A STUDY OF THE OXIDATION OF PYRETHROSIN

By

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INTRODUCTION

The history and characterization of pyrethrosin as a chemical individual has been thoroughly discussed by Stanton (29).

The research conducted by the author was directed toward the same goal as that of Stanton in that it sought to discover the structure of pyrethrosin. When the author began work on pyrethrosin the molecular formula was known to be $C_{17}H_{22}O_5$. Also known were the general physical properties and the existence of an acetate group, a double bond, an active hydrogen, and a probable lactone structure.

Neither the nature of the fifth oxygen atom nor the basic carbon skeleton were known. Likewise, the relationship which the various groups bore to each other was unknown.

The condition of the problem suggested two broad avenues of attack: First, an attempt could be made to determine the central carbon system, the most likely means of attack being dehydrogenation of pyrethrosin or some of its derivatives and identification of the resulting hydrocarbons. Second, attempts could be made to establish the nature of the fifth oxygen atom, the nature of the known double bond, the possible existence of other double bonds, and the relation which the known groups bore to each other. Here the most likely method of attack seemed to be degradation of the molecule into more simple structures by oxidation or other means. Mr. H. D. Anspon (1) of this laboratory had already started work on the dehydrogenation of pyrethrosin, so the author attempted a series of oxidative studies of the compound.

The unstable nature of pyrethrosin and the peculiar mixture of substances which results whenever the acetate grouping is destroyed, suggested that rather mild oxidative methods would probably be most productive. The knowledge that pyrethrosin possessed at least one double bond caused ozonization to appear to be a good method of degrading the molecule.

DISCUSSION

Discussion of the Ozonization of Pyrethrosin.

The ozonization reaction (14) has been of enormous value in the solution of structural problems by cleavage of unsaturated compounds. However, the complex mixture of aldehydes, ketones, acids, and peroxides which results from the various clevages of the ozonide, followed by secondary reactions, causes interpretation of the results to be none too simple. This is particularly true when the molecule contains other groups than double bonds which may be attacked by the ozone or during the decomposition of the ozonide. The formation of polymeric ozonides which cannot be broken up into desired fragments is also a great handicap to the value of the reaction. There is also some evidence indicating that not all ozonides have the generally accepted structure proposed by Staudinger (28) and consequently cleavage of the double bond should not always be expected. The gentler methods of decomposition of ozonides developed by Whitmore (3,31) and Fischer (8) reduce the number of products, but these methods are not always applicable.

The ozonization of pyrethrosin, unfortunately, is subject to many of the difficulties mentioned above. Its ozonide could not be decomposed by catalytic methods and apparently other centers than the double bond are attacked by the ozone or during the decomposition of the ozonide.

Pyrethrosin is known to possess at least one double bond, yet it does not absorb ozone mole for mole in either chloroform or acetic acid. It may be significant that pyrethrosin reacts with only about seven thenths of a mole of ozone per mole of pyrethrosin. This recalls

Stanton's (29) observation that only about eight tenths of a mole of permonophthalic acid is consumed, in chloroform, per mole of pyrethrosin. Dihydropyrethrosin absorbs less than a quarter of a mole of ozone before ozone is detected in the exit gases, yet ozone apparently attacks it because only a syrup could be obtained from ozonization of this compound.

Probably the most significant product obtained from the ozonization of pyrethrosin was formaldehyde. It was obtained in yields as high as forty five percent of theory for one mole of formaldehyde per mole of pyrethrosin. It was identified as the dimedone (30) derivative. The formation of formaldehyde in minute amounts is common in ozonolysis reactions even when the compound being ozonized has no structure which could logically produce it. However, the isolation of formaldehyde in such large quantities seems to indicate that pyrethrosin possesses a methylidene group. The yield of formaldehyde was better than that reported for many terpenoids known to have this structure (2,26). Dihydropyrethrosin yields no formaldehyde on ozonization so it would appear that in this molecule the double bond adjacent to the methylene group has been hydrogenated.

The presence of a methylidene group is very common in the sesquiterpenes (26,22,23,24) and their derivatives to which family pyrethrosin most probably belongs. The methylidene group in the terpenes is often part of an isopropenyl structure which is almost invariably associated with an isomeric form containing the isopropylidene group. This is true even with crystalline compounds in the terpene series according to Grignard (9,26) and others. Consequently a careful search for acetone, as an ozonization product, was made. No acetone was found nor could any methyl ketone or additional aldehyde be detected in the products. This seems to indicate that the methylidene group is probably attached to a ring. If the methylidene group is attached to a chain, then it must be branched off at a point further than one carbon from the end.

The failure to secure a higher yield of formaldehyde than was obtained may be due to several causes. Pyrethrosin apparently forms a polymeric ozonide which will be discussed later. The formation of this product would lower the yield of formaldehyde since no cleavage of the double bond occurs. Also there is evidence that ozone does not always cleave the carbon-carbon linkage in pyrethrosin but may make an epoxide such as that encountered by Ruzicka and Haagen-Smit (21) in the ozonization of the sesquiterpenol, guaiol. The fact that pyrethrosin does not appear to absorb as much as a mole equivalent of ozone may also be significant. The detection of small amounts of formic acid may also help account for the failure to get nearly quantitative yields of formaldehyde. Otherwise, the formic acid is not significant since it would be expected where formaldehyde is known to exist.

Acetic acid was obtained by ozonization in about a fifty percent yield of theory for one mole of acid per mole of pyrethrosin. However, no acetaldehyde could be detected and hence it must be assumed that the acetic acid was not formed by cleavage of a double bond but rather come from a disruption of the acetate group known to be present in the molecule. The possibility that hydrolysis of the ozonide leads exclusively to an acid splitting on one side seems a very unlikely one. Treatment of unozonized pyrethrosin in a manner identical with the ozonide decomposition process did not hydrolyze the acetate structure so it must be assumed that ozonization causes the acetate group to hydrolyze more easily.

The syrup obtained by the alkaline hydrolysis of pyrethrosin gave a yield of formaldehyde about the same as that from pyrethrosin itself. This would indicate that if pyrethrosin is an enol acetate as suggested by Stanton (29), the enolization was not responsible for producing the double bond adjacent to the methylene group. It does appear to be true that ozonization disrupts the acetate structure in some way, because ozonization in ethyl acetate and decomposition with boiling water yields a syrup which contains no acetate structure and appears generally similar to the syrup obtained by alkaline hydrolysis of pyrethrosin.

Two acids were obtained from the ozonization of pyrethrosin in ethyl acetate. The first was obtained from the water layer when the ozonide was decomposed by simply boiling it with water. Analyses and neutral equivalents indicated that this acid had the formula $C_{15}H_{24}O_7$. Both the acetate and lactone structures in pyrethrosin were hydrolyzed in the formation of this acid since the acid did not take up additional alkali after the first end point was reached. The fact that no carbon atoms were lost except those in the acetate structure shows that the ozone did not cause a cleavage of the double bond. This failure to cleave the double bond is unusual, but one example of such an occurrence has already been mentioned in Ruzicka's work on guaiol. Another example is the work done by Komppa and Roschier (12) on α fenchene. Any supposition that clevage did occur would indicate that the double bond was in a ring. Other evidence does not bear this out.

The above acid was obtained repeatedly but always in yields of about ten percent. Treatment of the decomposition mixture with hydrogen peroxide did not increase the yield. Attempts to prepare the acid by hydrolysis of pyrethrosin, simply boiling with water and an organic solvent without previous ozonization, failed in all cases. Ethyl acetate and water and dioxane with water gave back the pyrethrosin unchanged. Acetic acid and water gave only a syrup.

