原　著

Studies on Pyrocin, a New Compound found in the Dry Distillation Products of Pyrethrum Extract and Pyrethrum Flowers. Masanao MATSUI (Laboratories of the Nissin Chemical Co. and Department of Chemistry, College of Science, Kyoto University.) Received Jan. 31, 1950. *Bolyu-Kagaku* 15 : 1—20, 1950.

1. Pyrocin に就て

松井正直〔日新化學工業株式會社研究室(大阪)及び京都大學理學部化學敎室〕

25. 1. 31. 受理

長瀬氏が除虫菊エキス乾溜物中から得た一新物質は $C_{10}H_{16}O_2$ なる組成と lactone の性質を有し，酸化により *trans*-caron 酸と acetone とを與へる。著者は之にパイロシン (*Pyrocin*) と命名し，之を合成しその構造を明にした。

先づその酸化生成物から，その構造が次の何れかであることが推定される。

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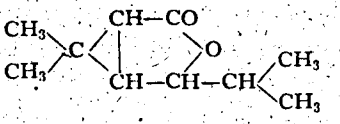

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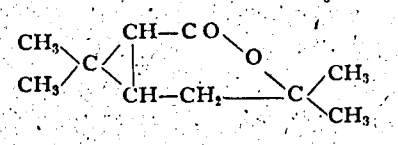
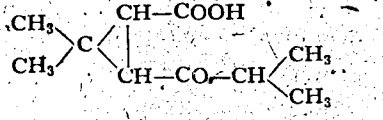


Pyrocin は d-*trans*- 第一菊酸を眞空封管中で 30 分間 400° 迄加熱し分子内轉位を起させて生ぜしめ得る。尙合成の dl-*cis*-*trans*- 第一菊酸を同樣に處理することにより dl-Pyrocin が生ずる。Pyrocin は mp 83.5°～84.5°, $[\alpha]_D^{21}=-75.5°$ (in ether), dl-Pyrocin は mp 59°～60° である。

今合成 *cis*-caron 酸から出發して III (mp 83°) を

III



作り之を Na-Hg で -CO- を還元して lactone を作ると之は油狀物で，dl-Pyrocin と性質全く異る。之に依り Pyrocin が II の構造を有することは先づ疑がないが，更に Pyrocin の alcohol 基を遊離のものとし，之に種々な第三級 alcohol 基反應を行うと何れもこの反應を示す。依つて Pyrocin の alcohol 基は第三級 alcohol 基であり從つてその構造は II であることが判明した。

尙 Pyrocin は相當の殺虫力があり，除虫菊花の燻煙中からはまだ分離されて居ないが恐らくその內に存在し，その殺虫力に相當の寄與をしてゐるものと考えられる。

INTRODUCTION

It was a question for number of years that what substances in the smoke of pyrethrum flowers (*Chrysanthemum cinerariaefolium*), has the insecticidal power.

For the substances discovered in the smoke of pyrethrum flowers, we can find many reports from R. Yamamoto [1], S. Takei, K. Wakasono et al [2], and M. Nagase [3]. Nagase found several substances in smoke of the flower besides pyrethrin which have insecticidal power. He concluded that the toxicity of the smoke owes to the combined actions of all these materials. In the course of previous study, he obtained also a new compound * by dry distillation of Pyrethrum flowers or its extract.

As this substance had a considerably high toxicity on mosquito, it became an interesting problem to confirm its structure and manifest the mechanism of its formation. After studying its properties, Nagase and present writer suggested a chemical structure which has a lactone and a cyclopropane ring [4].

Is it logical to establish this imaginary structure? From what substance in pyrethrum flower this compound was derived? Is there some element which has an insecticidal power, in the substances resembling to this structure? From these viewpoints

* Hereafter the writer wishes to name this lactone "*Pyrocin*".

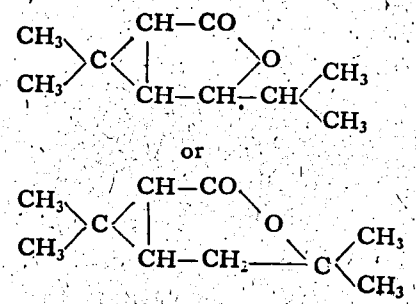
the writer has made this present study.

I Preparation of Pyrocin by Dry Distillation of Pyrethrum Flowers or Extract of the Flower.

The writer has repeated Nagase's experiments and obtained Pyrocin which has boiling point of ca. 110°/10 mm, ca. 127°/15 mm, ca. 130°/16mm, and melting point of 83.5°~84.5°.

The condensed pyrethrum extract(Pyrethrin content 40 %) or commercial pyrethrum extract (Pyrethrin content 15 %)or the powder of dry pyrethrum flowers was dry-distilled. After saponified with alkali, the distillate was steamed and removed from the neutral part, then acidified with sulphuric acid and subjected again to steam distillation. To the distillate was added sodium chloride and it was extracted with ether. The ether extract was washed with sodium carbonate solution several times and was removed from acids. From the ether solution, ether was distilled off and the remaining oil was distilled under reduced pressure. Pyrocin thus obtained as a colourless oil, crystallized in a short time as hexagonal plates. It was recrystallized from petroleum ether or ligroin in columner crystals which melts at 83.5°~84.5°, having a rotatory power $[\alpha]_D^{21} = -75.5°$ (in ether). This substance has a molecular formula $C_{10}H_{16}O_2$ and gives *trans*-caronic acid * and aceton on oxidizing with potassium permanganate.

From these experimental evidences, following structural formulae may be proposed for Pyrocin as shown in the previous article[4]



or

Experimental

1) Pyrocin from condensed pyrethrum extract (Pyrethrin content 40 %)**

10 g of condensed pyrethrum extract was distilled in 50 cc flask on a sand bath under slightly reduced pressure. The distillation was repeated ten times. The distillates were collected and saponified by boiling with 100 cc of 10 % methanolic potash on a water bath. The reaction product was treated with steam, methanol and volatile neutral substances were removed, after adding 50 cc of 30 % sulphuric acid, it was subjected to a steam-distillation until the distillate shows no longer acidity. Sodium chloride was added to the acidic distillate and it was extracted with ether in an extractor for 24 hrs. The ether extract was washed with each 10 cc of 10% sodium carbonate solution four times then with water three times. It was dried on anhydrous sodium sulphate and filtered. After removal of ether, the remaining oil was distilled under reduced pressure. The main part distilled at 105°~115°/10 mm. On leaving it stand in a refrigerator over night, the crystal——colourless hexagonal plates——was separated.

It was recrystallized from petroleum ether or ligroin in crystals which amounted to 1g, having melted at 83.5°~84.5°. It is called Pyrocin which smells like cinnamon.

Analysis:——

Sample mg	CO_2 mg	H_2O mg	C %	H %
2.509	6.565	2.115	71.36	9.61
$C_{10}H_{16}O_2$			71.42	9.52

2) Pyrocin from commercial pyrethrum extract(Pyrethrin content 15 %)

* The geometric structure of oxidation product of some compound does not always show the geometric structure of the starting substance, for example, furfural is oxidized to fumaric acid or maleic acid according to conditions. [Milas : J. Am. Chem. Soc. **49**, 2035 (1927)] Yataro Obata : J. Agr. Chem. Soc. Japan, **16**, 188 (1940)

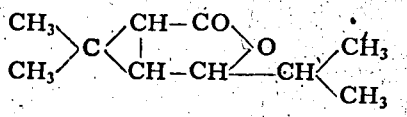
** cf. 4)

50 g of commercial pyrethrum extract was distilled from 100 cc flask by a direct heating. It was repeated six times and the distillates were collected. It was saponified with 400 cc of 10% methanolic potash by boiling for 3 hrs. The reaction product was treated as same as in 1) and 2g of Pyrocin —bp 125°~130°/15 mm, mp 83.5°~84.5°— was obtained.

