Fused small ring compounds
by Shi-Kuang Yao

A THESIS Submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry
Montana State University

Abstract:
Bicyclo(3.1.0)hexane-6-carboxylic acid [diagram not captured by OCR] has been synthesized by reaction of cyclopentene with ethyl diazoacetate in the presence of copper powder followed by alkaline hydrolysis. It has been observed that this compound does not undergo the Hell-Volhard-Zelinsky reaction.

Rearrangement of 6,6-dichlorobicyclo(3.1.0)hexane was found to occur on heating. Both the original dichloride and the rearrangement product gave the same l-chloro-6-acetoxy-l-cyclohexene when refluxed with potassium acetate and acetic anhydride.

The structure of the rearrangement product, 1,6-dichloro-l-cyclohex-ene, was proved by degradation and by preparing an authentic compound. The unknown and the authentic compound were found identical by both infrared and vapor phase chromatography analyses.

The following mechanisms are proposed: 1. 6,6-DichlorobicycIo(3,1.0)hexane* is heated at 150°C.: [diagrams not captured by OCR] 2. 6,6-Dichlorobicyclo(3.1.0)hexane reacts with potassium acetate in acetic anhydride: [diagrams not captured by OCR] * The number of members in the ring to the right exclusive of the members linking the two rings togethere are indicated by a number. Similarly the members of the smaller ring are designated. Lastly the members of the link (bridge) exclusive of the linking members are designated by number also. viz. bicyclo(3.1.0)hexane [diagram not captured by OCR] For the numbering of the compound, start numbering 1 at one of the carbons in the bridge as illustrated above.

FUSED SMALL RING COMPOUNDS

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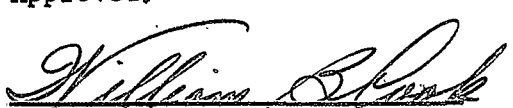
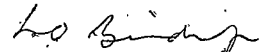
Approved:



Head, Major Department



Chairman, Examining Committee

Dean, Graduate Division

Bozeman, Montana
August, 1960

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Finally, thanks to my wife who has been so patient for the last few years.

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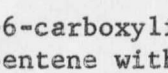
ABSTRACT

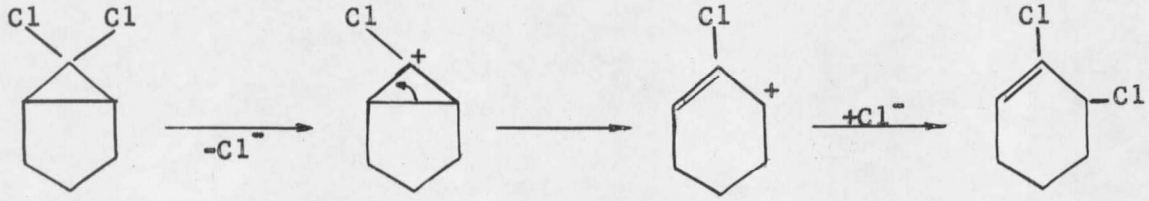
Bicyclo(3.1.0)hexane-6-carboxylic acid () has been synthesized by reaction of cyclopentene with ethyl diazoacetate in the presence of copper powder followed by alkaline hydrolysis. It has been observed that this compound does not undergo the Hell-Volhard-Zelinsky reaction.

Rearrangement of 6,6-dichlorobicyclo(3.1.0)hexane was found to occur on heating. Both the original dichloride and the rearrangement product gave the same 1-chloro-6-acetoxy-1-cyclohexene when refluxed with potassium acetate and acetic anhydride.

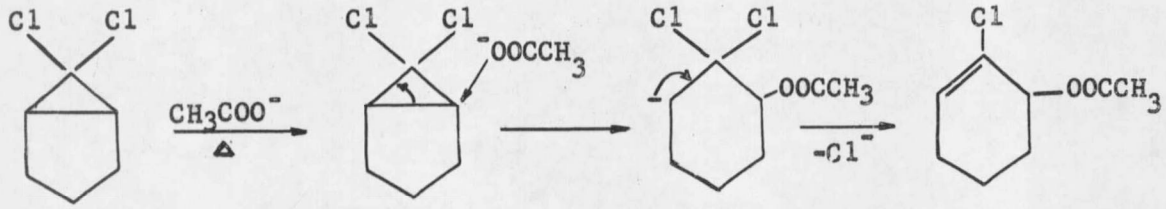
The structure of the rearrangement product, 1,6-dichloro-1-cyclohexene, was proved by degradation and by preparing an authentic compound. The unknown and the authentic compound were found identical by both infrared and vapor phase chromatography analyses.

The following mechanisms are proposed:

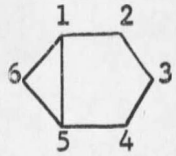
1. 6,6-Dichlorobicyclo(3.1.0)hexane* is heated at 150°C.:



2. 6,6-Dichlorobicyclo(3.1.0)hexane reacts with potassium acetate in acetic anhydride:



* The number of members in the ring to the right exclusive of the members linking the two rings togethere are indicated by a number. Similarly the members of the smaller ring are designated. Lastly the members of the link (bridge) exclusive of the linking members are designated by number also. viz. bicyclo(3.1.0)hexane

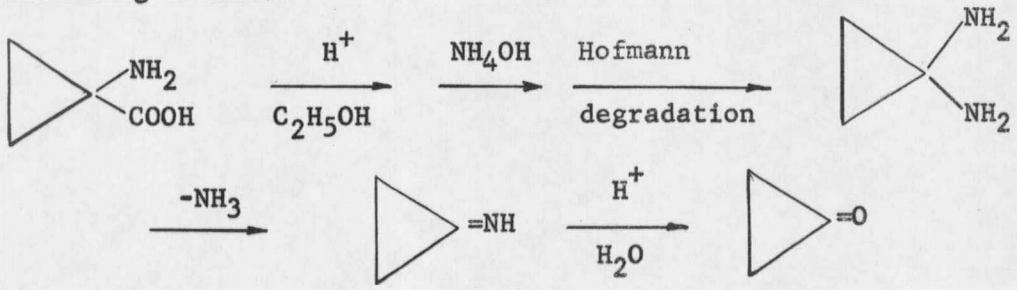


For the numbering of the compound, start numbering 1 at one of the carbons in the bridge as illustrated above.

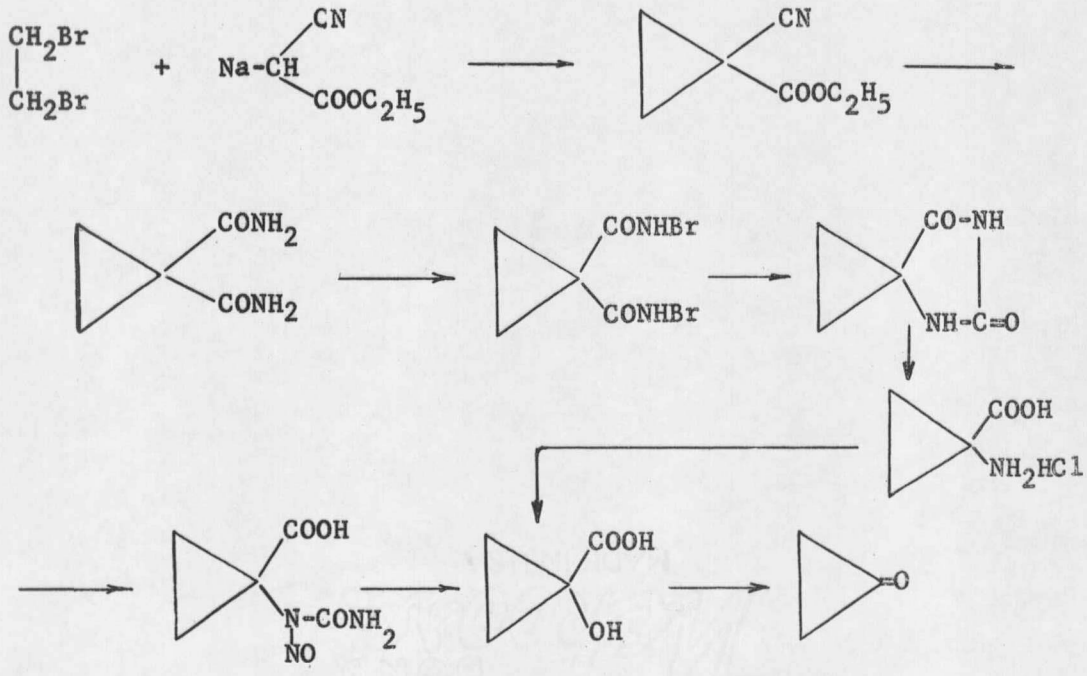
INTRODUCTION

There have been attempts to synthesize cyclopropanone for the past 40 years; however all these attempts have met with failure. This is undoubtedly due to the great strain on a three-membered ring.