It is interesting to note that this acid differs from an acid prepared by Rose and Haller (19) from alkaline hydrolysis of pyrethrosin by only an additional oxygen atom. This again suggests hydrolysis of the acetate structure and an epoxide oxygen across the double bond.

The other acid obtained from ethyl acetate ozonization came from the ethyl acetate layer of the decomposition mixture when this was allowed to evaporate slowly. It was obtained in very small amount and could not be obtained again. Analyses and neutral equivalent indicated that it had the formula $C_{15}H_{26}O_3$. This differs from the first acid by an additional molecule of water.

Ozonization in both chloroform and acetic acid gave a non-crystalline product melting, with evolution of gas, at 360-370°. It was insoluble in ethyl acetate but dissolved in alcohol after first turning to a gum. It was precipitated by the addition of water and dried to give a solid which could be ground into a fine white powder. Carbon and hydrogen analyses indicated that it corresponded closely to the formula $C_{17}H_{24}O_7$. It was not acid but took up excess alkali on standing. It failed to react with any carbonyl reagents and gave no free iodine with acidic potassium iodide. Pyrolytic distillation gave acetic acid. This substance is probably a polymeric ozonide.

The failure to obtain any crystalline aldehydes or ketones from the larger fragments of pyrethrosin or any pure carbonyl derivatives was a great handicap in the study of pyrethrosin by ozonization. Several methods of decomposition calculated to give aldehydes and ketones in good yield were tried (3,31), but all failed. The thick syrups invariably obtained, failed to give tests for aldehydes and no pure ketone derivative was ever obtained. It is probable that loss of the acetate group with consequent formation of the unworkable thick syrup which made progress difficult in other attacks on pyrethrosin was again responsible for failure to obtain pure compounds containing the greater part of the pyrethrosin molecule. The formation of the polymeric ozonides and epoxide compounds also complicated the investigation.

Failure to obtain formaldehyde from the ozonization of the pyrolysis product from the diazomethane-pyrethrosin adduct indicates that diazomethane adds across the double bond adjoining the methylene group.

Pyrethrosin, A Secondary Alcohol.

Four of the five oxygen atoms in pyrethrosin may be accounted for by the acetate and lactone structures known to be present in the molecule (29). No positive evidence as to the nature of the fifth oxygen atom existed when the author began work on the problem. Since all of the many attempts to prepare carbonyl and hydroxyl derivatives had failed, it was assumed that these groups were absent or in some way powerfully hindered. Alkoxyl determinations (4) show the absence of an ethoxyl or methoxyl group (29). The possibility of an ether linkage between larger fragments of the molecule existed.

The possibility of the existence of a powerfully hindered hydroxyl group was suggested by Stanton's (29) discovery that pyrethrosin possessed nearly one equivalent of active hydrogen. Dihydropyrethrosin also possesses a little less than one equivalent of active hydrogen.

The presence of a tertiary alcohol would be in accordance with most of this evidence.

However, pyrethrosin and dihydropyrethrosin are oxidized by chromic oxide in acetic acid and water to dehydropyrethrosin and dehydrodihydropyrethrosin respectively. These products (obtained in small yield) differ from the starting materials only by the loss of two hydrogen atoms and must be ketones since they yield 2,4-dinitrophenylhydrazones and oximes, yet give no tests for aldehydes. Hence pyrethrosin and dihydropyrethrosin must be secondary alcohols.

This evidence led to the repetition of many attempts made by earlier workers to prepare hydroxyl derivatives. These experiments as well as treatment with ketene and 3-nitrophthalic anhydride all failed to give hydroxyl derivatives of pyrethrosin. Pyrethrosin failed to react with any acetic anhydride in pyridine either under reflux (3 hrs.) or when allowed to stand eight days in the reagent. This latter evidence and the low yields of dehydropyrethrosin and dehydrodihydropyrethrosin raise doubt about the conclusion that the fifth oxygen atom is part of a secondary hydroxyl group. However, it is difficult to explain the formation of a ketone which differs from pyrethrosin only by the loss of two hydrogen atoms on the basis of any other structure. It is perhaps to be expected that the yield of dehydropyrethrosin would be low since oxidation might well attack the double bond or the rather sensitive acetate structure.

Active hydrogen determinations (11) on dihydropyrethrosin and dehydropyrethrosin support the theory that the fifth oxygen atom is that of a secondary alcohol, but the evidence is none too conclusive. In the first place, dihydropyrethrosin gives values ranging from six to eight tenths of an equivalent of active hydrogen. If this is due to the alcohol group, then dehydropyrethrosin should show no active hydrogen. However, it gives from two to three tenths of an equivalent. This fraction of an equivalent of active hydrogen may be due to enolization of the ketone.

Discussion of the Determination of Methyl on Carbon.

Oxidation of pyrethrosin with chromic oxide to determine the number of methyl groups attached to carbon using a modification of the method of Kuhn and Roth (13), gave results showing that two or slightly more than two molecules of acetic acid are formed per molecule of pyrethrosin. This formation of acetic acid shows the presence of at least two methyl groups attached to carbon. There may be more such groups since it has been shown that the yield of acetic acid depends upon the nature of the other groups attached to the methyl-carbon structure. There are many cases reported (13) where the yield of acetic acid is as low as fifty percent when calculated on the basis of methyl groups attached to carbon.

The determination of methyl on carbon for the high melting form of dihydropyrethrosin was interesting because it showed the existence of a minimum of three such groups. This is excellent corroboratory evidence of the presence of a double bond methylene group in pyrethrosin, since hydrogenation would yield an additional methyl group. This evidence also supports the earlier work indicating that the methylidene group is not a part of an isopropenyl linkage since the structure would give an extra methyl group on hydrogenation but could not form additional acetic acid on oxidation.

Discussion of Other Oxidations of Pyrethrosin.

In general all other oxidations of pyrethrosin did not produce significant results.

Selenium dioxide in boiling dioxane attacked pyrethrosin but yielded only thick syrups which could not be identified or conveniently characterized.

The Oppenauer (17) oxidation of pyrethrosin using aluminum tertiary butoxide in dry acetone and benzene failed to give any dehydropyrethrosin but apparently left the pyrethrosin unchanged.

Hydrogen peroxide oxidation by Fenton's method (7) failed to give any dehydrodihydropyrethrosin; excess hydrogen peroxide with pyrethrosin in boiling ethyl acetate failed to attack pyrethrosin to any considerable extent.

Nitric acid oxidation of pyrethrosin, dihydropyrethrosin and some alcohols obtained by hydrogenation of pyrethrosin yielded only syrupy mixtures of acids and neutral compounds which could not be purified or identified.

Potassium permanganate attacked pyrethrosin vigorously in the cold but no oxidation products could be obtained. Continuous ether extraction of a water soluble portion from cold permanganate oxidation of pyrethrosin yielded a few milligrams of a neutral crystalline substance melting at 120°. Efforts to repeat this work failed and only syrups were obtained.

It may be significant that dihydropyrethrosin is not attacked by permanganate in the cold for this fact is in general agreement with some other evidence indicating the absence of a double bond in dihydropyrethrosin.

Discussion of Absorption Spectrum of Pyrethrosin.

The ultraviolet absorption spectrum+ of pyrethrosin failed to show a maximum in the range investigated and tells little of a positive nature about the molecule. It indicates the absence of an unaltered carbonyl group or a carbonyl group conjugated with a double bond (5,15).

Pyrethrosin, A Mixture of Isomers.

The fact that pyrethrosin is a natural product and has a nucleus of fifteen carbons after the acetate group is removed suggests that it belongs to the sesquiterpenoid series. The presence of a methylidene group which is so common in the terpenoids supports this assumption. Since even the crystalline, naturally occurring sesquiterpenoids are usually mixtures of isomers where the positions of the double bonds vary (9,20,22,23,24,26), it seems logical to consider the possibility that pyrethrosin is a mixture of very similar isomers.

