, of the non-, mono-, di- and tri-deuterated ketone.



XV

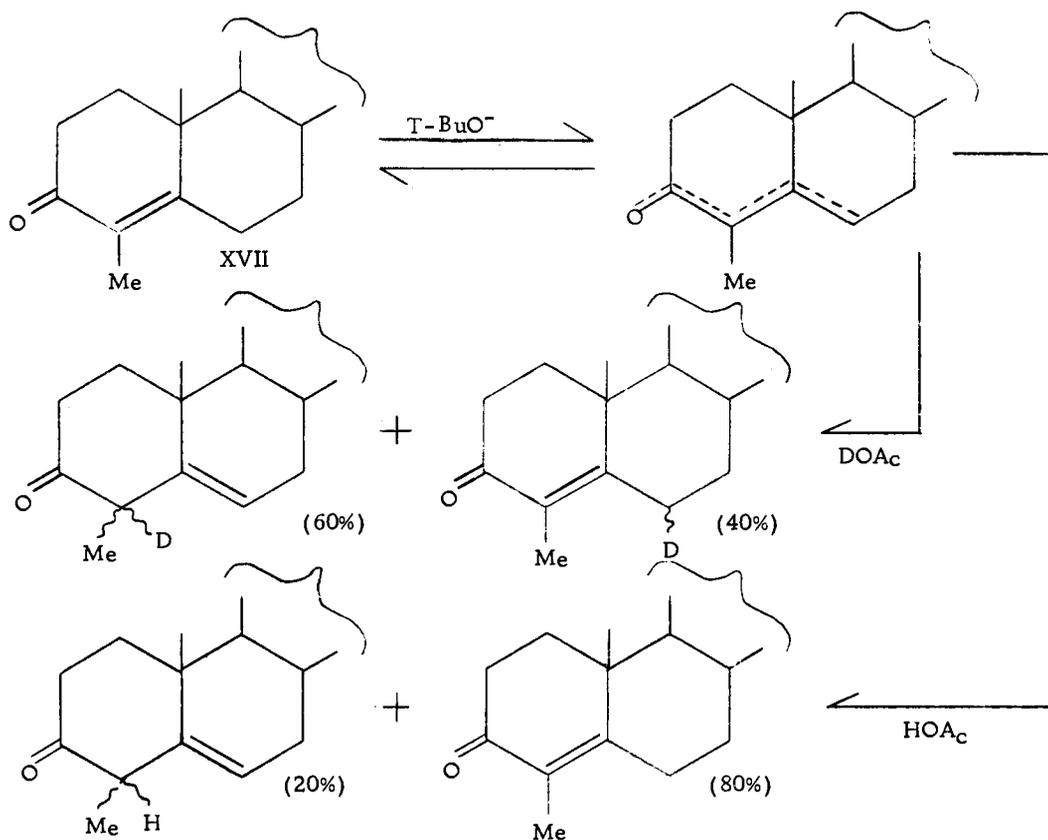
Ringold and his coworkers (24, 25, 26) have made a careful study of the rates of proton removal by base in  $\alpha, \beta$ - and  $\beta, \gamma$ -unsaturated ketones. A kinetically controlled deuterium exchange of  $\alpha, \beta$ -unsaturated ketone XVI showed that only the  $2, \beta$ -proton was exchanging. Thus the  $\alpha$ -proton is more rapidly removed than a  $\gamma$ -proton of the  $\alpha, \beta$ -unsaturated system. When the 4-methyl- $\Delta^4$ -3-keto