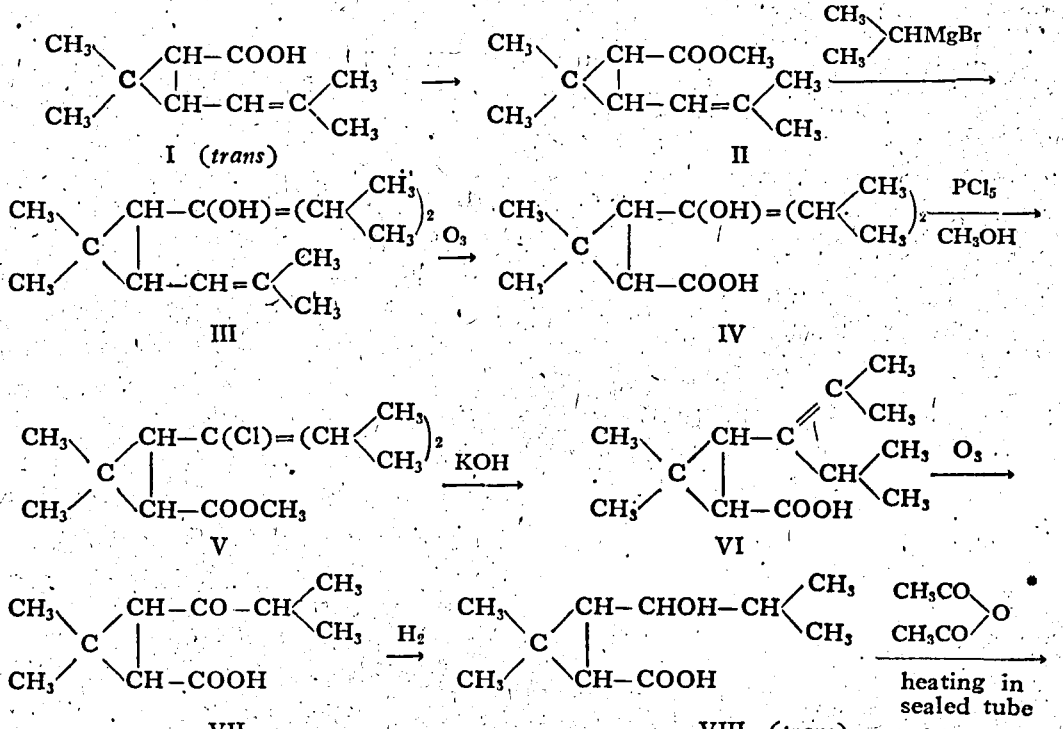
3) Pyrocin from dry pyrethrum flower. 100 g of dry powder of pyrethrum flowers (Pyrethrin content 0.9%) was dry-distilled from a Pyrex flask on a sand bath. This was repeated twenty times. The collected distillate was saponified with 1000 cc of 10% methanolic potash by boiling for 3 hrs. and subjected to the similar processes as stated in the former cases, 0.5 g of Pyrocin — bp 125°~135°/16 mm, mp 83.5°~84.5° — was obtained.

II. Preparations of *trans*-1,1-Dimethyl-2-diisopropyl-hydroxymethyl-cyclopropane carboxylic acid (3) and *cis*-1,1-Dimethyl-2-(1'-isopropyl-2'-methyl-2'-hydroxy-)-propyl-cyclopropane carboxylic acid (3) lactone.

At first the writer thought that Pyrocin should have a five-membered lactone ring, owing to the ordinary rule that a five-membered lactone ring is more stable than that of six-membered.

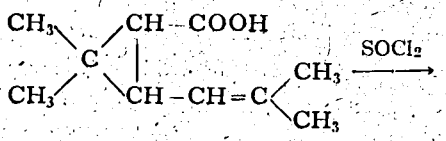


He, therefore, tried to synthesize this substance from chrysanthemum-monocarboxylic acid by the following scheme.

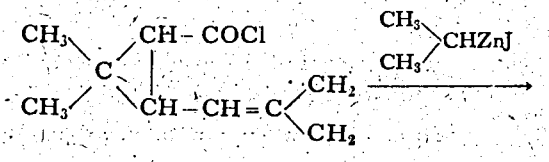


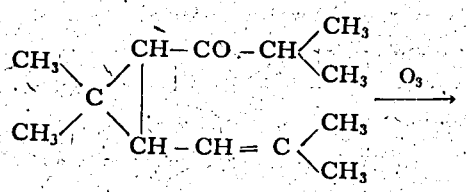
* *trans*-caronic acid and *trans*-homocaronic acid are converted to *cis*-anhydrides by the same condition, the writer therefore expected this reaction in this case.

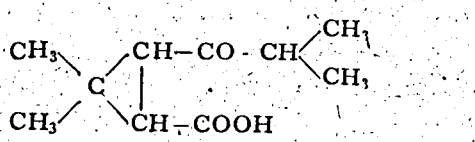
In this scheme, however, the reaction V to VI did not proceed as the writer has expe cted: the yield of V was so small and it was converted itself to the original IV by the alcoholic potash treatment. He, therfore, was obliged to give up this attempt. To get VII, the following processes should be adopted.



I

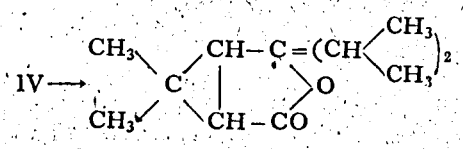






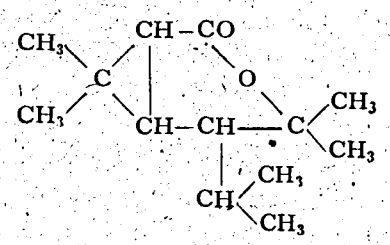
VII

In order to know the structure of Pyrocin, the writer now, tried to obtain *cis*-1,1-Dimethyl-2-diisopropyl-hydroxymethyl-cyclopropane carboxylic acid (3) lactone (X) from IV. For this purpose, IV was



X

treated with three volumes of acetic anhydride in a sealed tube at 230° for six hours, but no noticeable change has been occured, the starting material was recovered. In the meantime, it was found as described in the later article that chrysanthemum-monocarboxylic acid can be converted into Pyrocin by heating at 400° in a vacuum sealed tube. By the same treatment, IV was converted into a lactone, of which the structure, as described later, is not X but *cis*-1,1-dimethyl-



XI

2-(1′-isopropyl-2′-methyl-2′-hydroxy)-propyl cyclopropane carboxylic acid (3) lactone (XI). It was also obtained by another method as described in the next article.

Experimental

1) *trans*-Chrysanthemum-monocarboxylic acid (I)

This was prepared from pyrethrum extract by the ordinary method [5]. Colourless viscous oil, bp 145°～146°/13 mm.

2) Methyl *trans*-chrysanthemum-monocarboxylate (II)

This was obtained from (I) and diazomethane in ether solution. It boils at 86°～87°/10 mm.

3) *trans*-1,1-Dimethyl-2-diisopropyl-hydroxymethyl-3-isobuten-(1)-yl cyclopropane (III)

5 g of the above ester was added drop by drop under stirring and cooling in an ice-salt bath into the Grignard's reagent which has been prepared from 13 g of isopropyl bromide and 2.5 g of magnesium in dry ether. After leaving the reaction mixture over night, it was decomposed with ice and dil. sulphuric acid and extracted with ether. The ether extract was washed with water, dried on anhydrous sodium sulphate and then ether was removed. The remaining oil was distilled under a reduced pressure. The desired compound bp 114～

116°/9 mm) was obtained as a colourless viscous oil which amounted to 4.5 g.

Analysis :——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.560	10.499	4.038	80.43	12.60
$C_{16}H_{30}O$			80.67	12.61

4) *trans*-1,1-Dimethyl-2-diisopropyl-hydroxymethyl cyclopropane carboxylic acid (3) (IV)

2 g of the alcohol (III) was dissolved in 40 cc of chloroform and ozonized air was passed through it for 3 hrs. After this treatment the solvent was removed under reduced pressure at room temperature. To the remaining syrup some ice was added and left over night. The reaction mixture was then boiled for 3 hrs. on a water bath. On addition of 10 cc of 10 % caustic potash solution, it was extracted with ether to remove the neutral part. The residual alkali solution was acidified with dil. sulphuric acid and extracted with ether again. The ether extract was washed with water for three times and dried on anhydrous sodium sulphate. The solvent was removed and the residual oil was distilled under reduced pressure. The desired acid was distilled at 155°～160°/5 mm. It was a very viscous oil which crystallized in a refrigerator. After recrystallizing from petroleum ether it melts at 94°～95°.

Analysis :——

Sample mg	CO_2 mg	H_2O mg	C %	H %
4.610	11.535	4.406	68.24	10.62
$C_{13}H_{24}O_3$			68.42	10.52

5) Heat treatment of *trans*-1,1-dimethyl-2-diisopropylhydroxymethyl-cyclopropane carboxylic acid (3) with acetic anhydride.

1g of (IV) was heated with 3 g of acetic anhydride in a sealed tube at 230° for 6 hrs. After cooling, the content was distilled under reduced pressure. Acetic anhydride was recovered and then the main distillate boiling at 155°～160°/5 mm was collected. It crystallized, melting at 94°～95°. It was (IV) itself.

