

TOWARD THE SYNTHESIS
OF TRICYCLIC OCTANES

A Thesis
presented to
the Department of Chemistry
Washington and Lee University

by

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VITA

Robert Gillis Campbell was born in Tulsa, Oklahoma on December 24, 1946, the son of Bethel Cox Campbell and Robert N. Campbell. He attended elementary school in Oklahoma City, Oklahoma and graduated from Harding High School in Oklahoma City in June 1965. He entered Washington and Lee University in the fall of 1965 and is working toward a Bachelor of Science degree in Chemistry.

ACKNOWLEDGEMENT

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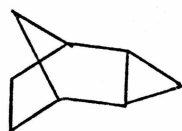
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INTRODUCTION

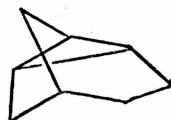
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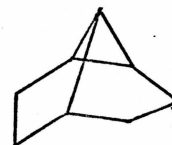
I began my research as a continuation of the summer research of Miss Julie Kugel of Northwestern University. She worked under a National Science Foundation grant. She had begun work on synthesizing Tricyclo (2.1.1.0^{3,4}) octane (Ia) or Tricyclo (2.1.1.0^{4,6}) octane (Ib) or Tricyclo (2.2.0^{1,5}.0^{4,5}) octane (Ic) or a mixture of all.



Ia

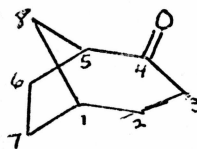
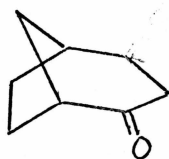


Ib



Ic

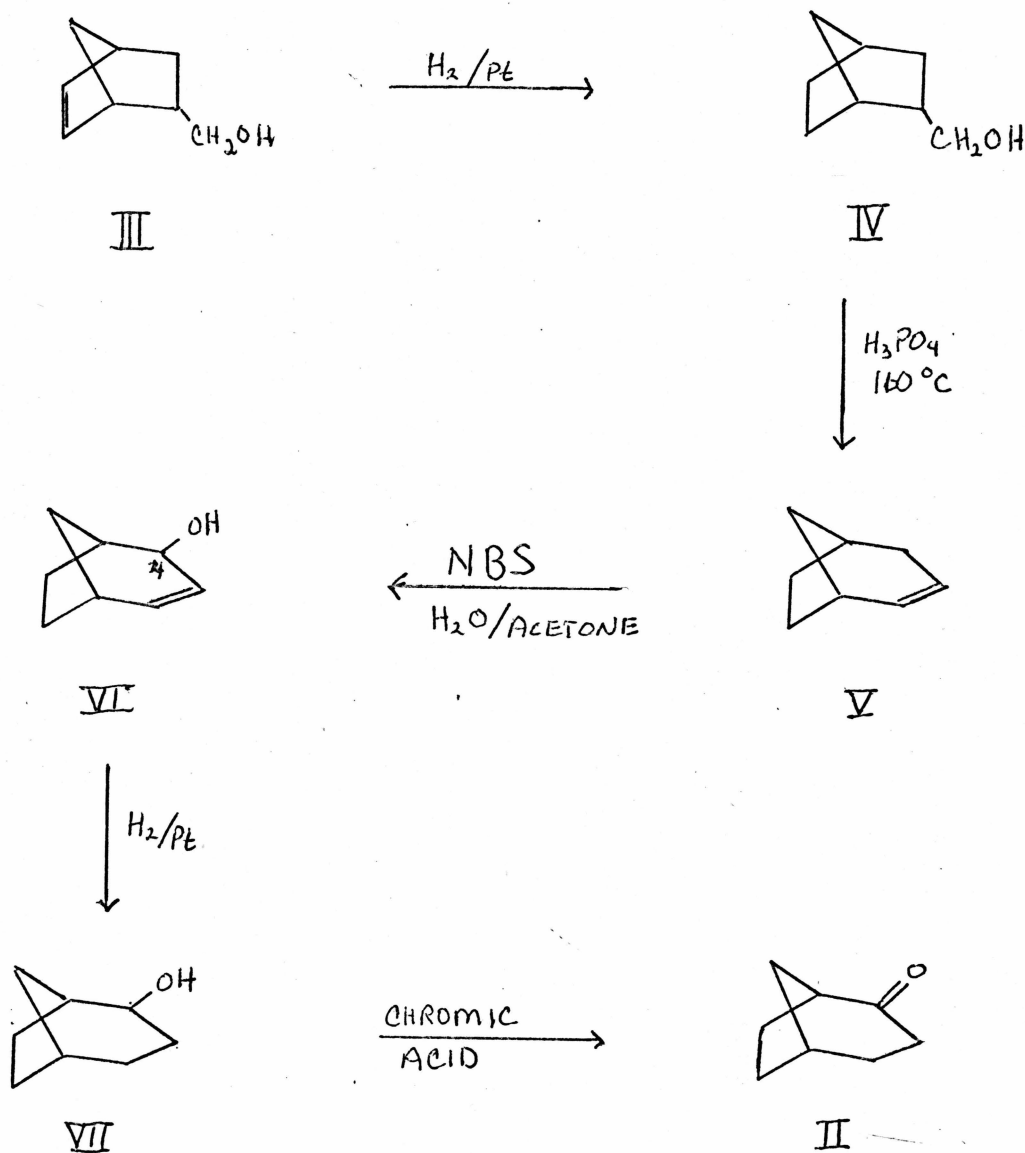
Miss Kugel worked on the synthesis of the desired starting product of Bicyclo (3.2.1) -4- octone (II). These two structures are