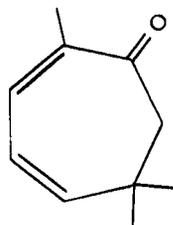
XVI

steroid XVII was treated with potassium tert-butoxide under

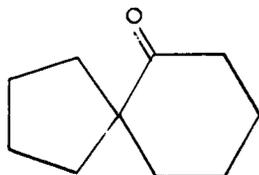
conditions which generated the most stable enolate ion, protonation gave a mixture of  $\Delta^4$ - and  $\Delta^5$ -ketones containing 20% of the  $\Delta^5$ - and 80% of the  $\Delta^4$ -ketone. Deuteration of the enolate under comparable conditions gave a 60/40 mixture of the the same ketones. This shows that during protonation, reformation of the enolate occurs rapidly and the irreversible protonation at  $C_6$  leads to the major product. Deuteration slows the reforming of the enolate sufficiently so that the non-conjugated ketone becomes the major product. Thus showing that the rate of proton removal by base is in the order  $\alpha$ -proton of  $\beta, \gamma$ -unsaturated ketone  $>$   $\alpha$ -proton of  $\alpha, \beta$ -unsaturated ketone  $>$   $\gamma$ -proton of  $\alpha$ - $\beta$ -unsaturated ketone.



Deuterium exchange with cyclic ketones has been studied. Corey and Burke (8) studied the rate of deuterium exchange of eucarvone (XVIII) in deuterated ethanol containing sodium ethoxide at 25° C. Two deuterium atoms were incorporated after five minutes under these conditions. Nesmeyanov and coworkers (17) studied the rate of deuterium exchange of some cyclohexanone derivatives in enriched water. 2, 2, 6-Trimethylcyclohexanone completely exchanges one hydrogen atom for deuterium after 70 hours at 100° C. Cyclohexanone exchanges one hydrogen atom for deuterium after 50 hours at 100° C. Spirg [4. 5] decan-6-one (XIX) incorporates between one and two deuterium atoms after 70 hours at 130° C. A study of the dione XX (18) showed that the compound exchanged two hydrogen atoms for two deuterium atoms after 70 hours at 17° C in a mixture of water, deuterium oxide and dioxane.



XVIII



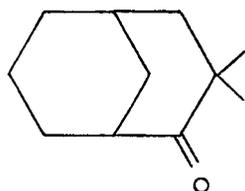
XIX



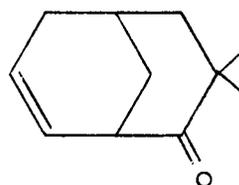
XX

## DISCUSSION

The rate of deuterium incorporation at the bridgehead position of saturated 3,3-dimethylbicyclo[3.3.1]nonan-2-one (XXI) has been studied and the rate constant was found to be 0.36 liter/mole-hour (30). Ringold and his coworkers (24, 25, 26) predict from their experimental results that the  $\alpha$ -proton of a  $\beta$ - $\gamma$ -unsaturated keto steroid is more acidic and thus will be exchanged faster than the  $\alpha'$ -proton of the  $\alpha$ , $\beta$ -unsaturated isomer. By the same reasoning one would predict a faster rate of deuterium exchange in the  $\beta$ - $\gamma$ -unsaturated ketone XXII than in the saturated analog XXI.



XXI



XXII

The rate of deuterium exchange of 3,3-dimethyl-7-bicyclo[3.3.1]nonen-2-one (XXII) was determined (Figure 2) at two different base concentrations. The rate constant,  $6.6 \times 10^{-3}$  liters/mole-hour ( $\pm 10\%$ ) is much smaller than predicted. A reasonable explanation for this decreased rate is that the introduction of a second endocyclic double bond, that of an enolate, is highly unfavorable in the

