SYNTHESSES IN THE BICYCLO[3.3.0]OCTANE SERIES

BY

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Submitted in Partial Fulfillment of the
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1951

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37-38
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SYNTHESSES IN THE BICYCLO[3.3.0]OCTANE SERIES

by

William Franklin Gorham

Submitted for the degree of Doctor of Philosophy to the
Department of Chemistry on August 22, 1951.

Abstract

1. The Linstead synthesis of cis- and trans-bicyclo[3.3.0]octane has been repeated. Numerous modifications have been introduced into the synthesis in order to increase the yields of several crucial steps.

2. The Tiffeneau-Demanjow ring expansion reaction has been applied to bicyclo[3.2.0]2-hepten-6-one and has been shown to yield a mixture of 85% bicyclo[3.3.0]2-octen-6-one and 15% bicyclo[3.3.0]2-octen-7-one.

3. The mixture of bicyclo[3.3.0]2-octen-6-one and bicyclo[3.3.0]2-octen-7-one has been converted to a mixture of bicyclo[3.3.0]octadienes. Attempts at catalytic dehydrogenation of this mixture of bicyclo[3.3.0]octadienes to pentatene have been unsuccessful.

4. Attempts at the conversion of the mixture of bicyclo[3.3.0]octadienes to pentatene by chemical methods have been carried out. Most of the results obtained indicate that the introduction of more than two double bonds into the bicyclo[3.3.0]octane ring system renders the resulting olefin too unstable to be isolated.

5. The reaction of the p-toluenesulfonates of bicyclo[3.3.0]2-octen-6-01 and bicyclo[3.3.0]2-octen-7-01 with organic tertiary amines has been shown to yield a mixture of bicyclo[3.3.0]octadienes and an acyclic "octatetraene."
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PART I

THE PREPARATION OF CIS- AND TRANS-BICYCLO[3.3.0]OCTANE
INTRODUCTION

The bicyclo[3.3.0]octane ring system is of interest to chemists for numerous reasons. Among the foremost of these are the relative stabilities of the cis- and trans-isomers in the series.

In any case where two ring systems are fused in the 1,2-position, cis-trans isomerism is theoretically possible. The most thorough study of cis-trans isomerism in the bicyclo[3.3.0]octane series was carried out by Linstead, Meade, Cook, and Barrett. These workers were the first to synthesize by unequivocal methods cis-bicyclo[3.3.0]octane, I, and trans-bicyclo[3.3.0]octane, II.

![Models of cis- and trans-bicyclo[3.3.0]octane](image)

Models show the cis-isomer to consist of two, essentially planar, strainless, cyclopentane rings, while in the trans-isomer both rings must be multiplanar and considerable distortion must exist from the regular tetrahedral valency angles between the adjacent carbon atoms of the ring. On the basis of the Sachse-Mohr theory of ring strain the
trans-isomer would be predicted to be the more unstable and energy rich. This has been confirmed by comparison of the heats of combustion \(^{1d}\) of the two isomers, I and II, and by comparison of the relative ease of formation of the two isomeric ring systems under identical reaction conditions. \(^{1b}\)
DISCUSSION

In order to have suitable reference compounds for the present study of the bicyclo[3.3.0]octane series the Linstead synthesis of I and II has been repeated. Numerous modifications have been introduced in order to improve the yields of certain critical steps. The modified synthesis is outlined in Fig. I.

The starting point in the synthesis is α-carbethoxy-cyclopentanone, III. Alkylation of III with ethyl bromoacetate yields α-carbethoxy-α-carbethoxymethylcyclopentanone, IV. Hydrolysis and decarboxylation of IV is effected with 20% hydrochloric acid, and yields 2-ketocyclopentanecetic acid, V. Direct esterification of V with ethanolic hydrogen chloride produces ethyl 2-ketocyclopentanacetate, VI. To this point in the synthesis the procedures described by Linstead and co-workers were followed and found to proceed as reported. As some minor modifications were introduced, the procedures used in this work are given in the experimental section.

The next step in the synthesis involves the condensation of VI with ethyl cyanoacetate. It is apparent that the English workers failed to recognize the equilibrium nature of the reaction. Using piperdine as solvent and a reaction time of fifteen days, the best yields reported
were 40% of the condensation product, VII. Five years later, Cope, Hofmann, Wyckoff, and Hardenbergh,\textsuperscript{2} in a thorough study of this type of condensation reaction, found that the yields could be considerably increased and the reaction time considerably shortened by distilling out the water as formed, thus forcing the equilibrium to the right. Using the best conditions reported by Cope and co-workers\textsuperscript{2} for unreactive ketones and aldehydes, the yield of VII has been increased to 68% and the reaction time shortened to fifteen hours.

The next step involves the reduction of the condensation product, VII, to the saturated, dihydro derivative, VIII. The English workers\textsuperscript{1d} were unable to carry out the reduction catalytically. Attempts at catalytic reduction of the double bond in the presence of Adam's platinum catalyst, Raney nickel, or palladium-on-barium sulfate, proved unsuccessful. The reaction was carried out by chemical reduction with aluminum amalgam followed by catalytic hydrogenation. It has been found in the present work that the reduction can be very smoothly carried out in the presence of freshly prepared palladium-on-carbon catalyst.

Hydrolysis and decarboxylation of VIII with boiling, concentrated hydrochloric acid leads to the formation of a mixture of cis- and trans-cyclopentane-1,2-diacetic acids, IX-A and IX-B respectively. The ratio of the two isomers obtained is dependent on the ratio obtained in the reduction
of the condensation product. The English workers reported the cis/trans ratio to be roughly 3:1 using chemical reduction. It was this unfavorable product ratio which prevented these same workers from entering the trans-bicyclo[3.3.0]-octane series for quite some period of time. It has been found that the cis/trans ratio obtained by catalytic reduction is roughly 1:1.

As mentioned above, a mixture of cis- and trans-cyclopentane-1,2-diacetic acids is obtained by hydrolysis and decarboxylation of VIII. The English workers found it inconvenient to separate the isomers by fractional crystallization of the acids or of salts of the acids. However, in an elegant piece of work, the same authors found that the cis-isomer, IX-A, could be "fractionally ketonized" with barium oxide at 280-300°, and that the trans-isomer, IX-B, could be recovered from the reaction residue. They were able to obtain absolute proof of the assigned configurations by resolution of IX-B by means of the neutral brucine salt. By fractional crystallization of the initial mixture of cis- and trans-acids they were also able to isolate the pure cis-isomeride, IX-A, which proved incapable of resolution, as required by theory. In the present work the separation by fractional ketonization has been substantiated.

From the fractional ketonization indicated above cis-β-bicyclo[3.3.0]octanone, X, is obtained.
trans-Cyclopentane-1,2-diacetic acid is ketonized with barium oxide at 340-350° to yield \(\text{trans-}\beta\text{-bicyclo}[3.3.0]\)octanone, XI. The English workers\(^1\) proved the structure of XI by oxidation to \(\text{trans-cyclopentane-1-carboxy-2-}
\)acetic acid.

It is of interest that only three saturated ketones in the bicyclo[3.3.0]octane series are apparently capable of existence as stable compounds. These are X, XI, and cis-\(\alpha\)-bicyclo[3.3.0]octanone. Linstead and Cook\(^1b\) found that both cis- and trans-cyclopentane-1-carboxy-2-propionic acids ketonized in the presence of barium oxide to yield cis-\(\alpha\)-bicyclo[3.3.0]octanone. As the trans-isomer required more drastic conditions it is believed that trans-\(\alpha\)-bicyclo[3.3.0]octanone is first formed, but due to the presence of the labile tertiary hydrogen is immediately converted to the more stable cis-isomer. A sample of cis-\(\alpha\)-bicyclo[3.3.0]octanone has been obtained.\(^5\) Fig. II shows the infrared curves of the three ketones, X, XI, and cis-\(\alpha\)-bicyclo[3.3.0]octanone.

To effect the conversion of X and XI to the respective cis- and trans-\(\beta\text{-bicyclo}[3.3.0]\)octanes, Linstead and Barrett\(^1\) employed the Kishner reduction of the semicarbazone of the ketone in the presence of sodium ethoxide. It has been found that the same reduction may be carried out more conveniently by a modified Wolff-Kishner reduction.\(^4\)
In assigning the *cis-* and *trans-*configurations to I and II it is assumed that, during the reduction of the keto group of X and XI, no other change has occurred in the structure of the molecule (i.e. no change in the configuration of the two fused rings, and no more fundamental rearrangement of the carbon skeleton). The infrared curves of I and II are given in Fig. III together with the infrared curve of an authentic sample of *cis*-bicyclo[3.3.0]octane. Both I and II are saturated to the usual reagents and the infrared curves are different from that of the most probable rearrangement product, bicyclo[4.2.0]octane.
Figure I

SCHEMATIC REPRESENTATION OF THE SYNTHESSES
OF CIS- AND TRANS-BICYCLO[3.3.0]OCTANE
Schematic Representation of the Syntheses of cis- and trans-Bicyclo(3.3.0)octane.

Etooc(CH₂)₄COOEt → Na → 75% → COOEt → Na → Br→CH₂COOEt → IV

1. HCl, H₂O → 2. HCl, C₂H₅OH → 82.6% overall → VI

CH₃COOEt → CN → CH₃COOH → CH₅C=O NH₄⁺ → VII

CH₃COOH → CN → CH₃COOEt

H₂N-NH₃⁺H₂O → KOH → 50% → H₂N-NH₃⁺H₂O → 68% → XI

CH₃COOEt → Na → Br→CH₂COOEt → 62% → XI-A → XI-B

1. H₂, Pd on C → 2. HCl, H₂O → 58.3% overall

Fig. 1
EXPERIMENTAL

α-Carbethoxycyclopentanone (III).—The synthesis was carried out according to the method of Organic Syntheses. In a typical run, 420 g. of diethyl adipate, b.p. 118-120° (5mm.), n$_D^25$ 1.4252, was converted to 244 g (75.3%) of III, b.p. 77-79° (2.7 mm.), n$_D^25$ 1.4505.

α-Carbethoxy-α-carbethoxymethylcyclopentanone (IV).—In a 5-l. three-necked flask equipped with stirrer, dropping funnel, reflux condenser, and protected from atmospheric moisture was placed 19.5 g. (0.85 g. atom) of sodium in 2 l. of anhydrous toluene. The solution was heated to reflux and stirred vigorously until all the sodium was converted to sodium sand. To this suspension was added dropwise 123.5 g. (0.79 mole) of III over forty minutes. The mixture was then heated to reflux and stirred for two hours and then 132 g. (0.79 mole) of ethyl bromoacetate was added dropwise over one hour. The solution was heated under reflux for an additional five hours. The reflux condenser was replaced by a still head and 1 l. of toluene distilled from the solution. After cooling, 300 ml. of ether was added and the organic layer washed successively with 1 l. of 8% sulfuric acid, two 400-ml. portions of water, 400 ml. of 5% sodium bicarbonate, and 300 ml. of water. The organic
layer was dried over magnesium sulfate and concentrated under reduced pressure. Distillation yielded 149 g. (78%) of IV, b.p. 114-117° (0.7 mm.), n\textsuperscript{25} D 1.4525.

Anal. Calcd. for C\textsubscript{9}H\textsubscript{18}O\textsubscript{5}: C, 59.45; H, 7.44. Found: C, 59.51; H, 7.66.

