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SYNTHESIS OF SOME NEW CHALCONES AND 3-HYDROXY CHROMONES

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SYNTHESIS OF SOME NEW CHALCONES AND 3-HYDROXY CHROMONES

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DISSERTATION COMMITTEE

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CHAPTER I

INTRODUCTION

The flavonoid compounds comprise a group of naturally occurring substances widespread in the plant kingdom, in which two aryl groups are linked by a propane bridge (C_6-C_3-C_6 unit) (Figs. 2 to 7). Some of these compounds have been reported to possess biological activity in animals (1). Although many flavonoid compounds have been synthesized, relatively few 3-hydroxy flavones have been previously synthesized which contain a heterocyclic or polycyclic ring in place of the benzene ring attached to carbon number two of γ-benzopyrone. (Fig. 1). Also, most of the flavonoid compounds have one or more free hydroxy groups attached to the ring. The various hydroxy groups, especially the one at carbon number three, possibly bear some relationship to the biological activity of these compounds. The present study was, therefore, undertaken to adapt known synthetic procedures to the preparation of those flavonoid type compounds containing a heterocyclic or polycyclic ring on carbon number two of the γ-benzopyrone as well as the hydroxy group on carbon number three of γ-benzopyrone. Where possible, the corresponding chalcones were also to be synthesized.

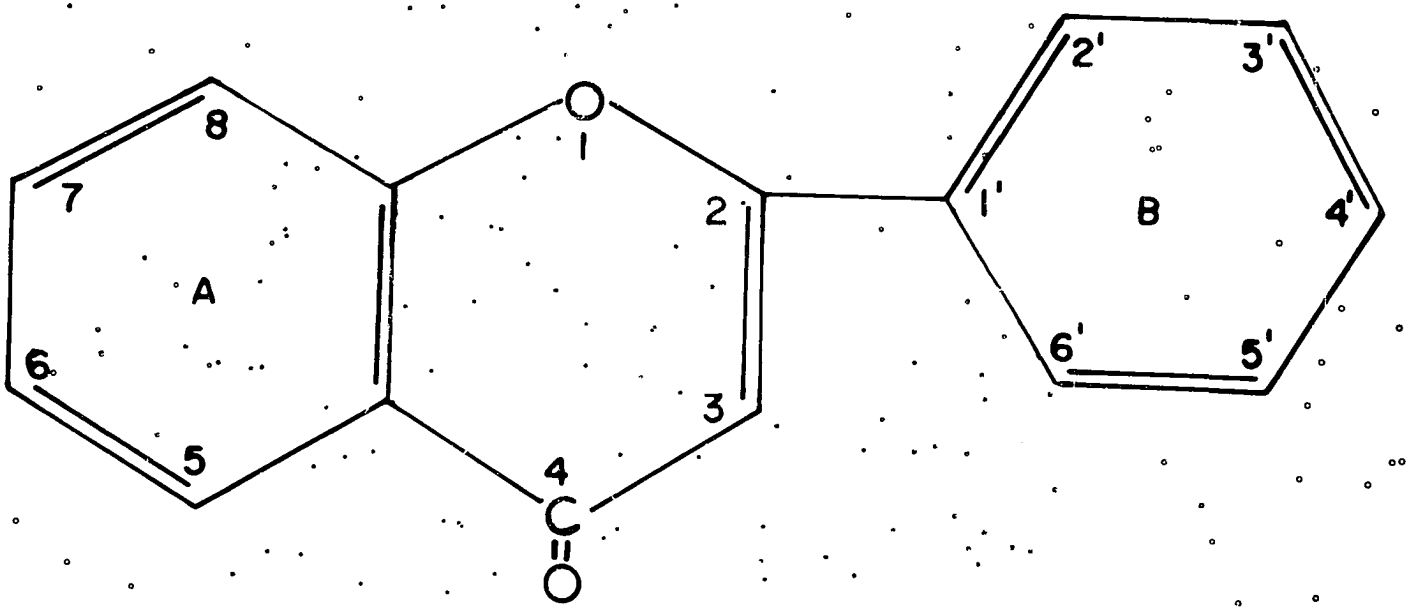
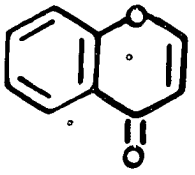


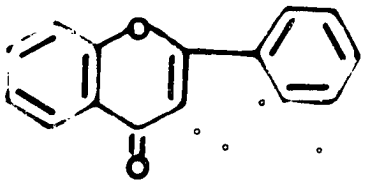
FIGURE 1

Structure of flavone (2-phenyl-γ-benzopyrone) showing the numbering system and the two benzene rings



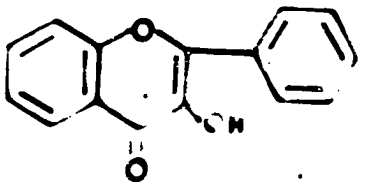
CHROMONE
(BENZOPYRONE)

FIGURE 2



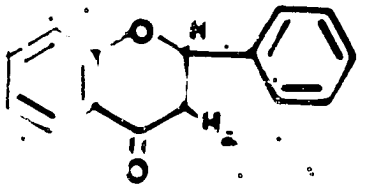
FLAVONE
(2-PHENYLBENZOPYRONE)

FIGURE 3



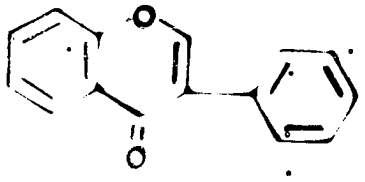
FLAVONOL
(3-HYDROXYFLAVONE)

FIGURE 4



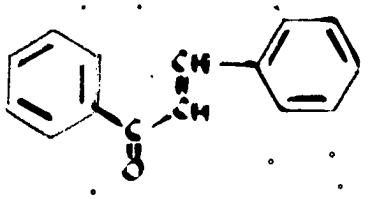
FLAVANONE

FIGURE 5



ISOFLAVONE

FIGURE 6



CHALCONE

FIGURE 7

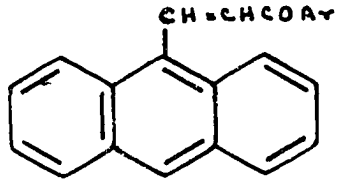
The idea of modifying the structure of the flavonoid compounds in order to study the changes in their biological activity is not new. Many workers have modified the flavonoid structure by introducing various substituent groups in the -benzopyrone ring or the "B" benzene ring.