6) *cis*-1,1-Dimethyl-2-(1'-isopropyl-2'-methyl-2'-hydroxy)-propylcyclopropane carboxylic acid (3) lactone (V)

1.2 g of the above acid (IV) was placed in a glass tube and it was evacuated to 7 mm -Hg, then sealed under this pressure. The sealed tube was heated up to 400° for 30 minutes in an electric furnace and then left stand to cool. The content was coloured very slightly and some water was observed on the inside wall of the tube. On opening, it was noticed that reduced pressure was kept, showing that any decomposition did not take place besides dehydration. The content was dissolved in ether and the ether solution was washed with 10 % sodium carbonate solution, then with water. After removal of the solvent, the remaining oil was boiled with 10 cc of 10 % methanolic potash for 2 hrs. After this procedure some water was added and methanol was removed under reduced pressure on a water bath. The water solution extracted with ether and acidified and extracted with ether again. The ether solution was washed with water, dried on anhydrous sodium sulphate, then distilled. The desired lactone was obtained as a colourless oil, boiling at 76°/13 mm, n_D^{12}= 1.4668, d_{15}=0.94, yield 0.7g.

Analysis:——

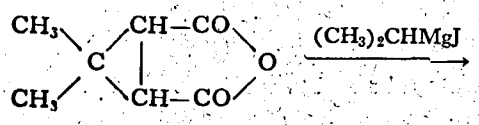
Sample mg	CO_2 mg	H_2O mg	C %	H %
2.9575	8.0789	2.8336	74.49	10.72
$C_{13}H_{20}O_2$			74.28	10.47

This is an isomer of the lactone which will be described in the next article.

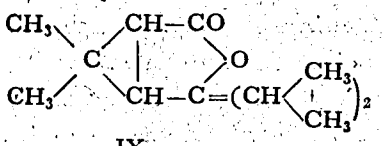
III Preparation of *cis*-1,1-Dimethyl-2-diisopropylhydroxymethyl-cyclopropane carboxylic acid (3) lactone.

In order to ascertain whether the lactone described in the previous article has a five-membered lactone ring or a six-membered, *cis*-1,1-dimethyl-2-diisopropylhydroxymethyl-

cyclopropanecarboxylic acid(3)lactone (IX) was synthesized. It was obtained from caronic anhydride, upon which isopropylmagnesiumiodide was reacted.



VIII



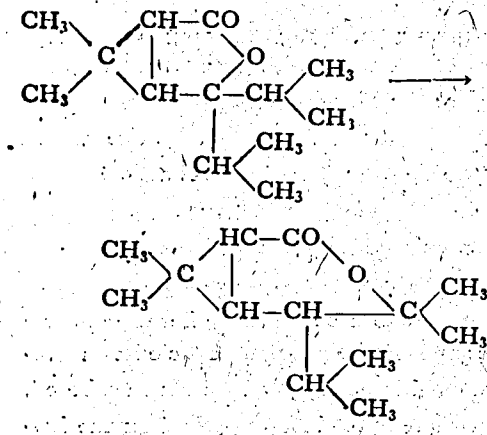
IX

The prepared lactone was colourless rhombic plate which melts at 46°~47° (from petroleum ether). The boiling point was 145°~147°/30 mm. It is easily soluble in chloroform and difficult soluble in petroleum ether and ligroin. It has the characteristics of lactone and a sweet fragrance and has some insecticidal power.

It is obvious from the synthesis that this lactone has a five-membered lactone ring[16]).

The lactone described in the previous article must have a six-membered ring, being quite different in properties from this lactone.

It is noteworthy that this lactone was converted into the lactone in the previous article by heating at 400° in vacuo.



Experimental

The starting material, caronic acid may be prepared by several methods[6.7.8]). The writer used the modified methods of Koetz[7]) and Perkin[8]). The processes were somewhat round about and the yields were not good. They were as follows:——

1) Ethyl isopropylidenmalonate (I)[7])

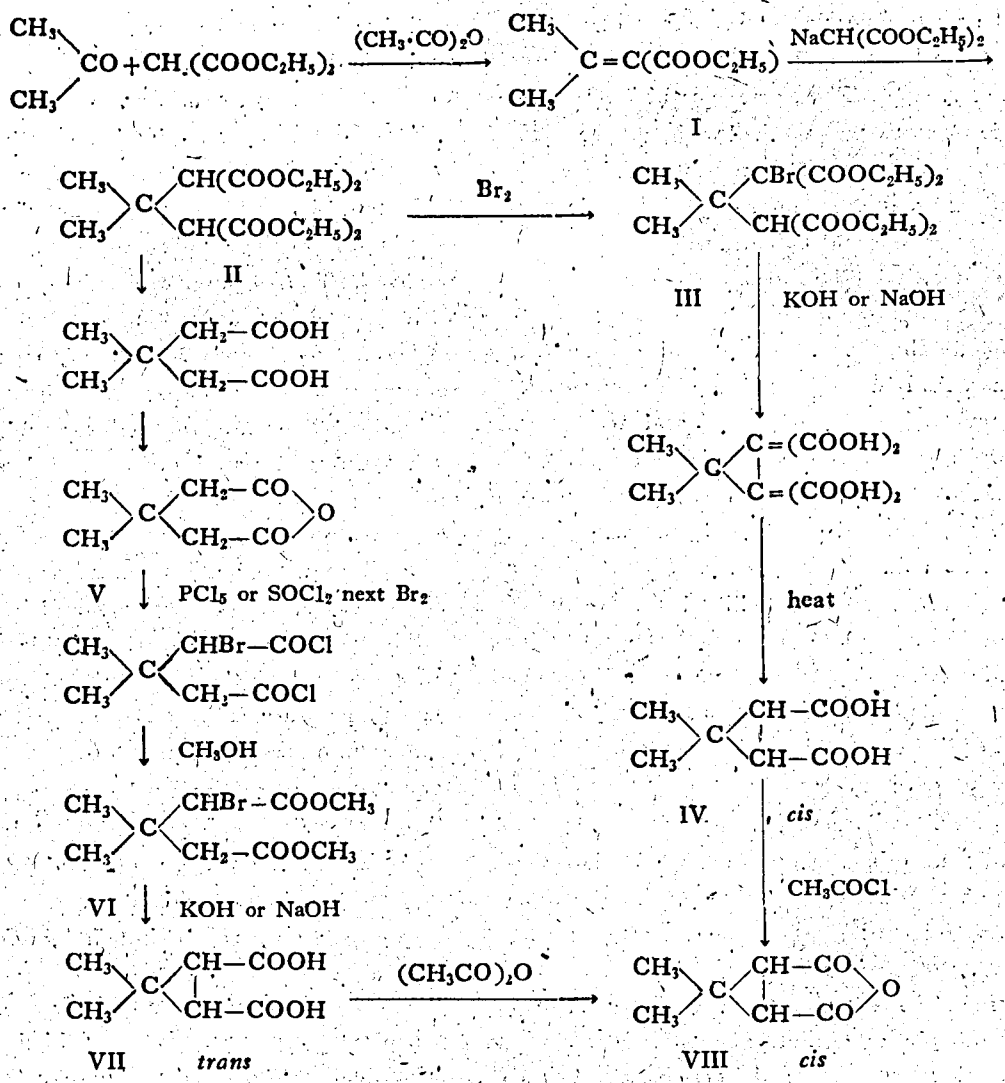
75 g of acetone, 160 g of ethyl malonate, 120 g of acetic anhydride and 10 g of zinc chloride (freshly fused) were placed in an autoclave and heated at 100° for 14 hours. After cooling the reaction mixture was poured into water and oily layer was separated. This was washed with saturated sodium carbonate solution until it showed no more acidity, then it was washed with water and dried on calcium chloride. After filtration, the oil was distilled. At first small quantity of ethyl acetate was obtained. Then it was distilled under reduced pressure.

a)	~	100°/25 mm	–
b)	100° ~	120°/25 mm	55 g
c)	120° ~	150°/25 mm	65 g
d)	150° ~	/25 mm	–

The greater part of(b)was recovered ethyl malonate, (c) was the mixture of ethyl malonate and ethyl isopropylidenmalonate. The greater part of (c) was the latter. By redistillation of this part, pure ethyl isopropylidenmalonate is obtainable which boils at 138°~141°/20 mm. But the redistillation was unnecessary in order to prepare next ethyl isopropylidendimalonate. The distillates (b) and (c) was used under that condition. The yield of the above condensation does not change in the scale of 640 g of ethyl malonate.

2) Ethyl isopropylidendimalonate (II)[7]);

The solution of 8 g of metallic sodium in 70cc of methanol was placed in an autoclave, and to it the distillate (b) (55 g) in above mentioned was added with stirring and then the distillate(c) was added in the same way.



After this, the mixture was heated at 90°~100° for 48 hours.

After cooling, water was added and the mixture was filtered using Buchner funnel on which charcoal is spread. Then filtrate was extracted with benzene. The benzene extract was washed with water and dried on calcium chloride. From this benzene solution, the solvent was removed and the remaining oil was distilled under reduced pressure. After unchanged ethyl malonate and ethyl isopropylidenmalonate were recovered at 130°/12 mm, the thermometer rose up suddenly and the ethyl isopropylidendimalonate was distilled at 190°~195°/12 mm. Yield, 18g.