There is much experimental evidence which can be construed to support this possibility. Pyrethrosin reacts with about eight tenths of an equivalent of permonophthalic acid (29) and about the same amount of ozone suggesting that part of the substance may have the double bond in a more hindered position. Likewise, pyrethrosin (29) and dihydropyrethrosin exhibit only about six to eight tenths of an equivalent of active hydrogen.

Pyrethrosin yields at least two isomers when a mole of hydrogen is added to form dihydropyrethrosin and at least two isomers when it reacts with diazomethane to give an adduct (29). Likewise permonophthalic acid gives a mixture of epoxide products. All these facts may be explained by assuming that pyrethrosin is a mixture of double bond

+The author is indebted to Mr. Herbert Wiseman for obtaining the absorption spectrum.

isomers.

The failure to obtain a better yield of formaldehyde may be due to the fact that not all the substance has the double bond adjacent to the methylene group.

The failure to obtain better yields of dehydropyrethrosin may be due to the presence of isomeric forms of pyrethrosin involving the hydroxyl group.

EXPERIMENTAL PART

Purification of Pyrethrosin.

The pyrethrosin used in these studies was obtained from some crudes supplied by McCormick Spice Company of Baltimore, Maryland. It was extracted with hot ethyl acetate and recrystallized from ethanol. As many as eight recrystallizations failed to give a product melting at 200-201°, which was the melting point obtained by Stanton (29) after three recrystallizations. However, a single recrystallization from acetone raised the melting point from 196-8° up to 199-201°. The prism type of crystals first noticed by Anspon (1) gradually changes on standing into the bipyramid type of crystal. Under the microscope the tiny bipyramids may be seen growing off the sides of the prisms. Both forms have the same melting point. The prisms may be grown quite consistently by rapidly cooling a saturated ethanolic solution.

Oxidation of Pyrethrosin by Selenium Dioxide.

Two grams of pyrethrosin dissolved in 40 ml. of ethanol was treated with .75 grams of selenium dioxide in 10 ml. of ethanol. The mixture was stirred and heated under reflux for eight hours. At the end of this time reaction had occurred to only a slight extent, so it was continued for an additional 24 hours. A test of some of the solution, using sulfur dioxide showed that some of the selenium dioxide remained.

Three grams of pyrethrosin dissolved in 30 ml. of dioxane was treated with 1.1 grams of selenium dioxide in 30 ml. of dioxane and the mixture was refluxed for four hours. A dark red color quickly developed and in less than an hour the walls of the flask were coated with selenium. A test with sulfur dioxide at the end of four hours showed no unreacted selenium dioxide.

No crystalline products were obtained from either of the two above oxidations and attempts to prepare bisulfite addition products, oximes, semicarbazones and 2,4-dinitrophenylhydrazones of the thick syrups obtained, resulted in failure in all cases.

Ozonization of Pyrethrosin Compounds

Description of the Ozonizer

An apparatus for generating ozone essentially like that described by Smith (27) was constructed. The transformer supplied 15,000 volts when connected to a 110 volt A. C. circuit. The oxygen was dried by passing it through concentrated sulfuric acid, two calcium chloride tubes, and finally through a tube containing Anhydrone. Three Berthelot+ tubes in series generated the ozone, and excess ozone was destroyed by bubbling it into acid solutions of potassium iodide. The concentration of ozone generated was measured by bubbling it into acid solutions of iodate free potassium iodide and titrating the liberated iodine with standard thiosulfate. The percent ozone in the ozonized oxygen varied between 4.5 and 6 percent under the conditions used in the experiments to be described.

Experiment I

Eight grams of pyrethrosin was dissolved in 30 ml. of dry chloroform and ozonized for 20 minutes in a salt-ice bath at -8°. The ozonization was stopped when the rubber tubing on the outlet cracked indicating that ozone was passing through the reaction mixture. Without changing the rate of flow of the gas stream, the amount of ozone being

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+The author is indebted to Dr. Frank Howard of the National Bureau of Standards for the loan of the Berthelot tubes.

produced in five minutes was determined iodimetrically and found to be about .0033 mols. Thus the .026 mols of pyrethrosin absorbed about .013 mols of ozone. The above experiment was repeated using 5 grams of pyrethrosin in 25 ml. of chloroform; in this experiment .0165 mols of pyrethrosin absorbed about .011 mols of ozone. The ozonide from the above two runs was decomposed by allowing the chloroform solution to drop slowly into 200 ml. of water containing 3 grams of powdered zinc and a trace of hydroquinone and silver nitrate. The water was heated to boiling and stirred. The chloroform distilled out the condenser of the flask and was collected in a trap cooled to -10°. The chloroform in the trap gave no test for aldehydes. The mixture in the flask was refluxed for 30 minutes. The gray solid which settled out on the bottom of the flask was filtered off and separated from the zinc by dissolving the solid in alcohol. The alcohol was evaporated to half its volume and about .5 grams of a grayish substance formed on cooling. After purification this material was shown to be pyrethrosin. Further concentration of the alcoholic solution gave another small amount of pyrethrosin and then a yellow solid which was leached with hot ethyl acetate to remove all pyrethrosin. This yellow solid was amorphous. It was purified by dissolving it in ethanol and precipitating it out by adding water. The resulting product could not be caused to crystallize but dried to a solid which was ground to a powder which possessed a yellow tinge. The final product melted at 360-370° and burned to leave a white residue which gave a color change from green to purple with dithizone showing the presence of zinc. Acidification of this compound gave only a sticky gum which could not be caused to crystallize.

The water soluble fraction from the ozonization was acid and reduced large amounts of potassium permanganate. Neutralization with sodium hydroxide produced a gelatinous, curdy precipitate of zinc hydroxide.

Experiment II

Five grams of pyrethrosin in 30 ml. of chloroform was ozonized at -10° for 10 minutes until the rubber exit tube cracked. The amount of ozone absorbed was about .6 moles per mole of pyrethrosin. This ozonization was repeated using another 5 grams of pyrethrosin; the ozone absorbed was about .5 moles per mole of pyrethrosin. The combined ozonides were decomposed by refluxing the chloroform solution with 200 ml. of water in a three necked flask. The chloroform distilled over and 7 grams of a gummy solid was formed on top the water. This solid was yellow at first but turned red on boiling. This substance was filtered off and washed with water. Observation under the microscope showed the substance was optically isotropic. Leaching with hot ethyl acetate removed the red color from the material. Over ninety percent of the solid remained. It was very slightly soluble in chloroform, water, benzene, ether and ethyl acetate. When dry, the solid was ground into a powder which melted at 360-370°. This powder was soluble in ethanol and dioxane, changing to a taffy-like material before dissolving. It could not be induced to crystallize from either solvent or from ethanol and dioxane mixed with other solvents. Repeated leaching with hot ethyl acetate and reprecipitation from ethanol by water did not change the character of the substance which remained optically isotropic and still melted at 360-370° with decomposition. This final product was ground into a powder, dried at 73° in vacuo for four hours and analyzed.

Mg. of Sample	Mg. of Water	Mg. of Carbon Dioxide	Percent C	Percent H
5.810	3.807	12.690	59.60	7.33
3.820	2.518	8.290	59.22	7.38

Calculated for $C_{17}H_{25}O_7$: % C = 59.80; % H = 7.39

On pyrolysis this substance yielded aclear liquid distillate which was identified as acetic acid by preparing its p-phenylphenacyl ester (6). This ester melted at 112-113 and showed no depression when mixed with the same ester prepared from acetic acid. The substance was not acid but took up excess alkali slowly. It would not form a 2,4-dinitrophenylhydrazone and gave no free iodine with acidic potassium iodide.