V. Kostanecki (2) and Tambur (3) who were first in this field synthesized a large number of flavonoid compounds. Chen et al. (4,5,6,7) have synthesized a number of flavonoid compounds containing halogens attached to various positions in the ring. Raval and Shah (8,9) have introduced amino and acetamino groups into position six of the flavones.

A few isolated examples are found in the literature where the "B" benzene ring in the flavone has been substituted by a polycyclic or heterocyclic ring. Virker and Shah (10) synthesized 2-(1-naphthyl) chromone; however they did not prepare the 3-hydroxy derivative of this compound. Schmudz. et al. (11) synthesized a large number of compounds for investigation of their analgesic and coronary dilatatory properties. Among the compounds they synthesized are some flavone type compounds in which the "B" benzene ring has been substituted by the pyridine or piperidine ring. These compounds; however, did not have a hydroxy group attached to carbon number three. The furyl ring has also been substituted in place of the "B" benzene ring. (12,13,14)

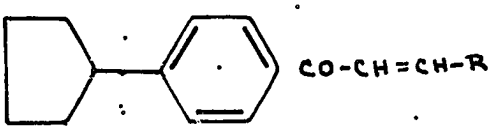
Other workers have prepared chalcones containing a polycyclic or heterocyclic "B" ring. In an effort to

investigate compounds with possible carcinogenic properties, chalcones containing the anthracene ring were prepared by N. P. Buu-Hoi. (15)



Ar = C_6H_5; C_6H_4Cl; C_6H_4I; C_4H_3S; C_4H_2BrS

As part of a general investigation on the relationship between tuberculostatic properties and chemical structure, Hai and co-workers (16) prepared several chalcones derived from p-cyclopentyl acetophenone of the type,

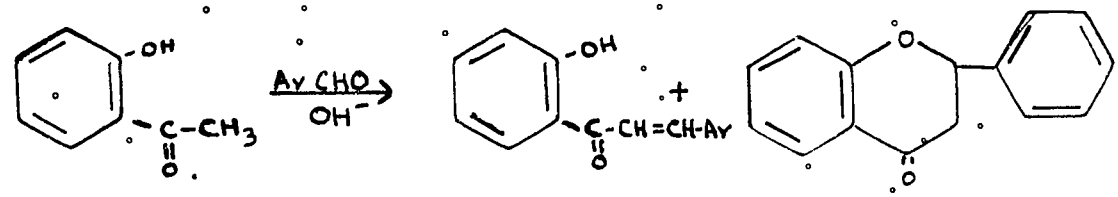


where R = 2-furyl, 2-thienyl, 1-naphthyl, 3-chlorophenyl and 3-methoxy phenyl, respectively.

Many chalcone derivatives of aldehydes or ketones of the thiophene series have also been prepared for the purpose of studying their anti-fungal or anti-bacterial properties. (17) None of the compounds synthesized in the research described here had been previously reported.

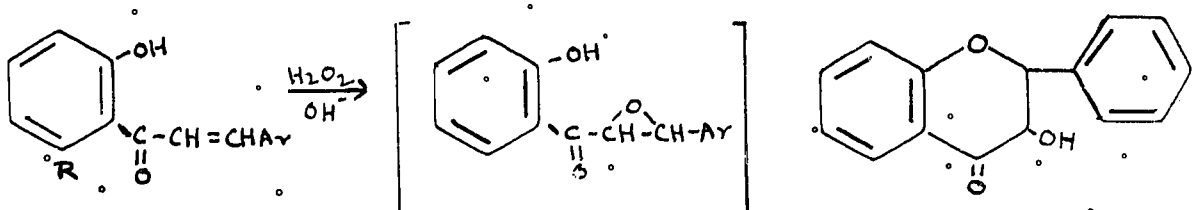
The 3-hydroxy flavone compounds were designated as flavonols by V. Kostanecki, who first synthesized flavonol itself from flavanone.

Flavonols can be prepared in a number of ways. Condensation of o-hydroxy acetophenones with aromatic aldehydes gives chalcones (benzal acetophenones) or flavanones which can be converted into flavones or flavonols in several ways.



o-Hydroxy acetophenone — A chalcone — Flavanone

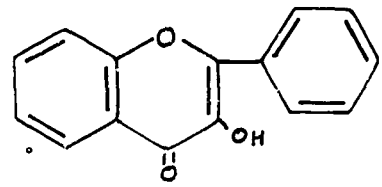
In 1934, Algar and Flynn (18) in Dublin, and independently Oyamada (19,20) in Japan, showed that chalcones or flavanones give the corresponding flavonols when treated with sodium hydroxide and hydrogen peroxide. This reaction has since been widely used for the synthesis of flavonols. Algar and Flynn suggested that the reaction proceeds through the chalcone to give an intermediate (II) which may then give a 3-hydroxy flavanone (III, R=H). This compound (III) which has been isolated in at least one case (21) is then oxidized to the flavonol (IV) (22).



I
A chalcone

II

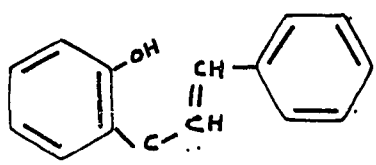
III
3-Hydroxy Flavanone



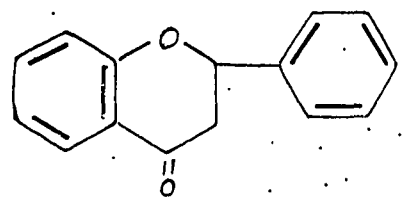
IV
Flavonol

3-Hydroxy flavanone may also be dehydrogenated to the flavonol by means of palladium using cinnamic acid or maleic anhydride as a hydrogen acceptor (23).

By boiling with alcoholic hydrochloric acid or by use of a dilute solution of alcoholic alkali, the chalcone is converted into flavanone.

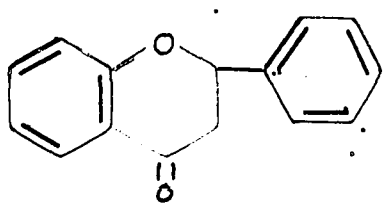


A chalcone

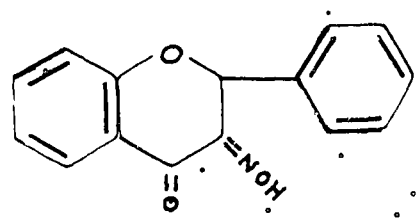


Flavanone

The resulting flavanone when treated with nitrous acid (amyl nitrite and concentrated hydrochloric acid) forms an oximino derivative.