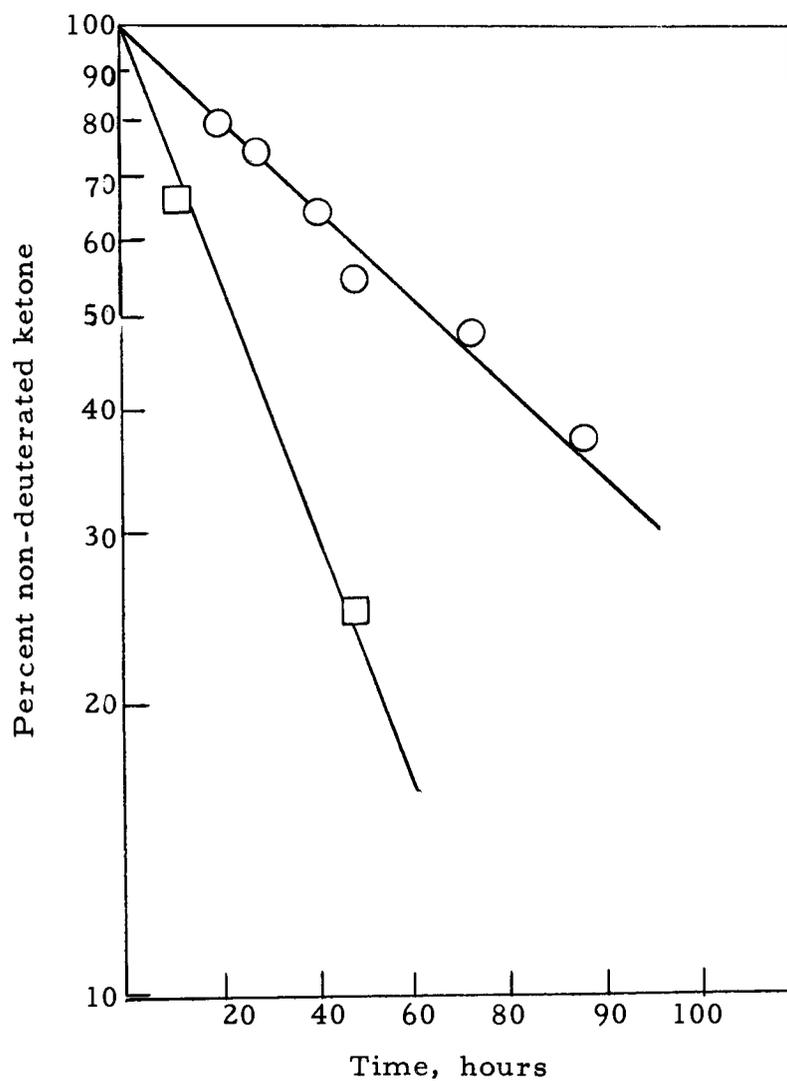
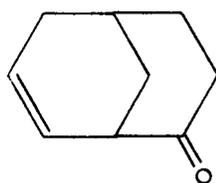


Figure 2. Percent non-deuterated ketone versus time, hours;

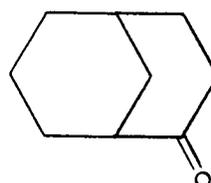
○  $[\text{CH}_3\text{O}^-] = 1.65$  molal ( $k=6.6 \times 10^{-3}$  liters/mole-hour),

□  $[\text{CH}_3\text{O}^-] = 4.13$  molal ( $k=7.0 \times 10^{-3}$  liters/mole-hour).

bicyclo[3.3.1] nonenone system. In support of this hypothesis it is noted that methylation of the unsaturated bicyclononenone XXIII could not be accomplished under the same reaction conditions which methylated the saturated bicyclononanone XXIV with ease (30). Methylation of XXIII was accomplished only by using a much stronger base.