Ethyl 2-Ketocyclopentaneacetate (VI).---In a 500-ml. round-bottomed flask was placed 149 g. (0.615 mole) of IV and 300 ml. of 20% hydrochloric acid. The reactants were heated under reflux for twenty hours. The solution was concentrated under reduced pressure to 90 g. (the theoretical yield of 2-ketocyclopentaneacetic acid was 87.5 g.) and the crude acid directly esterified by addition of 450 ml. of absolute ethyl alcohol containing 125 g. of anhydrous hydrogen chloride. The reactants were thoroughly mixed and allowed to stand at room temperature for twenty hours. The solution was concentrated under reduced pressure. Distillation yielded 86.5 g. (82.5% overall) of VI, b.p. 120-125° (11.5 mm.), n\textsuperscript{25} D 1.4503.

Anal. Calcd. for C\textsubscript{9}H\textsubscript{14}O\textsubscript{3}: C, 63.55; H, 8.23. Found: C, 63.50; H, 8.30.

Ethyl 2-Carbethoxymethylcyclopentylidine Cyanonacetate (VII).---In a 100-ml. round-bottomed flask was placed 17.3 g. (0.102 mole) of VI, 4.8 g. (0.08 mole) of acetic acid, 1.93 g. (0.025 mole) of ammonium acetate, 11.3 g. (0.10 mole) of ethyl cyanoacetate, and 30 ml. of benzene. The flask was
fitted with a water separator, which in turn was equipped with a reflux condenser. The flask was heated with a bath at 130-140° for fourteen hours. Water was removed at appropriate intervals. After cooling, 50 ml. of benzene and 30 ml. of ether were added and the mixture extracted with three 40-ml. portions of water. The combined washings were extracted with a small portion of benzene, the benzene layers combined, and dried over magnesium sulfate. The solution was concentrated under reduced pressure. Distillation through a 10 cm. Vigreux still head yielded 18 g. (68%) of VII, b.p. 172-174° (2.8 mm.), n_D^25 1.4831.

Analysis. Calcd. for C_{14}H_{19}O_{4}N: C, 63.40; H, 7.71; N, 5.28. Found: C, 63.39; H, 7.35; N, 5.39.

Preparation of a Mixture of cis- and trans-Cyclopentane-1,2-diacetic Acids (IX-A, and IX-B).---In a 1-l. reduction flask was placed 104 g. (0.39 mole) of VII, 300 ml. of 95% ethanol, and 2.5 g. of freshly prepared palladium-on-charcoal catalyst \(^8\) (7.5% palladium). The reduction was carried out under a pressure of 1-2 atmospheres. Over five hours the theoretical amount of hydrogen (0.39 mole) was taken up. The catalyst was removed by filtration and the ethanol by distillation under reduced pressure until the residue amounted to 110 g. The crude product was transferred to a 1-l. round-bottomed flask, 450 ml. of concentrated hydrochloric acid added, and the mixture heated under reflux
for fifteen hours. The boiling solution was filtered by 
gravity to remove a small amount of polymer and steam dis-
tilled until 1 l. of distillate was obtained. During the 
steam distillation the volume in the reaction flask was 
kept at approximately 500 ml. On cooling, a mixture of 
cyclopentane-1,2-diacetic acids crystallized from solution. 
A total of 58 g. of crude product was obtained. The crude 
product was dissolved in 500 ml. of boiling water and the 
solution treated with 2 g. of decolorizing carbon. The 
carbon was removed by filtration and the solution allowed 
to cool slowly to room temperature. On crystallization, 
35.5 g. of IX, m.p. 149.5°, was obtained. Concentration of 
the solution to 100 ml. and further crystallization yielded 
an additional 3 g. of IX, m.p. 138°. The total yield was 
38.5 g. (53.3% overall, 73% in each step). Using the melt-
ing point curve of Linstead and Barrett the composition 
of the first crop was 45% trans and 55% cis, and the com-
position of the second crop was 70% trans and 30% cis.

Anal. Calcd. for C₉H₁₄O₄: C, 58.05; H, 7.59. Found: 
C, 58.10; H, 7.59.

The above procedure combines the reduction of VII to 
VIII with the hydrolysis and decarboxylation of VIII to IX 
and was found to be the best procedure for the synthesis of 
large amounts of IX. In some instances VIII was isolated. 
In a typical synthesis, 24.2 g. of VII was converted to 
17.4 g. (71%) of VIII, b.p. 150-153° (1.5 mm.), nD²⁵ 1.4599.
From the steam distillate, obtained in the above procedure after the hydrolysis of VIII, it was possible to obtain small quantities of a semicarbazone, m.p. 193-194° (dec.). The semicarbazone proved to be identical with the semicarbazone of cis-β-bicyclo[3.3.0]octanone. This confirms the observation of Linstead and Meade\textsuperscript{1a} that cis-β-bicyclo[3.3.0]octanone is formed during the hydrolysis of VIII.

**cis-β-Bicyclo[3.3.0]octanone (X), and Isolation of**

**trans-Cyclopentane-1,2-diacetic Acid (IX-B).**---In a 100-ml. round-bottomed flask was placed 34 g. (0.183 mole) of IX-A and IX-B, m.p. 149.5°, and 2 g. of barium oxide. The flask was fitted with a 10 cm. Vigreux column and the flask heated with a Wood's metal bath from 280-300° over one hour, during which time organic material distilled freely, and from 300-305° for two hours to insure complete cyclization of the cis-isomer. The distillate was taken up in 50 ml. of ether and the ether layer washed with 25 ml. of 5% sodium bicarbonate solution and 25 ml. of water. The ether layer was dried over magnesium sulfate and the ether removed under reduced pressure. Distillation through a micro column$^9$ yielded 7.65 g. (61% based on percentage composition of starting material) of X, b.p. 88° (17 mm.), $n_25^D$ 1.4772.

The infrared spectrum is given in Fig. II.

The semicarbazone was prepared by the method of Fuson and Shriner. The product after crystallization from ethanol-water had m.p. 194-195° (dec.), (lit., m.p. 197-198° (dec.).


The 2,4-dinitrophenylhydrazone was prepared by the method of Fuson and Shriner. The product after recrystallization from ethanol had m.p. 115-116°.

Anal. Calcd. for $C_{14}H_{18}O_4N_4$: C, 55.30; H, 5.26; N, 18.42. Found: C, 55.61; H, 5.29; N, 18.39.

Isolation of $\text{trans}$-Cyclopentane-1,2-diacetic Acid (IX-B).---The tarry reaction residue from the cyclization was extracted with one 50-ml. portion and one 25-ml. portion of boiling 5% hydrochloric acid. It was necessary to treat the combined solutions three times with decolorizing carbon to remove all polymeric and tarry material. After cooling, the crude product was separated by filtration and purified by sublimation. The mother liquor was then concentrated to 25 ml. and the second crop of IX-B purified in a similar manner. A total of 10 g. (65% based on the percentage composition of the starting material) of pure IX-B, m.p. 133° (lit., m.p. 133°). was obtained.
trans-β-Bicyclo[3.3.0]octanone (XI).---In a 50-ml. round-bottomed flask equipped with a still head was placed 10 g. (0.054 mole) of IX-B, and 1.5 g. of barium oxide. The flask was heated with a Wood's metal bath. At 340° a vigorous reaction took place and organic material distilled freely while the temperature was raised slowly to 360° over two and one-half hours. The organic distillate was taken up in 30 ml. of ether and the ether layer washed with 25 ml. of 5% sodium bicarbonate solution and 25 ml. of water. The ether layer was dried over magnesium sulfate and the ether removed under reduced pressure. Distillation through a micro column9 yielded 3.23 g. (48%) of XI, b.p. 87-88° (22 mm.), nD 1.4755.

The infrared curve is given in Fig. II.


The semicarbazone was prepared by the method of Fuson and Shriner.10 The product after crystallization from ethanol-water had m.p. 243-244° (dec.), (lit., 1d m.p. 248-249° (dec.)).

The 2,4-dinitrophenylhydrazone was prepared by the method of Fuson and Shriner. The product after crystallization from ethanol had m.p. 156.5-157.5°.

Anal. Calcd. for C\textsubscript{14}H\textsubscript{16}O\textsubscript{4}N\textsubscript{4}: C, 55.30; H, 5.26; N, 18.42. Found: C, 55.22; H, 5.32; N, 18.66.

The residue from the cyclization was extracted with two 25-ml. portions of 5% hydrochloric acid. The combined portions were treated with decolorizing carbon and concentrated to 10 ml. After cooling the crude product was separated by filtration and on sublimation 1.1 g. of IX-B was recovered, m.p. 133°.

**cis-Bicyclo[3.3.0]octane (I).**—In a 50-ml. flask, fitted with a 10 cm. Vigreux column, was placed 1.8 g. (0.0145 mole) of X, 1.8 g. of hydrazine hydrate, and 12 ml. of butyl carbitol. To this was added a solution of 2.5 g. of potassium hydroxide in 12 ml. of butyl carbitol. The reactants were heated with a bath from 100-200° over ninety minutes. The distillate was taken up in 25 ml. of ether, and the ether layer washed with two 25-ml. portions of 5% hydrochloric acid and two 15-ml. portions of water. The ether layer was dried over magnesium sulfate and the ether removed by distillation at atmospheric pressure. Distillation through a micro column\textsuperscript{9} yielded 1.2 g. (75%) of I, b.p. 135-136°, n\textsubscript{D}^25 1.4580. **cis-Bicyclo[3.3.0]octane** prepared in
this way contained small amounts of ether. The ether was
removed by the silica-gel method of Cope and Hochstein. After five passages over silica gel, the refractive index
was constant at $n_25^D \ 1.4598$ (lit., $n_25^D \ 1.4595$).

The infrared curve is given in Fig. III.

Anal. Calcd. for $C_8H_{14}$: C, 87.30; H, 12.70. Found:
C, 87.04; H, 12.64.

Trans-Bicyclo[3.3.0]octane (II).---The synthesis was
carried out in an analogous manner to that described above
for cis-bicyclo[3.3.0]octane. In this way, 2 g. (0.016 mole)
of XI was converted to 1.14 g. (65%) of II, b.p. 136-136.5°,
$n_25^D \ 1.4568$. Product prepared in this manner was contaminated
with small amounts of ether which was removed by the silica-
gel method indicated above. After five passes over silica-gel
the refractive index remained constant at $n_25^D \ 1.4592$.

The infrared curve is given in Fig. III.

Anal. Calcd. for $C_8H_{14}$: C, 87.30; H, 12.70. Found:
C, 87.31; H, 12.73.
Infrared prism, solutions of 50 mg. of compounds in 0.50 ml. of carbon disulfide except in the regions 4.2-5.0\(\mu\) and 6.2-7.4\(\mu\) where carbon tetrachloride was used as solvent.

Curve 1. \textit{cis-}\(\alpha\)-Bicyclo[3.3.0]octanone.
Curve 2. \textit{cis-}\(\beta\)-Bicyclo[3.3.0]octanone.
Figure III

Infrared spectra: Baird spectrograph with NaCl prism. Pure samples of compounds in 0.025 mm. cell.

Curve 1. cis-Bicyclo[3.3.0]octane. Authentic sample prepared by Cope and Schmitz.\textsuperscript{4}

Curve 2. cis-Bicyclo[3.3.0]octane. Sample prepared by Wolff-Kishner reduction of X.