II

mirror image enantiomers. Her method of synthesis was as follows.

She hydrogenated Bicyclo (2.2.1) hept -5-ene-2 methanol (III) catalytically with hydrogen and platinum which yielded Bicyclo (2.2.1) hept-2- methanol. (IV). She then proceeded to react the product (IV) with Phosphoric acid heated to 160° C. This gave a mixture of products of which Bicyclo (3.2.1) -2-octene (V) was one.

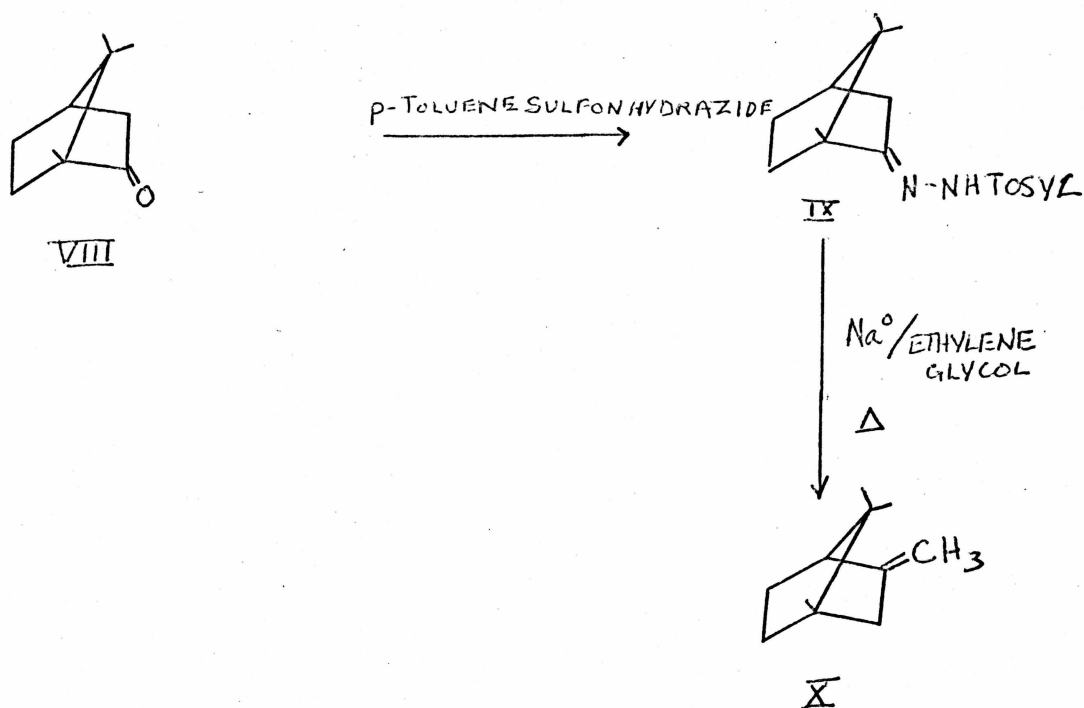


After she had separated the products by distillation, she followed the above reaction with the addition of bromine by using NBS to the number two carbon and followed this by hydration with a water and acetone mixture to form Bicyclo (3.2.1) -2-octene-4-ol (VI). She then attempted to catalytically hydrogenate the double bond to obtain Bicyclo (3.2.1) octane-4-ol (VII). She was going to follow by oxidizing this reaction with chromic acid to form the desired octane (II).¹ It was at this point I began my research.