In 1922, Ingold (1) reported the synthesis of cyclopropanone by the following method:



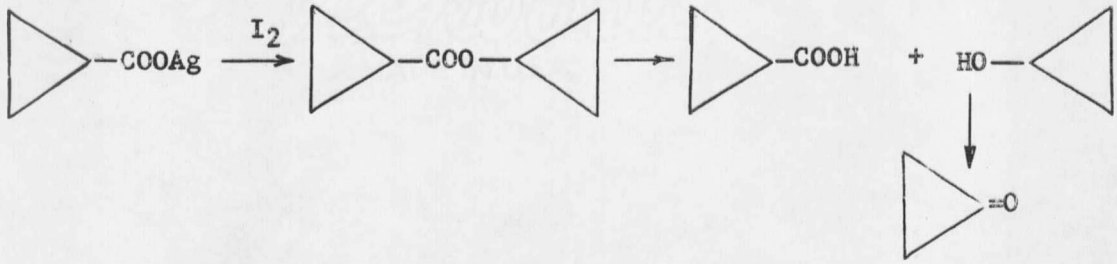
Demyanov and Feofilaktov (2) attempted to repeat Ingold's (1) work very carefully by the following scheme:



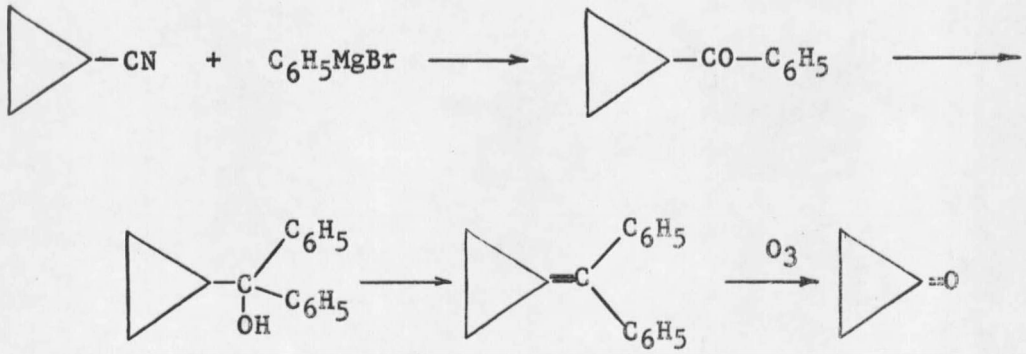
Actually, however, the work was not completed, and they suggest that the structure of the hydroxy acid, which was the last step they reached, will bear more study.

Demyanov and Feofilaktov (2) stated that with the evidence presented it was quite unlikely that Ingold actually had cyclopropanone. They also concluded that all the evidence points to the non-existence of Ingold's cyclopropanone, and probable great instability of the compound if, indeed, it exists at all.

Lipp (3) has attempted to synthesize cyclopropanone by the following method:



The final step gave only cyclopropane carboxylic acid and other degradation products. Lipp then tried the following method:

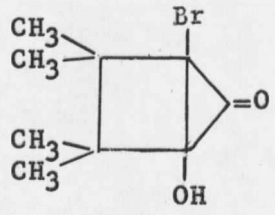


The synthesis was successful as far as diphenyl methylene cyclopropane, but only benzophenone was obtained on ozonolysis.

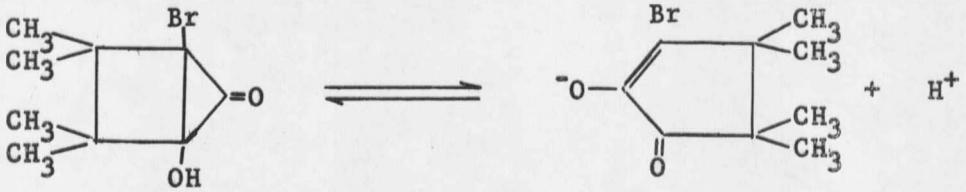
Lipp also tried diazomethane expansion of ketene (3), but this yielded only cyclobutanone which has been known for years.

Lipp has concluded that Ingold mistook 1,1-dihydroxy-cyclopropane for cyclopropanone.

Francis and Wilson (4) obtained a cyclic derivative of phorone for which they assigned the structure shown below:



Ingold and Shoppee (5) suggested that the compound prepared by Francis and Wilson was stabilized by tautomerism:



Guha and Seshadringar (6) have reported obtaining bicyclo(3.1.0)-hexan-1-on-2,6-diethyl carboxylate, but they failed to give any definite evidence.

In all cases, where the three-membered ring saturated ketone has been clearly identified, there have been geminal or large groups present on the three-membered ring or an adjacent ring of the condensed or spirane type. Known compounds include cyclopropan-1-on-2,2-dimethyl carboxylate (7), 1-bromo-2,2,3,3-tetramethyl-bicyclo(2.1.0)pentan-4-ol-5one (4),

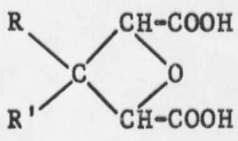
bicyclo(3.1.0)hexan-1-on-2,6-diethyl carboxylate (6), and cyclohexane-spiro-cyclopropanone (8).

The importance of steric effects on the stability of the following compounds

(I) (II)

has been discussed by Thorpe et al (9) (10) in Table I. The composition of the equilibrium mixture is definitely dependent on the nature of substituents, R and R', as shown by the data in Table I. This transformation, being an equilibrium and consequently directly related to the thermodynamic stabilities of the reactant and product, offers convincing evidence that gem-substituents or a condensed ring system may stabilize a three-membered ring, perhaps through an effect on bond angles.

The corrected structure of compound I has been reassigned by Wiberg and Holmquist (11) as follows:



The above compound still possesses the same effect (12) with which Thorpe et al have observed.

Stabilization by resonance is also possible as has been demonstrated by Breslow, Haynie and Mirra (13) who have synthesized diphenyl cyclopropenone from phenyl ketene dimethyl acetal with benzal chloride

TABLE I

Composition of Equilibrium Mixtures of I $\rightleftharpoons$ II

R	R'	% of I in Mixtures
hydrogen	hydrogen	0
methyl	methyl	0
methyl	ethyl	0
ethyl	ethyl	62
n-propyl	n-propyl	71
R and R' = $-(CH_2)_5-$		100

and potassium t-butoxide followed by hydrolysis in neutral aqueous solution. Thermal decomposition of diphenyl cyclopropenone at 130-40°C. causes evolution of carbon monoxide and diphenyl acetylene. The relatively high temperature at which decomposition occurs and the fact that diphenyl cyclopropenone can also be isolated from hydroxylic medium, show that the cyclopropenone system must have strong resonance stabilization indeed to compensate for its high angle strain.

Several other reactions which might have some bearing on the synthesis of cyclopropanone have been reported.

In the course of studies on the formation of dichlorocarbene as an intermediate in the alkaline hydrolysis of chloroform, Doering and Hoffmann (14) treated chloroform with cyclohexene in the presence of potassium t-butoxide and obtained 7,7-dichlorobicyclo(4.1.0)heptane. Other olefins were found by these workers to react similarly with chloroform and bromoform in the presence of strong bases to give gem-dihalocyclopropane and further examples of this reaction have been reported by Parham (15a, b, c), Skell (16a, b, c), and their co-workers.

Dale and Swartzentruber (17) tried to hydrolyze 2,2-dichlorocyclopropyl benzene in water in a sealed pyrex tube heated to 200-5°C. Only a black polymeric material was obtained. Under less drastic conditions only the starting material was observed.

McElvain and Weyna (18) have described the reaction of ketene acetals with dichlorocarbene to form 2,2-dichlorocyclopropanone acetals. These products can be isolated only by distillation under low pressure as