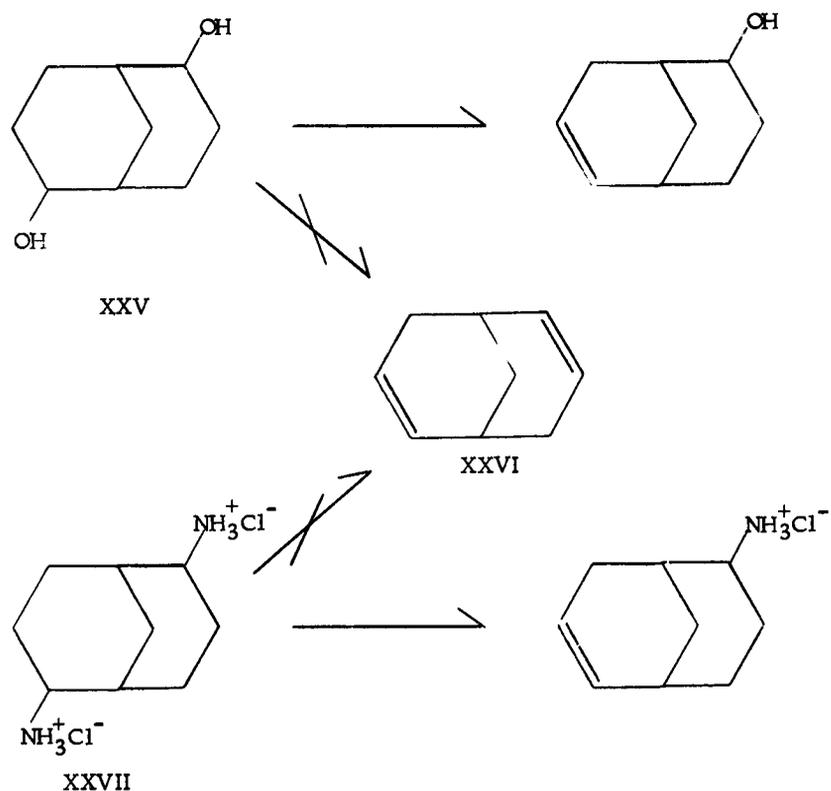


XXIII

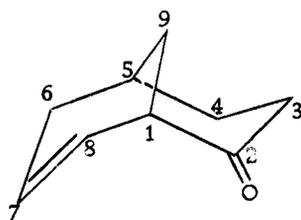


XXIV

It is interesting to note that Meerwein (15) was unsuccessful in his attempt to prepare the bicyclo [3.3.1] nonadiene XXVI by dehydration of the diol XXV or by deamination of the corresponding diamine XXVII. In each case the introduction of the second double bond was not observed. Although Meerwein did not use drastic conditions, it is obvious that the bicyclo [3.3.1] nonadiene is not formed under conditions which readily give the bicyclo[3.3.1] nonene.



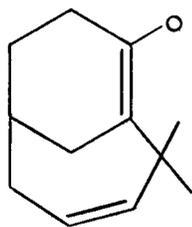
An examination of Dreiding molecular models helps explain these experimental results. The introduction of a double bond between



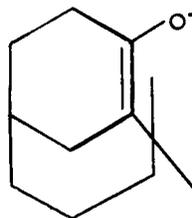
$C_7$  and  $C_8$  flattens the ring on that side and causes the  $C_1$ - $C_5$  distance to increase, thus widening the  $C_9$  carbon-carbon bond angle. The introduction of a similar double bond in the other ring will have the same effect. Apparently, the increase in strain due to a second double bond is sufficient to prevent the ready formation of a diene.

The fact that this compound is difficult to methylate can be rationalized on the basis that the second double bond, the enolate double bond, greatly increases the strain in the system.

The introduction of an enolate double bond at the bridgehead causes: (1) an increase in the bond angle at  $C_9$  and (2) a bending strain in the  $C_1-C_8$  bond. Both of these factors are more pronounced in XXII than in XXI. The  $C_9$  bond angle strain has been discussed above. The bending strain in the  $C_1-C_8$  bond can be most easily seen by Dreiding molecular models which show less orbital collinearity for XXVIII than for XXIX. (See simplified drawing below.)

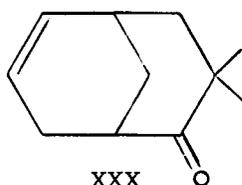


XXVIII



XXIX

It would be of interest to investigate an isomer of XXII, namely 3,3-dimethyl-6-bicyclo[3,3,1]nonen-2-one (XXX)(15). The rate of exchange should be decreased, relative to XXII, since the  $\gamma$ - $\delta$ -double bond would not stabilize the bridgehead enolate electronically but should introduce strain factors similar to those introduced by the  $\beta$ - $\gamma$ -double bond.