Curve 3. trans-Bicyclo[3.3.0]octane. Sample prepared by Wolff-Kishner reduction of XI.
PART II

THE RING EXPANSION OF BICYCLO[3.2.0]-2-HEPTEN-6-ONE
TO A MIXTURE OF BICYCLO[3.3.0]-2-OCTEN-6-ONE AND
BICYCLO[3.3.0]-2-OCTEN-7-ONE
THEORETICAL

Much of the present interest in the chemistry of the bicyclo[3.3.0]octane ring system has its origin in theoretical discussions concerning the stability or instability, and the possible existence or nonexistence of of pentalene (bicyclo[3.3.0]octatetraene), XXV, for which two equivalent resonance structures similar to the Kekule forms of benzene may be written.

XXV

Possibly the first authors to recognize the interest in this compound were Armit and Robinson\textsuperscript{11} who mentioned that the compound might be aromatic in character. In 1934 Ruzicka, de Almeida, and Brack\textsuperscript{12} suggested that a compound prepared by them, bicyclo[3.3.0]octan-2,6-dione, would be a good starting material for an attempted synthesis of pentalene. However they made no prediction as to what they believed its properties might be.

In 1936 Barrett and Linstead\textsuperscript{16} reported the first attempted synthesis of pentalene, by catalytic dehydrogenation of cis-bicyclo[3.3.0]octane.

For the past fifteen years much of the literature
on pentalene has been mathematical in nature. In 1940, Coulson and Rushbrooke\textsuperscript{13} examined pentalene by the molecular orbital method. Coulson and Rushbrooke, on the basis of their calculations feel that the mobile electrons (\(\pi\)-electrons) in pentalene might tend to accumulate on carbon atoms 1, 3, 5, and 7 at the expense of carbon nuclei 2, 4, 6, and 8. In cases such as this, Coulson and Rushbrooke report that, "Any predictions we might make from this (the molecular orbital) theory would have less theoretical basis than for molecules such as benzene and naphthalene."

Craig and Maccoll\textsuperscript{14,15} have recently made a thorough quantum-mechanical study of pentalene by both the valence-bond method and the molecular-orbital method. On the basis of their calculations they feel that considerable resonance energy should be associated with the molecule. However, these same authors found that calculation of the bond orders of pentalene by the method of Penney\textsuperscript{16} showed the bond joining the 1 and 5 carbon atoms, the central bond, should have a small negative order. This would indicate some repulsion between the \(\pi\)-electrons across the bond.

The more general molecular orbital theory of cyclic systems as developed by Hückel,\textsuperscript{17} however, ascribes special stability to those fully unsaturated, cyclic, planar, polyolefins which contain \((2 + 4n)\ \pi\)-electrons \((n = 0, 1, 2, \ldots)\). A \(\pi\)-electron by definition is an electron in a "\(\pi\)" orbital
which is used solely in the formation of multiple bonds through interaction with other $\pi$-electrons. Indeed it must be admitted that this rule holds in most cases as cyclobutadiene ($n = 1/2$), pentalene ($n = 1 1/2$), and heptalene ($n = 2 1/2$) have not been synthesized, while ethylene ($n = 0$), benzene ($n = 1$), naphthalene ($n = 2$), and anthracene ($n = 3$) are all well known compounds, and, with the exception of ethylene, can all be considered to be resonance-stabilized.

Huckel's rule appears equally applicable to cyclic resonating ions of either the carbanion or carbonium ion type. For example, cyclopentadiene very readily forms a carbanion, which possesses six $\pi$-electrons, by reaction with Grignard reagents but all attempts to form the corresponding carbonium ion, which possesses four $\pi$-electrons, have been unsuccessful. As a further example of the application of this rule to ionic species Boekelheide and Larrabee have recently reported the synthesis of perinaphthene. They found that all attempts to form the perinaphthenyl carbonium ion led to extensive decomposition of the reactants. The perinaphthenyl carbonium ion is seen to be an extremely symmetrical species. One may draw seven completely equivalent

![Perinaphthene](attachment:image.png)
resonance forms for the perinaphthenyl carbonium ion, which, it would seem should result in considerable stabilization. However the ion has twelve $\pi$-electrons which does not satisfy the $(2 + 4n)$ rule for cyclic resonating systems.

Doering and Detert, $^{18}$ and Dauben and Ringold $^{19}$ have recently explained the properties of cycloheptatraylum oxide, indicated below, by the fact that the molecular orbital theory predicts special stability for six electrons in a cyclic resonating system.

Baker, $^{20}$ in the Tilden Lecture in 1945, summarized the chemical evidence available at that time and came to the conclusion that pentalene would not be an aromatic type. His reasons were that pentalene was a fulvene derivative, the molecule would contain a moderate cyclic strain, and that each ring in pentalene does not contain the "aromatic sextet" of electrons present in all known aromatic types. There seems to be, however, a logical answer for each of these objections. With regard to the strain involved, both cyclopropene $^{21}$ and cyclobutene $^{22}$ have been synthesized and certainly considerably more strain occurs in these compounds than in pentalene. The objection that pentalene does not possess an
"aromatic sextet" of electrons in each ring can be answered by the calculations of Craig and MacColl,\textsuperscript{14, 15} which indicate that pentalene is considerably resonance stabilized. Finally, Patrick\textsuperscript{23} has noted that pentalene should no more be considered a fulvene derivative than benzene should be considered a cyclohexatriene derivative.

Recently M. J. S. Dewar\textsuperscript{24} has stated that he believes pentalene is probably not capable of stable existence and that Craig and MacColl's\textsuperscript{14, 15} calculations are not likely to be valid.

Brown,\textsuperscript{61, 62} has recently reported theoretical studies of some non-benzenoid hydrocarbons. Brown's calculations lead him to believe that pentalene should be a reasonably stable hydrocarbon, that it would be colored, and that the resonance energy would be 37 kcal. Brown, on the basis of his calculations, even predicted the point of attack by electrophilic, nucleophilic, and free radical species. Brown, in a summation of his work, reported that "It is likely pentalene is sufficiently stable to be isolated when a suitable synthesis has been devised."

From the above discussion it is obvious that considerable disagreement exists concerning the possible existence and properties of pentalene. It is also obvious that a decision can only be reached by attempted synthesis by all logical synthetic approaches. The object of this thesis has been to investigate one of these approaches.
GENERAL BICYCLO[3.3.0]OCTANE SYNTHESSES

It is of interest that the first compounds prepared containing the bicyclo[3.3.0]octane ring system are perhaps the most complicated compounds yet prepared containing this ring structure. Reimer,\textsuperscript{26} in 1881, reported that 2,3-diphenylsuccinic acid was converted to "dibenzyldicarbonid" on treatment with sulfuric acid. Roser\textsuperscript{27} investigated the reaction further and reported that the reaction product was 3,4,7,8-dibenzbicyclo[3.3.0]-3,7-octadien-2,6-dione. Brand\textsuperscript{28} found that reaction of this latter compound with two moles of phenyl magnesium bromide, followed by dehydration led to the formation of 2,6-diphenyl-3,4,7,8-dibenzpentalene.

\[\text{COOH}\]
\[\text{CH}\]
\[\text{H}_2\text{SO}_4\]

\[\text{COOH}\]
\[\text{CH}\]

\[2 \text{C}_6\text{H}_5\text{MgBr}\]
\[\text{Dehydration}\]
Brand then continued to make a thorough study of this ring system and made numerous other derivatives of dibenzpentalene. An account of much of his work and descriptions of many compounds of this structure are found in Elsevier. Some of the more interesting compounds of this structure prepared by Brand and Mueller were dihydrodibenzpentalene, 2,6-dichlorodibenzpentalene, and 2,6-dibenzalpentalene. The structures of these compounds are as follows:

Wawzonek has repeated and confirmed much of Brand's work. Even more recently Cope and Fenton have repeated
Brand's synthesis of 2,6-dichlorodibenzpentalene. Consequently there is no doubt but what these compounds do possess a true pentalene ring system. This does not, however, detract from the interest in pentalene itself as it has not yet been decided whether resonance interaction exists in the two central rings or if the double bonds are fixed.

Furthermore, the stabilizing effect of fused benzene rings on unstable ring systems is well exhibited in Lothrop's synthesis of dibenzocyclobutadiene, diphenylene. This latter compound is the only cyclobutadiene derivative known. For some time after its synthesis the structure of this compound was in doubt as an alternative structure, 2,3-benzpentalene, was proposed and seemed to explain some of the observed reactions. Lothrop prepared this interesting compound by the reaction of 2,2'-diiododiphenyl with cuprous oxide.
The product appeared to be reasonably stable, and aromatic in character. Lothrop's proof of structure included oxidation to phthalic anhydride and reduction in low yield to a sample of impure biphenyl. Baker, however, found that under different conditions for reduction the compound took up three moles of hydrogen forming an unidentified product. Uptake of three moles of hydrogen seemed to favor the 2,3-benzpentalene structure and Coulson soon after argued that the latter structure should be considerably more stable.

However, conclusive evidence in favor of the cyclobutadiene structure originally proposed by Lothrop was soon forthcoming in an electron diffraction analysis by Waser and Schomaker and an X-ray crystallographic analysis by Waser and Lee. Finally, Baker found that reduction of the reaction product in ethanol in the presence of Raney nickel led to the formation of biphenyl in 85% yield.

The ultraviolet spectrum of dibenzocyclobutadiene was investigated by Carr, Pickett, and Voris who showed that it was similar to the spectrum of naphthalene and fluorene and cited this as evidence in favor of the dibenzocyclobutadiene structure. Ilse has recently reinterpreted the spectrum as supporting the alternative 2,3-benzpentalene structure. The reduction in 85% yield to biphenyl seems, however, to settle the question beyond reasonable doubt in favor of the dibenzocyclobutadiene
structure.

While dibenzocyclobutadiene did not turn out to be 2,3-benzpentalene the synthesis of this latter compound is of considerable interest as it would be one step closer to the solution of the pentalene problem. Recently syntheses of compounds of this general structure have been reported by Baker and Jones; Baker, Coates, and Glockling; Clemo, Groves, Munday, and Swan; Groves and Swan and Dahn.

Baker and Jones have reported the synthesis of 2,3-benz bicyclo[3.3.0]-2-octene by the following series of reactions.

All attempts to catalytically dehydrogenate 2,3-ben zbicyclo[3.3.0]-2-octene by either chemical or catalytic methods were unsuccessful. The list of dehydrogenating
conditions and reagents in their unsuccessful attempts include practically all such conditions and reagents reported in the chemical literature.

Baker, Coates, and Glockling\(^6\)\(^3\) have reported that 3-keto-2-phenylcyclopentane-1-carboxylic acid is cyclized in the presence of fluorosulfonic acid to 2,3-benzbicyclo[3.3.0]2-octen-4,8-dione. This route to benzpentalene appears quite promising and the English workers report they are continuing their study of this interesting compound.

\[
\begin{align*}
\text{HOOC} & \quad \text{FSO}_3\text{H} \\
\begin{array}{c}
\text{C} \text{H} \\
\text{C} \text{H}_2-
\end{array} & \quad \text{C} \text{H}_2
\end{align*}
\]

Clemo, Groves, Munday, and Swan\(^6\)\(^4\) have reported the synthesis of 2,3-benzbicyclo[3.3.0]1(5),2-octadien-6-one.

\[
\begin{align*}
\text{CH}_2-\text{Cl} & \quad \text{CH}_2\text{COOR} \\
\text{COOR} & \quad \text{Hydrolysis} \\
\text{COOH} & \quad \text{CH}_2\text{CH}_2
\end{align*}
\]

\[
\begin{align*}
\text{S}_4\text{Cl}_4 & \quad \text{K}
\end{align*}
\]
Work with the cyclized ketone did not prove encouraging. Attempts at dehydrogenation of the ketone were unsuccessful as were attempts to convert the ketone by chemical methods to 2,3-benzpentalene.