The ethyl acetate leachings were combined and evaporated to leave about .2 grams of a light red colored gum which could not be caused to crystallize.

The aqueous layer from the decomposition of the ozonide was distilled until only 3 or 4 ml. remained. The distillate was acid and required 200 ml. of .069 N sodium hydroxide to neutralize it. The neutralized solution was concentrated to about 10 ml. and the p-phenylphenacyl ester of the acid prepared. After recrystallization the ester melted at 113° and showed no depression when mixed with the same ester of known acetic acid.

Experiment III

Five grams of pyrethrosin in 50 ml. of chloroform was ozonized at -10° for 20 minutes. A second similar ozonization was carried out and the combined solutions were run into 100 ml. of boiling water. The chloroform was distilled over and the water refluxed for one hour. A brown gum formed on top the water. The water layer was distilled over until about

5 ml. remained. A test portion of the distillate showed it was acid and would discolor permanganate. Another portion was treated with mercuric oxide according to directions given by Mulliken (16) and gave colloidal mercury indicating the presence of formic acid. The remainder of the distillate was neutralized with sodium hydroxide, made acid with acetic acid, and treated with a seven per cent solution of dimedone (30) in ethanol. A precipitate formed and was filtered off after standing over night. This precipitate was recrystallized once from ethanol and water. It melted sharply at 189°. The dimedone derivative of known formaldehyde melted at 189° and showed no depression when mixed with the sample prepared as above.

Several ozonizations of pyrethrosin were then made to determine what conditions of ozonization and decomposition would give the maximum yield of formaldehyde. Yields ranging from 9.5 percent to 39.6 percent of theory for one mole of formaldehyde per mole of pyrethrosin were obtained when chloroform was used as a solvent.

The ozonization which gave the yield of 39.6 percent of theory is described below. Two grams of pyrethrosin in 50 ml. of chloroform was ozonized for 25 minutes at -10° until ozone was detected in considerable concentration in the exit gases. The ozonide was decomposed by boiling with water, hydroquinone, zinc and silver nitrate for one hour. The aqueous layer was distilled and additional water added twice. The distillates yielded .75 grams of dimedone derivative melting at 189°. The chloroform layer was extracted twice with water and the water extract treated with dimedone. The yield of product melting at 189° was .032 grams.

In the various runs made, the amount of ozone was varied from one half a mole equivalent to several mole equivalents and the time of decomposition varied from 15 minutes to an hour and a half but in no case was the yield of formaldehyde greater than 40 percent of theory for one mole of formaldehyde per mole of pyrethrosin. The chloroform soluble matter from these ozonizations was saved for further study. If zinc dust, hydroquinone and silver nitrate were omitted from the decomposition mixture the yields of formaldehyde were cut in half.

Ozonization of Pyrethrosin in Ethyl Acetate.

One gram of pyrethrosin in 70 ml. of ethyl acetate was ozonized at -8° for 22 minutes until ozone appeared in the exit gas. The ozonide was decomposed by refluxing the ethyl acetate solution with 100 ml. of water, an excess of powdered zinc, and a trace of hydroquinone and silver nitrate. The water layer was distilled and combined with water used to extract the ethyl acetate layer. Treatment with dimedone gave .43 grams of product melting at 188°. It showed no depression when mixed with known formaldehyde dimedone derivative. This yield corresponded to 45 percent of theory. The ethyl acetate layer was evaporated to dryness. The residue was a brown sticky syrup. It gave no test for aldehydes with Schiff's reagent and failed to give a precipitate with dimedone. With 2,4-dinitrophenylhydrazine this syrup gave a red gum which could not be caused to crystallize or otherwise be purified.

Ozonization of the Syrup Obtained by Alkaline Hydrolysis of Pyrethrosin.

One and one-tenth grams of the dried syrup obtained by treating pyrethrosin with strong sodium hydroxide according to Stanton (29) was dissolved in 70 ml. of ethyl acetate and ozonized for 22 minutes at -9°. The ozonide was decomposed with water, zinc, hydroquinone and silver nitrate in the usual manner. The aqueous layer was treated with dimedone and gave .53 grams of product melting at 189°. This product showed no depression in melting point when mixed with an equal amount of the dimedone derivative of formaldehyde.

Ozonization of Dihydropyrethrosin.

One gram of dihydropyrethrosin (m. p. 198-205°) in 50 ml. of dry chloroform was ozonized for 20 minutes at -7° until ozone was evident in the exit gas by its reaction with potassium iodide. About one-fourth a mole equivalent of ozone appeared to be absorbed. The ozonide was decomposed by refluxing for one hour with 50 ml. of water containing excess zinc dust and a trace of hydroquinone and silver nitrate. The water and chloroform layers remained clear in contrast to the red color which developed in them when pyrethrosin ozonide was decomposed. The water layer was distilled, neutralized with sodium hydroxide, made acid with acetic acid and treated with dimedone. About .01 grams of a brownish precipitate formed. It melted with decomposition at around 170°. Recrystallization failed to give any product melting at 189°. The small amount of yellow gum which was insoluble in the water was not investigated. The results indicated that dihydropyrethrosin yields no formaldehyde on ozonization.

Acid from the Ozonization of Pyrethrosin.

One gram of pyrethrosin was dissolved in 70 ml. of ethyl acetate and ozonized for 20 minutes at -7° until ozone was detected in the exit gases. The solution was added to 50 ml. of water and refluxed for one hour. The water layer was evaporated under reduced pressure to almost dryness. On standing several hours a crystalline product formed. After recrystallization from ethanol, the product melted with decomposition at 204°. The weight of the product was 75 mg. Further recrystallization from ethanol did not raise the melting point but recrystallization from acetone yielded a pure product which melted at 209°. It was soluble in water and took up alkali in the cold. The ozonization was repeated using 4 grams of pyrethrosin in 200 ml. of ethyl acetate and the decomposition carried out as before. Half of the water layer from the decomposition was refluxed with 1 ml. of 30 percent hydrogen peroxide in an attempt to increase the yield of acid. However, each portion of the water layer yielded about .1 gram of the acid previously obtained. This acid was dried over phosphorous pentoxide at 78° in vacuo for one hour. The following neutral equivalents were determined in water solution.

Mg. of Sample	Ml. of .01002 N NaOH	Neutral Equivalent
13.990	4.52	309
24.080	7.67	314
20.783	6.70	310

Carbon and hydrogen analyses gave these results

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent H	Percent C
5.710	3.941	11.878	7.72	56.77
5.592	3.829	11.574	7.66	56.48
3.232	2.270	6.716	7.86	56.71
Calculated for $C_{15}H_{24}O_7$			7.65	56.90

Mol. wt. = 316.34

This acid would not take up any excess alkali which was run in after the first end point was reached.

Acid from the Ethyl Acetate Layer on Decomposition of Pyrethrosin Ozonide.

The ethyl acetate layer from the ozonization and decomposition of 4 grams of pyrethrosin was put in an open flask in the desk. When the ethyl acetate had evaporated to half its volume some triangular crystals were observed on the bottom of the flask. These were filtered off and dried. The substance melted at 190° with decomposition. It was very slightly soluble in ethyl acetate and chloroform but soluble in water and alcohol. Five recrystallizations from hot acetone gave about 70 mg. of small, hard crystals which melted at 219° with decomposition. A slight yellow tinge could not be removed by charcoal nor could the melting point be raised. The substance was acid. It was dried in vacuo at 78° for 2 hours and analyzed.