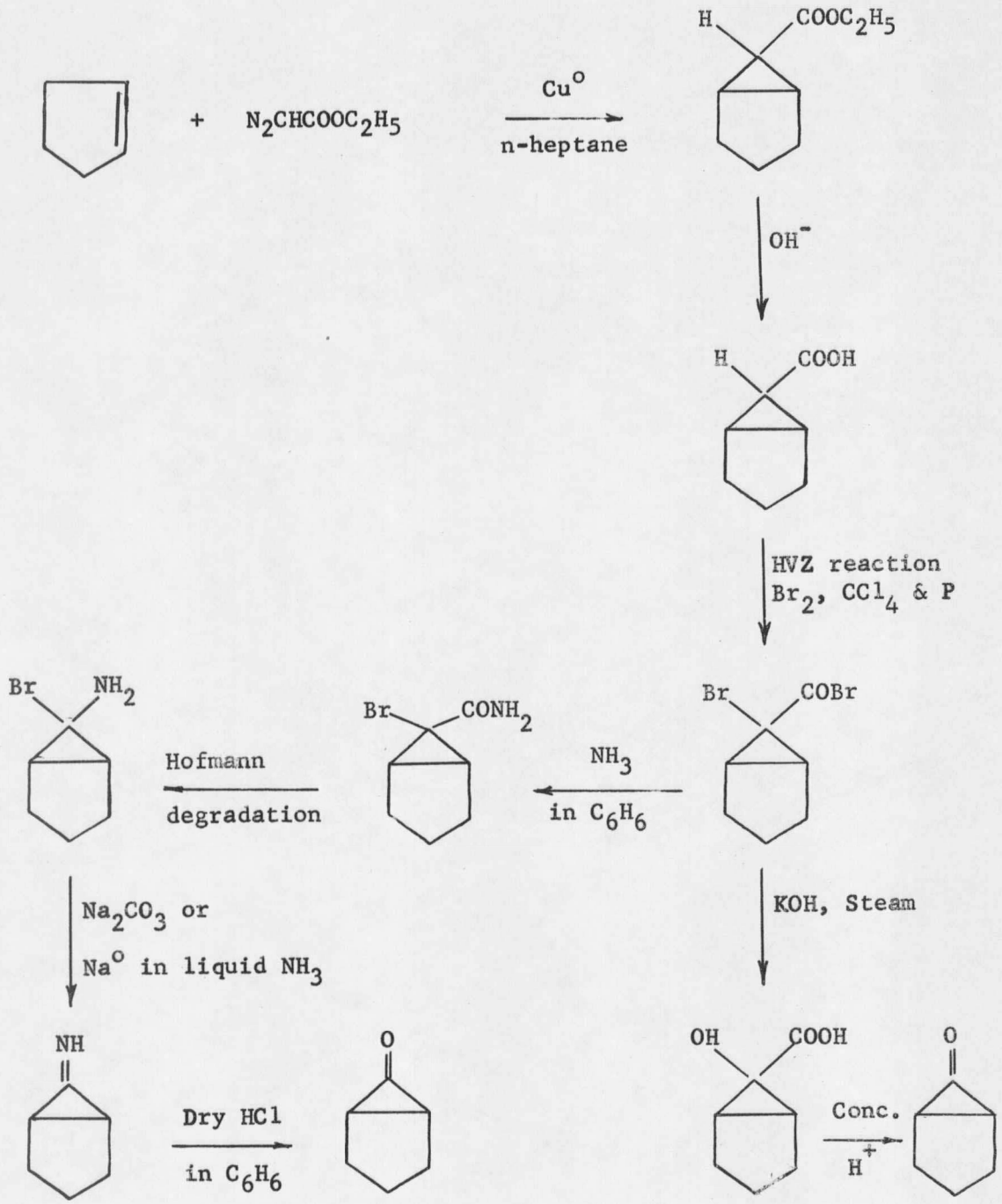
they undergo pyrolysis above 100°C. to α-chloroacrylic esters and an alkyl chloride.

All the procedures which have been attempted (1) (2) (3) for the preparation of cyclopropanone involved aqueous solutions. Even though cyclopropanone may exist, it would be expected that its hydrated form would be isolated from these solutions because in cyclopropanone the usual equilibrium between a ketone and its hydrate should be strongly shifted to the right as a result of the I-strain effect (19).

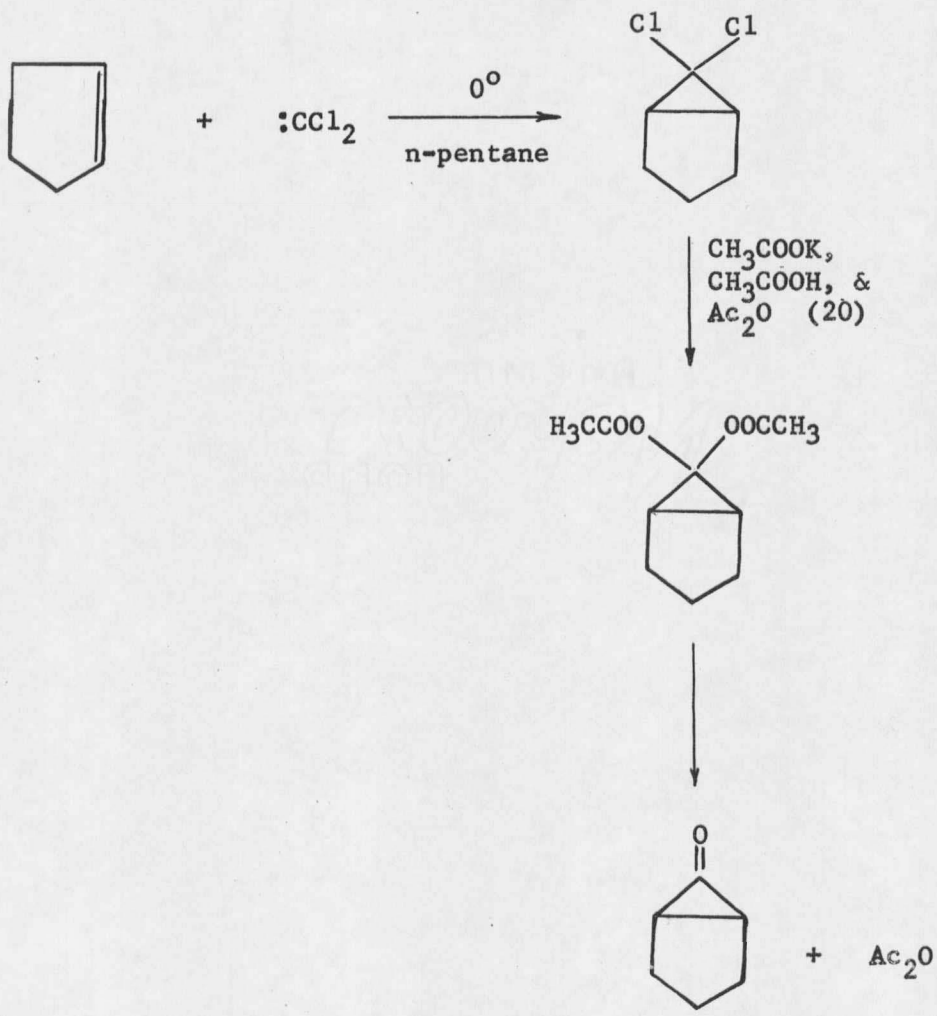
Therefore, it would seem wise to use non-aqueous solvents or no solvent at all, in order to avoid the possibility of hydrating any cyclopropanone that might be formed.

The proposition that a non-aqueous reaction sequence for the synthesis of cyclopropanone might be successful can be extended to simple substituted cyclopropanones which are not stabilized by resonance or the presence of geminal or large groups on the three-membered ring. The reaction schemes shown below were chosen in the hope of obtaining products which would be of interest for further studies.

SCHEME I


+ $N_2CHCOOC_2H_5$
Cu^o
n-heptane
H
$COOC_2H_5$
OH^-
H
COOH
HVZ reaction
Br_2, CCl_4 & P
Br
COBr
NH_3
in C_6H_6
Br
$CONH_2$
Hofmann
degradation
Br
NH_2
Na_2CO_3 or
Na^o in liquid NH_3
KOH, Steam
OH
COOH
O
Conc.
H^+
NH
Dry HCl
in C_6H_6
O

SCHEME II


Cl
Cl
+
:CCl2
0°
n-pentane
CH3COOK,
CH3COOH, &
Ac2O (20)
H3CCOO
OOCCH3
O
+
Ac2O

EXPERIMENTAL

Preparation of ethyl bicyclo(3.1.0)hexane-6-carboxylate.

Cyclopentene prepared by dehydration of cyclopentanol in the presence of 85% phosphoric acid (21), and then purified through a Todd Precise Fractionation Assembly, was collected at 39-40° at 641 mm.

A mixture of cyclopentene (76.4 g., 1.12 moles), n-heptane (180 ml.) and copper powder catalyst (3.0 g.) was heated at 53-8°. Ethyl diazoacetate (128 g., 1.12 moles) which was prepared from methylene aminoacetonitrile (22) (23) was added over a period of 4 hours with rapid stirring. The mixture was cooled to room temperature and the catalyst was removed by filtration. The filtrate was washed twice with 20 ml. portions of 10% sulfuric acid, one 100 ml. portion of water, one 50 ml. portion of saturated sodium bicarbonate and finally with saturated sodium chloride and dried over sodium sulfate. The solvent was removed in vacuo, and the residue was distilled through a 6" microfractionating column packed with stainless steel helices giving a main fraction boiling at 5 mm. : yield 53.3 g. (30.8%).

Preparation of bicyclo(3.1.0)hexane-6-carboxylic acid.

A mixture of 25 g. (0.162 moles) of ethyl bicyclo(3.1.0)hexane-6-carboxylate and 250 ml. of 2 N. potassium hydroxide was refluxed for 3 hours. The solution was filtered; the filtrate was neutralized with 50% sulfuric acid and repeatedly extracted with ether. The combined extracts were evaporated to dryness and the residue, recrystallized from alcohol as prisms, melted at 61.6-62.6°C. (corrected) : yield 15 g. (73.4%).

Analysis: Calculated for $C_7H_{10}O_2$: Neutralization Equivalent 126.16

Found: 126.04

Preparation of bicyclo(3.1.0)hexane-6-carbonyl bromide.

Two grams (0.0158 mole) of bicyclo(3.1.0)hexane-6-carboxylic acid was dissolved in 10 ml. of carbon tetrachloride and 0.2 g. of anhydrous red phosphorus which was first washed free of all acid and carefully dried was added. The mixture was heated to boiling and after the addition of 2.9 g. (0.018 mole) of bromine was refluxed for 15 minutes, vacuum distillation, gave a main fraction which boiled at 47° at 1.0 mm.