EXPERIMENTAL

My research was mainly done in two areas. The first was experimenting with how to get the Bicyclo (3.2.1) -4-octone (II) to the desired tricyclic compounds (Ia, Ib, Ic) if and when the bicyclic octone was isolated. The second area of research was to find a suitable synthesis for the starting material (II).

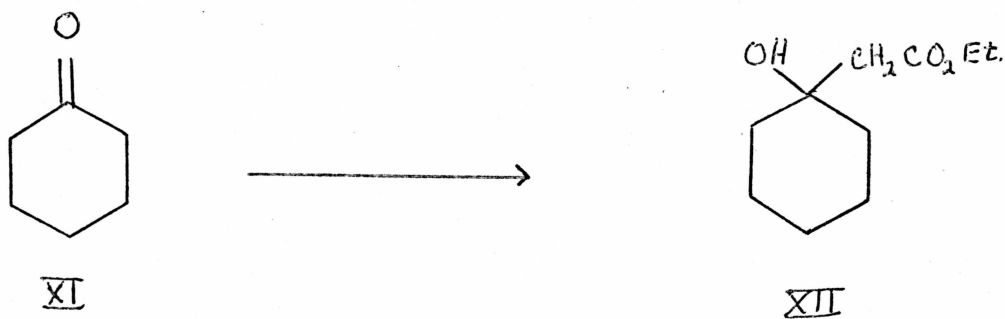
In the first area, I worked with camphor (VIII) which has a similar structure to the bicyclic octone (II). The purpose of the following reaction was to produce a third ring in the bicyclic octone and to give camphene (X) in this case. The reaction is described as follows. 9.09 g. of camphor was reacted with 11.5g of p-toluenesulfonylhydrazide. This was carried out by refluxing the camphor and p-toluenesulfonylhydrazide in an equivalent quantity of one percent HCl/EtOH solution for one half hour. This will form the tosylhydrazone of camphor (IX). This produced a total product of 6.3g. This was followed by a degradation by progressively heating the tosylhydrazone progressively with 25 ml of a 1.5 normal solution of sodium in ethylene glycol. This was supposed to produce camphene (X) which boils at 158-160° C. and melts at 46° C. However, this reaction did not work because the resultant product boiled at 115°-124° C.² The mechanisms of this reaction will be discussed later.



In the second area, consisted of a literature search followed by the synthesis of a suitable starting material. After consulting the literature, a synthesis using cyclohexanone as starting material was found and it was the method chosen. A mixture of 104 ml of cyclohexanone (XI) and 350 ml of toluene ~~and 400 ml~~ of 400 ml of benzene as a solvent mixture, was refluxed with 65g of zinc powder (cleaned with 100% H_2SO_4) in a three necked flask with an electric stirrer, a dropping funnel, and a reflux condenser afixed with a drying tube. To this refluxing mixture is added 85 ml of ethyl-bromoacetate, which had been previously prepared.³ Extreme care should be taken in handling ethylbromoacetate, because it is a very powerful lacrymator. The ethylbromoacetate is added as

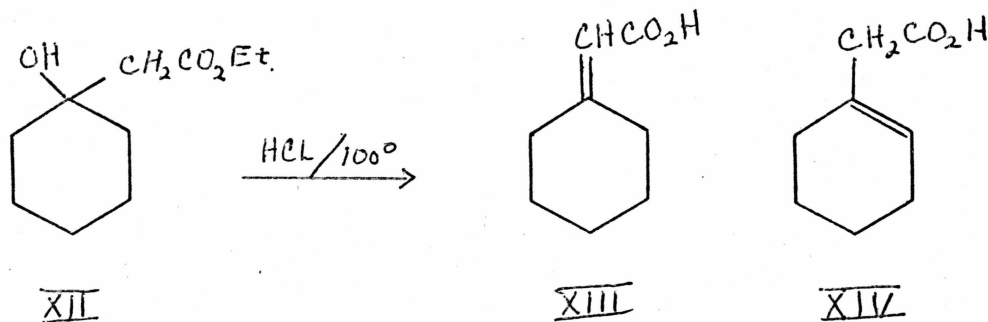
fast as the reaction will take it and remain at a gentle reflux. Completion is supposed to be indicated by a colorlessness of the reacting liquids. However after an hour a white milkiness appeared. I allowed the reaction vessel to reflux for two more hours. Upon completion of the reaction, I added 100-200 ml of dilute sulfuric acid to dissolve the zinc hydroxide and then separated the benzene-toluene layer and dried it over sodium sulfate.