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent C	Percent H
3.255	2.334	6.445	54.03	8.02
4.460	3.163	8.813	53.92	7.94

29.639 mg. of the acid required 4.65 ml. of .01945 N sodium hydroxide to produce a permanent pink using phenolphthalein as an indicator. Neutral equivalent = 328.

Calculated for $C_{15}H_{26}O_8$: % C = 53.88; % H = 7.79.

Mol. wt. = 334.36

The remainder of the ethyl acetate was allowed to evaporate at room temperature but no more crystalline matter formed. The red syrupy residue was soluble in chloroform but not in ether or benzene. A chloroform solution of it was extracted with 5 percent sodium hydroxide but only a syrup was obtained on acidifying this aqueous layer. The chloroform layer yielded a gum.

Investigation of the Chloroform and Ethyl Acetate Soluble Matter from Ozonization.

A neutral fraction of the gum obtained from the chloroform soluble material from decomposition of the ozonide was dissolved in ethanol and treated with 2,4-dinitrophenylhydrazine according to the method of Shriner and Fuson (25). A dark red, resinous material was obtained. After drying this residue could be pulverized to a red powder which melted over a range of 136-144°. This product was difficultly soluble in ethanol and formed a dark red gum when warmed with the alcohol. This substance could not be caused to crystallize from any solvent but in all cases came out as a gum which dried to a hard mass much like the original. An attempt to make a 2,4-dinitrophenylhydrazone of the gum obtained from ozonization of pyrethrosin in ethyl acetate failed.

Attempts to prepare a p-phenylphenacyl ester of some acid material from the various ozonizations failed to yield any crystalline material.

Attempts to Decompose the Ozonides of Pyrethrosin Catalytically (31)

One gram of pyrethrosin in 70 ml. of ethyl acetate at -7° was ozonized until one equivalent of ozone had been passed into the solution. The solution was then placed in a bomb and 2 grams of Raney nickel added. Hydrogen was run into the bomb to a pressure of 1000 pounds and the bomb was shaken for 15 minutes at room temperature. No drop in pressure was observed. After filtering off the nickel and evaporating the ethyl acetate, the residue was treated with a solution of 2,4-dinitrophenylhydrazine but no evidence of hydrazone formation was observed.

The above ozonization was repeated and the ethyl acetate solution was run into a well stirred mixture of 2 grams of Raney nickel in 30 ml. of ethyl acetate according to a procedure like that described by Whitmore (31). No heat was formed and no visible reaction occurred so the mixture was refluxed for 45 minutes. The nickel was filtered off and the solution evaporated to dryness. A few crystals were found imbedded in the syrup which comprised the main part of the residue. The crystals were identified as pyrethrosin. The syrup failed to show any reaction with a solution of 2,4-dinitrophenylhydrazine.

Ozonization of the Product Obtained by Pyrolysis of the Diazomethane Adduct of Pyrethrosin.

The diazomethane adduct of pyrethrosin was prepared according to the method described by Stanton (29). Two grams of the more insoluble adduct was put into a Pyrex test tube carrying a two-holed stopper through which passed a slow stream of nitrogen. The test tube was immersed in a metal bath and the temperature raised to 210°. The compound which melted with a vigorous evolution of gas, was kept at 210-220° for 5 minutes. The melt solidified on cooling to a clear glassy solid. This solid failed to give a test for nitrogen when treated with soda lime and failed to give a test for unsaturation with tetranitromethane.

Eight-tenths of a gram of this product was ozonized in 50 ml. of ethyl acetate at -3° until ozone was detected in the exit gas. The ethyl acetate solution was refluxed with 50 ml. of water containing zinc dust, hydroquinone and silver nitrate. The water layer failed to yield any derivative of dimedone when treated in the same manner as the water layer from ozonization of pyrethrosin. The ethyl acetate layer yielded a syrup which was not investigated.

Preparation of Dehydropyrethrosin.

Four grams of pyrethrosin in 40 ml. of 50 percent acetic acid was oxidized by adding 20 ml. of a 10 percent aqueous solution of chromic oxide to the well stirred solution heated to 85-90°. Addition of the chromic acid solution was at the rate of one drop every 4 or 5 seconds. The reaction mixture was poured on 100 grams of cracked ice and the solid which separated out on standing for one hour in the ice box was filtered off. After three recrystallizations from water and ethanol the product melted over a range of 174-178°. It behaved much like pyrethrosin on melting in that it never formed a char liquid if the temperature of the bath was raised slowly. Further recrystallization failed to raise the melting point to 178° which was the melting point reported for dehydropyrethrosin by Rose and Haller (19). However, the product was shown to be dehydropyrethrosin by carbon-hydrogen analysis. The yield of product was .21 grams. Dehydropyrethrosin failed to give an aldehyde test with Schiff's reagent, Fehling's solution, or Tollen's reagent. It also failed to give a positive iodoform test with iodine and sodium hydroxide.

<u>Preparation of the 2,4-Dinitrophenylhydrazone of Dehydropyrethrosin.</u>

Fourteen-hundredths of a gram of dehydropyrethrosin was dissolved in 8 ml. of ethanol and .10 grams of 2,4-dinitrophenylhydrazine was added. The solution was heated to boiling and .2 ml. of concentrated hydrochloric acid was added. The solution changed to a canary yellow color and a yellow precipitate quickly formed. This product was almost totally insoluble in ethanol. It melted at 248-250° with decomposition, after darkening at 240°. Two recrystallizations from chloroform and ethanol failed to change the melting point. The compound was dried in vacuo at 78° over phosphorus pentoxide for one hour and analyzed.

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent C	Percent H
5.408	2.475	11.275	56.89	5.12
6.325	2.850	13.085	56.48	5.04

4.292 mg. gave .432 ml. of N_2 by Dumas analysis. Temp. = 24.2

Pressure = 767 mm. % N = 11.66

Calculated for $C_{23}H_{24}N_4O_8$: % C = 57.02 % H = 4.99 % N = 11.56.

Preparation of Dehydrodihydropyrethrosin.

Four grams of dihydropyrethrosin (m. p. 203-207°) was dissolved in 40 ml. of 50 percent acetic acid and oxidized by adding 20 ml. of 10 percent aqueous chromic oxide at the rate of one drop every 3 or 4 seconds. The solution was well stirred and kept at 80-90° throughout the addition of chromic acid, after which it was poured on 100 grams of cracked ice. The solid material which formed on standing for one hour was filtered off and recrystallized from ethanol and water; it weighed .53 grams. Two additional recrystallizations from ethanol and water gave a product which melted at 193-195°. Further recrystallization did not change the melting point. The compound gave no test for aldehydes with Schiff's reagent. It was dried in vacuo at 78° for two hours and analyzed.

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent C	Percent H
3.931	2.580	9.600	66.64	7.34
4.264	2.800	10.403	66.65	7.35

Calculated for $C_{17}H_{22}O_5$: % H = 66.65 % C = 7.24

Preparation of the 2,4-Dinitrophenylhydrozone of Dehydrodihydropyrethrosin.

One-tenth of a gram of dehydrodihydropyrethrosin was treated with .08 grams of 2,4-dinitrophenylhydrazine in 8 ml. of ethanol and the solution heated to boiling. On the addition of .2 ml. of concentrated hydrochloric acid the solution turned yellow and a precipitate formed. It was filtered off and recrystallized twice from chloroform and ethanol. This substance melted at 245-248° with decomposition after darkening at 240°. Further recrystallization failed to change the melting point. After drying in vacuo at 78° over phosphorus pentoxide for one hour, the substance was analyzed.

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent C	Percent H
4.055	1.980	8.422	56.68	5.46
4.080	1.990	8.465	56.62	5.46

Dumas nitrogen*

3.308 mg. gave .330 ml. of N_2 at 20.6° and 773 mm.