3) Ethyl bromoisopropylidendimalonate (III)[7]

20 cc of carbon tetrachloride was added to 50 g of ethyl isopropylidendimalonate, and to this mixture 8 cc of bromine was added drop by drop with stirring and cooling with ice and salt. After the addition was completed, the mixture was left over night. If the colour of bromine does not discharge, the mixture was warmed on a water bath until the decolourization is completed. After cooling, the mixture was poured into the water and heavy oily layer is separated.

The water layer was extracted with benzene and the benzene extracts were combined to the oily layer. The benzene-carbontetrachloride solution was washed with 10% sodium carbonate solution, then with water. After the solution was dried on calcium chloride, the solvents were removed and the remaining oil was distilled. The substance boiling at 145°~180°/2mm was 37 g. The remainder was considerably large quantity of carbonized mass. As Koetz reported, the halogenization seems to be not completed and moreover dehalogenization took place in some portion during distillation. However, if this distillation was carried out, the crystallization of caronic acid was very easy. But in order to obtain caronic acid this distillation was unnecessary. After removing the solvents under reduced pressure, the remaining oil was reacted with methanolic soda or potash. The yield of caronic acid seems to be better in this case.

4) *cis*-Caronic acid (IV)[7]

37g of ethyl bromoisopropylidendimalonate was added drop by drop from the top of reflux condenser to the warm solution of 40 g of caustic soda or potash in 150 cc of methanol and kept boiling gently. After the completion of addition, boiling was continued for 10 hours on a water bath. Then water was added and the methanol was removed under reduced pressure. The remaining mixture was extracted with benzene and the neutral materials were removed. After this, the solution was acidified with hydrochloric acid and extracted with ether in an extraction apparatus. From the ether extract, the solvent was removed and the remaining syrup was added to three volumes of chloroform and was placed in a refrigerator. Crystal *cis*-caronic acid was separated and recrystallized from water. The melting point was 171°~172°. Its melting point was not depressed by admixing with *cis*-caronic acid from chrysanthemum-monocarboxylic acid. Yield, 6 g.

5) β, β-Dimethylglutaric anhydride (V)

40 g of ethyl isopropylidendimalonate was boiled with 40 g of 50% sulphuric acid for 12 hours. Upper layer is extracted with ether and from the ether extract solvent was removed. The remaining oil was saponified with 70 g of 30% caustic soda solution on boiling for four hours. If oily layer is remaining, this will be removed by ether extraction. The water solution was acidified with hydrochloric acid and extracted with ether in an extraction apparatus.

From the ether extract, the solvent was removed and to the remaining syrup was added 40 cc of acetic anhydride and boiled for 3 hours. The greater part of acetic acid and acetic anhydride was removed under ordinary pressure. The remaining part was distilled under reduced pressure. Distillate from 160° to 180°/30 mm (the greater part 164°~166°)was crystallized soon after distillation. This was dried on unglazed porcelain plate, mp 140°. Yield 16 g.

6) Methyl-α-brom-β, β-dimethylglutarate (VI)

To 13 g of the above anhydride 25 g of phosphorous pentachloride was added and the mixture was warmed under reflux condenser on a water bath until the phosphorous pentachloride dissolved completely (this chlorination was also carried out with thionyl chloride). Then the mixture was cooled with ice-salt, and 5.5 cc of bromine was added drop by drop. After violent evolution of hydrogenbromide was over, the mixture was warmed on a water bath until the colour of bromine completely discharged. After it cool down, the mixture was poured into 100 cc of cooled anhydrous methanol drop by drop and this was left stand over night. The reaction mixture was poured into 80 cc of water and the heavy oil was se-

parated, the upper layer was extracted with ether four times and the ether extracts were combined to the oily layer. The combined solution was washed with 10% sodium carbonate solution, then with water. The ether solution was dried on calcium chloride. Little oil was separated when the sodium carbonate washing was acidified with hydrochloric acid. From the ether solution, the solvent was removed and the remaining oil was distilled. The desired material was collected at 180°~185°/40 mm. By redistillation, it boils at 172°/20 mm and weighed 19 g.

7) dl-*trans*-Caronic acid (VII)

20 g of methyl-α-brom-β,β-d methylglutarate was added drop by drop to the warm solution of 20 g of caustic soda or potash in 60 cc of methanol and the mixture was boiled for 10 hours on a water bath. Then water was added and the methanol was removed. It was acidified with hydrochloric acid and treated once with active carbon. After this, it was extracted with ether in an extraction apparatus. From the ether extract, the solvent was removed. Remaining syrup crystallized in a short time, three volumes of chloroform was added to it and the mixture was placed in an ice box. The crystal was collected and wahsed with chlorform. It was recrystallized from water, yield 6 g, mp 210°. The test of the melting point, admixing with authentic substance, proved to be *trans*-caronic acid.

8) Caronic anhydride (VIII)

i. Five grams of *trans*-caronic acid was heated with 15 cc of acetic anhydride at 220° in a sealed tube for six hours. After cooling, the tube was unsealed and the content was distilled. The distillate at 143°/20 mm soon crystallized. It was recrystallized from dry ether. Colourless crystal mp 56° was obtained. Yield 3.5 g. It coincides with next caronic anhydride from *cis*-caronic acid by the test.

ii. Five grams of *cis*-caronic acid was treated with 15 cc of acetyl chloride until the evolution of hydrogen chloride ceased. Then the solution was distilled under reduced pressure. Caronic anhydride was collected at 123°~126°/8 mm. It was recrystallized from dry ether, mp 56°, yield 3.6g.

Analysis:——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.751	8.120	2.105	59.61	6.34
$C_7H_8O_3$			59.74	5.76

9) dl-*cis*-1,1-Dimethyl-2-diisopropyl-hydroxymethyl-cyclopropane-carboxylic acid (3),lactone

6.9 g of caronic anhydride which was dissolved in 20 cc of dry benzene, was added with stirring and cooling into the Grignard's reagent which was prepared from 20 g of isopropyl iodide, 2.7 g of magnesium and 40 cc of dry ether by the ordinary method. When addition was completed, the mixture was gently boiled for two hours. After cooling, it was poured in to ice and dil. sulphuric acid was added until precipitate dissolves. The mixture was extracted with ether and the ether extract was washed with water. From the ether solution, the ether was removed. The remaining oil was saponified with 25 g of 25% caustic soda solution by boiling for four hours. 33 cc of water was added and the neutral oil was removed by ether extraction. The water solution was acidified with hydrochloric acid and extracted with ether once. The ether extract was washed with water and dried on the anhydrous sodium sulphate. From the ether solution, the solvent was removed and the remaining oil was distilled under reduced pressure. The distillate at 140°~150°/30mm was collected. It was dissolved in ether and the ether solution was washed with 5% sodium carbonate solution three times and with water three times. The ether solution

was dried on anhydrous sodium sulphate. After filtration, ether was removed and remaining oil was distilled once more. The distillate at 140°～150°/30mm was collected. It crystallized slowly. It was cooled in a refrigerator and the crystals were separated. It was recrystallized from petroleumether. The crystal was colourless hexagonal or rhombic plate, mp 46°～47°, yield 4.5 g.

Analysis: ——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.860	10.42	3.685	73.62	10.68
$C_{13}H_{22}O_2$			74.22	10.48

10) The heat treatment of *cis*-1,1-dimethyl-2-diisopropylhydroxy-methyl-cyclopropane carboxylic acid (3) lactone

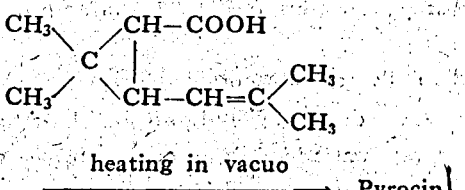
2 g of crystalline lactone (IX) was heated up to 400° in a vacuum (8mm-Hg.) sealed tube in 30 minutes, then heating was stopped. After cooling the tube was opened. It was kept vacuum and the content was almost colourless. The content was dissolved in ether and washed with 10% sodium carbonate solution three times then with water. The ether solution was dried on anhydrous sodium sulphate then distilled. As the distillate, the following two fractions were obtained (i) bp 74°～78°/13 mm (83°/25mm) ca. 0.5 g (ii) bp 140°～150°/30 mm (135°～145°/25 mm) ca. 1.2 g. Fraction (i) has the same elementary composition and index of refraction $n_D^{12} = 1.4670$ as the lactone described in the previous article. Thus, it is obvious that the five-membered lactone converted into the six-membered lactone by the heat.

The fraction (ii) crystallized and melted at 46°～47°, ie. the unchanged lactone (IX).