After drying, the benzene-toluene mixture was vacuum distilled over. The product was never distilled over because a suitable pressure could not be obtained. The product (XII) was to boil at 86-89°C. at 2 millimeters of pressure but I could only get about 60 mm. and was afraid I might pyrolyze the product.



Following this, the product was dehydrated by heating it on a steam bath and passing dry hydrogen chloride gas through the product (XII). This dehydration produces cyclohexylideneacetic acid (XIII)

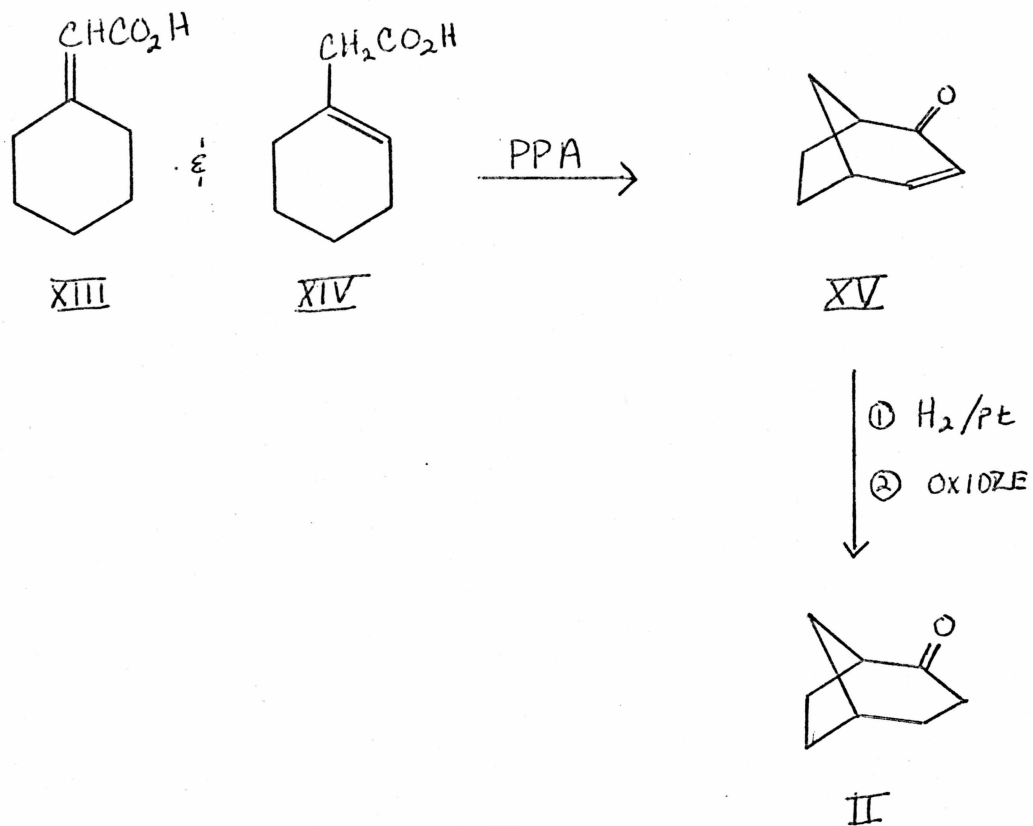
and cyclohexyl-1-ene-1 acetic acid (XIV). The mixture was to be collected from 159-160° at 22 mm. A pressure of 26 mm. to 31 mm. was maintained while heating in a wood's metal bath. The product was collected up to 210° C. as read on the thermometer in the wood's metal bath. A yield of 28 ml of liquid was obtained along with a considerable amount of dark brown goo.⁴