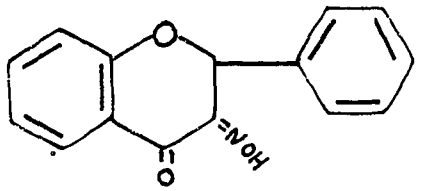
Flavanone



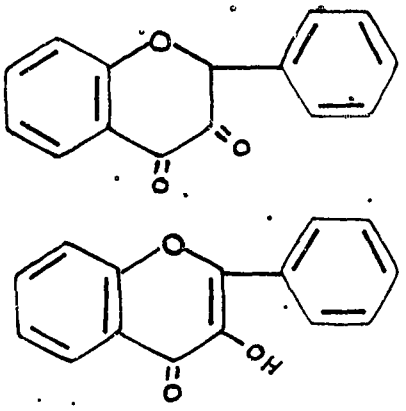
Oximino derivative

The oximino derivative when boiled with 10% sulphuric

acid in acetic acid solution, gives flavonol. The oximino group is first hydrolyzed to a ketonic group and subsequently the flavonol is formed by enolic rearrangement.



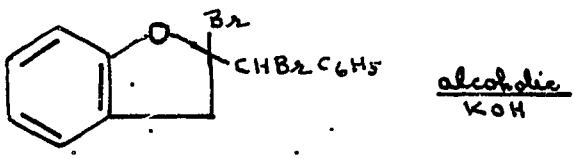
Oximino derivative



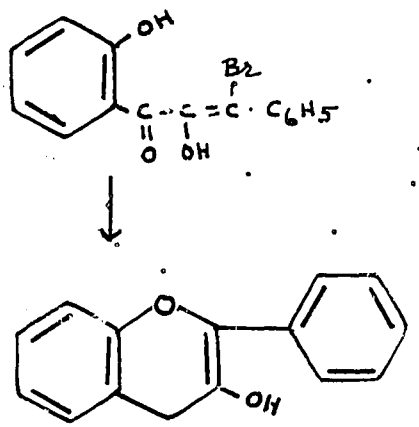
Flavonol

An improvement was made by Seshadri (24,25) who obtained the flavonol in one operation from flavanone.

According to Auwers and Muller (26), coumaran-3-ones can be converted into flavonols. 2-Benzylidene coumaran-3-one dibromide when treated with potassium hydroxide gives flavonol. The reaction is expressed:

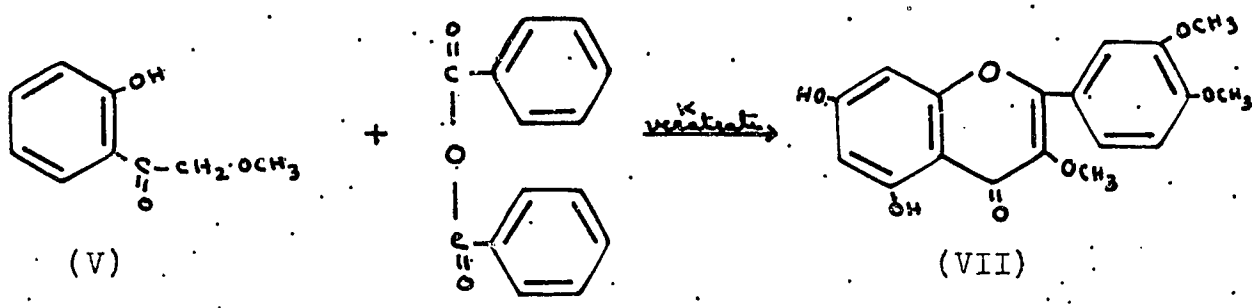


2-Benzylidene coumaran-3-one dibromide



Flavonol

Robinson (27) has developed a method for the synthesis of flavonol derivatives which is analogous to the one used in the preparation of flavones. Omega-methoxy acetophenone (or its derivative) is condensed with the ~~aldehyde~~ anhydride of an appropriate phenolic acid in the presence of its alkali salt. Quercetin, a typical flavonol, has been synthesized in this manner. Omega-methoxy chloro-acetophenone (V) is condensed with the anhydride of veratric acid (VI) in presence of potassium veratrate to give 3,3', 4', -trimethyl quercetin (VII).



(V) (VI) (VII)

One molecule of veratric acid is regenerated with simultaneous closing of the ring.

On demethylation with hydriodic acid, the trimethyl derivative of quercetin gives quercetin.

A one step synthesis of flavonols from o-hydroxy acetophenone and aldehyde has been described by Limaye (28), who has designated this reaction as the "Ranjorwa Reaction". Benzaldehyde (0.5 g.), (0.005 mole) 5-methyl-2-hydroxy acetophenone (0.75 g.) (0.005 mole) and 1.5 ml. of 10 N sodium

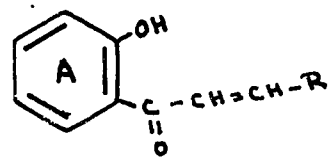
hydroxide solution in 30 ml. of 95% ethanol are placed in a 700 ml. bottle which is rolled on its side for one month with occasional exposure to air. The red sodium salt which precipitates is acidified with dilute hydrochloric acid. The precipitate, crystallized from acetic acid or ethanol, gives 3-hydroxy-6-methyl flavone. This reaction has been extended to the synthesis of furoflavonols from o-hydroxy acetyl benzofurans. It has been demonstrated that air is consumed and chalcones are formed as intermediates. Limaye (29) has also synthesized flavonols from chalcone dibromides. Limaye's method has not been extensively used for the synthesis of flavonols, although it appears to be very simple.

In the present study, 3-hydroxy chromones with a heterocyclic or polycyclic ring attached to carbon number two have been synthesized. From the analogy of known flavonoid compounds, these synthesized chromones may be of biological interest. The Ranjorwa reaction and Algar-Flynn reactions have been used for the preparation of these compounds. Properties of these compounds such as their ultra-violet spectra, infra-red spectra, color reactions and melting points have been studied. All the compounds have been purified by chromatography.

CHAPTER II

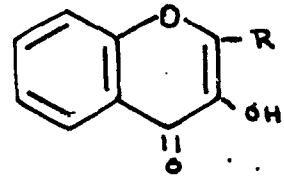
EXPERIMENTAL

In the following pages, experimental procedures for the newly synthesized compounds will be described. The word 'chalcone' will be used henceforth in this dissertation as a general term to apply to those compounds which have a structure of the type



where the benzene ring 'A' may be further substituted. Compounds of this general structure may also be named as hydroxy chalcones. R is a cyclic group.