4.424 mg. gave .440 ml. of N_2 at 20° and 771 mm.

% N = 11.56 and 11.51

Calculated for $C_{23}H_{26}N_4O_8$: % C = 56.78; % H = 5.39; % N = 11.51.

Preparation of the Oxime of Dehydrodihydropyrethrosin.

Two-tenths of a gram of dehydrodihydropyrethrosin was treated with hydroxyl amine hydrochloride and sodium hydroxide according to directions given by Shriner and Fuson (25) for the preparation of oximes. The product which formed on ice cooling was filtered off and recrystallized from ethanol and water. The product consisted of fine silky needles which melted with decomposition at 229-230°, after darkening at 215°. Three more recrystallizations brought the melting point up to 232°, the first darkening occurring at 225°.

Two-tenths of a gram of dehydrodihydropyrethrosin was treated with hydroxylamine hydrochloride in pyridine and absolute ethanol (25) and refluxed for two hours. The solvent was evaporated and the residue triturated with water and filtered. After four recrystallizations from ethanol and water the white silky needles melted at 233° with decomposition. Further recrystallization did not raise the melting point. The yield of product was about .2 grams or about twice the yield by the other

*The author is indebted to Mr. Daniel Kauffman for these analyses.

method. The oxime was dried in vacuo at 78° over phosphorus pentoxide for two hours and analyzed.

Mg. of Sample	Mg. of Water	Mg. of CO_2	Percent C	Percent H
3.379	2.199	7.840	63.39	7.26
3.904	2.503	8.988	62.82	7.17

7.640 mg. by Dumas method gave .289 ml. of N_2 at 22.8° and 769 mm.

$$\% N = 4.41$$

Calculated for $C_{17}H_{23}NO_5$: % C = 63.53; % H = 7.21; % N = 4.36.

<u>Attempts to Increase the Yield of Ketones from Pyrethrosin and Dihydropyrethrosin.</u>

While dihydropyrethrosin gave about twice as much ketone as did pyrethrosin, the yields from both were small. In attempts to increase these yields, the amount of chromic oxide was varied from one equivalent to four, the temperature was varied from room temperature to 100° and the time of heating from 15 to 45 minutes. In no case was the yield of ketone better than that obtained in the experiment described above (.53 grams of dehydrodihydropyrethrosin from 4 grams of dihydropyrethrosin).

The aqueous acetic acid solutions from the oxidations were extracted with various solvents in attempts to obtain more ketone. Ether and benzene took out inappreciable amounts of any product present. When chloroform was used to extract the mixture, the solvent took on a light yellow color. Evaporation of the chloroform left a thick yellow syrup which amounted to about 70 percent of the original dihydropyrethrosin. This syrup was soluble in ethanol but not in water. Various attempts to crystallize the syrup failed. When an ethanol-water solution of this syrup was left to stand open in the desk for five days, some crystals grew out of the oil which first formed on the bottom of the beaker. These crystals were dissolved in ethanol, and water was added to a faint turbidity which was removed by additional alcohol. On standing some long, soft crystals formed; they could not be separated from the syrup adhering to them and attempts to repeat this growth of crystals failed.

Determination of Methyl on Carbon.

The method used was a modification of the micro-method described by Kuhn and Roth (13). Ordinary Pyrex glass was used in place of the quartz equipment described by these authors.

Determinations run on known compounds gave results which were invariably too high no matter how carefully the acetic acid was distilled. A blank for the determination was then found using the same amount of reagents as was used in actual runs on pyrethrosin and dihydropyrethrosin. One hundred and fifty ml. of distillate was collected in all cases and an average blank of .90 ml. of .1490 N sodium hydroxide was required to neutralize the acid which distilled over. The samples were digested with the chromic oxide mixture for one and a half hours in all cases. In the results tabulated below the amount of standard alkali required to neutralize the distillate has been corrected for the blank.

Number of Run	Weight of Pyrethrosin	Ml. of .1490 N NaOH	Equivalents of Acetic Acid per Mole of Pyrethrosin
1	.1305	5.30	1.86
2	.1000	4.35	1.99
3	.1000	4.90	2.24
4	.1000	4.85	2.22

Thus the results show that pyrethrosin yields about two equivalents of acetic acid per mole of pyrethrosin. This establishes the existence of at least two methyl groups on carbon. Determination of methyl on carbon for dihydropyrethrosin (m. p. 203-208°)

Run	Wt. of Sample	Ml. of .1490 N NaOH	Equivalents of Acetic Acid per mol of Dihydropyrethrosin
1	.1002	6.80	3.09
2	.1003	6.60	3.01

The above determinations indicate the existence of at least 3 methyl groups attached to carbon in the dihydropyrethrosin molecule.

Oxidation of Pyrethrosin According to Oppenauer (17)

Ten grams of pure dry pyrethrosin was dissolved in 100 ml. of acetone which had been distilled from potassium permanganate and dried over Drierite. To this mixture was added 100 ml. of benzene which had been distilled from sodium. This was refluxed on an oil bath at 80-85°, whereupon 8 grams of aluminum tertiary butoxide in 100 ml. of dry benzene was added. The mixture was refluxed for eleven hours on the oil bath at 80-85°. The condenser was equipped with Drierite tube at the top. After the mixture was cool it was treated with 20 ml. of water and acidified with 50 ml. of 10 percent sulfuric acid. The benzene layer was separated and washed with 50 ml. of concentrated aqueous sodium bicarbonate. The benzene layer was then washed three times with 50 ml. portions of water. The benzene layer was dried by filtering it twice through sodium sulfate. It was evaporated down to 40 ml. Some crystals formed on the walls of the flask. They weighed about one gram and were identified as pyrethrosin by melting point and mixed melting point determinations. A thick yellow liquid remained when the pyrethrosin was filtered off. This liquid was evaporated on the steam bath to a yellow semisolid material which was recrystallized from ethanol to give 4 grams of a product melting at 185-190°. Three additional recrystallizations gave a product which melted at 190-191°. Recrystallization from acetone and two additional recrystallizations from ethanol raised the melting point to 192-193°. Sintering began at 189° and no clear liquid was ever obtained even at a temperature of 250°. The general behavior on melting was much like that of pyrethrosin except that the loss of crystalline form began about 9 degrees lower. A mixed melting point with an equal amount of pyrethrosin showed a typical loss of crystalline form at 187-188°.

This product (.5230 grams) in 13 ml. of chloroform gave a negative rotation of -1.15° with sodium vapor light at 25°. $\alpha^{D}_{25} = -31.2$; pyrethrosin has $\alpha^{D}_{25} = 33.6$ in chloroform. This product which did not form a dinitrophenylhydrazone was dried at 78° in vacuo over phosphorus pentaxide for 2 hours and analyzed.

4.234 mg. of sample gave 2.795 mg. of water and 10.294 mg. of carbon dioxide.

% C = 66.37 % H = 7.39

Calculated for $C_{17}H_{22}O_5$: % C = 66.65; % H = 7.24

The aqueous layer from acidification of the oxidation mixture was combined with water used to wash the benzene layer and the whole evaporated down to 50 ml. Three grams of a heavy gum was obtained. It could not be caused to crystallize. Benzene extracts of the acidified sodium bicarbonate washings yielded only a brown syrup.

Active Hydrogen Determinations on Dihydropyrethrosin and Dehydropyrethrosin.

These determinations were made using the "Grignard machine" described by Kohler, Fuson and Stone (11).