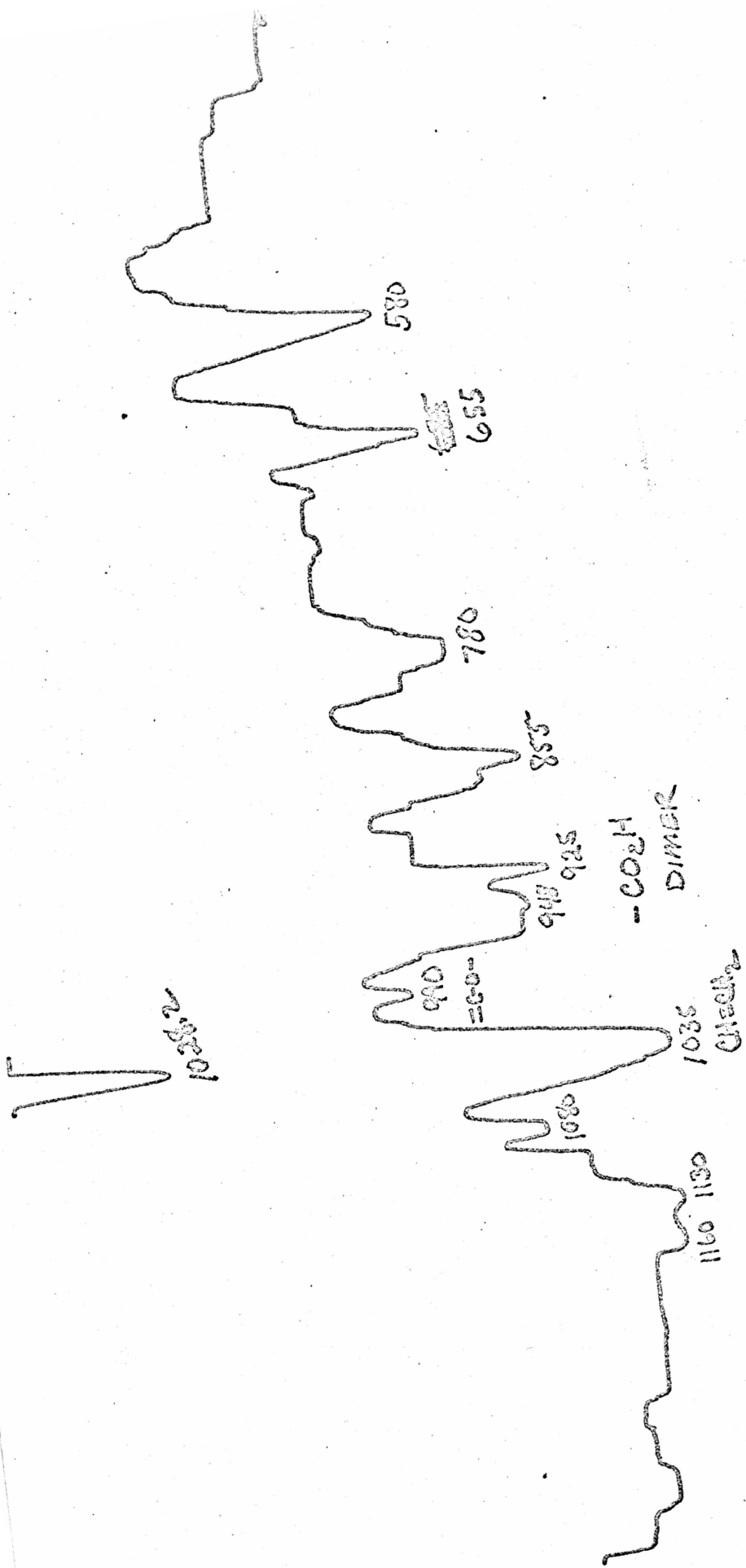


Compound (XIII) melts at 91° C. and the other compound (XIV) melts at 38° C. The mixture is supposed to have more of the lower melting compound. The next two pages are copies of the I.R. data run on the resulting liquid portion isolated.