Groves and Swan have reported the synthesis of 2,3-benzbicyclo[3.3.0]-2-octen-7-one by a synthesis resembling the Linstead synthesis of cis-β-bicyclo[3.3.0]octanone. Groves and Swan converted the former ketone to 2,3-benzbicyclo[3.3.0]-2,6-octadiene by standard procedures. This latter olefin could not be dehydrogenated and attempts to introduce allylic bromines with N-bromosuccinimide followed by dehydrohalogenation led only to the formation of black, polymeric material.

Dahn has also reported syntheses in this series. His starting material was indanone which was converted by the Stobbe condensation and cyclization of the resulting product to 2,3-benz-8-carbethoxybicyclo[3.3.0]-1(5),2-octadien-6-one.
Dahn's plan of attack then involved reaction of the keto ester with excess methyl magnesium bromide followed by dehydration. This would lead to the formation of a fulvene derivative which would be isomeric with 2-methyl-4-isopropyl-6,7-benzpentalene. The dehydration step was unsuccessful and Dahn was only able to isolate polymeric material. While the final step was unsuccessful the approach to the problem is novel and most interesting.
All the above work on benzpentalene has been reported in 1951. From the evidence now at hand it seems safe to conclude that benzpentalene can not be prepared by dehydrogenation and that preparation by chemical methods does not appear promising.

Georgi,42 and independently Stobbe,43 were probably the first to prepare a compound having the simple bicyclo[3.3.0]octane ring system. Their synthesis involved 1,4 addition of cyclopentanone to benzalacetophenone, in the presence of piperdine, and subsequent pinacol reduction with sodium amalgam in alcohol.

In 1922 Schroeter44 suggested that the condensation of chloral with dimethyl malonate, under conditions not reported in the experimental section, led to the formation of a highly complex bicyclo[3.3.0]octane derivative. By a series of decarboxylations and reductions the product was reduced to a hydrocarbon. The properties reported by
Shroeter for this hydrocarbon are in close agreement with the accepted properties of cis-bicyclo[3.3.0]octane.

\[
\text{CCl}_3\text{CH}_3 + \text{CH}_3\text{-O-CH}_2\text{-O-CH}_3 \rightarrow ?
\]

It must be admitted that the above condensation is a rather unusual reaction. Schroeter further mentions that the product had been converted by Vossen to bicyclo[3.3.0]octan-3,7-dione. As this latter compound would be of great interest as a precursor in an attempted synthesis of pentalene, the condensation should probably be further investigated.

Another reported synthesis of bicyclo[3.3.0]octane derivatives involves the rearrangement of decalin in the presence of aluminum halides. This rearrangement has been studied by Zelinsky and Turowa-Pollack, and by Jones and Linstead. These workers feel the rearrangement leads to the formation of either 2,6-dimethylbicyclo[3.3.0]octane or 2,8-dimethyl-bicyclo[3.3.0]octane.

The structure proof of the products was interesting but not adequate. In line with this work it should be
It is difficult to believe that the steric effect of two methyl groups would prevent either of the two proposed rearrangement products of decalin, 2,6- or 2,8-dimethylbicyclo[3.3.0]octane, from undergoing the more complex rearrangement exhibited by cis-bicyclo[3.3.0]octane under identical conditions.

In 1934 Ruzicka, de Almeida, and Brack reported the synthesis of diethyl bicyclo[3.3.0]octan-2,6-dion-3,7-dicarboxylate. The synthesis involved a double Dieckmann condensation. Degradation of the diester led to the formation of bicyclo[3.3.0]octan-2,6-dione.

The Swiss workers reported that they believed bicyclo[3.3.0]octan-2,6-dione would be a good starting material for an attempted synthesis of pentalene but
apparently had not investigated the possibility further.

In 1934-36 Linstead, Cook, Meade, and Barrett reported in a series of papers the synthesis of cis- and trans-bicyclo[3.3.0]octane, cis- and trans-β-bicyclo[3.3.0]-octanone, and cis-α-bicyclo[3.3.0]octanone. Some of this work has been reported in Part I of this Thesis. The English workers also investigated many of the fundamental properties of the ring system. Their work is by far the most thorough and reliable study of this particular ring system yet reported. Most of the work being carried out in the field today relies on ultimate comparison of the compounds prepared with those of the English workers. The approach of the English workers involved barium oxide ring closures of cis- and trans-cyclopentane-1,2-diacetic acids and cis- and trans-cyclopentane-1-carboxy-2-propionic acids.

Bardhan and Banerjee; Mitter and Banerji; and Banjeree have reported the synthesis of several bicyclo[3.3.0]octane derivatives with alkyl, carbethoxy, and keto groups on various positions in the ring. All of these syntheses start with substituted cyclopentane compounds and form the bicyclo[3.3.0] octane ring by a Dieckmann condensation.

In 1943 Wawzonek reported the synthesis of 2,6-diphenylbicyclo[3.3.0]-2,6-octadiene and 2,6-diphenylbicyclo[3.3.0]-1,5-octadiene. His starting material was
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bicyclo[3.3.0]octan-2,6-dione, prepared by the method of Ruzicka, de Almeida, and Brack. 12

![Chemical structure](image)

Dehydration

As neither of the diphenylbicyclo[3.3.0]octadienes would form well-defined addition products with bromine, Wawzonek concluded that 2,6-diphenyl-pentalene does not exist as a stable aromatic compound.

Another method of entry into the bicyclo[3.3.0]octane ring system involves dicyclopentadiene as starting material. The approach was originally studied by Bruson and Reiner66 but it remained for Bennett67 to develop an acceptable synthesis of cis-bicyclo[3.3.0]octane-2,4-dicarboxylic acid by this route.
Recently Cope and Schmitz have reported that sulfuric acid hydrolysis of the eight-membered cyclic dimer of chloroprene led to the formation of bicyclo[3.3.0]1(5)-octen-2-one. This interesting reaction is believed to involve initial hydrolysis of the dimer to cyclooctan-1,4-dione, which, under the reaction conditions is converted to the bicyclic ketone.

The above survey of bicyclo[3.3.0]octane syntheses is not intended to be a complete survey of all known compounds of this ring system but it is intended to describe most of the synthetic routes into this series which have been used by other investigators. A compilation of many of the known compounds of this ring system is found in Elsevier.
DISCUSSION

In 1940 Brooks and Wilbert\textsuperscript{52} reported the synthesis of bicyclo[3.2.0]-2-hepten-6-one, XII, from the reaction of cyclopentadiene and ketene. The ketone XII was of interest in this work as it provided the starting material for a new method of entry into the bicyclo[3.3.0]octane ring system.

The reaction of ketoketenes and conjugated dienes to give substituted cyclobutanones had been investigated earlier by Staudinger and Suter,\textsuperscript{53} and Staudinger and Rheimer,\textsuperscript{54} but the work of Brooks and Wilbert represents the first reported example of the reaction of ketene and a conjugated diene to give a substituted cyclobutanone.

Brooks and Wilbert reported a partial structure proof of XII which involved catalytic reduction of the double bond to give the dihydro derivative, XIII, and permanganate oxidation of XIII to glutaric acid. The most probable alternative structure for the initial reaction product is dehydronorcamphor, XII-B. It is easily seen after the reduction of the double bond of both XII and XII-B that glutaric acid could only arise from the dihydro form of XII on oxidation.
The reaction of ketene with conjugated dienes has recently been reinvestigated by Blomquist and Kwiatek.\textsuperscript{55} In further work with XIII they found that on careful oxidation of this compound with dilute nitric acid \textit{cis}-cyclopentane-1,2-dicarboxylic acid could be isolated. This provides absolute proof of 1,2-addition of ketene to cyclopentadiene rather than possible 1,4-addition.

It is seen that XII consists of a five-membered ring, containing an isolated double bond, fused in the 1,2-position to a four-membered ring containing a carbonyl group. The four-membered ring has been expanded to a five-membered ring by the Tiffeneau-Demanjow\textsuperscript{60} reaction thereby giving rise to a bicyclo[3.3.0]octane derivative with a double bond in one ring and a carbonyl group in the other.

In this work the preparation of XII has been carried out on a much larger scale than that previously reported. Brooks and Wilbert isolated the desired reaction product, XII, by direct distillation of the reaction mixture. It was found that XII prepared in this manner is contaminated with considerable amounts of dicyclopentadiene. In order to obtain a pure product it was found convenient to convert the ketone to the semicarbazone, and regenerate the ketone by steam distillation of an aqueous solution of the semicarbazone and oxalic acid.
Further work on the structure of XII has been carried out. Dehydronorcamphor, XII-B, the most probable alternative reaction product of ketene and cyclopentadiene, had been previously prepared in the M.I.T. Laboratories and direct comparison of the physical properties of suitable derivatives of the two ketones indicated beyond doubt that the two are different compounds. The infrared spectrum of XII has been obtained and is given in Figure V. The carbonyl band occurs at 5.6 $\mu$ which is quite specific for a carbonyl group in a four-membered ring. Two further points concerning the structure of XII are the stereochemistry of the two fused rings and the position of the double bond. There seems to be little doubt that the ring fusion is cis since considerable strain would be involved if the juncture were trans. Even if the initial addition of ketene to cyclopentadiene were trans, the presence of the carbonyl group next to the bridge and a labile tertiary hydrogen on the bridge would in all probability result in isomerization to the more stable cis form.

The position of the double bond in XII is dependent on whether the carbonyl group of ketene becomes attached to carbon atom 1 or 2 of 1,3-cyclopentadiene during the addition reaction. If the carbonyl group becomes attached to carbon atom 1, XII is the product, if the point
of attachment is carbon atom 2, XII-A is the product. The question has been settled for the dimethylketene-cyclopentadiene adduct, and for the diphenylketene-cyclopentadiene adduct. In both cases the carbonyl group adds to carbon atom 1. Some evidence has been obtained which indicates that in XII the addition is in the same direction and the carbonyl group of ketene becomes attached to carbon atom 1 of 1,3-cyclopentadiene. Inspection of XII shows that it is an $\alpha$-$\gamma$ unsaturated ketone, while XII-A is a $\beta$-$\gamma$ unsaturated ketone. A control experiment has been run with a 2,4-dinitrophenylhydrazone of a $\beta$-$\gamma$ unsaturated aldehyde under the conditions of which the derivative was converted to the more stable $\alpha$-$\beta$ form. Under the same conditions the 2,4-dinitrophenylhydrazone of XII was unaffected.