The flavonol-type compounds synthesized have the general formula



where R = 9-anthracyl, 9-phenanthryl, 1-naphthyl, 2-naphthyl, 2-thienyl, 2-pyridyl, 3-pyridyl, 2-pyridyl -6-methyl, and 2-quinonyl, respectively. In one case, the 'A' ring has been further substituted. For the preparation of these compounds, 2-hydroxy acetophenone and an aldehyde of the appropriate

polycyclic or heterocyclic compound were used. In one case, 2-hydroxy 5-methyl acetophenone instead of 2-hydroxy acetophenone was used. The 1-naphthaldehyde used was obtained from L. Light & Co., Ltd., England. The other aldehydes and the acetophenone compounds used were obtained from Aldrich Chemical Company, Milwaukee, Wisconsin.

Two different methods were tried for the attempted 3-hydroxy chromone synthesis from each aldehyde studied. The first method was to prepare the chalcone and then try to convert the chalcone to the 3-hydroxy chromone by the Algar-Flynn oxidation using alkaline hydrogen peroxide. The other method tried was to prepare 3-hydroxy chromone in one step by the Ranjorwa reaction. The Ranjorwa reaction gave good results in a few cases only. The majority of the 3-hydroxy chromones were prepared by first synthesizing the chalcones and then by converting the chalcones to 3-hydroxy chromones with alkaline hydrogen peroxide. In all cases, the final product was purified by passage through a chromatographic column. Since the methods of preparation and purification are nearly the same for each compound synthesized, details of the experimental procedure have been described only for the first synthesis.

Preparation of 1-(2-hydroxyphenyl) 3-(9-anthracyl) propenone

First method for preparation of chalcones.

In a 125 ml. Erlenmeyer flask, 2.06 g. (0.01 mole)

of 9-anthraldehyde and 1.3 g. (0.01 mole) of 2-hydroxy acetophenone were dissolved in 30 ml. of 95% ethanol. To this solution, 5 ml. of 50% potassium hydroxide solution was added in portions. The flask was shaken after each addition. The color of the solution became orange. The flask was then stoppered and kept at room temperature (25°C.) for 48 hours. The resulting deep red solution was diluted with water and the chalcone was precipitated by bubbling a current of carbon dioxide through the solution. The red precipitate was crystallized from acetone. M.P. 166-167°C. The yield was 1.9 g. (58%).

Second method for preparation of chalcones.

In a 125 ml. Erlenmeyer flask, 2.06 g. (0.01 mole) of 9-anthraldehyde and 1.36 g. (0.01 mole) of 2-hydroxy acetophenone were dissolved in 30 ml. of 95% ethanol and 5 ml. of 50% potassium hydroxide solution was slowly added to it. The flask was shaken mechanically for 4 hours. The solution, which had now become deep red, was acidified with 5% ice-cold hydrochloric acid. The red precipitate formed was crystallized from acetone. M.P. 166-167°C. The yield was 2.1 g. (64.8%).

The 1-(2-hydroxyphenyl) 3-(9-anthracyl) propenone obtained by both methods was purified further by column chromatography. A chromatographic column was prepared by adding a slurry of Magnesol brand magnesium silicate (Food Machinery and Chemical Corp., N.Y.) in methanol to a chromatographic

tube and packing the absorbant under 10 lbs. of pressure. This column of magnesol was washed with 50 ml. of methanol. The solution of chalcone in methanol was poured onto the column, and the pressure was reduced to 5 lbs. A small amount of impurity remained adsorbed on the top of the column, but most of the chalcone passed through the column. The chalcone was obtained from the colored methanol eluate by the evaporation of methanol at room temperature. The chalcone was crystallized from acetone. M.P. 166-167°C.

Preparation of 2-(9-anthracyl)3-hydroxy chromone by the Algar-Flynn reaction

One gram (0.003 mole) of 1-(2-hydroxyphenyl) 3-(9-anthracyl) propenone was dissolved in 50 ml. of 95% ethanol, and then 20 ml. acetone and 6 ml. of 1 N alcoholic potassium hydroxide solution were added to it. This red solution was heated on a water bath, and 10 ml. of 30% hydrogen peroxide was added. There was a vigorous reaction, and the solution slowly turned yellow. The mixture was then heated on a water bath for 30 minutes. The yellow solution was allowed to stand for two hours. Yellow crystals deposited and were separated and recrystallized from benzene. M.P. 331-332°C. The yield was 0.2 g. (17.9%). From the alcoholic solution, a small amount of yellow crystalline substance melting at 246-247°C. was isolated. This latter compound has not been identified.

Preparation of 2-(9-anthracyl) 3-hydroxy chromone by the Ranjorwa reaction

In a 125 ml. Erlenmeyer flask, 2.06 g. (0.01 mole) of 9-anthraldehyde and 1.36 g.(0.01 mole) of 2-hydroxy acetophenone were dissolved in 30 ml. of 95% ethanol and 5 ml. of 50% potassium hydroxide solution was added slowly. The flask was shaken mechanically for one hour with the solution exposed to air. The flask was then stoppered and kept at room temperature. The procedure was repeated daily for 30 days. At the end of the 30 days, the red sodium salt that had deposited in the flask was separated and treated with dilute hydrochloric acid. The red salt turned yellow. This yellow solid was crystallized from benzene. M.P. 331-332°C. The yield was 1.00 g.(29.6%).

The 2-(9-anthracyl) 3-hydroxy chromone was purified further by chromatography. A chromatographic column was prepared by adding a slurry of magnesol in dry benzene to a chromatographic tube. The absorbant was packed under a pressure of 10 lbs. The column was washed with anhydrous benzene by pouring 50 ml. of the anhydrous benzene onto the absorbant and passing it through the column under a pressure of 10 lbs. The benzene solution of the chromone was next passed through the magnesol column, under a pressure of 5 lbs. The column was developed with additional benzene. The chromone was present just at the top of the column in a yellow zone, and a chalcone appeared as an orange zone just below it. Immediately after washing the column with anhydrous benzene, the

magnesol was extruded from the top of the column. This was accomplished by applying air pressure to the constricted lower end of the chromatographic tube. By holding the tube horizontally, one inch above a stainless steel tray, and applying the pressure very slowly, it was possible to ease the magnesol from the top of the column. In this manner, the magnesol retained its cylindrical shape. The magnesol was then cut by a stainless steel spatula into three portions. The top zone contained impurities and was set aside. The second zone was eluted with acetone, and the desired chromone was obtained after evaporation of the acetone. The chromone was crystallized from benzene. M.P. 331-332°C.