Analysis: Calculated for C_7H_9BrO : Br, 42.26%

Found: 43.02%

Preparation of bicyclo(3.1.0)hexane-6-carboxamide:

Two grams of bicyclo(3.1.0)hexane-6-carbonyl bromide was added dropwise to an excess ice-cold concentrated aqueous ammonia solution with vigorous agitation. The precipitate, after filtration, washing with water and recrystallization from alcohol as needles, melted at 193-94°C. (uncorrected).

Analysis: Calculated for $C_7H_{11}NO$: N, 11.19%

Found: 10.73%

Preparation of 6,6-dichlorobicyclo(3.1.0)hexane.

One hundred and thirty-six grams (2 moles) of purified cyclopentene, 510 ml. of n-pentane and 284.5 g. (2.54 moles) of potassium t-butoxide (10% excess) were added to a 2 liter 3-necked flask which was equipped with mercury sealed stirrer, condenser and dropping funnel. The entire

apparatus was placed in an ice-bath. The potassium t-butoxide was prepared from 90.0 g. (2.30 moles) of metallic potassium by adding excess of t-butyl alcohol, and distilling off the excess aldohol. It was then dried in evacuated oven at 95°C. for 16 hours. The suspension was cooled to 0°C. and stirred throughout the whole reaction. Two hundred thirty-eight and eight-tenths grams (2 moles) of chloroform were added dropwise at such a rate that the temperature remained between 0 and 5°C. Following the addition of the chloroform (which required 4 hours), the mixture was stirred for an additional hour, and then poured into ice water. The organic layer was separated and the aqueous layer was extracted with two 250 ml. portions of n-pentane which were combined with the organic layer, after drying with anhydrous calcium chloride, the solvent was evaporated and the residue distilled in vacuo. A main fraction (102 g., 33.8%), b.p. 57-8°C. at 13 mm. pressure was obtained through the Todd Precise Fractionation Assembly at the reflux ratio of 50:1.

$D_{25}^{25} = 1.1605$ $\eta_D^{25} = 1.4942$

Analysis: Calculated for $C_6H_8Cl_2$: Cl, 46.96%

Found: 47.17%

Examination of this material by vapor phase chromatography showed only 6,6-dichlorobicyclo(3.1.0)hexane and 1,6-dichlorocyclohexene in the ratio 92.3 : 7.7. The major component was isolated by vapor phase chromatography and was shown by infrared analysis to be pure 6,6-dichlorobicyclo-(3.1.0)hexane. In the vapor phase chromatography analyses, two columns were employed; (1) 5 ft. x 0.25 in. Ucon Polar column operated at 96°C.

with helium flow rate 9.5 cm^3./sec., and (2) 5 ft. x 0.5 in. Craig column operated at 114°C. with helium flow rate 8.5 cm^3./sec.

The infrared spectrum of 6,6-dichlorobicyclo(3.1.0)hexane showed the usual cyclopropane absorption at 3.35 μ (3070 cm^{-1}.) and 9.8 μ (1020 cm^{-1}.).

Preparation of 1,6-dichloro-1-cyclohexene.

(a) Fifty grams of 6,6-dichlorobicyclo(3.1.0)hexane were refluxed at 150°C. for one hour, and then distilled through the Todd Precise Fractionation Assembly giving a main fraction boiling at 83-4°C. at 15 mm.; yield 47.5 g. (95%).

(c) An authentic compound was prepared from cyclohexanone by chlorination (24) and subsequent reaction with phosphorous pentachloride at 0°C. The reaction mixture was poured into ice-water and extracted with ether. The solvent was evaporated in vacuo and a main fraction that had a boiling point of 82-4° at 15 mm. was obtained.

The authentic compound was separated by vapor phase chromatography in order to obtain a pure product, and then checked with infrared analysis, the spectrum was superimposable with the 1,6-dichloro-1-cyclohexene (25) primarily obtained. The results are presented in figures 5 and 6.

Analysis: Calculated for $C_6H_8Cl_2$: Cl, 46.96%

Found: 46.33%

Preparation of 1-chloro-6-acetoxy-1-cyclohexene from 6,6-dichlorobicyclo-(3.1.0)hexane.

Thirty-eight and one-half grams (0.255 mole) of 6,6-dichlorobicyclo(3.1.0)hexane, 50 g. (0.51 mole) of anhydrous potassium acetate, 77 ml.

of glacial acetic acid and 38.5 ml. of acetic anhydride were refluxed at 92-5°C. for 72 hours, and poured into ice-water. The organic layers was separated, the aqueous layer was extracted with two 30 ml. portions of benzene. The combined organic solutions were distilled until the benzene was gone, and the residue distilled in vacuo through a Todd Precise Fractionation Assembly. A main fraction, b.p. 83-4°C. at 5 mm., was obtained; yield 30.7g. (69%).

Mousseron et al (26) report the following constants for this compound:

b.p. 107-8°C. at 15 mm. ; $D_{25}^{25} = 1.168$; $\eta_D^{25} = 1.4805$

Analysis: Calculated for $C_8H_{11}ClO_2$: Cl, 20.31%

Found: 20.31%

Detailed vapor phase chromatography studies, similar to those mentioned on page 20 showed that the product was contaminated by 0.1% of 6,6-dichlorobicyclo(3.1.0)hexane.

Preparation of 1-chloro-6-acetoxy-1-cyclohexene from 1,6-dichloro-1-cyclohexene.

The procedure described in the preceding section was followed using 38.5 g. (0.255 mole) of 1,6-dichloro-1-cyclohexene, 77 ml. of glacial acetic acid and 50.0 g. (0.51 mole) of anhydrous potassium acetate. Reflux temperature was 130-32°C. The product boiled at 83-4°C. at 5 mm., and was shown by infrared analysis and vapor phase chromatography to be the same as the one mentioned above.

Preparation of bicyclo(3.1.0)hexane.

The method described by Doering and Hoffmann (14) for the reduction

of 7,7-dibromobicyclo(4.1.0)heptane was employed. Following the complete reaction of the sodium metal (31 g., 2.0 g. atoms) with wet methanol (10 ml. of water to 300 ml. of methanol), and 30 ml. of ether as solvent, 100 ml. of water was added, the ether layer was separated, and the aqueous layer was extracted twice with 20 ml. portions of ether. From 10.2 g. (0.0675 mole) of 6,6-dichlorobicyclo(3.1.0)hexane the yield was 2.85 g. (51.7%) of bicyclo(3.1.0)hexane as a colorless liquid, b.p. 74°C. (641 mm.).

An infrared analysis showed the usual cyclopropane absorption at 3.35 μ (3084 cm^{-1}) and 9.77 μ (1024 cm^{-1}) and showed no absorption for unsaturation which would have appeared at 6-6.5 μ (1668-1548 cm^{-1}).

Vapor phase chromatography proved the homogeneity of the product.

The reduction of 1,6-dichloro-1-cyclohexene with sodium and methanol.

1,6-Dichloro-1-cyclohexene (10.2 g., 0.0675 mole) was reduced with 31 g. (2.0 g. atoms) of sodium and 200 ml. of wet methanol in the above manner. The product obtained (3 g., 54.5%) was identified with known cyclohexene by both infrared and vapor phase chromatography analyses.

Preparation of 1-chloro-6-hydroxy-1-cyclohexene.

A solution of 35 g. (0.624 mole) of potassium hydroxide and 10 g. (0.0755 mole) of 1-chloro-6-acetoxy-1-cyclohexene in 200 ml. of 90% ethyl alcohol was refluxed for 3 hours. The solution was filtered and the filtrate was neutralized with 50% sulfuric acid and then refiltered. This filtrate was diluted with 100 ml. of water and extracted twice with benzene. The extracts were distilled until the benzene was removed and the residue was distilled in vacuo. A main fraction, b.p. 86-7°C. at 15 mm.,

was obtained; yield 4.74 g. (62.5%).

Mousseron et al (26) report the following constants:

b.p. 86-7°C. at 15 mm. ; $D_{25}^{25} = 1.184$; $\eta_D^{25} = 1.5066$

Analysis: Calculated for C_6H_9ClO : Cl, 26.74%

Found: 26.49%

Preparation of 1-chloro-cyclohex-1-en-6-one.

Potassium dichromate (1.48 g., 0.0050 mole) was dissolved in 20 ml. of water and 4 ml. of concentrated sulfuric acid was added. The mixture was added dropwise to 2 g. (0.0151 mole) of 1-chloro-6-hydroxy-1-cyclohexene, keeping the temperature between 25 and 30°C. Following addition of the potassium dichromate the reaction mixture was heated in a beaker of water at 60°C. for 20 minutes. Fifty milliliters of water was then added and the solution cooled in a cooling bath for 2 hours. After the precipitate had been separated by suction, it was washed with ice-water and dried in desiccator. After recrystallization from alcohol it had a m.p. of 75.6-76.4 (corrected); yield 1.2 g. (61%). Mousseron et al (27) report a m.p. of 70°C.

Analysis: Calculated for C_6H_7ClO : Cl, 27.15%

Found: 27.11%

Semicarbazone (recrystallized from alcohol) melted at 195-97°C. reported at 195-98°C. by Mousseron et al (27).