Dihydropyrethrosin and dehydropyrethrosin are not appreciably soluble in isoamyl ether so the samples were dissolved in toluene which had been dried by refluxing for 4 hours over sodium and distillation from the sodium. The toluene was shown to have a negligibly small blank. Each sample was dissolved in 7 ml. of toluene. The reaction chamber was swept out for 15 minutes before adding the Grignard reagent. The mixture of reagent and sample was heated to 100° for 10 minutes. After addition of water the reaction chamber was again heated to 100° for 5 minutes.

	I	II
Mols of Grignard reagent	.00139	.00139
Mols of Dihydropyrethrosin	.000334	.000374
Mols Methane from sample	.000229	.000312
Mols Methane per mole of sample	.69	.84
Mols reagent used	.0011	.00105
Mols reagent used per mole of sample	3.3	2.8

	I	II
Mols of Grignard reagent	.00118	.00133
Mols of Dehydropyrethrosin	.000357	.000385
Mols of Methane from sample	.000074	.000121
Mols of Methane per mole of sample	.21	.31
Mols of reagent used	.00075	.00093
Mols of reagent used per mole of sample	2.1	2.4

Investigation of Products Obtained by Drastic Hydrogenation of Pyrethrosin.

Sixty-eight grams of pyrethrosin was dissolved in 450 ml. of dioxane and 23 grams of copper-chromite catalyst was added to the mixture in the bomb. The mixture was hydrogenated at 300° and 7000 pounds pressure for 4 hours, until hydrogen was no longer absorbed. After the catalyst had been filtered from the solution, the latter had a slight blue color. The dioxane was removed under the pressure of the water pump by warming on the steam bath. The residue was fractionally distilled under 1-2 mm. pressure. Four cuts were made of the distillate.

	Weight	Boiling range	Pressure
I.	6 grams	60-90°	1-2 mm.
II.	14 grams	110-130°	1-2 mm.
III.	12 grams	130-148°	1-2 mm.
IV.	8 grams	150-190°	1-2 mm.

The first fraction was a clear liquid of low viscosity and was given to Anspon (1) who had shown that it was a hydrocarbon mixture.

The second fraction had been shown by Anspon (1) to be chiefly a mixture of alcohols corresponding closely to the formula $C_{15}H_{28}O$. Six ml. of this alcohol mixture was dehydrated by passing it through a tube containing alumina at 295-300° at the rate of about 3 drops per minute. About 4.5 ml. of a green liquid of low viscosity was obtained. This liquid gave a strong tetranitromethane test. It was dried over drierite in ether and distilled after removing the ether. It started to reflux at an oil bath temperature of 230°. Refractive index, n_D^{26} = 1.484.

Two and five-tenths ml. of this liquid was dissolved in 50 ml. of 30-60° petroleum ether which had been carefully purified. The purification was carried out by stirring the petroleum ether with fuming sulfuric acid for 20 hours. The petroleum ether was washed with sodium hydroxide and dried over phosphorus pentoxide. The final product gave negative tests for unsaturation when treated with tetranitromethane, permanganate, and bromine.

The petroleum ether solution was ozonized for 40 minutes at -6° until ozone was detected in the exit gas. The ozone absorbed was almost exactly one mole of ozone per mole of hydrocarbon if the hydrocarbon was assumed to be $C_{15}H_{26}$. The ozonide was observed to be an amorphous white substance in the petroleum ether. The solvent was evaporated; there remained a viscous syrup which was transferred to a flask containing 50 ml. of water and 10 ml. of hydrogen peroxide and refluxed for 30 minutes. The mixture was left to stand over night and a thick oil formed on the water. This oil was taken up in ether and dried over Drierite. The ether was evaporated; a viscous yellow liquid remained. A neutral equivalent of this material indicated that the substance contained considerable non-acid material. Hence it was partitioned between ether and an aqueous solution of sodium hydroxide. The acid obtained on acidification of the alkali amounted to about one-third the original product. An attempt to make a p-phenylphenacylester of this fraction gave only a brown oil which could not be crystallized. The neutral fraction from the ether layer was an oil which was treated with 2,4-dinitrophenylhydrazime. It gave only a brown gum which could not be crystallized.

The water layer from the decomposition of the ozonide was neutralized with sodium hydroxide, taken to dryness, dissolved in water, acidified with sulfuric acid to congo red paper and distilled. The distillate was neutralized with 2.54 ml. of .1490 N sodium hydroxide and treated with an equivalent amount of p-phenylphenacylbromide. The ester which formed was recrystallized twice from ethanol and melted at 110°. Mixed with an equal amount of known p-phenylphenacylester of acetic acid is showed no depression in melting point.

Active hydrogen was determined on the hydrogenation fraction boiling at 130-143° under 1-2 mm. (III). .1812 grams of sample yielded .00080 mols of methane when treated with an excess of Grignard reagent. A total of .00091 mols of reagent was consumed. If the alcohol mixture is assumed to correspond to $C_{15}H_{28}O$, .99 mols of methane was liberated per mole of alcohol and 1.12 moles of Grignard reagent was consumed per mole of alcohol.

Both of the alcohol mixtures distilling at 110-130 (II) and 130-143 (III) were treated with iodine and sodium hydroxide but no iodoform was formed in either case.

Ten grams of the fraction distilling at 130-143° under 1-2 mm. (III) was oxidized with concentrated nitric acid but only thick syrups which could not be purified or identified were obtained. About half of the products were acidic and half were neutral.

Anspon (1) has shown by carbon-hydrogen analyses that the fraction distilling above 150° under 1-2 mm. (IV) contained a higher percent of oxygen than the lower boiling fractions. The analysis agreed fairly well with the formula $C_{15}H_{26}O_2$. Active hydrogen determinations showed less than half an equivalent of active hydrogen. Determination of alkoxyl by Clark's modification of Viebock method (4) showed the absence of any methoxyl or ethoxyl groups.

Potassium Permanganate Oxidation of Pyrethrosin.

Two and six-tenths grams of pyrethrosin in 30 ml. of acetone was run into a three-necked flask containing 50 ml. of acetone and 1 gram of powdered potassium permanganate. The solution was stirred until the pink color disappeared. An additional 3 grams of permanganate was added in 1 gram portions during the course of an hour and stirring was continued until the pink color was gone. The manganese dioxide was filtered off and the acetone evaporated to leave a small amount of a brown liquid. The manganese dioxide was extracted three times with boiling water. The water was made acid to congo red paper with dilute sulfuric acid and extracted continuously for 24 hours with ether. After the ether layer had been evaporated, about .1 gram of a brown gum which was insoluble in water and only slightly soluble in ethanol remained. This gum was dissolved in benzene and alcohol and left to stand in the open over night. Some very thin, long crystals which formed in the brown gum at the bottom of the beaker were removed, washed with alcohol and recrystallized from benzene and alcohol. This product weighed about 20 mg. and melted sharply at 120°. It was a neutral substance. Since this product was more soluble in benzene than ether, the water extract of the manganese dioxide was extracted continuously with benzene for 24 hours. Only a gum was obtained and it could not be caused to crystallize. All attempts to repeat the formation of the product melting at 120° failed. No crystalline material could be obtained from the acetone soluble material resulting from the oxidation with permanganate.

Dihydropyrethrosin does not reduce permanganate in the cold.

Oxidation of Pyrethrosin with Hydrogen Peroxide.

Five grams of pyrethrosin in 200 ml. of ethyl acetate and 10 ml. of 30 percent hydrogen peroxide was refluxed for one and a half hours; 4.5 grams of pyrethrosin was recovered unchanged. A small amount of a slightly yellow material melting at 175-185° and degassing at 190-200° was also isolated. Further fractional recrystallization of this material from ethanol gave an additional small amount of pyrethrosin and about 50 mg. of a material which melted and decomposed over a range of 180-195°. This product was not investigated further.