On the basis of the direction of addition found with both diphenylketene and dimethylketene with cyclopentadiene, and the evidence cited above, the double bond is assigned to the $\delta$-$\gamma$ position. Blomquist and Kwiatek have reported that they are investigating this point further.
On the basis of the evidence presented above, it is felt that the structure of the reaction product of ketene and cyclopentadiene is best represented as XII, below.

\[ \text{XII} \]

The first step in the ring expansion of XII involves the formation of the cyanohydrin, XIII. It was found that the cyanohydrin could be best formed by reaction of XII with anhydrous hydrogen cyanide at 0° in the presence of a catalytic amount of piperidine. The cyanohydrin was never isolated as such but was acetylated with a mixture of acetic anhydride and acetyl chloride to give the cyanohydrin acetate, XIV. The cyanohydrin acetate XIV is believed to be a mixture of two stereoisomers (i.e. the cyano group may be either cis or trans with respect to the hydrogens at the ring junction). Reduction of XIV to the amino alcohol, XV, was carried out using lithium aluminum hydride as reducing agent. As with XIV the amino alcohol XV is believed to be a mixture of the two possible stereoisomers.

\[ \text{XII} + \text{HCN} \overset{\text{piperidine}}{\rightarrow} \text{XIII} \] \[ \text{XIII} \xrightarrow{\text{Ac}_2\text{O}, \text{AcCl}} \]
Deamination of XV with nitrous acid resulted in ring expansion and formation of bicyclo[3.3.0]2-octen-7-one, XVII, and bicyclo[3.3.0]2-octen-6-one, XVI. The ring expansion is pictured as involving, (1) diazotization of the amino group, (2) loss of nitrogen to form a carbonium ion, and (3) rearrangement and loss of a proton to form one of the two ring-expanded ketones. The rearrangement step is depicted below.

Rearrangement proceeding by path (a) involves migration of a primary alkyl group with its bonding pair of
electrons, while, rearrangement by path (b) involves migration of a secondary alkyl group with its bonding pair of electrons. It was of considerable interest to determine which alkyl group migrated. Reduction of the double bond of XVI and XVII lead to the formation of a mixture of α- and β-bicyclo[3.3.0]octanone. The infrared curve of this latter mixture indicated a composition of 85% of the α-isomer and 15% of the β-isomer and was identical to the infrared curve, within experimental error, of an authentic mixture of this composition. Thus in the case studied, the primary alkyl group displayed the greater migratory aptitude (rearrangement by path (a)).

Tchoubar, however, has shown that the nitrous acid deamination of 1-hydroxy-1-aminomethyl-2-methylcyclopentane gives chiefly 3-methylcyclohexanone.

In this latter case, then, the secondary alkyl group with its bonding pair of electrons migrated
preferentially to the primary group. Consequently it is impossible to generalize and say that either a primary or secondary alkyl group will migrate predominantly in rearrangements of this type. It is possible, however, that accurate predictions on the predominant course of rearrangements of this type could be made if the stereochemistry of the amino alcohol intermediates were known.

The structure proof of XVI and XVII was completed by Wolff-Kishner reduction of the mixture of α- and β-bicyclo[3.3.0]octanone indicated above. The product isolated from the reaction was pure cis-bicyclo[3.3.0]octane, I. The isolation of pure cis-bicyclo[3.3.0]octane from this reaction indicates that the stereochemistry of the two fused rings (cis-juncture) is retained during the ring expansion.
Figure IV

SCHEMATIC REPRESENTATION OF THE RING EXPANSION OF BICYCLO-[3.2.0]-2-HEPTEN-6-ONE AND SUBSEQUENT WORK IN THE BICYCLO-[3.3.0]OCTANE SERIES
Schematic Representation of the Ring Expansion of Bicyclo (5.2.0)-2-hepten-6-one, and Subsequent Work in the Bicyclo (5.3.0) octane Series.

Fig. 4
EXPERIMENTAL

Ketene.---Ketene was prepared by pyrolysis of reagent acetone in a ketene generator similar to that described by Williams and Hurd. The generator was calibrated by passing ketene through two sodium hydroxide solutions, of known normality, in series and back titrating the excess base with standard acid. In the preparation of XII the ketene was collected by passing the ketene through two Dry-Ice traps in series partially filled with sodium-dry toluene.

Cyclopentadiene.---Cyclopentadiene was prepared by cracking redistilled dicyclopentadiene, b.p. 84° (40 mm.). The dicyclopentadiene was placed in a round-bottomed flask, which was attached to a 60 x 1.5 cm. glass-helix packed column, and heated to the point where cyclopentadiene distilled freely. The cyclopentadiene was collected in an ice-cooled receiver. All material was used immediately after preparation and had b.p. 40-42°.

Bicyclo[3.2.0]-2-hepten-6-one Semicarbazone.---In a steel hydrogenation bomb, which had been previously cooled to -78°, was placed a mixture of 0.9 mole of ketene in 80 ml. of dry toluene and 160 g. (2.5 mole) of cyclopentadiene.
The bomb was immediately sealed and heated to 100° for one and one-half hours. A second run was made using the same quantities and the liquid products from the two runs combined. The liquid products were placed in a 1-l. round-bottomed flask and distilled through a 20 cm. Vigreux still head taking two fractions. The lower boiling fraction had b.p. < 60° (45 mm.) and consisted of acetone, toluene, and ketene dimer. The higher boiling fraction had b.p. 60° (45 mm.) to 60° (10 mm.) and consisted of small amounts of ketene dimer, XII, and dicyclopentadiene. About 280 ml. of higher boiling material was obtained. The higher boiling fraction was transferred to a 1-l. Erlenmeyer flask and 500 ml. of 95% ethanol, 80 g. (0.71 mole) of semicarbazide hydrochloride, and 120 g. of sodium acetate trihydrate added. The solution was heated to reflux on a steam bath for fifteen minutes and cooled. The solid products were collected by filtration on a Büchner funnel. The residue was heated for fifteen minutes with 400 ml. of boiling water (to remove inorganic salts). On cooling the solid product was collected on a Büchner funnel and air dried as thoroughly as possible. The residue was crystallized from 300 ml. of ethanol. The product was collected on a Büchner funnel and dried under vacuum in a desiccator. A total of 88.5 g. (0.535 mole) of semicarbazone was obtained, m.p. 221-222° (dec.) (lit., 52 m.p. 221-222° (dec.).
The yield was 11% based on cyclopentadiene.

**Anal.** Calcd. for C₈H₁₁ON₃: C, 58.20; H, 6.67; N, 25.45. Found: C, 58.00; H, 6.95; N, 25.56.

**Bicyclo[3.2.0]2-hepten-6-one (XII).**---In a 500-ml. round-bottomed flask was placed 20 g. (0.12 mole) of bicyclo[3.2.0]2-hepten-6-one semicarbazone, 15 g. (0.12 mole) of oxalic acid dihydrate, and 200 ml. of water. The solution was steam distilled until 200 ml. of distillate was obtained. The distillate was extracted with two 50-ml. portions of ether and then continuously with ether for six hours. The ether layers were combined, dried over magnesium sulfate, and the ether removed under reduced pressure. Distillation through a 10 cm. Vigreux still head yielded 11.5 g. (88%) of XII, b.p. 83-84° (51 mm.), n²⁵ D 1.4801, (lit., ⁵⁵ b.p. 62-63.5° (20 mm.), n²⁰ D 1.4819).

The infrared curve is given in Figure V.

**Anal.** Calcd. for C₇H₉O₇: C, 77.80; H, 7.42. Found: C, 77.75; H, 7.55.

The 2,4-dinitrophenylhydrazone was prepared by the ¹⁰ method of Fuson and Shriner. After crystallization from ethanol the product had m.p. 114-115°.

Hydrogen Cyanide.---Hydrogen cyanide was prepared by the method of Organic Syntheses,\textsuperscript{72} and was dried over calcium chloride before use. In a typical run 74 g. (1.5 mole) of sodium cyanide was converted to 30 ml. (21 g., 50\%) of hydrogen cyanide.

6-Acetoxy-6-cyanobicyclo[3.2.0]3-heptene (XIV).---In a 500-ml. round-bottomed flask, immersed in an ice bath, was placed 84.5 g. (0.78 mole) of XII and 32 ml. (0.83 mole) of anhydrous hydrogen cyanide. The reactants were thoroughly mixed and 0.25 ml. of piperdine added. The flask was tightly stoppered and the reactants thoroughly mixed. There was considerable heat of reaction. The flask was placed in an ice bath for twenty-four hours. The piperdine was neutralized by addition of 0.25 ml. of concentrated sulfuric acid and 0.1 g. of sulfonic acid ion exchange resin. The cyanohydrin was acetylated by addition of 50 ml. of anhydrous ether, 150 ml. of acetic anhydride and 5 ml. of acetyl chloride. The reactants were thoroughly mixed and kept at 0\textdegree{} for twenty-four hours. The flask was then allowed to stand at room temperature for seven days. The excess hydrogen cyanide and ether were removed by distillation at atmospheric pressure, the acetic acid and acetic anhydride by distillation through a 20 cm. Vigreux column under reduced pressure. Distillation of the residue yielded 95 g. (67\% overall) of
XIV, b.p. 106-110° (3 mm.), n$_D^{25}$ 1.4785.

The infrared curve is given in Fig. V.

**Anal.** Calcd. for C$_{10}$H$_{11}$O$_2$N: C, 67.80; H, 6.22; N, 7.91. Found: C, 67.80; H, 6.44; N, 7.77.

6-Aminomethyl-6-hydroxybicyclo[3.2.0]2-heptene (XV), Bicyclo[3.3.0]2-octen-6-one (XVI), and Bicyclo[3.3.0]2-octen-7-one (XVII).---In a 2-l. three-necked flask equipped with stirrer, addition funnel, reflux condenser, and protected from atmospheric moisture was placed 16 g. (0.42 mole) of lithium aluminum hydride in 400 ml. of sodium-dry ether. To the stirred solution, 42.5 g. of XIV (0.24 mole) in 75 ml. of anhydrous ether was added dropwise over forty minutes. The reaction was then heated to reflux for forty-five minutes. The reaction flask was immersed in an ice bath, 25 ml. of water cautiously added to destroy the excess reagent, and 800 ml. of 20% sodium potassium tartrate solution added. The solution was vigorously stirred for fifteen minutes and transferred to a separatory funnel. The ether layer was removed and the aqueous layer extracted with 300 ml. of ether and continuously with ether for three days. The ether layers were combined and dried over calcium oxide. The ether was removed under reduced pressure until the crude product had been concentrated to 40 g. One tenth of the crude product was then removed for purification and the remainder directly
converted to XVI and XVII as follows: The larger portion of crude amino alcohol, 36 g., was transferred to a 1-l. round-bottomed flask equipped with stirrer, reflux condenser, and addition funnel. The flask was placed in an ice bath and over ten minutes a solution of 15 g. (0.23 mole) of acetic acid in 225 ml. of water was added. The solution was stirred until homogeneous. A solution of 16 g. (0.23 mole) of sodium nitrite in 50 ml. of water was then added over five minutes, the mixture stirred at 0° for forty minutes, heated on the steam bath for forty minutes, and allowed to stand at room temperature for twenty hours. The solution was steam distilled until 450 ml. of distillate was obtained. The distillate was extracted with three 80-ml. portions of ether and continuously extracted with ether for twenty hours. The ether layers were combined, dried over magnesium sulfate, and concentrated under reduced pressure. Distillation yielded 14.5 g. (55% overall, 74% per step) of XVI and XVII, b.p. 80-82.5° (17 mm.), n°25 D 1.4902.

The 2,4-dinitrophenylhydrazone was prepared by the method of Fuson and Shriner. The product after crystallization from ethanol had m.p. 145°.