Analysis: Calculated for $C_{23}H_{14}O_3$

C = 81.64% H = 4.17%

Found C = 81.41% H = 4.12%

C = 81.57% H = 4.25%

Preparation of the acetate of 2-(9-anthracyl) 3-hydroxy chromone

The synthesized 2-(9-anthracyl) 3-hydroxy chromone (0.5 g.) was refluxed for an hour with acetic anhydride (2 ml.) and pyridine (3 drops). The resulting mixture was poured onto crushed ice. The yellow solid formed was crystallized from 95% ethanol. The yellow needles melt at 194-195°C.

Analysis: Calculated for $C_{25}H_{16}O_4$

C = 78.97% H = 4.24%

Found C = 78.90% H = 4.42%

C = 79.05% H = 4.16%

Preparation of 1-(2-hydroxy 5-methyl phenyl) 3-(9-anthracyl) propenone

First method:

In a 125 ml. Erlenmeyer flask, 2.06 g.(0.01 mole) of 9-anthraldehyde and 1.3 g.(0.01 mole) of 2-hydroxy 5-methyl acetophenone were dissolved in 30 ml. of 95% ethanol. To this solution, 5 ml. of 50% potassium hydroxide solution was added slowly. The flask was shaken after each addition, and the color of the solution became orange. The stoppered flask was kept at room temperature (25°C.) for 48 hours. The chalcone was obtained from this solution in the same manner as described above for 1-(2-hydroxyphenyl) 3-(9-anthracyl) propenone. The chalcone was crystallized from acetone as red needles melting at 171-172°C. The yield was 2.1 g. (62%).

The same chalcone could be prepared by the second method also. It was purified chromatographically the same way as has been described before for the magnesol purification of 1-(2-hydroxyphenyl) 3-(9-anthracyl) propenone.

Preparation of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone

1-(2-Hydroxy 5-methyl phenyl) 3-(9-anthracyl) propenone, 1.1 g. (0.003 mole), was dissolved in 50 ml. of 95% ethanol and then 20 ml. of acetone and 3 ml. of 1 N alcoholic potassium hydroxide solution were added. The resulting red solution was heated on a water bath, and 10 ml. of 30%

hydrogen peroxide was added. The solution was treated the same way as described before for preparation of 2-(9-anthracyl) 3-hydroxy chromone. Yellow crystals melting at 305-306°C were obtained. The yield was 0.4 g. (3[illegible].1%).

Analysis: Calculated for $C_{24}H_{16}O_3$

C = 81.80% H = 4.58%

Found C = 81.82% H = 4.76%

Preparation of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone by the Ranjorwa reaction

9-Anthraldehyde, 2.06 g. (0.01 mole), and 2-hydroxy 5-methyl acetophenone, 1.5 g. (0.01 mole), gave 1.2 g. (35.4%) of the chromone by this method.

Further purification of this 2-(9-anthracyl) 3-hydroxy 6-methyl chromone was made by chromatography. A chromatographic column was prepared by adding a slurry of magnesol in anhydrous benzene to a chromatographic tube. The absorbant was packed under a pressure of 10 lbs. and was washed with anhydrous benzene. The solution of the chromone in anhydrous benzene was poured onto the column and the pressure was reduced to 5 lbs. More benzene was added and the yellow colored benzene eluate was collected. The first 100 ml. gave a small amount of a compound melting at 315-316°C. One hundred ml. of anhydrous acetone were then added to the column and the acetone eluate collected. This gave a yellow compound which was crystallized from benzene. The melting point was. 305-306°C.

Preparation of the acetate of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone

A mixture of 0.2 g. of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone, 3 ml. of acetic anhydride, and 3 drops of pyridine were refluxed for 30 minutes and then diluted with ice-cold water. The white solid was crystallized from 95% ethanol; M.P. 283-285°C.

Analysis: Calculated for $C_{26}H_{18}O_4$

C = 79.17% H = 4.60%

Found C = 79.10% H = 4.73%

Preparation of 1-(2-hydroxyphenyl) 3-(9-phenanthryl) propenone

Phenanthrene-9-aldehyde, 2.06 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), were dissolved in 30 ml. of 95% ethanol, and 5 ml. of 50% potassium hydroxide solution was added slowly. The color of the solution became orange, and the flask was shaken mechanically for 2 hours. Then the solution was acidified with ice-cold dilute hydrochloric acid. The resulting orange precipitate was crystallized from acetone. Yellow needles melting at 158-159°C. were obtained. Yield 3.0 g. (92.6%) This chalcone was purified by passing it through a column containing magnesol.

Preparation of 2-(9-phenanthryl) 3-hydroxy chromone

1-(2-Hydroxyphenyl) 3-(9-phenanthryl) propenone, 1.1 g. (0.003 mole), was dissolved in 50 ml. of 95% ethanol and

20 ml. of acetone. Three ml. of 1 N potassium hydroxide solution was added. The solution was heated on a water bath, and 10 ml. of 30% hydrogen peroxide was added. There was a vigorous reaction and the solution was boiled on a water bath for 20 minutes, and then let stand for 1 hour. The yellow crystals that deposited were dissolved in anhydrous benzene and passed through a column containing magnesol. A brown substance remained at the top of the column. The other components passed through the column. The benzene eluate which gave a greenish yellow fluorescence under ultra-violet light was collected. From this solution crystals melting at 248-249°C. were obtained. Yield was 0.19 g. (16.9%)

Analysis: Calculated for $C_{23}H_{14}O_3$

C = 81.64% H = 4.17%

Found C = 81.47% H = 4.15%

Preparation of the acetate of 2-(9-phenanthryl) 3-hydroxy chromone

A mixture of 0.2 g. of 2-(9-phenanthryl) 3-hydroxy chromone, 3 ml. of acetic anhydride, and 3 drops of pyridine were refluxed for 30 minutes and diluted with ice-cold water. The white solid was crystallized from 95% ethanol. M.P. 179-181°C.

Analysis: Calculated for $C_{25}H_{16}O_4$

C = 78.94% H = 4.24%

Found C = 78.68% H = 4.16%

Attempted preparation of 2-(9-phenanthryl) 3-hydroxy chromone by the Ranjorwa reaction

Phenanthrene-9-aldehyde, 2.06 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), were dissolved in 30 ml. of 95% alcohol and 5 ml. of 50% potassium hydroxide solution was added. The flask was shaken mechanically for one hour with the solution exposed to the air. The flask was then stoppered and kept at room temperature. This procedure was repeated daily for 30 days. The solution was then filtered, and the solid obtained was treated with dilute hydrochloric acid solution and extracted with benzene. The benzene extract after evaporation gave a yellow substance which was found to be identical on mixed melting point determination with 1-(2-hydroxyphenyl) 3-(9-phenanthryl) propenone.