The reaction of 1-chloro-6-hydroxy-1-cyclohexene with potassium permanganate solution.

The method described by Crossley and Haas (28) was employed with

only a slight modification as follows:

Two grams of 1-chloro-6-hydroxy-1-cyclohexene were suspended in 30 ml. of water and a cold, saturated solution of potassium permanganate added until the color of latter remained permanent. After filtering the separated manganese dioxide, a small amount of sodium bisulfite was added in order to destroy the excess permanganate and the liquid was evaporated to a very small volume. acidified with sulfuric acid and repeatedly extracted with ether. After recrystallization from chloroform, the m.p. of the product was 96.5-7.5°C.; yield 0.5 g. This m.p. was indicative of glutaric acid which was the product expected from this reaction.

This substance was further identified as glutaric acid, by a mixed m.p. determination with known glutaric acid. No melting point depression was observed.

The reaction of 1-chloro-6-hydroxy-1-cyclohexene with thionyl chloride.

A solution of 1.2 g. (0.00905 mole) of 1-chloro-6-hydroxyl-1-cyclohexene and 1.6 g. (0.0134 mole) of thionyl chloride was refluxed on the steam-bath until hydrogen chloride gas evolution had ceased (about 2 hours). The excess thionyl chloride was removed under vacuum leaving a product which boiled at 68-9°C. at 7.5 mm.

This material was shown by infrared and vapor phase chromatography analyses to be 1,6-dichloro-1-cyclohexene.

Dehydrogenation of 1-chloro-6-acetoxy-1-cyclohexene in the presence of sulfur or chloranil.

The methods described by Cocker (29) and Arnold (30) were followed:

(a) A solution of 5 g. (0.0286 mole) of 1-chloro-6-acetoxy-1-cyclohexene and 1.84 g. (0.0572 mole) of sulfur was refluxed at 220-40°C. for 24 hours. The product was then distilled. About 70% of unreacted material was recovered, and a small amount of low boiling material which was not investigated was also obtained.

(b) A solution of 5 g. (0.0286 mole) of 1-chloro-6-acetoxy-1-cyclohexene and 13.76 g. (0.126 mole) of chloranil in 30 ml. of xylene was refluxed for 14 hours, cooled, and filtered. The filtrate was diluted with an equal quantity of ether, washed with diluted alkali, dried over sodium sulfate and fractionated.

No 2-chloro-1-phenoxy acetate, the expected product, could be isolated.

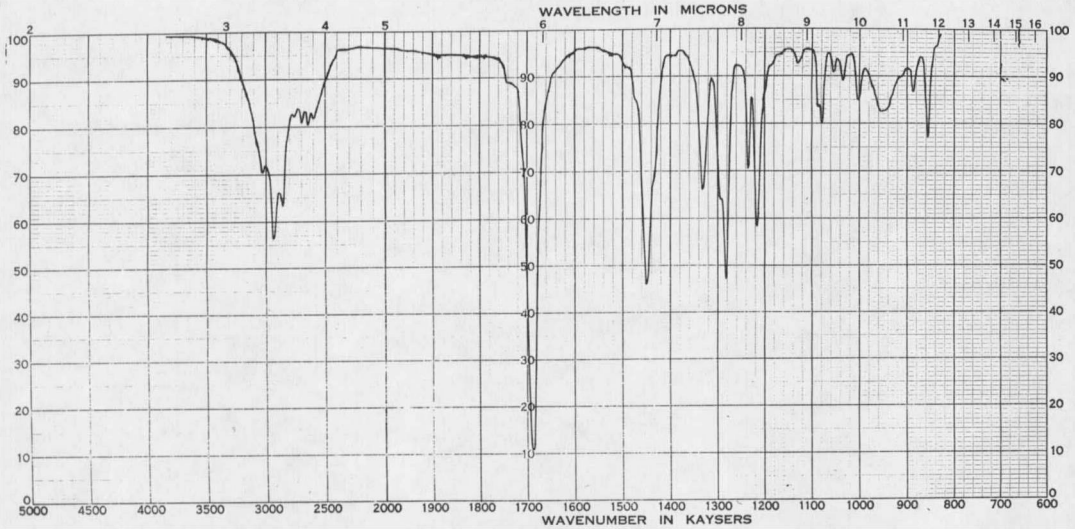


Figure 1. Bicyclo(3.1.0)hexane-6-carboxylic acid (5% w/w in CCl_4)

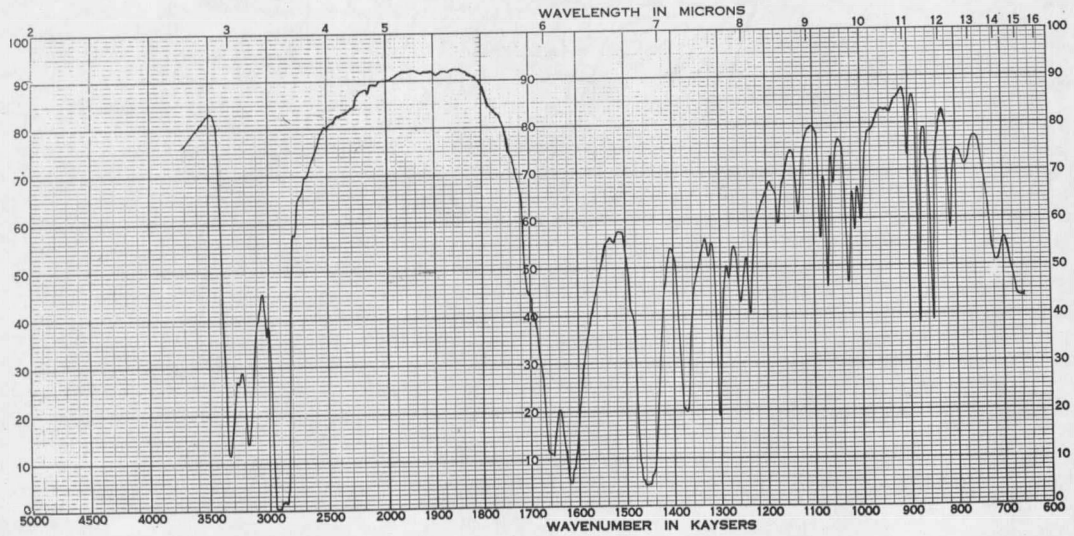


Figure 2. Bicyclo(3.1.0)hexane-6-carboxamide (Nujol mull)

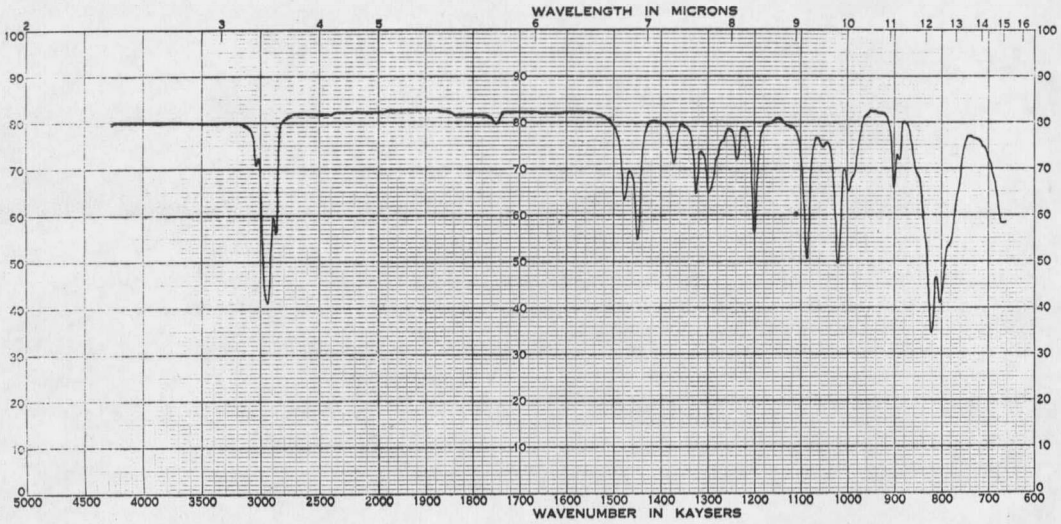


Figure 3. 6,6-Dichlorobicyclo(3.1.0)hexane (capillary film)

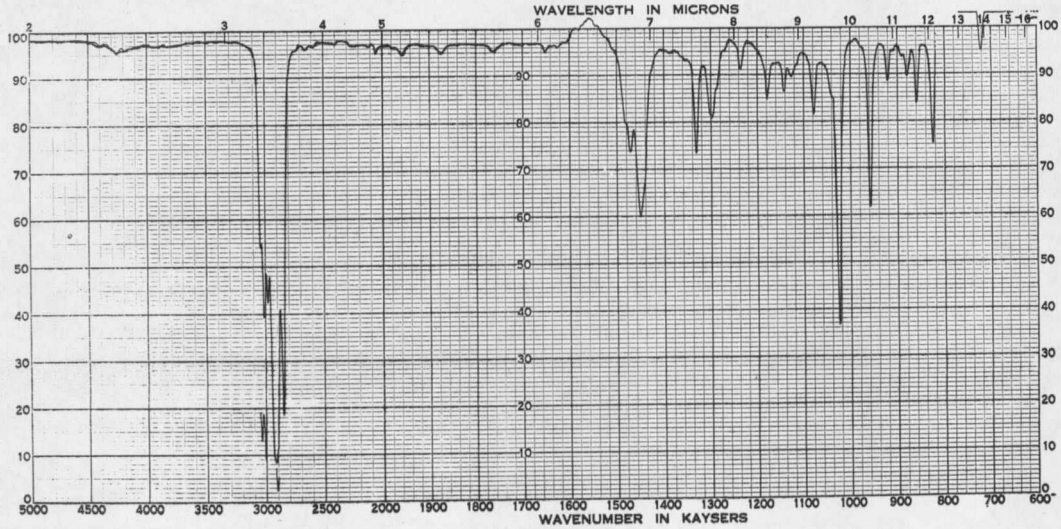


Figure 4. Bicyclo(3.1.0)hexane (20% v/v in CCl_4)