XXX

## EXPERIMENTAL

2-Carboxy-3-(3-cyclohexen-1-yl) propionic acid

This reaction was carried out according to the method of Sturmer (30).

A mixture of 101 g. (0.4 mole) of ethyl-2-carbethoxy-3-(3-cyclohexen-1-yl) propionate in 750 ml. of 10% potassium hydroxide solution was heated at reflux with vigorous stirring for 22 hrs. The cooled solution was washed with 60 ml. of ether and acidified (pH=1) with concentrated sulfuric acid. The aqueous layer was extracted with four 350 ml. portions of ether. The ethereal layer was washed with saturated sodium sulfate solution and was dried over magnesium sulfate. Removal of the solvent in vacuo gave 71.6 g. (0.364 mole) of 2-carboxy-3-(3-cyclohexen-1-yl) propionic acid (91% yield); m. p. (recrystallized) 120-121° C. A melting point of 120-121° C has been reported (30) for this acid.

3-(3-Cyclohexen-1-yl) propionic acid

This reaction was carried out according to the method of Sturmer (30).

Crude 2-carboxy-3-(3-cyclohexen-1-yl) propionic acid (80.6 g., 0.41 mole) was heated under reflux for 6.5 hrs in 1 l. of xylene.

The solvent was removed in vacuo and the product was distilled giving 55.2 g. (0.36 mole) of 3-(3-cyclohexen-1-yl) propionic acid (88% yield); b. p. 105° C (0.35 mm.), m. p. 33-35°C. A melting point of 33-35.5°C (30) has been reported for this compound.

3-(3-Cyclohexen-1-yl) propionyl chloride

This reaction was carried out according to the method of Sturmer (30).

To a solution of 18.5 g. (0.12 mole) of 3-(3-cyclohexen-1-yl)-propionic acid and six drops of pyridine in 350 ml. of dry benzene was added 20 ml. (0.238 mole) of oxalyl chloride over 2 hrs. The reaction mixture was kept at 10-15°C with a cold water bath during the addition and for two hours thereafter. It was cooled then to 5-10°C and stirred 3.5 hrs. longer. The solvent was removed in vacuo and the residue was taken up in 150 ml. of n-hexane. After removal of non-soluble material by filtration, the solvent was removed in vacuo. The residue was distilled, bath temp. 100-110°C (4.7 mm.), giving 19.8 g. (0.115 mole) of 3-(3-cyclohexen-1-yl) propionyl chloride (96% yield). A boiling point of 80-90° C (1.5 mm.) has been reported (30) for this acid chloride.

7-Bicyclo[3.3.1] nonen-2-one

Anhydrous stannic chloride (11.7 ml., 0.10 mole) was added

over a 1 hr. period to a well-stirred solution of 8.16 g. (0.0475 mole) of 3-(3-cyclohexen-1-yl)propionyl chloride in 300 ml. of chloroform. The reaction mixture was stirred 5 hrs. at room temperature. Successive additions of 100 g. of ice, 20 ml. of concentrated hydrochloric acid and 100 ml. of water were made and the mixture was stirred for 3 hrs. The organic layer was separated and washed with 50 ml. of saturated sodium carbonate solution, six 100 ml. portions of water and finally, saturated sodium sulfate solution. After the solution had been dried over magnesium sulfate, the solvent was removed in vacuo. The residue was distilled through a small alembic, bath temp. 120° C (3.0 mm.) yielding 4.20 g. (0.031 mole) of 7-bicyclo[3.3.1]nonen-2-one (purity 85% by vapor phase chromatogram)(55% yield). A mixture of the product and an authentic sample showed a single peak in the vapor phase chromatogram.

7-Bicyclo[3.3.1]nonen-2-one was isolated in 96-97% purity (by vapor phase chromatogram) from the crude reaction mixture by distillation through a six-inch column, packed with glass helices, bath temp. 60° C (0.05 mm.).  $\nu = 3030(w), 2850(s), 2750(s), 1700(s), 1650(w), 1270(m), 1220(m), 900(m)$  and  $670(m) \text{ cm}^{-1}$ . The infrared data is in agreement with that reported for 7-bicyclo[3.3.1]nonen-2-one (30).