Preparation of 1-(2-hydroxyphenyl) 3-(1-naphthyl) propenone

Alpha-naphthaldehyde, 3.12 g. (0.02 mole), and 2-hydroxy acetophenone, 2.72 g. (0.02 mole), were dissolved in 30 ml. of 95% ethanol, and 5 ml. of 50% potassium hydroxide solution was added slowly. The yellow solution was shaken for two hours, at which time the solution was dark red. This solution was acidified with cold dilute hydrochloric acid. The yellow precipitate that formed was separated and then was crystallized from acetone. The crystals were yellow needles melting at 115-116°C. The yield was 0.9 g. (16.4%).

The 1-(2-hydroxyphenyl) 3-(1-naphthyl) propenone was purified further using benzene and magnesol by the column

chromatography procedure described previously.

Preparation of 2-(1-naphthyl) 3-hydroxy chromone

Chromatographically pure 1-(2-hydroxyphenyl)-3-(1-naphthyl) propenone, 3.43 g. (0.013 mole), was dissolved in 100 ml. of 95% ethanol, and 8 ml. of 1 N alcoholic potassium hydroxide solution was added. The red solution was heated on the water bath to about 70°C., and 25 ml. of 30% hydrogen peroxide was added. The solution was boiled for about 15 minutes and then set aside for 4 hours; a yellow crystalline precipitate appeared. This was separated and crystallized from benzene. M.P. 231-232°C. Yield was 1.3 g. (36.1%). This compound was further purified by chromatography.

Preparation of 2-(1-naphthyl) 3-hydroxy chromone by the Ranjorwa reaction

Alpha-naphthaldehyde, 1.56 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), were dissolved in 40 ml. of 95% alcohol, and 5 ml. of 50% potassium hydroxide solution was added to the solution. For thirty days, the mixture was shaken each day for one hour in contact with air, then the flask was stoppered until the next day. After 30 days, the mixture was dark colored. No precipitate of sodium salt of the flavonol was found. The solution was acidified, therefore, with dilute hydrochloric acid and extracted with benzene. The brick red benzene solution was boiled to remove water by azeotropy.

A column of magnesol was prepared and washed with anhydrous benzene. The crude flavonol solution was passed through this column and developed with more benzene. The first 500 ml. of eluate gave a red syrup after all the benzene was evaporated. The next 500 ml. eluate gave a yellow syrupy mass. After repeated crystallization with 95% alcohol, yellow needles melting at 231-232°C. were obtained from this yellow syrup. The yield was 0.28 g. (10%).

Analysis: Calculated for $C_{19}H_{12}O_3$

C = 79.15% H = 4.19%

Found C = 79.07% H = 4.06%

Preparation of the acetate of 2-(1-naphthyl) 3-hydroxy chromone

A mixture of 0.2 g. of 2-(1-naphthyl) 3-hydroxy chromone, 3 ml. of acetic anhydride and 3 drops of pyridine were refluxed for 30 minutes and then diluted with ice-cold water. The cream colored solid was crystallized from 95% alcohol. M.P. 190-192°C.

Analysis: Calculated for $C_{21}H_{14}O_4$

C = 76.35% H = 4.27%

Found C = 76.52% H = 4.43%

Preparation of 1-(2-hydroxyphenyl) 3-(2-naphthyl) propenone

2-Naphthaldehyde, 1.56 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), were dissolved in 30 ml. of 95% ethanol and 5 ml. of 50% potassium hydroxide solution

was slowly added. The flask was shaken mechanically for 3 hours. Then the red solution was acidified with ice-cold dilute hydrochloric acid solution. The yellow precipitate was crystallized from acetone. The chalcone was purified further by dissolving it in anhydrous benzene and passing the solution through a column, and small impurities were adsorbed by the column. The chalcone crystallized from acetone in yellow needles melting at 155-156°C. The yield was 1.5 g. (54.9%).

Preparation of 2-(2-naphthyl) 3-hydroxy chromone

1-(2-Hydroxyphenyl) 3-(2-naphthyl) propenone, 2.74 g. (0.01 mole), was dissolved in 40 ml. of 95% ethanol, and 6 ml. of 1 N potassium hydroxide solution was added. The solution was heated on a water bath, and 10 ml. of 30% hydrogen peroxide was added. There was a vigorous reaction and the solution was boiled for 15 minutes and then let stand for 2 hours. The yellow crystals which separated were dissolved in benzene, and the benzene solution was passed through a column containing magnesol. More benzene was added and the benzene eluate fraction which gave a bright yellow fluorescence under ultra-violet light produced yellowish needles melting at 208-209°C. The yield was 0.72 g. (25%).

Analysis: Calculated for $C_{19}H_{12}O_3$

C = 79.15% H = 4.19%

Found C = 78.98% H = 4.14%

Preparation of the acetate of 2-(2-naphthyl) 3-hydroxy chromone

A mixture of 0.2 g. of 2-(2-naphthyl) 3-hydroxy chromone, 3 ml. of acetic anhydride and 3 drops of pyridine were refluxed for 30 minutes and then diluted with ice-cold water. The cream colored solid was crystallized from 95% ethanol. M.P. 145-146°C.

Analysis: Calculated for $C_{21}H_{14}O_4$

C = 76.35% H = 4.27%

Found C = 76.41% H = 4.35%

Preparation of 1-(2-hydroxyphenyl) 3-(2-thienyl) propenone

Thiophene 2-carboxylic aldehyde, 2.2 g. (0.02 mole), 2-hydroxy acetophenone, 2.7 g. (0.02 mole) and ethanol, 20 ml., were mixed, and 5 ml. of 50% potassium hydroxide solution was added slowly. The flask was then stoppered and kept at room temperature (25°C.) for 48 hours. The resulting deep red solution was diluted with water, and the chalcone was precipitated by bubbling a current of carbon dioxide through the solution. The yellow precipitate was crystallized from 95% ethanol. M.P. 99-100°C.

The 1-(2-hydroxyphenyl) 3-(2-thienyl) propenone obtained above was purified further using benzene and magnesol by the column chromatography procedure previously described. A small impurity remained at the top of the column. The first 100 ml. of the yellow colored benzene eluate gave most of the

chalcone. This was crystallized from 95% ethanol. Yellow needles melting at 99-100°C. were obtained. Yield = 2.7 g. (58.7%).