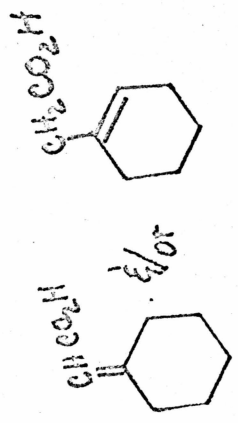
If I had had more time, I would have reacted each of the isolated materials, the liquid and the goo, with polyphosphoric acid which hopefully would yield Bicyclo (3.2.1)-2-ene-4-octone (XV). This would then be either catalytically hydrogenated and

re-oxidized to produce the bicyclic octone (II) or would be used directly in a reaction to try to produce the tricyclic octane(s).





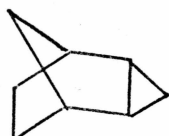
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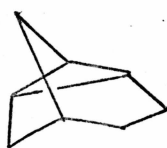
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DISCUSSION

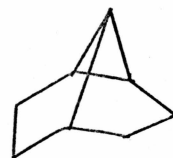
The formation of the tricyclic compound or mixture of compounds Ia, Ib, Ic will be initiated through degradation of a tosylhydrazone of the bicyclic octone (II).



Ia

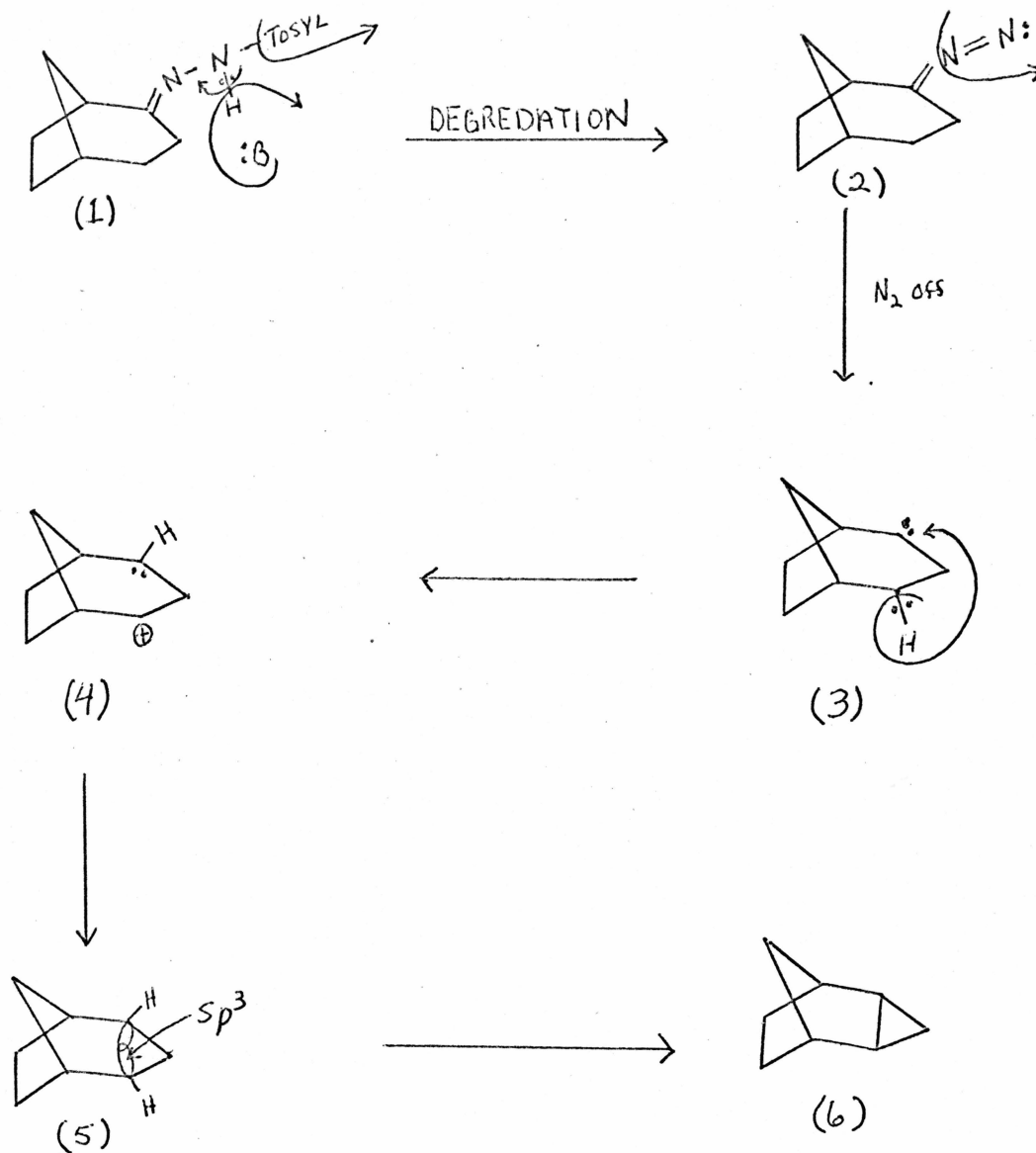


Ib



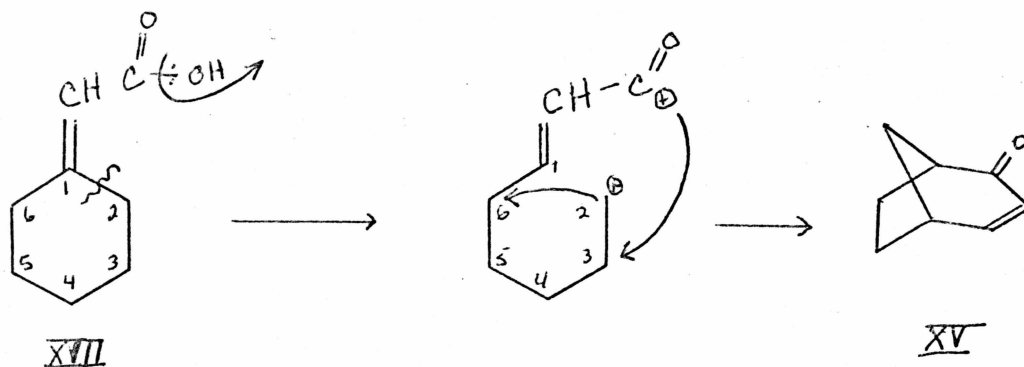
Ic

The mechanism arises from the basic abstraction of the hydrogen on the nitrogen bonded to the ring. When this hydrogen leaves, it leaves its electrons behind (1). As this happens, the tosyl group pops off, leaving two doubly bonded nitrogens doubly bonded to the