### Cyclization of 3-(3-cyclohexen-1-yl) propionic acid

A mixture of 4.07 g. (0.026 mole) of 3-(3-cyclohexen-1-yl)-propionic acid and 59.4 g. of polyphosphoric acid (82-84% phosphorus pentoxide) was heated on a steam bath for 2.5 hrs. The mixture was shaken every 30 min. The reaction mixture was diluted to 200 ml. with ice and was extracted with six 100 ml. portions of ether. The ethereal layer was washed with water and saturated sodium sulfate solution and dried over magnesium sulfate. Removal of the solvent in vacuo, followed by distillation, bath temp. 68-78° C (0.35 mm.), yielded 2.66 g. (0.0196 mole) of 4,5,6,7-tetrahydroindanone (purity 93-94% by vapor phase chromatogram)(74% yield). A pure sample of the compound, isolated with the preparative vapor phase chromatograph, gave the following data:  $\lambda_{\max} = 238 \text{ m}\mu$ . (log E = 4.10), 2,4-dinitrophenylhydrazone (m. p. 237-238° C), semicarbazone (m. p. 240.5-241° C). Literature values were  $\lambda_{\max} = 236 \text{ m}\mu$ . (log E = 4.09)(11); 2,4-dinitrophenylhydrazone (m. p. 228° C)(11), (m. p. 238.5-239.5° C)(14); semicarbazone (m. p. 240° C)(11), (m. p. 242.5-243° C)(14).

### Methylation of 7-bicyclo[3.3.1]nonen-2-one

#### Potassium *tert*-butoxide catalyzed methylations

Methylation procedures I and II were carried out on a

Friedel-Crafts reaction mixture containing 85% (by the vapor phase chromatogram) 7-bicyclo[3.3.1] nonen-2-one.  $\nu = 3030(w)$ ,  $2850(s)$ ,  $2750(s)$ ,  $1700(s)$ ,  $1650(2)$ ,  $1270(m)$ ,  $1220(m)$ ,  $900(m)$  and  $670(m) \text{ cm}^{-1}$ .

The tert-butyl alcohol was distilled from sodium prior to use.

Procedure I. A solution of potassium tert-butoxide (0.70 g., 6.2 mole) and 0.3 g. of the Friedel-Crafts mixture in 30 ml. of tert-butyl alcohol was heated to  $40^\circ \text{C}$ . A solution of 3.4 g. (0.024 mole) of methyl iodide in 20 ml. of tert-butyl alcohol was added in one portion. The reaction mixture was stirred at  $40^\circ \text{C}$  for 5 hrs., at which time 20 ml. of water was added. The alcohol was removed in vacuo and the aqueous layer was extracted with four 100 ml. portions of n-hexane. The organic layer was dried over magnesium sulfate and the solvent removed in vacuo.

The entire procedure was repeated twice again on the reaction product. The vapor phase chromatogram of the final product (0.16 g.) showed that the major component (35% of the total area) was not 7-bicyclo [3.3.1] nonen-2-one. An infrared spectrum of the crude product showed a band at  $1355(m) \text{ cm}^{-1}$  in addition to all bands present in the starting material.

Procedure II. To a solution of 1.0 g. of the Friedel-Crafts mixture in 10 ml. of tert-butyl alcohol was added a solution of 1.63 g. (0.0145 mole) of potassium tert-butoxide in 12 ml. of tert-butyl alcohol. After the 30 min. addition period, the mixture was allowed

to stir for 15 min. at 40° C. Methyl iodide (8.88 g., 0.0625 mole) in 10 ml. of tert-butyl alcohol was added over a 1 hr. period and the solution was stirred at 45° C for 19 hrs. Water (20 ml.) was added, the alcohol was removed in vacuo, and the aqueous layer was extracted with four 100 ml. portions of n-hexane. After the organic layer had been dried over magnesium sulfate, the solvent was removed in vacuo.