Preparation of 2-(2-thienyl) 3-hydroxy chromone

1-(2-Hydroxyphenyl) 3-(2-thienyl) propenone, 1.15 g. (0.005 mole), was dissolved in 20 ml. of 95% ethanol, and 5 ml. of 1 N alcoholic potassium hydroxide solution was added. The red solution was heated on the water bath to about 70°C. and then 5 ml. of 30% hydrogen peroxide was added. The solution was boiled for 15 minutes and then set aside for 4 hours. The solution was acidified with dilute sulphuric acid and the resulting precipitate was crystallized from 95% ethanol. M.P. 205-206°C.

The 2-(2-thienyl) 3-hydroxy chromone was purified further by passing it through a magnesol column using benzene as previously described. A yellow zone developed at the top of the column followed by a brown zone. The column was extruded and the yellow zone was extracted with acetone. The acetone was evaporated at room temperature and the yellow solid was crystallized from 95% ethanol. M.P. 205-206°C. Yield was 0.3 g. (24.6%).

Analysis: Calculated for $C_{13}H_8O_3S$

	C = 63.92%	H = 3.30%	S = 13.13%
Found	C = 64.10%	H = 3.40%	S = 13.29%
	C = 63.93%	H = 3.28%	S = 13.07%

The acetate of 2-(2-thienyl)· 3-hydroxy chromone prepared by the previously described method above, melts at 152-153°C.

Analysis: Calculated for $C_{15}H_{10}O_4S$

S = 11.20%

Found S = 11.21%

Preparation of 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone

In a 125 ml. Erlenmeyer flask, pyridine 2-carboxaldehyde, 1.07 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), were dissolved in 20 ml. of 95% ethanol. This solution was cooled to 0°C., and 5 ml. of 50% potassium hydroxide solution was slowly added. The color of the solution became red. The solution was shaken for 2½ hours and then acidified with ice-cold 5% hydrochloric acid. After acidification, the pH of the solution was 5. A yellow precipitate separated, and then it was crystallized from 50% ethanol. The crystals were dissolved in anhydrous benzene and passed through a column containing magnesol. A slight impurity remained adsorbed at the top of the column, but most of the chalcone passed through the column. The chalcone was obtained from this benzene eluate by the evaporation of benzene, at room temperature. The chalcone was crystallized from 50% ethanol. M.P. 101-102°C. The yield was 1.2 g. (53.3%).

Preparation of 2-(2-pyridyl) 3-hydroxy chromone .

Three grams (0.013 mole) of 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone were dissolved in 60 ml. of 95% ethanol, and 6 ml. of 1 N alcoholic potassium hydroxide solution was added. The yellow solution became red. The solution was warmed on a water bath to 70°C. and then 18 ml. of 30% hydrogen peroxide was added. The solution was stirred vigorously, heated on the water bath for 15 minutes, and then kept at room temperature for 4 hours. This solution was next acidified with ice-cold dilute sulphuric acid and extracted with benzene. The benzene extract was washed with water and then was boiled for a few minutes to remove some of the water.

The benzene solution was passed through a column containing magnesol. A yellow zone at the top of the column was separated by extruding the column as already described in the purification of 2-(9-anthracyl) 3-hydroxy chromone. A yellow compound was isolated and was crystallized from 95% ethanol. M.P. 178-179°C. The yield was 1.5 g. (46.1%).

Analysis: Calculated for $C_{14}H_9O_3N$

C = 70.29% H = 3.79% N = 5.85%

Found C = 70.04% H = 3.57% N = 5.84%

The acetate of 2-(2-pyridyl) 3-hydroxy chromone was prepared by the described method and crystallized from 95% ethanol. M.P. 138-140°C.

Analysis: Calculated for $C_{16}H_{11}N_1O_4$

N = 4.98%

Found N = 5.08%

Preparation of 1-(2-hydroxyphenyl) 3-(3-pyridyl) propenone

This compound was prepared by the same method described for 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone. From 1.07 g. (0.01 mole) of pyridine 3-carboxaldehyde and 1.3 g. (0.01 mole) of 2-hydroxy acetophenone, 0.65 g. (25.8%) of the chalcone was obtained. M.P. 161-162°C.

Preparation of 2-(3-pyridyl) 3-hydroxy chromone

This compound was prepared in the same way as described for the preparation of 2-(2-pyridyl) 3-hydroxy chromone. From 2.25 g. (0.01 mole) of 1(2-hydroxyphenyl) 3-(3-pyridyl) propenone, 0.52 g. (21.7%) of the chromone was obtained. M.P. 207-208°C.

Analysis: Calculated for $C_{14}H_9O_3N$

C = 70.29% H = 3.79% N = 5.85%

Found C = 70.43% H = 3.71% N = 5.95%

The acetate of 2-(3-pyridyl) 3-hydroxy chromone prepared by the described method melted at 109-110°C.

Analysis: Calculated for $C_{16}H_{11}O_4N$

N = 4.98%

Found N = 5.08%

Preparation of 1-(2-hydroxyphenyl) 3-(4-pyridyl) propenone

This compound was prepared by the same method described for the preparation of 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone. Pyridine-4-carboxaldehyde, 1.07 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), gave 0.24 g. (10%) of a yellow compound which was crystallized from 95% ethanol. M.P. 119-120°C. This chalcone was purified by chromatography in the same way described for 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone.

The 1-(2-hydroxyphenyl) 3-(4-pyridyl) propenone decomposed when heated on a water bath. The corresponding hydroxy chromone was not obtained from this chalcone.

Analysis: Calculated for $C_{14}H_{11}O_2N$

N = 6.22%

Found N = 6.28%

Preparation of 1-(2-hydroxyphenyl) 3-(2-pyridyl-y-methyl) propenone

This compound was prepared in the same way as has been described for the preparation of 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone. 6-Methyl-2-pyridine carboxaldehyde, 1.21 g. (0.01 mole), and 2-hydroxy acetophenone, 1.36 g. (0.01 mole), gave 0.9 g. (37.5%) of the chalcone. This product was further purified by using magnesol and benzene.

Preparation of 2-(2-pyridyl-6-methyl) chromone

This compound was prepared from 1-(2-hydroxyphenyl) 3-(2-pyridyl-6-methyl) propenone by the Algar-Flynn reaction. From 0.6 g. (0.0025 mole) of the chalcone, 0.4 g. (63.4%) of chromone was obtained. M.P. 208-209°C.

This compound was purified by dissolving it in anhydrous benzene and passing the solution through a column containing magnesol. The column was washed with 100 ml. of anhydrous benzene and then 100 ml. of acetone. It was then washed with ethyl acetate saturated with water. The ethyl acetate-water eluate gave a yellow substance which was crystallized from 95% ethanol. M.P. 208-209°C.