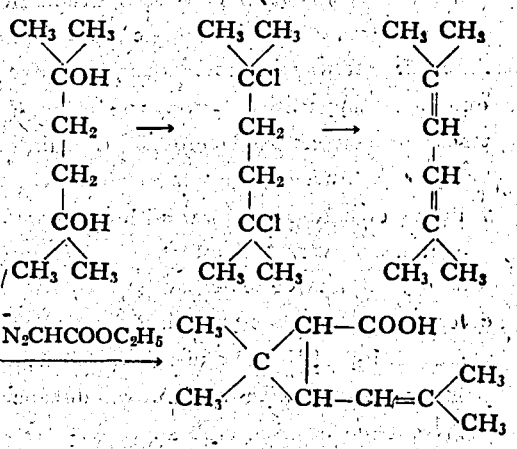
IV Preparation of Pyrocin

In the beginning of these synthetic studies, as it was already described, from the fact that Pyrocin yielded caronic acid and acetone by the oxidation, the writer considered that Pyrocin has been derived from chrysanthemum-monocarboxylic acid. Many trials have been made in vain to prepare it from the acid. For examples; boiling it with sulphuric, hydrochloric or hydrobromic acid of different concentrations. Distillation with a small quantity of sulphuric acid or iodine, heating it in a sealed tube etc.

A method of heating it in a tube sealed under reduced pressure was contrived, by which the preparation of Pyrocin from chrysanthemum-monocarboxylic acid has been achieved at last.



Chrysanthemum-monocarboxylic acid has already been synthesized by Staudinger and Ruzicka [9], as follows:



Therefore it can be said that the total synthesis of Pyrocin has been completed.

About the lactone ring of Pyrocin, it will be discussed in the later article.

Experimental

1) *trans*-Chrysanthemum-monocarboxylic acid. This is prepared as in article II

2) Pyrocin

5g of chrysanthemum-monocarboxylic acid was placed in a glass tube and this was

evacuated to the pressure of 8 mm-Hg, and the tube was sealed. Then this was heated up to 400° in an electric furnace for thirty minutes, then the electric current was off. After cooling in room temperature the tube was opened. The content was kept in the evacuated condition and was scarecely coloured. This shows that the decarboxylation has not been occurred. The content was saponified with 50 cc of 10% methanolic potash by boiling on a water bath for three hours. Then water was added, and from this solution, methanol was removed. The water solution was washed with ether in order to remove some neutral materials which might be produced. The water solution was then acidified with hydrochloric acid and left for a short time. This acidic solution was extracted with ether and the ether extract was washed with 10% sodium carbonate solution four times and then with water three times. The ether solution was completely separated from washing. After removal of the solvent from the ether extract, the remaining oil was soon crystallized. The mixture was placed in an ice box overnight. The crystal was separated and washed with small quantity of petroleum ether. The filtrate and washing were combined and from this, the petroleum ether was removed, the remaining oil was once distilled over, and again this distillate was placed in a refrigerator. The second crop was obtained. It was also recrystallized from ether. The combined crystal weighed 2.5 g, mp 83°~84.5°.

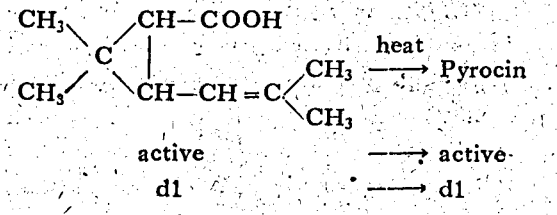
The test of its melting point admixing with authentic Pyrocin obtained from pyrethrum extract did not cause the depression of the melting point.

Analysis:——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.700	9.725	3.250	71.68	9.83
$C_{10}H_{16}O_2$			71.43	9.52

V Preparation of dl-Pyrocin

In the previous article, the writer has described the preparation of Pyrocin. The compound was obtained from optical active chrysanthemum-monocarboxylic acid and had also an optical activity $[\alpha]_D^{21} = -75.5°$ in ether. It was obtained by heating the active chrysanthemum-monocarboxylic acid at 400° in a vacuum sealed tube. In the same way dl-Pyrocin should be obtained from synthetic chrysanthemum-monocarboxylic acid which is a mixture of dl-*trans* and dl-*cis*-chrysanthemum-monocarboxylic acids.



dl-Pyrocin thus obtained was optically inactive and colourless crystal which melted at 59°~60°, it melted at 62°~64° admixing with ca. equal quantity of active Pyrocin which melts at 83°~84.5°.

The starting dl-chrysanthemum-monocarboxylic acids were obtained by the method of Staudinger, Ruzicka et al.[2]*

Experimental

1) dl-Chrysanthemum-monocarboxylic acids [2]

10 g of 1, 1, 4, 4-tetramethylbutadiene and 5 g of ethyl diazoacetate were heated in an autoclave at 80°~100° for 24 hrs. and then 120°~150° for 24 hrs.

The reaction product was distilled and the fraction of 95°~110°/11 mm was collected. It amounted to ca. 2 g. It was saponified with 10% alcoholic potash boiling on a water bath for 4 hrs. Then water was added. Alcohol was distilled off.

The water solution was treated with ether

* The improved method has been reported by Campbell and Harper [J. Chem. Soc. 283 (1945). Chemical Abstract 39, 4319 (1945)]

in order to remove neutral substances. The remaining water solution was acidified with dil. sulphuric acid and it was extracted with ether. The ether extract was washed with water several times and ether was removed from the solution. Remaining oil was distilled under reduced pressure. The substance distilling at 140°～145°/12 mm was collected. It weighed ca. 0.8 g.

Analysis:——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.890	10.205	3.410	71.55	9.74
$C_{10}H_{16}O_2$			71.43	9.52

2) dl－Pyrocin

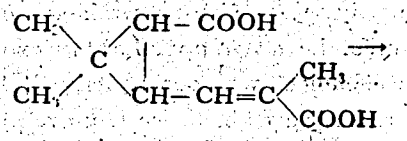
0.5g of dl-chrysanthemum-monocarboxylic acids was heated in a glass tube sealed under the pressure of 8 mm-Hg up to 400° in 30 minutes then the heating was ceased. After cooling, the content was dissolved in ether and the ether solution was washed with 10% sodium carbonate solution several times, then with water. Ether was distilled off from the solution. The remaining oil was saponified with 10% alcoholic potash for 4 hrs. Water was added to the reaction mixture. Alcohol was removed from it. The water solution was extracted with ether and neutral substances were removed. The remaining water solution was acidified with dil. sulphuric acid and it was extracted with ether several times. The ether extract was washed with water. Ether was removed from the solution and remaining oil was distilled under reduced pressure. The fraction boiling at 140°～150°/20 mm was collected. It amounted ca. 0.2 g. It was left for a long time in room temperature. The crystals were collected. They were recrystallized from petroleum ether. The yield of the substance melting at 59°～60° was ca. 50 mg. It melted at 62°～64° admixing with ca. equal quantity of active pyrocin (mp 83.5°～84.5°).

Analysis:——

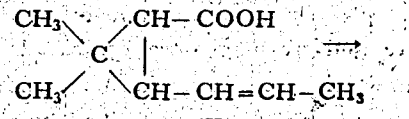
Sample mg	CO_2 mg	H_2O mg	C %	H %
2.733	7.170	2.310	71.54	9.38
$C_{10}H_{13}O_2$			71.43	9.52

VI Preparation of *cis*-1,1-Dimethyl-2-α-hydroxypropyl-cyclopropane-carboxylic acid (3) lactone (Pyrocin β)

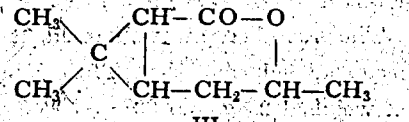
If, in the smoke of pyrethrum flower, there is Pyrocin that is derived from chrysanthemum-monocarboxylic acid, there must be formed in the same way a lactone from chrysanthemum-dicarboxylic acid. The writer, therefore, tried to prepare this lactone* from chrysanthemumdicarboxylic acid (I). Staudinger and Ruzicka has already prepared 1,1-dimethyl-2-propen(1')-yl cyclopropane carboxylic acid (3) (II) by the thermal decomposition of *trans*-chrysanthemum-dicarboxylic acid[10]. If this yield is true, in the same manner as chrysanthemum-monocarboxylic acid, this must rearrange to a *cis*-lactone (III), by heating. Therefore, chrysanthemum-d carboxylic acid was heated in a vacuum sealed tube at 400°. As it was expected, the desired lactone has been obtained, though its amount was too small.



I



II



III

It was an oil boiling at 116°～119°/17 mm and it was confirmed by analysis. Besides the above lactone, an acid boiling at 130°～135°/12 mm was also formed. This was undoubtedly 1,1-dimethyl-2-propenyl cyclopropane carboxylic acid (3) (II) which has been prepared by Staudinger and Ruzicka.

* The writer wishes to name this "*Pyrocin β*"

The above lactone, however, has not been separated from the smoke of pyrethrum flowers. It dues perhaps to reasons that (a) it is an oil, (b) it has the boiling point near that of Pyrocin and (c) it yields in very small quantity etc.