Anal. Calcd. for C\textsubscript{14}H\textsubscript{14}O\textsubscript{4}N\textsubscript{4}: C, 55.60; H, 4.65; N, 18.65. Found: C, 55.92; H, 5.05; N, 18.33.

The semicarbazone was prepared by the method of
Fuson and Shriner\textsuperscript{10}. The product after crystallization from ethanol-water had m.p. 166-167°.

\textbf{Anal.} Calcd. for C\textsubscript{9}H\textsubscript{13}ON\textsubscript{3}: C, 60.30; H, 7.25; N, 23.50. Found: C, 60.30; H, 7.51; N, 23.20.

The mixture of XVI and XVII prepared in this manner showed a weak hydroxyl band in the infrared curve. This is believed to be due to the presence of bicyclo[3.2.0]2-hepten-6-ol, which would be formed during the reduction of the cyanohydrin acetate, XIV, by preliminary reduction of the acetoxy group and reversal of the cyanohydrin synthesis prior to the reduction of the nitrile group. The ketone was easily purified by conversion to the semicarbazone, and regeneration of the ketone by steam distillation of a solution of semicarbazone in the presence of oxalic acid. Details for a procedure of this type have been given in the preparation of XII. In this way 80% of the ketone could be recovered pure. The pure ketone had b.p. 81-83° (17 mm.) \( n^\text{D} \) 1.4880. The infrared curve is given in Fig. V.

\textbf{Anal.} Calcd. for C\textsubscript{8}H\textsubscript{10}O: C, 78.70; H, 8.20. Found: C, 78.39; H, 8.30.

It is believed that the percentage of reversal of the cyanohydrin synthesis is dependent on the activity of the lithium aluminum hydride used. In preparations where a freshly opened can of lithium aluminum hydride was used the mixture of ketones, XVI and XVII, was obtained
essentially pure on the first distillation and infrared showed no hydroxyl band.

Distillation through a micro column of the portion of amino alcohol set aside for purification yielded 2.26 g. (68%) of XV, b.p. 80-83° (0.9 mm.). Nitrogen analysis indicated the product contained approximately 90% amino alcohol. The other component, as mentioned above, is believed to be bicyclo[3.2.0]2-hepten-6-ol. The amino alcohol was purified by dissolving the mixture in 70 ml. of 5% sulfuric acid and continuously extracting the solution with ether for twenty-four hours. The aqueous layer was then made basic by addition of 5 g. of sodium hydroxide and the basic solution continuously extracted with ether for twenty-four hours. The ether layer was dried over calcium oxide and the product concentrated under reduced pressure. Distillation through a micro column yielded 0.9 g. of XV, b.p. 83-84° (1.5 mm.).


The picrate of V could not be prepared in the usual manner. It was finally prepared by heating equivalent amounts of the amino alcohol and picric acid in benzene and allowing the benzene to evaporate. The picrate was re-crystallized by dissolving in benzene-ethanol and then adding hexane. The picrate crystallized in this manner had
m.p. 137-138°.

Anal. Calcd. for C₁₄H₁₈O₈N₄:  C, 45.65;  H, 4.35;  N, 15.20.  Found:  C, 45.76;  H, 4.30;  N, 15.17.

Hydrogenation of XVI and XVII to \( \alpha \)-Bicyclo[3.3.0]octanone and cis-\( \beta \)-Bicyclo[3.3.0]octanone, and Hydrogenation and Wolf-Kishner Reduction of XVI and XVII to cis-Bicyclo-

[3.3.0]octane.---A solution of 3 g. of XVI and XVII in 25 ml. of ethanol was hydrogenated at room temperature and atmospheric pressure in the presence of 0.6 g. of prereduced Adam's platinum oxide. Reduction to the point that the solution no longer decolorized permanganate required 1.3 molar equivalents of hydrogen. Previous work had indicated that reduction of the double bond competed with reduction of the carbonyl group. The catalyst was removed by filtration and the solution concentrated by distillation to 8 ml. The ketone was converted to the semicarbazone by the method of Fuson and Shriner and purified by crystallization. The ketone was regenerated by steam distillation of a solution of the semicarbazone and oxalic acid. A typical procedure for this reaction has been given in Part I for the preparation of bicyclo[3.2.0]-2-hepten-6-one. Distillation yielded 1 g. of the reduced mixture of ketones, b.p. 84-86° (18 mm.), \( n^\text{D} 1.4758 \). The infrared curve is given in Fig. V together with the infrared curve of an authentic mixture.
of 85% α-bicyclo[3.3.0]octanone and 15% β-bicyclo[3.3.0]-octanone. Catalytic hydrogenation of 1.5 g. of XVI and XVII followed by Wolff-Kishner reduction (for a typical procedure see preparation of cis-bicyclo[3.3.0]octane, Part I) of the crude mixture of ketones yielded 0.5 g. of cis-bicyclo[3.3.0]octane. After purification by the silica-gel method the refractive index was constant at $n^\text{D}_{25} 1.4590$. The infrared curve was identical, within experimental error, to that of authentic cis-bicyclo-[3.3.0]octane.

**Anal Calcd. for C$_8$H$_{14}$:** C, 87.27; H, 12.73. **Found** C, 87.28; H, 12.61.
Figure V

Infrared Spectra: Baird spectrograph with NaCl prism, solutions of 50 mg. of compounds in 0.50 ml. of carbon disulfide except in the regions 4.2-5.9 μ and 6.3-7.4 μ where carbon tetrachloride was used as solvent.

Curve 1. Bicyclo[3.2.0]-2-hepten-6-one (XII).
Curve 2. 6-Acetoxy-6-cyanobicyclo[3.2.0]-2-heptene (XIV).
Curve 3. Synthetic Mixture of Bicyclo[3.3.0]-2-octen-6-one (XVI) and Bicyclo[3.3.0]-2-octen-7-one (XVII).
Curve 4. Authentic Mixture of 85% α-Bicyclo[3.3.0]-octanone and 15% cis-β-Bicyclo[3.3.0]octanone.
Curve 5. Catalytic Reduction Product of XVI and XVII.
PART III

THE PREPARATION AND REACTIONS OF A
MIXTURE OF BICYCLO[3.3.0]OCTADIENES
HISTORICAL

The introduction of double bonds into the unsubstituted bicyclo[3.3.0]octane ring system has not been widely studied. Cope and Schmitz \(^{69}\) have reported the preparation of a mixture of bicyclo[3.3.0]octenes by Wolff-Kishner reduction of bicyclo[3.3.0]-1(5)-octen-2-one. Cope and Keller \(^{73}\) have recently converted this latter ketone to bicyclo[3.3.0]-1(5),2-octadiene by the following reactions.

\[
\text{LiAlH}_4 \quad \begin{array}{c}
\text{O} \\
\text{OH}
\end{array} \quad \text{I}_2
\]

The bicyclo[3.3.0]octadiene prepared in this manner proved to be relatively unstable and extremely acid sensitive. Cope and Keller also attempted the preparation of a bicyclo[3.3.0]octatriene but were unable to isolate any product.

The above syntheses represent practically all reported attempts at the introduction of double bonds into the
unsubstituted bicyclo[3.3.0]octane ring system. In Part II of this thesis the preparation of olefins with either benzene rings fused to the ring system or phenyl groups attached to the ring system was discussed.

It is of interest to consider the number of isomers possible for the various olefins in this series. There appear to be four bicyclo[3.3.0]octenes, A, B, C, and D, theoretically capable of existence.

Olefin A belongs to the cis-bicyclo[3.3.0]octane family, olefin B to the trans-bicyclo[3.3.0]octane family, while in olefins C and D, the double bond, attached to either one or both of the bridge carbon atoms, has destroyed the stereochemical specificity of the two fused rings.

With the introduction of the second double bond the number of isomers increases to ten, bicyclo[3.3.0]-octadienes E to N.
Olefins E and F belong to the cis-bicyclo[3.3.0]-octane family, and, on theoretical grounds, would be predicted to be capable of stable existence as the double bonds are not in conjugation. Olefins G and H belong to the trans-bicyclo[3.3.0]octane family and it is quite probable that they would be converted to the more stable cis-family in the presence of strong bases. Olefins I through N belong to neither family due to the attachment of a double bond to at least one of the bridge carbon atoms. Olefins I, K, and M are substituted cyclopentadiene derivatives, while olefins L and N are butadiene derivatives. It is quite probable that all the olefins of this latter group, I, K, L, M, and N, would show a marked tendency to polymerize. Olefin J has isolated double bonds and for this reason would be predicted to be reasonably stable.

With the introduction of the third double bond the number of isomers decreases to six, none of which belong to either the cis- or trans-bicyclo[3.3.0]octane family.
It is quite probable that all of the trienes would be considerably more unstable than the dienes or monoolefins in the series. It is of interest that all the above olefins are isomeric with cyclooctatetraene.

With the introduction of the fourth double bond the possibility of isomerism disappears and on paper it is possible to write only one structure, that of pentalene, XXV.

XXV

The arguments for and against the stability of this compound have been discussed in Part II.
DISCUSSION

The mixture of bicyclo[3.3.0]-2-octen-6-one, XVI, and bicyclo[3.3.0]-2-octen-7-one, XVII, synthesized by the ring expansion of bicyclo[3.2.0]-2-hepten-6-one, has been used as the starting material in the synthesis of a mixture of bicyclo[3.3.0]octadienes.

All preparative methods studied for this conversion involved initial reduction of XVI and XVII with lithium aluminum hydride to bicyclo[3.3.0]-2-octen-6-ol, XVIII, and bicyclo[3.3.0]-2-octen-7-ol, XIX. It is believed that both XVIII and XIX are mixtures of the two possible stereoisomers (i.e., the hydroxyl group may be either cis or trans with respect to the tertiary hydrogens on the bridge). Trevoy and Brown have found that reductions of this type are not stereospecific. These workers found that reduction of camphor under very mild conditions, -80°, led to the formation of both borneol and isoborneol. Plattner, Heusser, and Feurer, and Fieser, Fieser, and Chakravarti have found that in the lithium aluminum hydride reduction of several keto steroids both epimers are formed.

\[ \text{XVI} + \text{XVII} \xrightarrow{\text{LiAlH}_4} \text{XVIII} \xrightarrow{\text{H}^+} \text{XIX} \]
The products obtained on dehydration of XVIII and XIX proved to be dependent on the reaction employed. The best synthetic procedure for the preparation of a mixture of bicyclo[3.3.0]octadienes proved to be the Chugaev reaction.

The product from the Chugaev reaction is believed to be best represented as a mixture of three dienes, bicyclo[3.3.0]-2,6-octadiene, XX, bicyclo[3.3.0]-2,7-octadiene, XXI, and bicyclo[3.3.0]-1,6-octadiene, XXII. The mixture of dienes took up two moles of hydrogen on catalytic hydrogenation and the reduction product proved to be pure cis-bicyclo[3.3.0]octane. The ultraviolet spectrum showed no maximum in the region 220-350 nm. This would seem to indicate that the double bonds were not conjugated. The mixture of dienes was colorless, and stable enough to be stored for several months at 0° without decomposition.

A second method of dehydration studied was the
reaction of the p-toluenesulfonates of XVIII and XIX with various organic tertiary amines. The reaction took an unexpected course and for quite some period of time gave misleading results. The product from this reaction had a distinct yellow color, not unlike that of cyclooctatetraene, and catalytic hydrogenation of several samples required varying amounts, but always more than two moles of hydrogen. The infrared curve indicated the presence of the expected mixture of dienes and some other product. The same colored mixture was obtained when either diethylaniline, 2,6-dimethylpyridine, or 2,4,6-trimethylpyridine was used as the tertiary amine but the percentage of the yellow component varied from preparation to preparation under apparently identical reaction conditions.