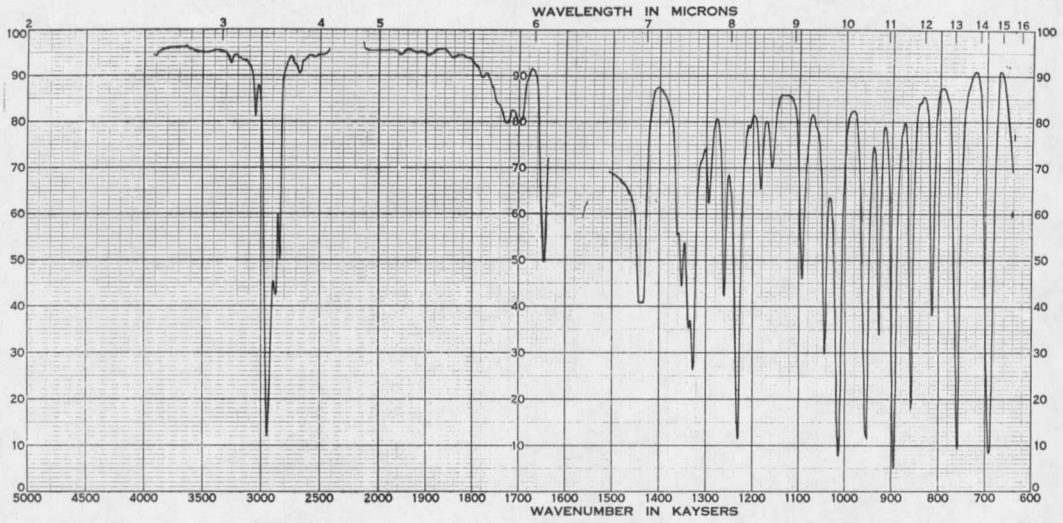


Figure 5. 1,6-Dichloro-1-cyclohexene (20% v/v in CS_2)

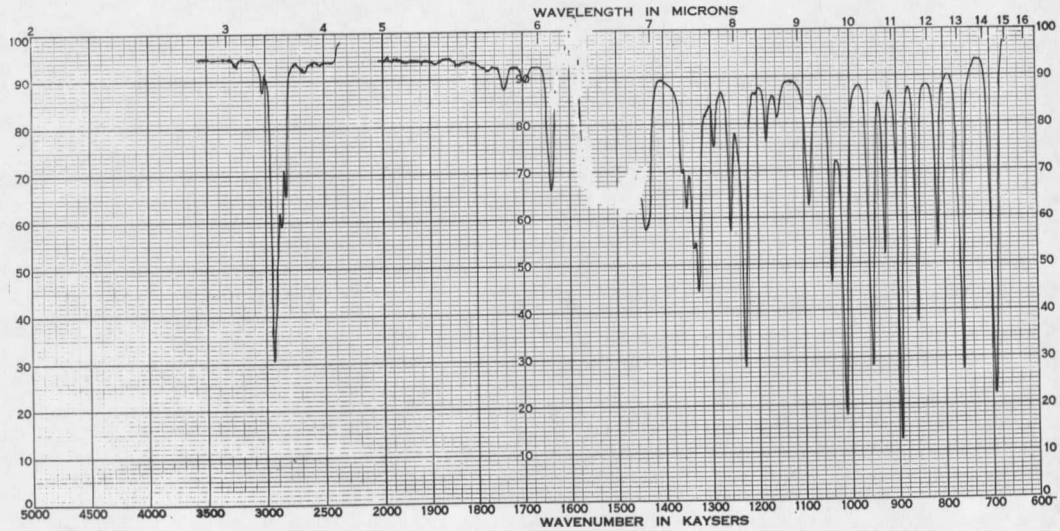


Figure 6. Authentic compound of 1,6-dichloro-1-cyclohexene (20% v/v in CS_2)

DISCUSSION

Although neither of the reaction schemes outlined in the introduction for the synthesizing of bicyclo(3.1.0)hexan-6-one was realized a number of interesting points developed in the course of the investigation.

Reaction sequence I was carried as far as bicyclo(3.1.0)hexane-6-carboxylic acid, but the introduction of bromine into the acid by the well-known Hell-Volhard-Zelinsky reaction failed.

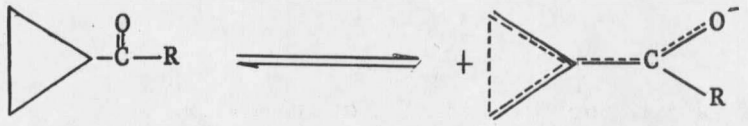
The Hell-Volhard-Zelinsky reaction normally substitutes bromine on the α-carbon. Repeated attempts under most of the known conditions gave only starting material. Even reaction of bromine with the acid chloride, which is presumed to be an intermediate in the Hell-Volhard-Zelinsky reaction, gave negative results.

The bromine molecule in Hell-Volhard-Zelinsky reaction acts as an electrophilic reagent. The proposed mechanism is: (31)

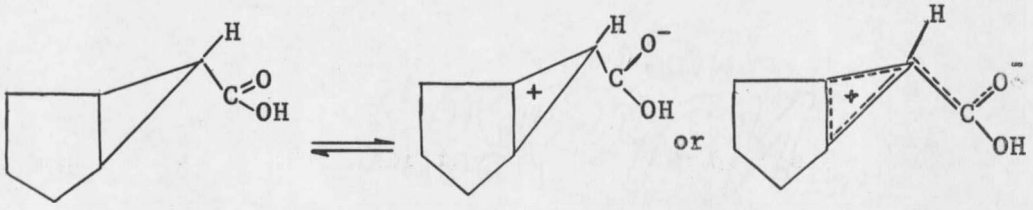
1. $3RCH_2COOH + PBr_3 \longrightarrow 3RCH_2COBr + P(OH)_3$
2. $RCH_2COBr + Br^+Br^- \longrightarrow RCHBrCOBr + HBr$
3. $RCHBrCOBr + RCH_2COOH \longrightarrow RCHBrCOOH + RCH_2COBr$

The cyclopropane ring has been classified as a nucleophilic group because the carbon-carbon bonds of the cyclopropane ring are abnormally weak and cyclopropane derivatives might be expected to be readily attacked by electrophilic reagents. However, the electronegative group which is directly attached to cyclopropane ring would diminish the additive activity of cyclopropane toward bromine through exercise of inductomeric or mesomeric electron attraction away from the nucleophilic center (32).

Kosower (33) has demonstrated electron delocalization in alkyl propyl ketones:



A similar delocalization could occur in bicyclo(3.1.0)hexane-6-carboxylic acid.

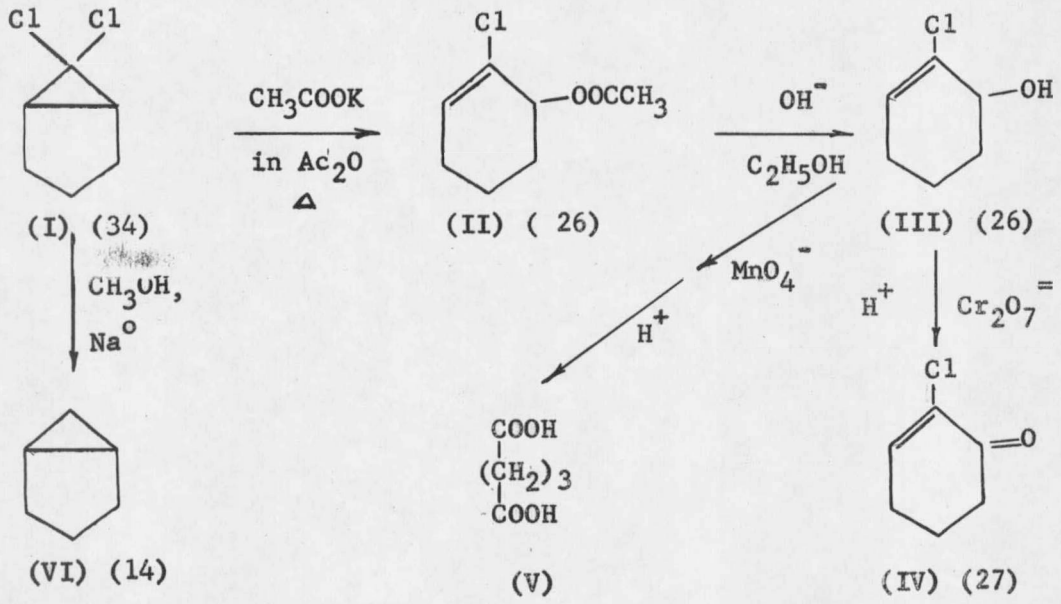


This may be the reason why the Hell-Volhard-Zelinsky reaction was unsuccessful.