The structure of Pyrocin β may be shown by formula III which will be discussed in the next article.

Experimental

1) Chrysanthemum-dicarboxylic acid (I)

This is obtained from concentrated pyrethrum extract by the ordinary method [1]. Colourless crystal, mp 164°.

2) Pyrocin β

10 g of the above acid was placed in a glass tube which was then evacuated to pressure of 8 mm-Hg and sealed. This was heated up to 400° about 30 minutes in an electric furnace and kept at this temperature for 15 minutes, then left to natural cooling. After reaching to room temperature, the tube was opened and positive pressure was noticed.

The content was considerably coloured and carbonized and a small quantity of water was observed on the inside wall of the tube. From these facts it was known that decarboxylation and dehydration has been taken place.

The content was taken out and once it was distilled over. The distillate was ca. 1.2 g. This was saponified with 10 cc of 10% methanolic potash by boiling for 3 hrs. Then water was added to it. From the mixture methanol was removed completely and the solution was washed with ether in order to remove neutral substances. Then the solution was acidified with hydrochloric acid and left for a short time. The mixture was extracted with ether and the ether extract was washed with 10% sodium carbonate solution five times, then with water three times. The ether solution was dried on anhydrous sodium sulphate. After removal of the solvent, the oil was distilled. After twice distillations, the lactone was collected as a fraction boiling at 117°~119°/17 mm. It was a colourless oil which has a fragrance resembling to that of Pyrocin.

Analysis:——

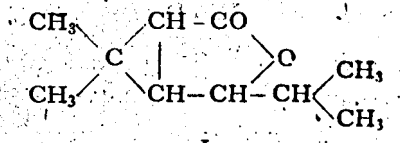
Sample mg	CO_2 mg	H_2O mg	C %	H %
4.880	11.29	3.650	70.54	9.33
$C_9H_{14}O_2$			70.13	9.15

3) 1,1-Dimethyl-2-propenyl cyclopropane-carboxylic acid (3) (II)

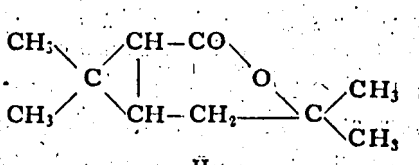
10% sodiumcarbonate washings in experiment [2] were combined. It was washed with ether, then acidified with hydrochloric acid and extracted with ether. The ether extract was washed with water and dried on the anhydrous sodium sulphate. From the ether solution the solvent was removed, the remaining oil was distilled. 1,1-Dimethyl-2-propenylcyclopropane carboxylic acid (3) was obtained as a faint yellowish oil boiling at 130°~135°/12 mm, yield 0.5 g.

VII Structure of Pyrocin

As described in the preceeding articles, it is obvious that Pyrocin has one of the two following formulae,

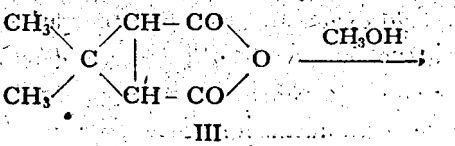


I

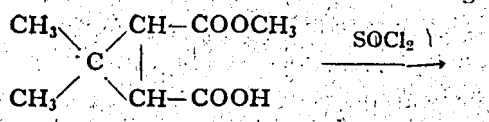


II

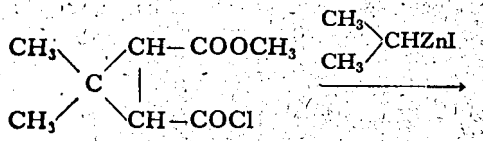
To decide the structure directly, the writer tried to synthesize I in the following scheme:



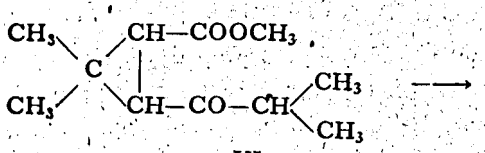
III



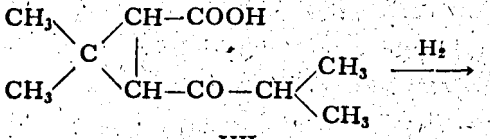
IV



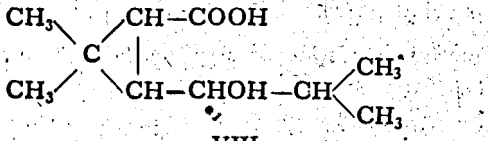
V



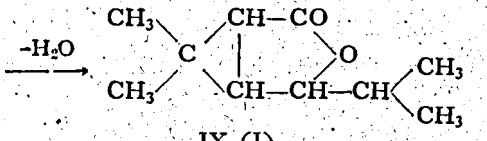
VI



VII



VIII

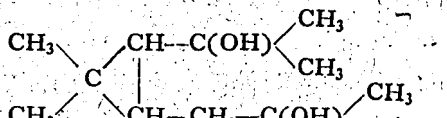


IX (I)

The processes up to VII were successful, but hydrogenation VII to VIII did not proceed smoothly. The writer could not obtain VIII or IX in a pure state. Therefore he was obliged to confirm the structure of Pyrocin by an indirect method.

First, as described in article II, lactone which is obtained from *trans*-1, 1-dimethyl-2-diisopropyl-hydroxymethyl-cyclopropane-carboxylic acid(5) by thermal rearrangement is not the same as *cis*-1,1-dimethyl-2-diisopropylhydroxymethyl-cyclopropane-carboxylic acid(3) lactone which has a five-membered lactone ring, the former consequently should have a six-membered lactone ring. This shows that the compound which has a cyclopropane ring in the α position to carboxyl and a double bond which may be resulted by dehydration) conjugated to the cyclopropane ring, rearranges to a six-membered lactone by heat treatment. Therefore Pyrocin also may have a six-membered lactone structure. Moreover, by oxidation of Pyrocin β, with hydrogene peroxide a ketonic acid *cis*-1,1-dimethyl-2-α-ketopropyl-cyclopropane-carboxylic acid [12] has been obtained. On the contrary, no compound besides recovered Pyrocin has been obtained from Pyrocin by oxidizing with the same reagent. This shows that Pyrocin has tertiary alcohol group and Pyrocin β has secondary one, that is to say, Pyrocin should have the structure II.

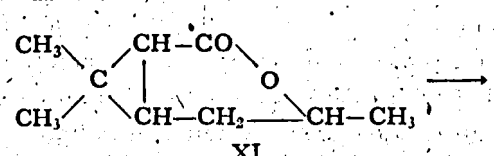
In addition, on treating sodium salt of Pyrocin with Nessler's reagent, coloured precipitate was not obtaind. It shows that the alcohol group of Pyrocin is tertiary one. A diol (X) was derived from Pyrocin by the action of methyl magnesiumiodide.



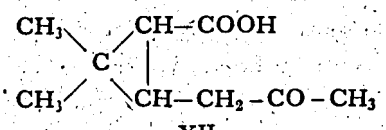
X

The diol gave no coloured precipitate as in the case of sodium salt of Pyrocin on treatment with Nessler's reagent. Then the diol was shaken with chromic anhydride in glacial acetic acid or carbontetrachloride, but it was not oxidized. These facts show that each of the two alcohol group is tertiary one. Thus it has been confirmed that Pyrocin has a six-membered lactone ring, that is to say, its structure is 1,1-dimethyl-2-(α-hydroxy-α-methyl)-propylcyclopropane-carboxylic acid(3) lactone (II). By analogy, it is almost doubtless, Pyrocin β has also a six-membered lactonering and its structure is shown as XI. It is understood to be

convertible into a ketonic acid (XII) by oxidation.



XI



XII

Experimental

1) Caronic anhydride (III)

This was prepared by the method described in the previous article.

2) dl-methyl-hydrogencaronate (IV)

To 10.4 g of caronic anhydride (1 mol) 2.4 g of methanol (1 mol) was added and the mixture was warmed on a water bath for 2 hrs. The reaction mixture was chilled with ice. Methylhydrogen caronate was crystallized. It was separated and was recrystallized from petroleum ether, mp 76°, yield 7 g.