The entire procedure was repeated twice again on the reaction product and 0.57 g. of the final product mixture was recovered. A vapor phase chromatogram showed that the major component (22% of the total area) was neither 7-bicyclo[3.3.1]nonen-2-one nor the major component of Procedure I. An infrared spectrum showed bands at 1730(s), 1380(w) and 1360(w)  $\text{cm}^{-1}$  in addition to all the bands of the starting material.

#### Sodium hydride catalyzed methylation

A solution of 3.26 g. of the Friedel-Crafts mixture and 7.1 g. (0.296 mole) of sodium hydride in 70 ml. of dry benzene was stirred at 65° C for 2 hrs. Dimethyl sulfate (15.5 g., 0.248 mole) was added in one portion and the reaction mixture was refluxed for 108 hrs. Hydrogen evolution was still noted at the end of this time. The solution was hydrolyzed with 20 ml. of methanol and the solvent was removed in vacuo. The vapor phase chromatogram of the product indicated

that no significant change in the starting material had occurred.

#### Potassium triphenylmethide catalyzed methylation

A mixture of 12.2 g. (0.05 mole) of triphenylmethane and 1.84 g. (0.047 g-atom.) of potassium metal in 25 ml. of dry 1,2-dimethoxyethane was refluxed for 12 hrs. under a nitrogen atmosphere. After the solution had been cooled to room temperature, 1.88 g. (0.014 mole) of 7-bicyclo[3.3.1]nonen-2-one (96% pure) was added in one portion and stirring was continued for 20 min. Methyl iodide (20.5 g., 0.145 mole) was then added over a 10 min. period and stirring was continued for 10 hrs. The solution was filtered and the solvent was removed in vacuo. Distillation, bath temp. 60° C (0.05 mm.), through a six-inch column packed with glass helices yielded 2.12 g. of product mixture. The major component (53% by the vapor phase chromatogram) was 3,3-dimethyl-7-bicyclo[3.3.1]nonen-2-one (49% yield),  $\nu = 3030(m), 2850(s), 2750(s), 1700(s), 1650(m), 1380(m), 1360(m), 1260(m)$  and  $710(m) \text{ cm}^{-1}$ . The n. m. r. spectrum showed multiplets centered near 5.8 $\delta$ (2H), 2.9 $\delta$ (1H), 2.4 $\delta$ (1H), 2.2 $\delta$ (2H), 1.9 $\delta$ (4H), and singlets at 1.1 $\delta$ (3H), and 1.05 $\delta$ (3H).  
Anal. Calc'd for C<sub>11</sub>H<sub>16</sub>O: C, 80.44%; H, 9.82%.

Found: C, 79.91%; H, 10.02%.

Deuterium exchange study of  
3, 3-dimethyl-7-bicyclo-  
[ 3. 3. 1 ] nonen-2-one

Series A

A solution of 239  $\mu$ l. of deuterated methanol containing 96.6 mg. (0.59 mmole) of 3, 3-dimethyl-7-bicyclo[ 3. 3. 1 ] nonen-2-one and 22.9 mg. (0.394 mmole) of 93% active sodium methoxide was divided into seven aliquots which were sealed into bombs. The samples were placed into a constant temperature bath at 100.7° C ( $\pm 0.1^\circ$  C) and removed at given time intervals. The bombs were opened and the contents were taken up in 2 ml. of water and extracted with five 2 ml. portions of carbon tetrachloride. The organic layer was washed with saturated sodium sulfate solution, dried over magnesium sulfate, and the solvent removed in vacuo. The sample was taken up in a measured amount of carbon tetrachloride and the deuterium content of the samples was determined by quantitative infrared analysis. The extinction coefficient of 0.690 liter/mole-mm. was calculated from the infrared spectra of a number of samples which had been analyzed for deuterium content by mass spectrometry. The rate constant was calculated as  $6.6 \times 10^{-3}$  liters/mole-hour ( $\pm 10\%$ ). This calculation was made assuming the following rate law:

$$-dA/dt = \text{Rate} = k[\text{CH}_3\text{O}^-] [\text{C} = \text{O}]$$

$$k = \ln 2 / T_{1/2} [\text{CH}_3\text{O}^-]$$

### Series B

A solution of 152  $\mu\text{l}$ . of deuterated methanol containing 82.2 mg. (0.505 mmole) of 3,3-dimethyl-7-bicyclo [3.3.1] nonen-2-one and 36.3 mg. (0.626 mmole) of 93% active sodium methoxide was divided into four aliquots which were sealed into bombs. The samples were placed in a constant temperature bath at 100.7° C ( $\pm 0.1^\circ$  C) and removed at given time intervals. The samples were worked-up and analyzed for deuterium content as described in Series A. The rate constant was calculated as  $7.0 \times 10^{-3}$  liters/mole-hour ( $\pm 15\%$ ) with the same assumptions for the rate expression that were made in Series A. Because the deuterium content of only two of the four samples could be plotted in a straight line with the origin on the rate curve, it is felt that the rate constant from Series A is the more valid of the two.

### Quantitative infrared analyses

The infrared analyses were made with a Perkin-Elmer Model 21 infrared spectrophotometer equipped with a sodium chloride micro-cell of path length 0.2 mm. Instrument settings were: resolution 927, gain 6.0, response 1, suppression 2 and speed 4. The deuterium

concentration was determined from the absorption at  $2180\text{ cm}^{-1}$ .

The  $I_0$  and  $I$  values were determined by measuring the distance from the base line of no absorption to the point of zero transmission and from the peak to point of zero transmission respectively. Samples of known concentration of the deuterated compound in carbon tetrachloride were used to establish a standard curve and to calculate the extinction coefficient.

#### Infrared spectra

All spectra were obtained for the neat material unless otherwise indicated. The instrument for all non-quantitative spectra was a Beckman IR 8 infrared spectrophotometer.

#### Nuclear magnetic resonance spectra

The Varian A-60 Resolution NMR Spectrometer was used for all spectra. The material being studied was dissolved in carbon tetrachloride containing tetramethylsilane as an internal standard.

#### Vapor phase chromatography

All analyses were run on the same  $6' \times 1/4''$  unopolar column. A Perkin-Elmer Model 154C vapor fractometer was used with helium as carrier gas at 15 psi pressure. All vapor phase chromatographic purifications were done on a  $5' \times 1/4''$  silicone column in an

Aerograph Model A-700 Autoprep.

Ultraviolet spectrum

The ultraviolet spectrum was taken in ethanol on a Beckman DB Spectrophotometer.

Boiling points

All boiling points were uncorrected.

Melting points

Melting points above 200° C were taken on a Fisher-Johns melting point block. All other melting points were taken on a Büchi melting point apparatus. All melting points were uncorrected.

## SUMMARY

2-Carboxy-3-(3-cyclohexen-1-yl)propionic acid, 3-(3-cyclohexen-1-yl)propionic acid and 3-(3-cyclohexen-1-yl)propionyl chloride were prepared in sequence. Cyclization of 3-(3-cyclohexen-1-yl)propionic acid in phosphoric acid resulted in the formation of 4, 5, 6, 7-tetrahydroindanone which was identified by its ultraviolet spectrum and its physical properties.

7-Bicyclo[3.3.1]nonen-2-one (XXIII) was prepared by the cyclization of 3-(3-cyclohexen-1-yl)propionyl chloride. It was identified by its infrared spectrum and its physical properties.

3,3-Dimethyl-7-bicyclo[3.3.1]nonen-2-one (XXII) was prepared by methylation of 7-bicyclo[3.3.1]nonen-2-one. It was characterized by its infrared and nuclear magnetic resonance spectra and its carbon-hydrogen analysis.

The rate of deuterium exchange of 3,3-dimethyl-7-bicyclo[3.3.1]nonen-2-one (XXII) was studied and an explanation for the unexpectedly slow rate was offered.

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