ring (2). Following this, the two nitrogens leave as N_2 and the ring is left with a pair of electrons left by the leaving nitrogen (3). At this point, it is assumed that a hydrogen on one of the second carbons away from the electron possessing carbon, migrates to the carbon with the pair of electrons. This causes the carbon from which the hydrogen migrates, electron deficient (4). Now somehow the carbon sp^3 bond reaches out and manages to share the electrons that are present on the carbon which has the free electron pair (5). Thus the third bond is formed (6).

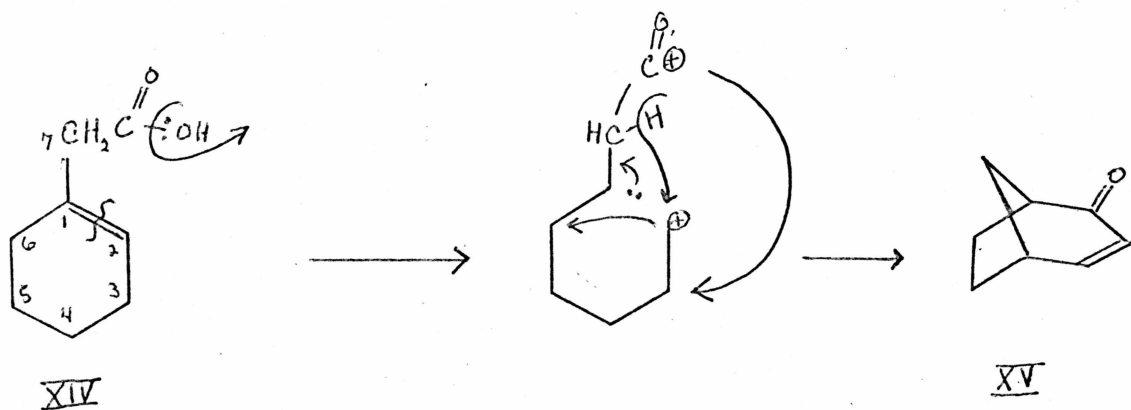


The following is a proposed explanation and mechanism for the formation of the Bicyclic (3.2.1)-2-ene-4-octone (XV). The ring closure is done with polyphosphoric acid. This acid dehydrates the carboxylic acid leaving a positively charged carbon. At the same time, the six membered ring is broken between carbons 1 and 2. This forms an intermediate (XVI). From this

point the bicyclic compound (XV) is formed by a concerted double ring closure. The carbon number 2 forms a bond with carbon number 6 and the carbonium form from dehydration of the acid closes on carbon number 3.