In one preparation using 2,4,6-trimethylpyridine as the tertiary amine, a sample was obtained which on catalytic hydrogenation required 3.35 moles of hydrogen. The infrared curve indicated a small percentage of the mixture of bicyclo[3.3.0]octadienes, XX, XXI, and XXII. This fact, coupled with the hydrogenation data, requires that the other component be a tetraene. The analysis of this fraction agreed well with the formula C₈H₁₀ and precluded the possibility that the additional unsaturation observed was due to dehydrogenation of the bicyclo[3.3.0]octane ring. The requirements of the unknown component proved to be a molecular
formula of $C_8H_{10}$ and the presence of four double bonds. These requirements are satisfied only by an acyclic octatetraene. Excluding cis-trans isomerism and compounds with allene-type bonding, there appear to be four possible tetraenes, XXIII-A, XXIII-B, XXIII-C, and XXIII-D.

\[ \begin{align*}
CH_2 &= CH(-CH = CH)_2 - CH = CH_2 \\
CH_2 &= \text{H}_2C=O
\end{align*} \]

\[ \begin{align*}
XXIII-A \\
XXIII-B
\end{align*} \]

\[ \begin{align*}
CH_2 &= CH - CH = CH - CH = CH_2 \\
\text{H}_2C=O
\end{align*} \]

\[ \begin{align*}
XXIII-C \\
XXIII-D
\end{align*} \]

Of these, XXIII-A may exist as three geometrical isomers and XXIII-B as two geometrical isomers. Tetraene XXIII-B may be excluded however as there is no reasonable way it can be formed by a double cleavage of the two fused five-membered rings of the bicyclo[3.3.0]octane ring system. Possible mechanistic interpretations of the formation of the other three tetraenes are given in Fig. VI.

The only acyclic tetraene reported in the chemical literature is XXIII-A, octatetraene, the preparation of which has been reported by Woods and Schwartzman. Their
POSSIBLE MECHANISTIC INTERPRETATIONS OF THE FORMATION OF THREE ACYCLIC TETRAENES FROM THE REACTION OF THE p-TOLUENESULFONATE OF XVIII WITH TERTIARY AMINES.

**Figure VI**

CH$_2$ = CH(C=C)$_2$CH = CH$_2$

XXIII-A

CH$_2$ = CH(C=C)$_2$CH = CH$_2$

XXIII-C

CH$_2$ = CH(C=C)$_2$CH = CH$_2$

XXIII-D
product was a white, highly explosive solid. Woods and Schwartzman give no indication as to which of the three geometrical isomers their product may be.

The ultraviolet spectrum of the mixture of tetraene and bicyclo[3.3.0]octadienes was then obtained. The spectrum of a solution of the freshly prepared mixture exhibited a maximum at 260 m\(\mu\), \(\log \epsilon_{\text{Max}} 3.66.\) On standing for six weeks at 0° the maximum shifted to 248 m\(\mu\), \(\log \epsilon_{\text{Max}} 3.87.\) The ultraviolet spectra are given in Fig. VII. In some cases the ultraviolet spectrum of the freshly prepared solution exhibited this latter maximum, 248 m\(\mu\), \(\log \epsilon_{\text{Max}} 3.87.\)

There appear to be at least two explanations as to why the spectrum should change on standing. The first is that a change in the geometrical configuration has occurred (i.e. change in the cis-trans configuration of a double bond). The second possibility is that an actual change in the nature of the bonding within the molecule has occurred.

\[
\text{CH}_2=\text{CH}-\begin{array}{c}
\text{CH} \\
\text{CH} \\
\text{H} \\
\text{CH} \\
\text{CH} \\
\end{array}
\rightarrow
\text{CH}_2=\text{CH}-
\]

An example of this latter phenomenon has recently been reported by Cope and Hochstein. 6

\[
\begin{array}{c}
\text{[cycle]} \\
\rightarrow \\
\text{[cycle]} \\
\end{array}
\]
Separation of the tetraene from the mixture of bicyclo[3.3.0]octadienes proved difficult. Attempted fractionation in an efficient center-tube column was unsuccessful. Attempts at the formation of the picric acid or 1,3,5-trinitrobenzene addition complex of the tetraene were also unsuccessful. Chromatographic methods of separation were then investigated but no suitable adsorbent could be found.

The only successful method of separation involved formation of the maleic anhydride adduct of the tetraene. It was first found that addition of maleic anhydride to a benzene solution of the tetraene-diene mixture resulted in the slow disappearance of the characteristic yellow color of the tetraene and on gentle refluxing the solution became clear and colorless. After removal of the benzene and bicyclo[3.3.0]octadienes by distillation under reduced pressure it was possible to isolate by sublimation a colorless solid which analyzed correctly for the mono-maleic anhydride adduct of the tetraene. The adduct on catalytic hydrogenation took up three moles of hydrogen as required by theory.

The above procedure represented a separation of the tetraene but it proved inconvenient to separate the bicyclo[3.3.0]octadienes from the solvent, benzene. It was found finally that separation could be achieved by adding maleic
anhydride directly to the mixture of tetraene and bicyclo-
[3.3.0]octadienes and allowing the mixture to stand at room
temperature for several days. In contrast to the clean
reaction in benzene the reaction without solvent led to
extensive decomposition. It was possible, however, to
distill the colorless mixture of bicyclo[3.3.0]octadienes
directly from the reaction mixture under reduced pressure.
The adduct of the tetraene was then separated and purified
by sublimation. Some evidence was obtained which indicated
that two isomeric mono-maleic anhydride adducts are obtained.
All efforts to obtain the di-maleic anhydride of the tetraene
have proven unsuccessful. It was further observed that the
tetraene slowly decomposed on standing, leaving the colorless
mixture of bicyclo[3.3.0]octadienes.

Attempts were made to catalytically dehydrogenate the
mixture of bicyclo[3.3.0]octadienes to pentalene. Standard
dehydrogenation procedures were used involving passage
of the vaporized compound over platinized-asbestos and platin-
ized-charcoal catalysts. In no case did it appear that
dehydrogenation was taking place. The conditions used were
found sufficient to dehydrogenate cyclohexene to benzene.
These findings are in accord with the observation of Barrett
and Linstead that cis-bicyclo[3.3.0]octane is resistant to
catalytic dehydrogenation and the observations of numerous
investigators that the 2,3-benzbicyclo[3.3.0]-2-
octene series is incapable of either chemical or catalytic
dehydrogenation to benzpentaland.

Scouting reactions were then run to investigate possible synthesis by chemical methods of either a bicyclo[3.3.0]octatriene or of pentalene from the mixture of bicyclo[3.3.0]octadienes. Most of the syntheses attempted involved reaction of the mixture of bicyclo[3.3.0]-octadienes with either one or two moles of N-bromosuccinimide. This initial reaction was apparently successful as in every case it was possible to isolate the theoretical quantity of succinimide. Both the monobromide and dibromide decomposed, however, on attempted distillation. Reaction of either the monobromide or dibromide with quinoline at 0° resulted in extensive decomposition and no products could be isolated. Reaction of the crude dibromide with magnesium, in an attempt to bring about intramolecular removal of bromine to form a triene, was unsuccessful.

The most promising approach appears to be reaction of the mixture of bicyclo[3.3.0]octadienes with mercuric acetate. Conditions were worked out in which a small yield of a monoacetoxo compound could be obtained. The acetoxo compound could be distilled and in general appeared to be considerably more stable than the corresponding bromo derivative.
\[ \text{Structure 1} + \text{Hg(OAc)}_2 \rightarrow \text{Structure 2} + \text{H}_2 + \text{HO}^\cdot + \text{CH}_3 \]
EXPERIMENTAL

Bicyclo[3.3.0]-2-octen-6-ol (XVIII) and Bicyclo-[3.3.0]-2-octen-7-ol (XIX).---In a 500-ml. three-necked flask equipped with stirrer, addition funnel, reflux condenser, and in an atmosphere of dry nitrogen was placed 3.8 g. (0.1 mole) of lithium aluminum hydride in 200 ml. of dry ether. To the stirred solution was added dropwise 21.6 g. (0.177 mole) of XVI and XVII in 50 ml. of dry ether over twenty-five minutes. The solution was heated to reflux for forty minutes. The flask was immersed in an ice bath and the excess reagent and reaction complexes destroyed by the careful addition of 20 ml. of water followed by 150 ml. of 12% sulfuric acid solution. The ether layer was separated and the aqueous layer extracted with two 50-ml. portions of ether and then continuously with ether for two days. The ether layers were combined, dried over magnesium sulfate, and concentrated under reduced pressure. Distillation yielded 18.4 g. (84%) of XVII and XIX, b.p. 91-94° (17 mm.), n_D 1.5025.


Solid derivatives of XVIII and XIX proved difficult to crystallize and had wide melting point ranges which might be expected from the mixture present. The acetate of XVIII
and XIX was prepared as follows: To a solution of 1 g. (0.008 mole) of XVIII and XIX in 4 ml. of pyridine was added 1 g. of acetyl chloride with stirring over five minutes. The reaction mixture was allowed to stand at 0° for five hours and at room temperature for one hour. The reaction mixture was poured into 25 ml. of water and the mixed acetates extracted with 25 ml. of ether. The ether layer was washed with 25 ml. of 1N hydrochloric acid, 25 ml. of 5% sodium bicarbonate, and 25 ml. of water. The ether layer was dried over magnesium sulfate and concentrated under reduced pressure. Distillation yielded 0.95 g. of the mixed acetates, b.p. 91-94° (16 mm.), n^25_D 1.4675.

Anal. Calcd. for C_{10}H_{14}O_2: C, 72.30; H, 8.43. Found: C, 72.04; H, 8.69.

The formate of XVIII and XIX was prepared by heating a solution of 4 g. (0.032 mole) of XVIII and XIX and 25 ml. of 98-100% formic acid on a steam bath for one hour. After cooling the mixture was poured into 100 ml. of water and the formate extracted with three 50-ml. portions of ether. The ether layer was washed with 100 ml. of 10% sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure. Distillation yielded 3.4 g. (75%) of XVIII and XIX formate, b.p. 98-100° (28 mm.), n^25_D 1.4838.

Chugaev Reaction of Bicyclo[3.3.0]-2-octen-6-ol (XVIII) and Bicyclo[3.3.0]-2-octen-7-ol (XIX).---In a 200-ml. three-necked flask equipped with stirrer, addition funnel, reflux condenser, and in an atmosphere of dry nitrogen was placed 1 g. (0.042 mole) of sodium hydride in 50 ml. of dry ether. To the stirred suspension 2.7 g. (0.022 mole) of XVIII and XIX in 30 ml. of dry ether was added over ten minutes. The suspension was heated under reflux and stirred for twenty hours. A solution of 5 ml. of carbon disulfide in 20 ml. of dry ether was then added over five minutes and the stirring and heating under reflux continued for six hours. Methyl iodide (5 ml.) dissolved in 20 ml. of ether was added over five minutes, and the stirring and heating under reflux continued for twenty hours. The reaction flask was immersed in an ice bath and the excess sodium hydride destroyed by the careful addition of 25 ml. of water. The reaction mixture was transferred to a separatory funnel and all inorganic salts extracted from the ether layer with 25 ml. of water. The aqueous washings were extracted with 25 ml. of ether, the ether layers combined, dried over magnesium sulfate, and concentrated under reduced pressure. The crude xanthate was transferred to a
50-ml. round-bottomed flask and pyrolyzed by heating the flask with a Wood's metal bath from 180-220° over forty minutes. Gas evolution was steady during this period and organic material distilled over regularly. The pyrolysate was taken up in 35 ml. of ether and sulfur-containing compounds removed by thorough extraction of the ether layer with 50 ml. of 20% sodium hydroxide solution. The ether layer was dried over calcium chloride and concentrated by distillation at atmospheric pressure. Distillation of the residue through a micro column yielded 1.23 g. (53%) of the mixture of bicyclo[3.3.0]octadienes, XX, XXI, and XXII, b.p. 129-131°, n\textsubscript{D} 1.4852. With purification of the olefin by the silica-gel method the refractive index became constant at n\textsubscript{D} 1.4865.