Five-tenths of a gram of dihydropyrethrosin in 40 ml. of acetone with .2 grams of ferrous sulfate and .2 ml. of 30 percent hydrogen peroxide was left to stand for 24 hours. The dihydropyrethrosin was recovered unchanged.

Other Unsuccessful Experiments with Pyrethrosin.

Four grams of pyrethrosin in 80 ml. of dry acetone at 0° was treated with 4 moles of ketene per mole of pyrethrosin. The pyrethrosin was recovered unchanged.

The above experiment was repeated and a small drop of concentrated sulfuric acid was added to the acetone. The sulfuric acid was removed by stirring with precipitated calcium carbonate. Evaporation of the acetone left a thick liquid which yielded about 1 ml. of acetic acid on distillation. The residue formed a tough resinous cake on standing. It could not be caused to crystallize.

Two grams of pyrethrosin and .6 grams of maleic anhydride were refluxed for 7 hours in 40 ml. of xylene. A sticky film formed on the flask. Addition of 30-60° petroleum ether caused a clear gummy material to separate out. It could not be crystallized.

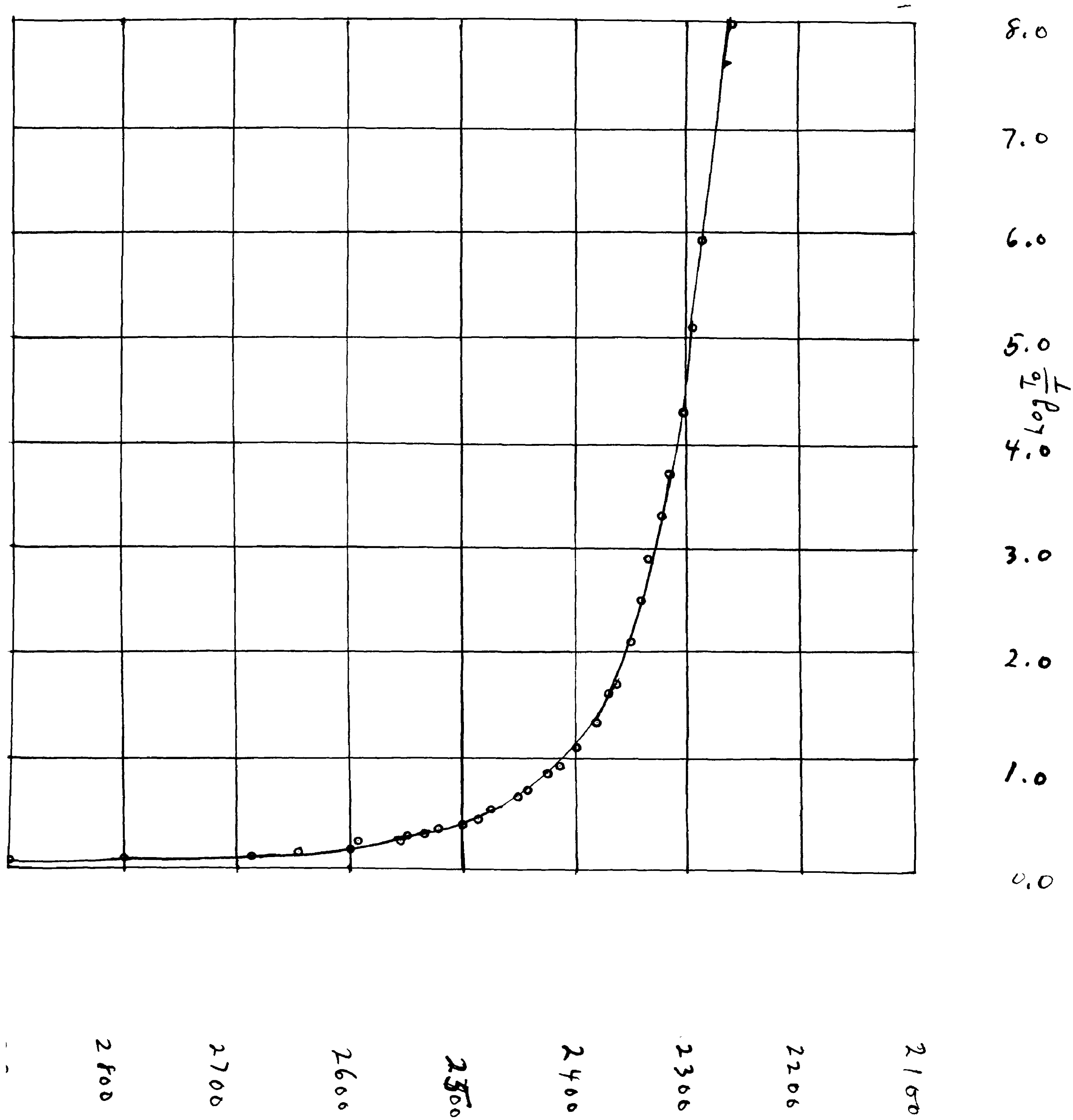
One gram of pyrethrosin and 3 grams of 3-nitrophthalic anhydride were refluxed in 20 ml. of dry toluene for 3 hours. The toluene was removed under the water pump; a yellow gum remained which could not be caused to crystallize.

Five grams of pyrethrosin in 200 ml. of dry benzene was treated with about 7 moles of phenyl magnesium bromide per mole of pyrethrosin. The mixture, containing 50 ml. of ether, was refluxed for 30 minutes, cooled and poured on cracked ice. It was acidified with sulfuric acid and the products were worked up. Except for a small amount of biphenyl no crystalline matter was obtained. The main product was a hard brown glassy material.

Twenty grams of pyrethrosin was pyrolyzed (10) and about 1 ml. of a green liquid distillate collected. It gave a faint yellow color with tetranitromethane. The resinous looking residue gave a similar test. This residue failed to give formaldehyde on ozonization.

Pyrethrosin in Methyl Alcohol

38.5 mg per 50 ml.



SUMMARY AND CONCLUSIONS

1. The ozonization of pyrethrosin yields 45 percent of a mole of formaldehyde per mole of pyrethrosin. This indicates that pyrethrosin possesses a methylidene group.

2. No other aldehydes or methyl ketones are formed by ozonization. This fact suggests that the methylidene group may be attached to a ring and is not a part of an isopropyl carbon skeleton.

3. The isolation from the ozonization of pyrethrosin of two acids which have lost no carbon atoms but those in the acetate group suggests that ozonization may have failed to cleave the double bond in at least a part of the substance.

4. Pyrethrosin appears to absorb less than a mole of ozone per mole of pyrethrosin which suggests that part of the substance may have the double bond in a more hindered position.

5. Pyrethrosin apparently forms a polymeric ozonide when ozonization is conducted in chloroform or acetic acid.

6. Pyrethrosin and dihydropyrethrosin are oxidized by chromic acid to give dehydropyrethrosin and dehydrodihydropyrethrosin, respectively. These products are ketones which differ from the starting material only by the loss of two hydrogen atoms. Hence pyrethrosin and dihydropyrethrosin are secondary alcohols.

7. Pyrethrosin, when oxidized by the chromic oxide method of Kuhn and Roth yields two molecules of acetic acid per mole of pyrethrosin. Thus pyrethrosin has at least two methyl groups attached to carbon. The higher melting isomer of dihydropyrethrosin has at least three methyl groups attached to carbon. This supports the theory that pyrethrosin possesses a methylidene group.

8. Dehydropyrethrosin shows about two or three-tenths of an equivalent of active hydrogen while pyrethrosin and dihydropyrethrosin show about six to eight-tenths of an equivalent of active hydrogen. This fact indicates that the active hydrogen in pyrethrosin is due to the secondary alcohol group which has been oxidized to a ketone group in dehydropyrethrosin.

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