Analysis: ——

Sample mg	CO_2 mg	H_2O mg	C %	H %
1.760	3.612	1.150	55.97	7.31
$C_8H_{12}O_4$			55.80	7.03

3) dl-methyl-*cis*-1,1-dimethyl-2-isobutyryl-cyclopropane-carboxylate (VI)

30 cc of petroleum ether was added to 40 g of the above halfester and to the mixture 40 g of thionyl chloride was added under cooling by ice. This was left for 30 minutes and then warmed on a water bath for 30 minutes. When the evolution of hydrogen chloride ceased, the solvent and excess of thionyl chloride was removed under reduced pressure. The remaining oil weighed 47 g. As described in another paper, it was mainly composed of V and V transformed a part into its *trans*-isomer by a distillation. The oil, therefore, was used without distillation for the further reaction. To 47 g of this crude ester acid chloride, under stirring and cooling with salt, was added the Blaise's reagent which had been prepared from 70g of isopropyl iodide, 21 g of zinc and 35 cc of petroleum ether.* After leaving for 3 hrs. the reaction mixture was decomposed with ice and then neutralized with dil. sulphuric acid. This was extracted with ether. The ether extract was washed twice with 10% sodium carbonate solution which contains a small amount of sodium sulphite then washed with sodium carbonate solution twice and then with water. After the ether solution was dried on anhydrous sodium sulphate, the ether was removed and the remaining oil was distilled. The ketonic acid ester was collected as an oil, boiling at 115°~120°/10 mm. It weighed 21 g. But this was not pure enough, due to contaminating a small quantity of sulphur compounds. The pure ester was prepared by esterification of the free acid with diazomethane. It boiled at 110°/8 mm.

Analysis: ——

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.592	8.769	2.896	66.56	9.12
$C_{11}H_{18}O_3$			66.66	9.09

4) *cis*-1,1-Dimethyl-2-isopropyl-oxomethyl-cyclopropane-carboxylic acid (3) (VII)

9 g of the above ketonic ester was saponified with 20 cc of 20% methanolic soda by boiling on a water bath for 3 hrs., water was added to the reaction mixture and methanol was distilled off completely. The water solution was concentrated to 30 cc it was once filtered and acidified with conc. hydrochloric acid. An oil separated which crystallized in a short time. The crystal was separated and recrystallized from petroleum ether. It weighed 5 g, mp 88°.

* This is the general method of Blaise to obtain ketones [13].

Analysis:—

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.530	8.410	2.815	64.98	8.92
$C_{10}H_{16}O_3$			65.16	8.75

5) *cis*-1,1-Dimethyl-2-isopropylhydroxymethylcyclopropane carboxylic acid (3) lactone

The writer tried in vain to reduce carbonyl to hydroxymethyl in VI and VII by several methods: e. g. catalytic reductions of the free acid in acetic acid and the salt in alcohol or in water, using platinous oxide or palladious oxide, and reduction of the ester by aluminium isopropylate, etc.

Only by using sodium amalgam, the reduction was carried through. But the yield of lactone was very small and the greater part of reduction products seemed to be a ketonic acid which has no more cyclopropane ring.

3 g of the above ketonic acid (VII) were neutralized with sodium carbonate solution and the water solution was made to 100 cc, 40 cc of 50 % methanol was added to it and it was stirred with 36 g of 5 % sodium amalgam at 10° for 4 hrs. The quicksilver was filtered off. From the filtrate methanol was removed completely on a water bath and the solution was acidified with hydrochloric acid. It was extracted with ether, the ether solution was washed with each 5 cc of 7.5 % sodium carbonate solution four times and then with water three times. The ether solution of lactone part was preserved. The sodium carbonate washing was acidified with hydrochloric acid and a small amount of crystal of the ketonic acid was put in. Unchanged ketonic acid crystallized soon. It was separated, which amounting to 4 g, when it was wet. The recovered ketonic acid was neutralized and reduced with 22 g of 4 % sodium amalgam, and the ether solution of lactone part was obtained. The recovered ketonic acid (ca. 3g wet) was again reduced with 25 g of 4 % sodium amalgam, and the ether solution of lactone part was also obtained. This was combined with previous two ether solutions, and washed with each 5 cc of 30 % sodium carbonate solution five times and then with water three times. From this, ether was evaporated and the remaining oil was distilled. The main fraction distilled at 130°~145° (temperature of oil bath)/7 mm. It was colourless oil which amounted to ca. 0.3 g. This substance has characteristic sweet fragrance resembling to that of *cis*-1,1-dimethyl-2-diisopropyl-hydroxymethyl-cyclopropane-carboxylic acid (3) lactone. Even being left stand for a long time no crystallization was observed and seeding with crystal of dl-Pyrocin did not induce any crystallization at all. But it was too little quantity to be purified further by distillation.

Analysis:—

Sample mg	CO_2 mg	H_2O mg	C %	H %
4.010	10.125	3.530	68.86	9.85
4.200	10.650	3.810	69.20	10.15
$C_{10}H_6O_2$			71.42	9.52

It was soluble in caustic alkali solution and insoluble in alkali carbonate solution, it is therefore almost same as *cis*-1, 1-dimethyl-2-isopropylhydroxymethyl-cyclopropane-carboxylic acid (3) lactone, although this lactone was not completely pure.

6) Oxidation of Pyrocin β with hydrogen peroxide.

250 mg of Pyrocin β was saponified with equivalent molecule of caustic soda in 1 cc of water by warming on a water bath. After the oil layer has disappeared, it was cooled to room temperature. A drop of ferric chloride solution was added to the solution, then 3.5 cc of 3 % hydrogen peroxide was added by stirring. The mixture was left stand over night. This was acidified with hydrochloric acid and extracted with ether. The ether extract was washed with each 2 cc of 10 %

sodium carbonate solution four times. From the ether solution, after evaporating the solvent, 150 mg of Pyrocin β was recovered. The sodium carbonate washings were combined, and after washed with ether, it was acidified with hydrochloric acid and extracted with ether. The ether extract was washed with water three times. The ether solution was separated from water with caution, the ether was then evaporated. 50 mg of oil was remained. The oil was dissolved in 2 cc of methanol and to it 50 mg of semicarbazide hydrochloride and 50 mg of sodium acetate, was added. The mixture was boiled for one hour on a water bath. After this 1 cc of water was added. The solution was then left in an ice box. It crystallized in a few days. The crystal was separated and washed with water, yield 5 mg. It was recrystallized from 80% methanol, 3 mg of compound —mp 175° (with decomposition) —was obtained. This is considered to be semicarbazone of *cis*-1,1-dimethyl-2-(-α-ketopropyl)-cyclopropane-carboxylic acid(3) (XII)

Analysis: —

Sample mg	N_2 cc	T°	P mm	N %
1.068	0.159	9	769	17.92
$C_{10}H_{17}O_3N_3$				18.50

7) Oxidation of Pyrocin with hydrogen peroxide

With 0.5 g of Pyrocin, experiment was carried on as same as above mentioned. No oxidation product was obtained. Pyrocin was recovered almost completely.

8) 1.1-dimethyl-2(2′-hydroxy)-isopropyl-3-(2″-methyl-2″-hydroxy)-propylcyclopropane(X)

500 mg of Pyrocin was dissolved in 2 cc of dry ether, to this was added the Grignard's reagent which has been prepared from 2.5 g. of methyl iodide, 0.5 g of magnesium and 5 cc of dry ether under stirring and cooling. The reaction mixture was left stand at room temperature over night, then decomposed with ice and dil. sulphuric acid. The decomposed mixture was extracted with ether. The ether extract was washed with water. The ether was removed from the ether solution. Viscous oil was remained. This oil was saponified with 4 cc of 10% methanolic potash by boiling on a water bath for 3 hrs.. Water was added and methanol was removed completely on a water bath under reduced pressure. The mixture was then extracted with ether and the ether extract was washed with water three times. The ether layer was separated completely from water. After complete removal of the solvent from the ether solution under reduced pressure, the remaining oil was dried in vacuum desiccator on phosphorous pentoxide for 4 days.

Analysis: —

Sample mg	CO_2 mg	H_2O mg	C %	H %
3.764	9.969	4.170	72.23	12.30
$C_{12}H_{18}O_2$			72.00	12.00

9) Reaction of the above diol and chromic anhydride.

0.1 g of the above diol was dissolved in 2cc of acetic acid or carbon tetrachloride and to it was added 0.05 g of chromic anhydride. The mixture was shaken throughly and was left stand at room temperature. Any change did not observed.

10) Reaction of the diol and Nessler's reagent.

1 cc of Nessler's reagent was added to 0.1 g of the diol and the mixture was heated for 10 minutes. Any coloured precipitate was not obtained.

11) Reaction of sodium salt of Pyrocin and Nessler's reagent.

1cc of Nessler's reagent was added to 0.1 g of sodium salt of Pyrocin in 0.5 cc of water and the mixture was heated for 10 minutes. Any coloured precipitate was not obtained.

VIII Insecticidal Power of Pyrocin and 1,1-Dimethyl-2-diisopropylhydroxymethyl-cyclopropane-carboxylic acid (3) lactone,

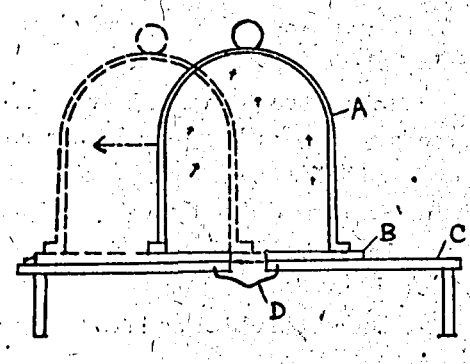
Among the lactones described in the preceeding articles, two Pyrocins and 1,1-dimethyl-2-diisopropylhydroxymethyl-cyclopropane-carboxylic acid(3)lactone were tested for their insecticidal powers on fly (*musca domestica*) by a fumigation method.