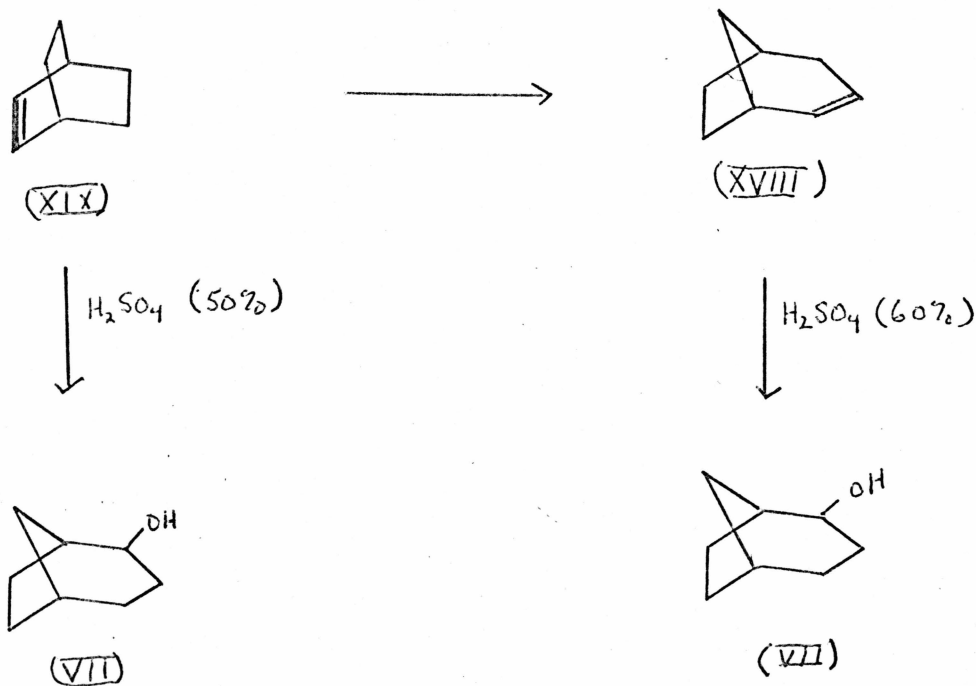
The mechanism for (XIV) might be as follows. The polyphosphoric simultaneously dehydrates the carboxylic acid and breaks the double bond between carbons one and two. The electrons freed migrate to form a double bond between carbons one and seven (XVII). The mechanism from this point on would parallel the above.



SUMMARY

IS NOT MADE,

In the future, if the use of the above method¹ for producing a starting Bicyclo (3.2.1) -2- octanol, another way may be through the use of Bicyclo (3.2.1) -2-octene (XVIII).⁵ The hydration of (XVIII) will give the desired bicyclic alcohol. The hydration in question was carried out by 60 per cent sulfuric acid. The Bicyclo (3.2.1)-2-octene can be made using Bicyclo (2.2.2)-2-octene (XIX) as a starting material. However, it was also found that the alcohol can be formed directly from Bicyclo (2.2.2)-2-octene by using fifty percent sulfuric and shaking at 20-25°C. This gave yields of 73%.⁶ This may be the best way of producing the desired alcohol (VII) depending on the availability of (XIX).



This has been a very fascinating and rewarding year for me. I have gained a lot of lab technique and have been well oriented to the literature of research. Again I wish to thank the Robert E. Lee Research Foundation for making this possible.

Footnotes

1. Summer Research notebook of Miss Julie Kugel.
2. W. R. Bamford and T. S. Stevens, J. Chem. Soc., 4735 (1952).
3. Organic Synthesis Vol. III, p. 381.
4. Samuel Natelson and Sidney P. Gottfried, J. Amer. Chem.Soc. 61, 1970 (1939).
5. A. F. Bickel, J. Kontnerus, F. C. Kooyman, and G. C. Vegter, Tetrahedron V. 9, 230-236 (1960).
6. M. S. Newman and Y. Tien Yu, J. Amer. Chem. Soc., 74, 507 (1952).