The infrared curve is given in Fig. VIII.

\textbf{Anal. Calcd. for C}_{8}\textsubscript{H}_{10}: \text{C}, 90.57; \text{H}, 9.43. \text{Found: C}, 90.28; \text{H}, 9.62.

In general, good analyses of the olefin were difficult to obtain due to the high volatility of the product.

Microhydrogenation of two samples of the olefin in glacial acetic acid, in the presence of pre-reduced Adam's platinum catalyst, required 102 and 103% of two molar equivalents of hydrogen. The reduction product was obtained by reduction of a 1.2 g. sample of the mixture of dienes in glacial acetic acid followed by neutralization
of the acetic acid with 10% sodium hydroxide solution and extraction of the reduction product with ether. After working up the ether layer in the usual manner distillation through a micro column\textsuperscript{9} yielded 0.6 g. (50%) of cis-bicyclo[3.3.0]octane, b.p. 135-137\textdegree, $n_2^5$ 1.4584. After five passages over silica gel the refractive index was constant at $n_2^5$ 1.4593. The infrared curve is given in Fig. VIII and is identical within experimental error to that of authentic cis-bicyclo[3.3.0]octane, I.

Reaction of the Mixture of Bicyclo[3.3.0]octadienes with Mercuric Acetate.---In a 15 ml. centrifuge tube was placed 0.6 g. (0.0056 mole) of the mixture of bicyclo[3.3.0]-octadienes and 1.8 g. (0.0056 mole) of mercuric acetate. The air was displaced by dry nitrogen and the tube fitted with a cold-finger condenser. The tube was heated with an oil bath from 150-160\textdegree for ten hours. Considerable decomposition occurred. After cooling 3 ml. of ether was added and the liquid products thoroughly extracted. The solid products were centrifuged into the bottom of the tube and the liquid layer removed. Distillation through a micro column\textsuperscript{9} yielded 0.06 g. (8%) of a product with b.p. 94\textdegree (17 mm.), $n_2^5$ 1.4910. The product is believed to be chiefly bicyclo-[3.3.0]-2,6-octadien-4-ol acetate or an isomer thereof.

\textbf{Anal. Calcd. for C\textsubscript{10}H\textsubscript{12}O:} C, 73.20; H, 7.32.

\textbf{Found:} C, 72.29; H, 7.36.
Reaction of the p-Toluenesulfonates of Bicyclo[3.3.0]2-octen-6-ol (XVIII) and Bicyclo[3.3.0]2-octen-7-ol (XIX) with 2,4,6-Trimethylpyridine.—In a 100-ml. round-bottomed flask was placed 2.5 g. (0.02 mole) of XVIII and XIX, 3.84 g. (0.02 mole) of p-toluenesulfonyl chloride (m.p. 69°), and 3.5 ml. of dry pyridine. The reactants were thoroughly mixed, allowed to stand at 0° for three hours, and at room temperature for twelve hours. The reaction mixture was taken up in 60 ml. of ether and the ether layer washed with three 25-ml. portions of 1N hydrochloric acid, two 25-ml. portions of 5% sodium bicarbonate, and 25 ml. of water. The ether layer was dried over potassium carbonate and concentrated under reduced pressure (final pressure 0.5 mm.). All attempts at crystallization of the p-toluenesulfonates failed. A mixture of the crude p-toluenesulfonates and 25 ml. of 2,4,6-trimethylpyridine (b.p. 172°), in a 200-ml. round-bottomed flask equipped with a reflux condenser and protected from atmospheric moisture, was heated with an oil bath from 150-160° for two and one-half hours. After cooling the reaction mixture was taken up in 100 ml. of ether and the solution transferred to a separatory funnel. The 2,4,6-trimethylpyridine was thoroughly extracted with 150 ml. of iced 10% sulfuric acid. The ether layer was washed with two 25-ml. portions of water and dried over magnesium sulfate. After concentration by distillation at atmospheric
pressure the residue was distilled taking fractions through a micro column as follows: Fraction I, 0.37 g., b.p. 70-74° (158 mm.), \(n^D_2 1.5078\); Fraction II, 0.38 g., b.p. 74-75° (160 mm.), \(n^D_2 1.5010\); Fraction III, 0.27 g., b.p. 74-75° (160 mm) \(n^D_2 1.4950\).

The infrared curve of Fraction I is given in Fig. VIII. The analysis of Fraction I was as follows:


Microhydrogenation of a portion of Fraction I required 3.35 molar equivalents of hydrogen.

The ultraviolet spectrum of Fraction I was determined for a solution in purified cyclohexane with a Beckman model DU quartz ultraviolet spectrophotometer. The spectrum is given in Fig. VII. Curve A represents the spectrum of the freshly prepared solution and Curve B the spectrum of the solution after standing for six weeks at 0°.

The refractive index of Fraction II indicated a composition of approximately 40% tetraene, 60% bicyclo[3.3.0]-octadienes. Fraction II was added to a solution of 0.35 g. of maleic anhydride in 5 ml. of benzene. The solution initially had the characteristic yellow color of the tetraene. After standing for two hours the solution was nearly colorless. The solution was heated to reflux for four hours and all liquid products distilled under vacuum into a Dry-Ice
trap. Sublimation of the solid residue at 70° (1 mm.)
yielded 0.2 g. of maleic anhydride. Sublimation at 150°
(1 mm.) yielded two products, a solid (0.035 g.), m.p.
96-98°, and a liquid which solidified on standing for two
weeks, m.p. 64-76°. The solid product, m. p. 96-98°
analyzed correctly for a monomaleic anhydride adduct of a
C₈H₁₀-tetraene.

Anal. Calcd. for C₁₂H₁₂O₃: C, 70.60; H, 5.88.
Found: C, 70.34; H, 5.70.

Microhydrogenation of a sample of the solid prod-
uct, m.p. 96-98°, required 105% of three molar equivalents
of hydrogen.

Reaction of the p-Toluenesulfonates of XVIII and
XIX with 2,6-Dimethylpyridine and Separation of the Tetraene
_and Bicyclo[3.3.0]octadienes._—The p-toluenesulfonates of
2.5 g. of XVIII and XIX were prepared and worked up exactly
as described above in the reaction of the p-toluenesulfonates
with 2,4,6-trimethylpyridine. After concentration under vac-
uum a solution of the crude p-toluenesulfonates and 25 ml. of
2,6-dimethylpyridine, in a 300-ml. round-bottomed flask
equipped with a reflux condenser, was heated with an oil
bath from 150-155° for three and one-half hours. The re-
action mixture was taken up in 100 ml. of ether and the
2,6-dimethylpyridine extracted with 200 ml. of iced 12°
sulfuric acid. The ether layer was washed with two 35-ml.
portions of water, dried over magnesium sulfate, and con-
centrated by distillation at atmospheric pressure. Dis-
tillation of the residue through a micro column taking
fractions proceeded as follows: Fraction I, 0.42 g., b.p.
76-78° (166 mm.), n_2^25 1.4970; Fraction II, 0.32 g., b.p.
73-80° (165 mm.) n_2^25 1.4930; Fraction III, 0.22 g., b.p.
80-82° (163 mm.), n_2^25 1.4868. The three fractions were
combined and 0.27 g. of maleic anhydride added. The mix-
ture was allowed to stand at room temperature for four days.
Considerable decomposition occurred. Distillation of all
liquid products into a Dry-Ice trap under reduced pressure
yielded 0.525 g. of the colorless mixture of bicyclo[3.3.0]-
octadienes. Sublimation of the solid residue at 70° (1 mm.)
yielded a small amount of maleic anhydride. Sublimation at
150° (1 mm.) yielded 0.15 g. of the crude maleic anhydride
adduct of the tetraene. After two more sublimations 0.105
g. of the white, crystalline adduct was obtained, m.p. 96-
99° (softens 88-90°). Microhydrogenation of a portion of
the adduct in methanol in the presence of pre-reduced
Adam's platinum oxide required three molar equivalents of
hydrogen.

Reaction of the p-Toluenesulfonates of XVIII and
XIX with Diethylaniline.---The p-toluenesulfonates of
5.05 g. of XVIII and XIX were prepared and worked up in a similar manner to that described above. After concentration, the crude p-toluenesulfonates were heated with 120 ml. of diethylaniline for three hours at 160-170°. The reaction mixture was taken up in 150 ml. of ether and the diethylaniline extracted with 450 ml. of iced 12% sulfuric acid. The ether layer was washed with two 100-ml. portions of water and dried over magnesium sulfate. After concentration by distillation at atmospheric pressure the residue was distilled through a 10 cm. Vigreux still head taking fractions as follows: Fraction I, 0.365 g., b.p. 74-76° (152 mm.), $n_{D}^{25} 1.4935$; Fraction II, 1.65 g., b.p. 76-78° (152 mm.), $n_{D}^{25} 1.4892$; Fraction III, 0.63 g., b.p. 78-80° (152 mm.), $n_{D}^{25} 1.4870$. 
Figure VII
Ultraviolet Spectra

Curve 1. Freshly prepared solution of bicyclo[3.3.0]octadiene-''octatetraene'' mixture (n^25_D 1.5078) in cyclohexane.

Curve 2. Spectrum of same solution after standing at 0° for six weeks.
Figure VIII

Infrared spectra: Baird spectrograph with NaCl prism, solutions of 50 mg. of compounds in 0.50 ml. of carbon disulfide except in the regions 4.2-5.0μ and 6.2-7.4μ where carbon tetrachloride was used as solvent.

Curve 1. Mixture of bicyclo[3.3.0]octadienes prepared by Chugaev reaction of XVIII and XIX.

Curve 2. Reduction product of the mixture of bicyclo[3.3.0]octadienes.

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BIOGRAPHICAL NOTE

The author was born August 13, 1926, in Brandon, Vermont, and received his early education in the elementary school of that town. He was graduated from Brandon High School, Brandon, Vermont, in June 1944.

In July 1944 the author enlisted in the United States Naval Reserve, and, after four months of recruit training, entered the V-12 Naval Officers Training Program at Alma College, Alma, Michigan. After one year in the V-12 Program the author was transferred to the NROTC Officers Training Program at Miami University, Oxford, Ohio. At the conclusion of the Great War the author was discharged from the United States Navy and in September 1946 he returned to Miami University to complete his undergraduate studies. He received the degree A. B. in June 1948.

In September 1948 the author entered the Graduate School of the Massachusetts Institute of Technology to study in the field of Organic Chemistry.