Skell and Garner (16b) have prepared 6,6-dibromobicyclo(3.1.0)-hexane, but reported no chemical properties.

Reaction sequence II was carried as far as 6,6-dichlorobicyclo-(3.1.0)-hexane (34). 6,6-Dichlorobicyclo(3.1.0)hexane was found to be inert to bromine in carbon tetrachloride, but reacted readily with potassium permanganate solution. The compound showed no absorption at 6-6.5 μ (1668-1548 cm^{-1}) which is consistent with the absence of a double bond. The chloride was remarkably active in displacement reactions. There was precipitation with alcoholic silver nitrate within 3 minutes at room temperature. The reaction of the chloride with potassium acetate in acetic anhydride gave only the rearrangement product, 1-chloro-6-acetoxy-1-cyclohexene. The structure of this compound was demonstrated by a series of

reactions as follows:

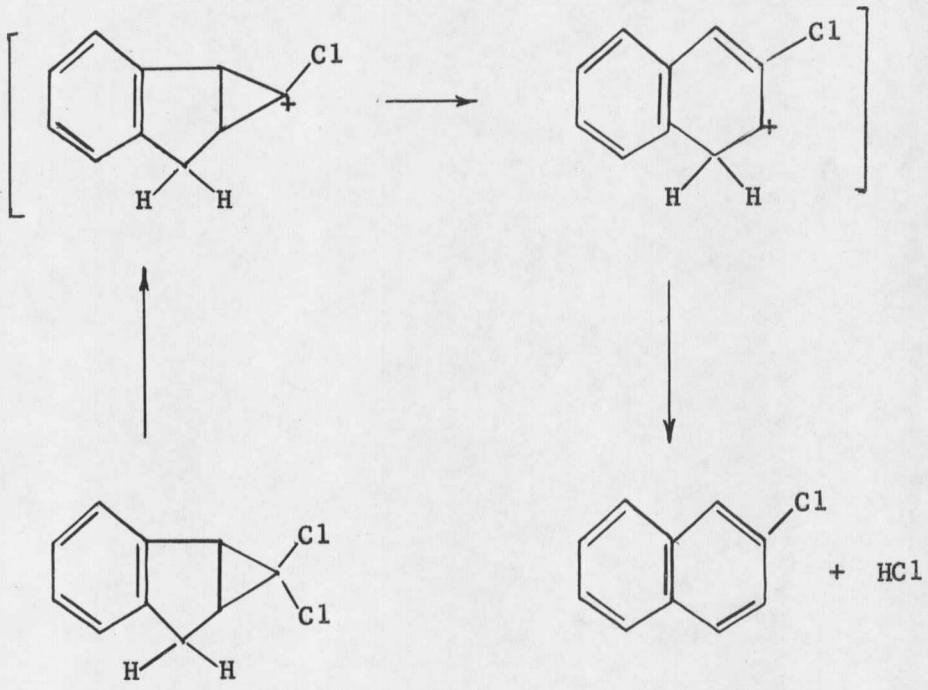


A number of similar rearrangements have been reported in the literature. The reaction of pyrrole (35) (36) (37) and indole (38) (39) with chloroform and base has given rise to, respectively, 3-chloro-pyridine and 3-chloro-quinoline, in addition to the expected aldehyde.

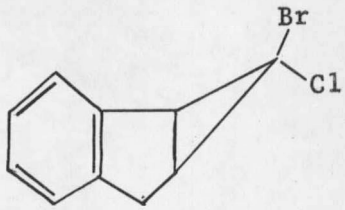
Skell and Sandler (34) have reported the rearrangement of 6,6-dihalobicyclo(3.1.0)hexane with electrophilic reagents. Treatment with alcoholic silver nitrate, yielded 6-hydroxy-1-cyclohexene. According to these authors the strain in the 5-3 ring system results in greatly enhanced reactivity, 6,6-dibromobicyclo(3.1.0)hexane being 200 times as reactive as the analogous 7,7-dihalobicyclo(4.1.0)heptane, wnich has a 6-3 ring system.

Parham, Reiff and Swartzentruber (15a) have reported the reaction of indenylsodium with chloroform in excess indene. 2-Chloronapthalene

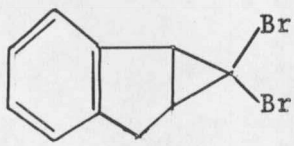
was the product when the reaction mixture was steam distilled, but they also found 1,1-dichloro-1a,6a-dihydrocycloprop(a)indene when non-polar solvents were employed in processing the crude reaction mixture. The proposed mechanism follows:



Farham and Twelves (15b) have reported dibromochloromethane, indene and base should lead preferentially to the formation of the following compounds:

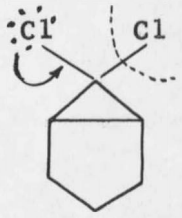


and



The crude cyclopropyl derivatives obtained from this reaction, proved to be thermally unstable. However, when the crude product was distilled a high yield of a mixture of the 2-bromonaphthalene and 2-chloronaphthalene was obtained.

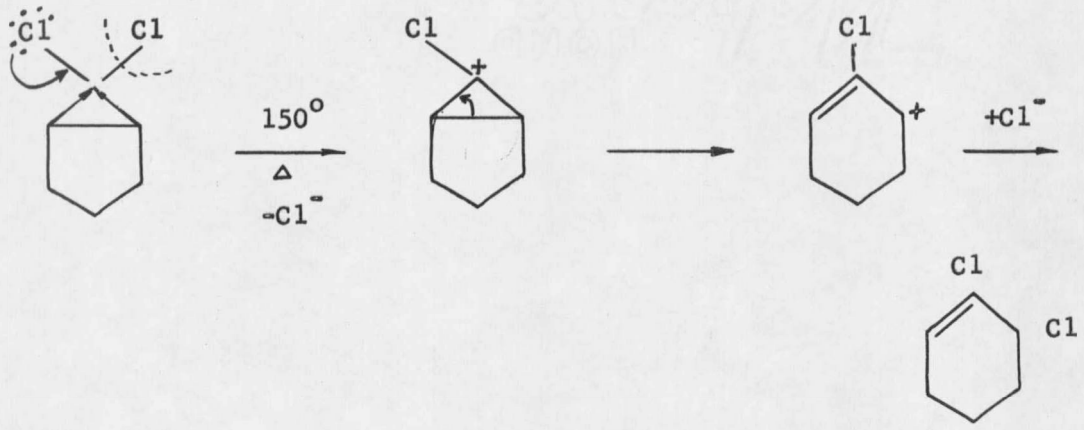
The compound 6,6-dichlorobicyclo(3.1.0)hexane appears to undergo a similar thermal rearrangement when heated at 150°C.



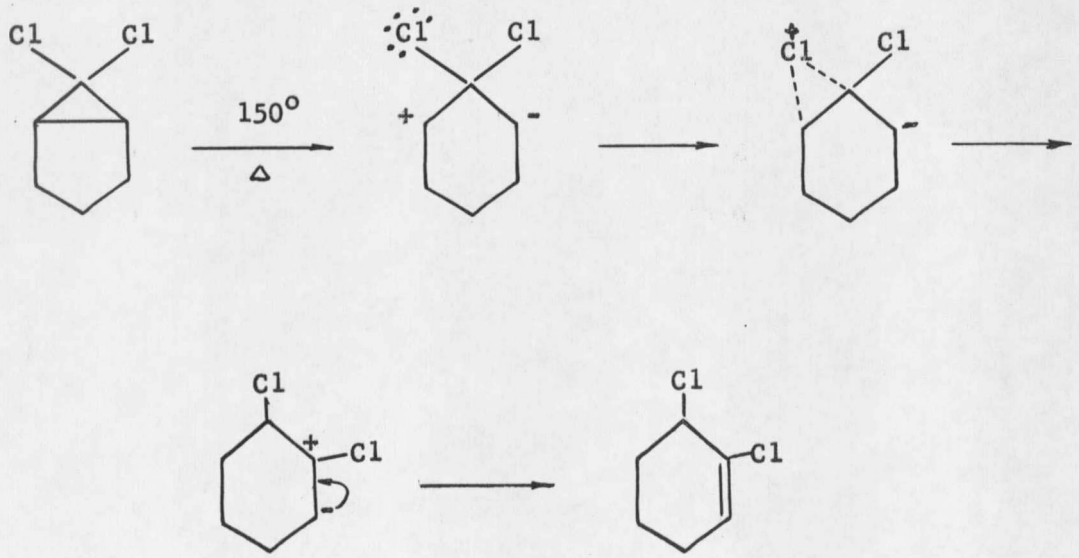
Presumably, the bond between carbon atoms 1 and 5 is the weakest bond and it will break during a rearrangement reaction. The weakness of this bond is due to the ring strain in the 5-3 ring system. During the rearrangement of the 6,6-dichlorobicyclo(3.1.0)hexane, the removal of one of the chlorine atoms is assisted by the mesomeric effect of the other chlorine atom attached to the same carbon atom. The mesomeric effect of the other chlorine atom will tend to stabilize the intermediate cyclopropane carbonium ion.