Control materials were D.D.T., benzophenone and Pyrethrin. Pyrethrin, which could not be obtained as pure state, was tested in 1% petroleum ether solution. The effect of the solvent—petroleum ether—was shown negligibly small by another test.

The apparatus of the fly killer and the method for test was as follows:—

1) Apparatus:

It is consist of a glass vessel (A) (content 8.4 litre), a rubber plate (B) which has a hole in the center and a table (C) which has also a hole with the same diameter as above and



a metallic dish which is fitted to the holes as shown in the diagram.

2) Fly (*Musca domestica*):

It is breeded one. Breeding temperature was 30° and humidity 70%.

3) The method of test:

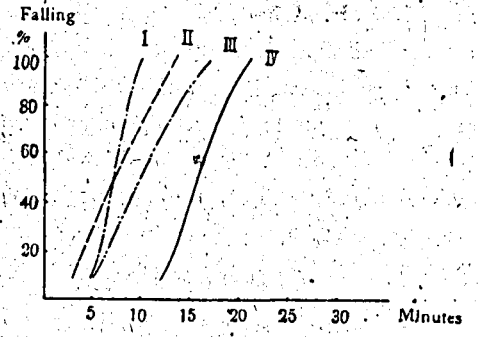
At first, the flies from ten to thirty in number, were driven in the glass vessel and the dish, on which was placed the weighed material for test, was set into the holes. The dish was heated with a alcohol lamp and let the sample evaporate. After the evaporation was completed (within one minute), the glass vessel was slided aside with the rubber plate and the holes were closed. The number of flies which fell and laid down on the back were calculated. The measurement of time was taken at the beginning of the heating.

The results of test are shown in graphs I, II, III and IV.

From the beginning of the fumigation, the state of flies were observed. In the cases of lactones and Pyrethrin, the effect appeared at first as a paralysis of hind legs and

Fig. I

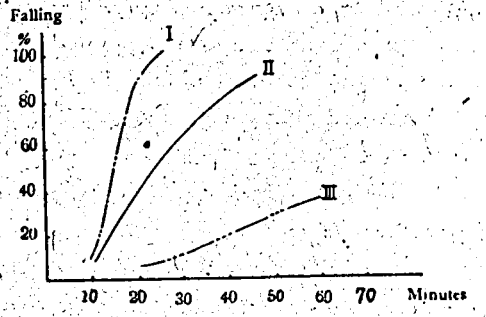
Test temperature: 23° Humidity: 65%
Flies: 7 days after incubation



I D.D.T. 5mg. II 1% Pyrethrin extract 10 mg.
III Benzophenone 5 mg. IV Pyrocin 10 mg.

Fig. II

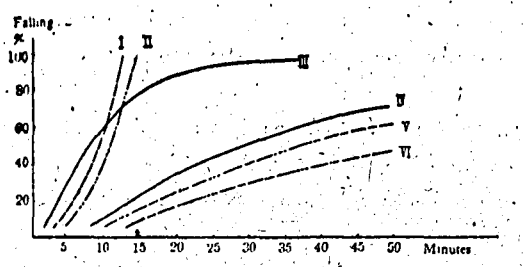
Test temperature: 23° Humidity: 65%
Flies: 7days after incubation



I Benzophenone 5 mg. II Pyrocin 5 mg.
III 1, 1-Dimethyl-2-diisopropylhydroxy-methylcyclopropane-carboxylic acid lactone (D.M.C.A.L.) 5 mg.

Fig. III

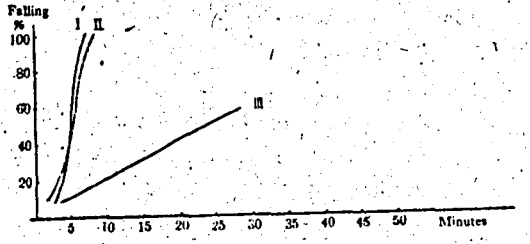
Test temperature: 23° Humidity: 65%
Flies: 5 days after incubation



I Benzophenone 4 mg. II D.D.T. 4mg.
III 1% Pyrethrin extract 0.2 mg.
IV 1% Pyrethrin extract 0.03 mg.
V D.M.C.A.L. 20 mg.
VI D.M.C.A.L. 10 mg.

Fig. IV

Test temperature: 23° Humidity: 65%
Flies: 10 days after incubation



I Pyrocin 10 mg. II Benzophenone 5 mg
III Pyrocin 5 mg.

the paralysis reached to the rest legs, then to the whole body. In the cases of D.D.T. and benzophenone, the agony of whole body soon came about.

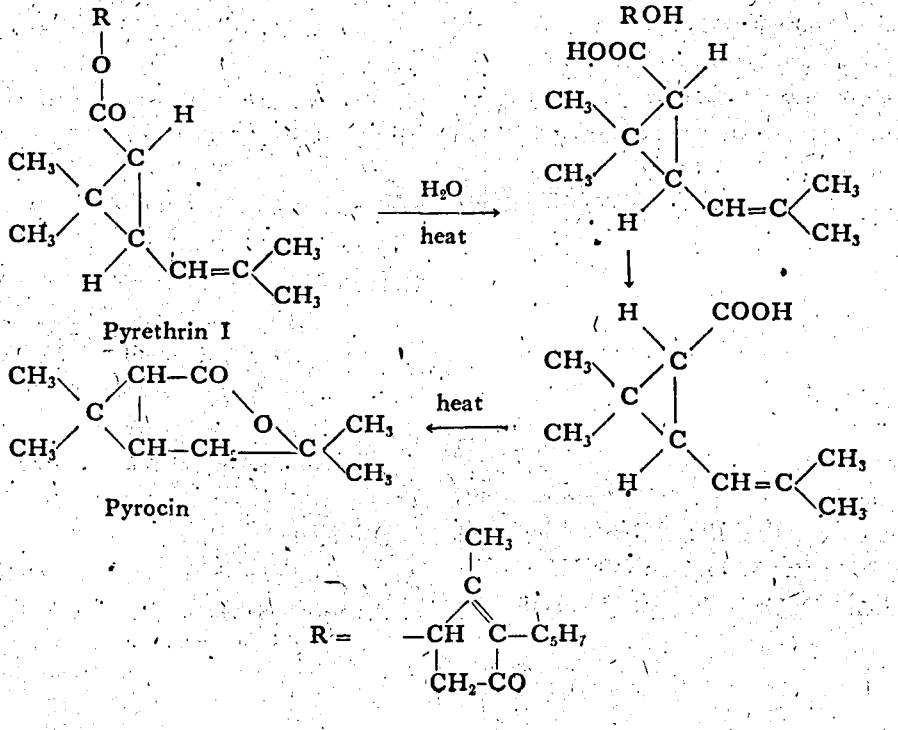
From the above tests, it is obvious that Pyrocin has a considerably strong insecticidal power on flies. As it has been shown that the tests of flies are parallel with those of mosquitoes [13], Pyrocin must have also a powerful toxicity on mosquitoes. Actually, the previous simple test on mosquito has shown this fact [4].

Consequently, Pyrocin must have been taken a prominent part of the insecticidal power of the smoke of mosquito coils.

CONCLUSION

As described in the preceeding articles, Pyrocin has been synthesized and confirmed its structure. From the fact that Pyrocin was prepared from chrysanthemum-monocarboxylic acid. The writer has all reason to believe that Pyrocin from dry distillation products of pyrethrum flowers has been derived from Pyrethrin-I.

The mechanism of its formation will



probably be as follows, Pyrethrin-I are saponified by a small quantity of water at high temperature into chrysanthemum-monocarboxylic acid and Pyrethrolone. The former is isomerized into *cis*-form and this then converted into the lactone.

Pyrocin has a considerably strong insecticidal power. It is very stable and composed of carbon, hydrogen and oxygen. It is expected to be less poisonous to human body than other synthetic insecticides. If it is manifested to be true, it can be used as insecticide in the future, though its preparation is not simple and rather expensive at present.

SUMMARY

1) From dry distillation product of pyrethrum flowers or pyrethrum extract, a new compound (Pyrocin) mp 83.5°~84.5° was obtained.

2) Pyrocin has been synthesized and confirmed to be 1,1-dimethyl-2-α-hydroxy-α-methylpropyl-cyclopropane carboxylic acid (3)lactone.

3) Concerning to the above preparation, some other compounds resembling to Pyrocin in structure were synthesized.

4) The tests of insecticidal power of Pyrocin and other synthesized materials were carried out. By this experiment it was manifested that Pyrocin has a considerably strong toxicity.

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