The bond between carbon atoms 1 and 5 breaks because of the increased ring strain on the cyclopropane ring which results from the formation of a carbonium ion center at carbon atom 6.

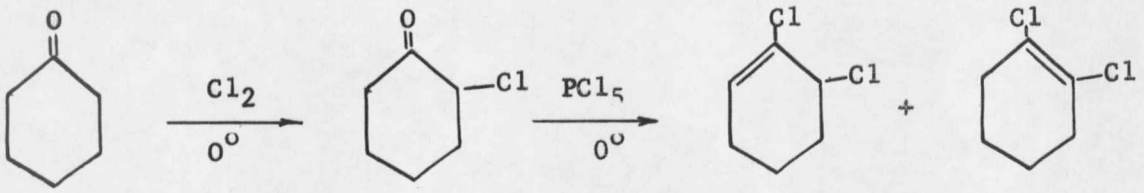
The mechanism of the rearrangement most likely in effect follows on the next page:



Because of the increased internal energy of the molecule at 150°C., it is possible that the rearrangement is initiated by the creating of the bond between carbon atoms 1 and 5. The resulting intermediate could be stabilized by the participation of the neighboring chlorine atom to form a chloronium ion. An alternative concerted mechanism may be postulated for this reaction:



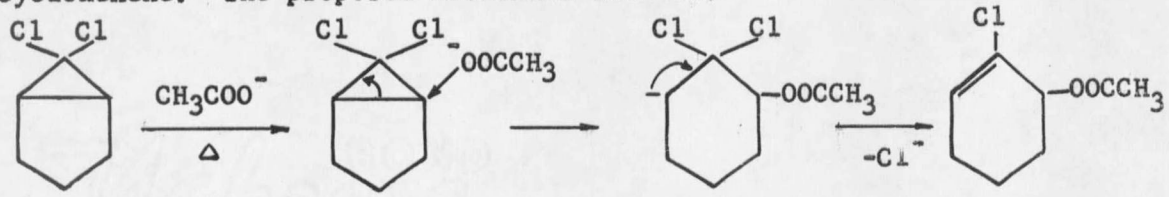
1,6-dichloro-1-cyclohexene has been synthesized by Mousseron (25). This compound and 1,3-dichloro-1-cyclohexene both on oxidation with potassium permanganate would give glutaric acid. Therefore, the authentic compound was synthesized by passing chlorine gas through cyclohexanone (24) followed by the reaction of phosphorous pentachloride as follows:



The authentic compound was separated from 1,2-dichloro-1-cyclohexene by distillation. The authentic compound was further purified by vapor phase chromatography analysis and was identified by infrared analysis. 1,2-Dichloro-1-cyclohexene (40) was found to be melted at 26-7°C.

When 6,6-dichlorobicyclo(3.1.0)hexane and 1,6-dichloro-1-cyclohexene were reacted individually with anhydrous potassium acetate in acetic anhydride and refluxed at 92-5°C., both gave 1-chloro-6-acetoxy-1-cyclohexene, whereas 6,6-dichlorobicyclo(3.1.0)hexane when heated alone at 95°C. for an hour gave no rearrangement product.

In this case, the rearrangement was probably due to the nucleophilic activity of the acetate ion. This causes a fission of the ring giving cyclohexene derivative which was characterized to be 1-chloro-6-acetoxy-1-cyclohexene. The proposed mechanism follows:



The infrared spectra of some representatives of bicyclo(3.1.0)-hexanes are shown in figures 1, 2, 3 and 4. Each of the bicyclo(3.1.0)-hexane derivatives has medium to strong absorption peaks between 9.77 - 9.96 μ (1024 and 1004 cm^{-1}). Allen and co-workers (41) have pointed out that in a random selection of organic compounds 42% contained one or more moderate or strong absorption peaks between 9.7 - 10.05 μ (1033-995 cm^{-1}). The same authors noted that absorption at 3.2 μ region which previously had been ascribed to the methylene group of the cyclopropane structure is also unreliable. The spectra of figures 1, 2, 3 and 4 show no absorption at 3.2 μ, but a shoulder appears consistently at 3.35 μ.

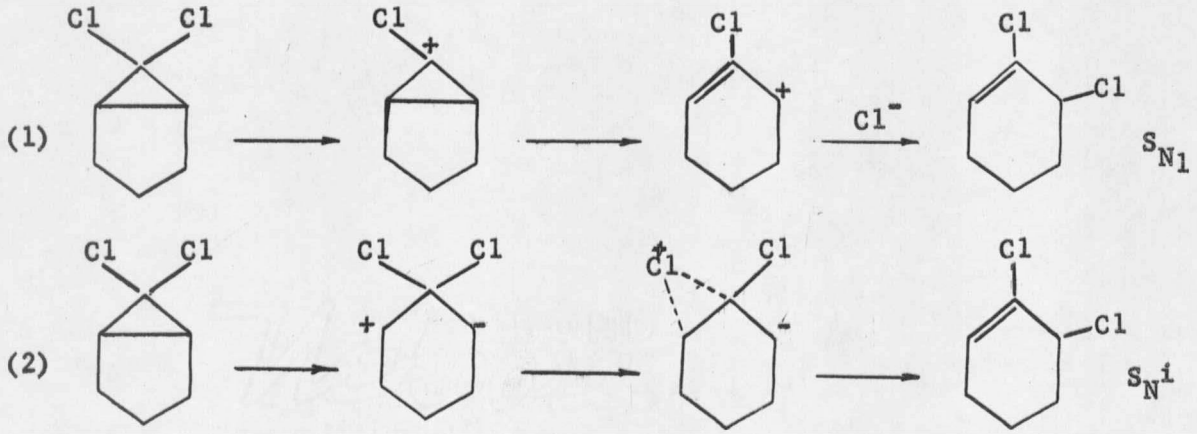
THE POSSIBILITIES OF FUTURE RESEARCH

1. A further investigation should be made of the reaction of dichlorocarbene with cyclobutene, cyclohexene, cycloheptene, cyclooctene and other like compounds:

Theoretically, it would be hard to prepare a seven-membered ring analogous to 1,6-dichloro-1-cyclohexene from 7,7-dichlorobicyclo(4.1.0)-heptane because of the stability of the six-membered ring and the steric influences existing possibly in seven-membered rings. However, it may be feasible to prepare a higher membered ring than a seven-membered one, which then might indeed be a novel ring expansion method.

2. It may be possible by the use of labelled chlorine (Cl^{38}) to determine the mechanism of the rearrangement of 6,6-dichlorobicyclo(3.1.0)-hexane by heating. The procedure of Roberts and Mazur (42) could be modified by using NaI^{131} in acetone or HCl^{38} in benzene in order to carry out the above reaction for labelling purposes.

3. The kinetic studies of the following mechanisms might be investigated to advantage if intermediate compounds can be isolated.



The rate of rearrangement of scheme (1) could be expected to be more rapid than the rate of rearrangement of scheme (2). This can be determined only if intermediate compounds can be isolated.

4. From the evidence presented on pages 30 and 31, the bicyclo-(3.1.0)hexane-6-carboxylic acid could be expected to be attacked by nucleophilic reagents such as potassium permanganate. Therefore, it may be feasible to prepare bicyclo(3.1.0)hexane-6-hydroxy-6-carboxylic acid with potassium permanganate. The α-hydroxy acid could be expected to undergo oxidation with concentrated sulfuric acid resulting in the formation of bicyclo(3.1.0)hexan-6-one. This would be in keeping with Meinwald and Gassman (43).

SUMMARY

1. Bicyclo(3.1.0)hexane-6-carboxylic acid has been synthesized from cyclopentene with ethyl diazoacetate in the presence of copper powder and followed by the alkaline hydrolysis. Its amide derivative was also obtained. These are new compounds.

2. The reaction of this acid by the Hell-Volhard-Zelinsky method has been discussed. Evidence indicates this method can not be applied to this compound.

3. 6,6-Dichlorobicyclo(3.1.0)hexane has been synthesized from cyclopentene with dichlorocarbene in n-pentane. This confirms previous synthesis with dichlorocarbene.

4. Rearrangement occurred when 6,6-dichlorobicyclo(3.1.0)hexane is heated at 150°C. or refluxed with acetate ion at 92-5°C. These are new findings. The mechanisms are proposed.

5. Both 6,6-dichlorobicyclo(3.1.0)hexane and 1,6-dichloro-1-cyclohexene have been shown to give same 1-chloro-6-acetoxy-1-cyclohexene, the former a new finding.

6. 1,6-Dichloro-1-cyclohexene is further proved by preparing an authentic compound which checked completely by infrared and vapor phase chromatography analyses and also checked by the degradation of 1-chloro-6-keto-1-cyclohexene to glutaric acid.

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