Analysis: Calculated for $C_{15}H_{11}O_3N$

N = 5.53%

Found N = 5.61%

The acetate of 2-(2-pyridyl-6-methyl) chromone melts at 118-119°C.

Analysis: Calculated for $C_{17}H_{13}O_4N$

N = 4.74%

Found N = 4.87%

Preparation of 1-(2-hydroxyphenyl) 3-(2-quinonyl) propenone

This compound was prepared the same way as has been described for the preparation of 1-(2-hydroxyphenyl) 3-(2-pyridyl) propenone. Quinoline-2-aldehyde, 1.57 g. (0.01 mole) and 2-hydroxy acetophenone 1.36 g. (0.01 mole) gave an

orange colored compound melting at 125-126°C. This compound was purified by chromatography using magnesol and anhydrous benzene. The yield was 0.8 g. (29.0%).

Preparation of 2-(2-quinonyl) 3-hydroxy chromone

This hydroxy chromone was prepared from 1-(2-hydroxy-phenyl) 3-(2-quinonyl) propenone, by the Algar-Flynn reaction as has been described for the preparation of 2-(2-pyridyl) 3-hydroxy chromone. One gram (34.6%) of red crystals of 2-(2-quinonyl) 3-hydroxy (0.01 mole) chromone, M.P. 253-254°C, was obtained from 2.71 g. (0.01 mole) of the chalcone.

Further purification of this chromone was made by chromatography. Crystals of 2-(2-quinonyl) 3-hydroxy chromone were dissolved in benzene and passed through a column containing magnesol. The column was developed by adding 100 ml. of acetone. The orange zone which developed was separated from the column by extruding the magnesol. From this orange zone, red needles melting at 253-254°C. were obtained.

Analysis: Calculated for $C_{18}H_{11}O_3N$

N = 4.84%

Found N = 5.01%

The acetate derivative of this chromone melts at 181-182°C.

Analysis: Calculated for $C_{20}H_{13}O_4N$

N = 4.23%

Found N = 4.17%

Attempted preparation of 1-(2-hydroxyphenyl) 3-(3-indol) propenone

Indole-3-aldehyde, 2.9 g. (0.02 mole) and 2-hydroxy acetophenone, 1.7 g. (0.02 mole) and 95% ethanol, 80 ml. were heated on a water bath at 60-65°C. and 10 ml. of 50% potassium hydroxide solution was added slowly. The mixture was heated on a water bath for one hour. The color of the solution slowly changed from orange to red. The solution was then shaken for two hours and ice-cold dilute hydrochloric acid added. The yellow precipitate which separated was crystallized from 95% ethanol. M.P. 202-203°C.

The precipitate was dissolved in 160 ml.of anhydrous benzene and passed through a column containing magnesol. More benzene was added. A brown impurity remained at the top of the column and the yellow benzene solution which came out was collected. The benzene was evaporated and the yellow solid crystallized from 95% ethanol. M.P. 202-203°C.

Analysis: Calculated for $C_{19}H_{13}O_2N$

N = 5.32%

Found N = 9.64% and N = 9.79%

The compound obtained, therefore, is not the anticipated 1-(2-hydroxyphenyl) 3-(3-indole) propenone.

CHAPTER III

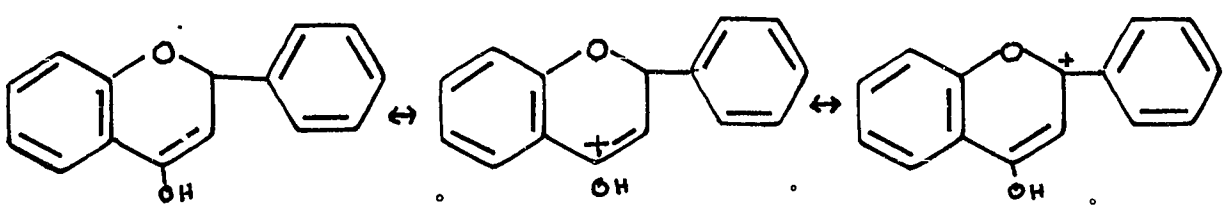
PROPERTIES

Color Reactions

Since the synthesized compounds are chalcones or 3-hydroxy chromones, the color reactions of these compounds with the common flavonoid color producing reagents (30) have been investigated.

Ferric Chloride: The production of colors with ferric chloride is a general property of polyhydroxy flavonoid compounds. A 5% solution of ferric chloride was added to the alcoholic solution of the compounds. The results are given in Table 1.

Concentrated Sulphuric Acid: Flavones and flavonols dissolve in sulphuric acid to give intensely yellow solutions which probably contain the oxonium (flavylium) salts of the following genral structure:



The color obtained with each of these synthesized compounds is reported in Tables 1 and 2.

Antimony Pentachloride: In this test, 5-10 mg. of the compound to be tested was dissolved in 5 ml. of anhydrous carbon tetrachloride, and 1 ml. of 2% anhydrous carbon tetrachloride solution of antimony pentachloride was added. The chalcones usually give red to red-violet colors and flavonols generally give yellow colors. Results on the synthesized compounds are given in Tables 1 and 2.

Magnesium-Hydrochloric Acid Reduction: The test is carried out by adding the acid dropwise to an alcoholic solution of the compound. Characteristic colors develop within a minute or two, and the subsequent addition of more acid often causes modification of the color in a manner characteristic of the compound being examined. With flavonols, pink, scarlet, crimson or occasionally green or blue colors are obtained. The results obtained on the synthesized compounds are reported in Table 1.

Appearance on Paper Chromatograms under Ultra-violet Light: Only limited generalizations can be made regarding the relationship between the structure of flavonoid compounds and their appearance under ultra-violet light. Flavonols generally fluoresce brightly with greenish-yellow colors. This behavior is attributed to the effect of the 3-hydroxy group. The flavones, lacking this 3-hydroxy group, appear brown under ultra-violet light. The colors obtained for the synthesized compounds have been listed in Table 1.

TABLE 1

COLOR REACTIONS OF THE SYNTHESIZED 3-HYDROXY CHROMONES

Compound	5% $FeCl_3$ Soln.	H_2SO_4 conc!	Sb Cl_5 in CCl_4	Mg+HCl	Appearance on Paper Chromatogram under Ultra-violet light
2-(9-anthracyl) 3-hydroxy chromone	yellow	Orange red	yellow	--	Blue
2-(9-anthracyl)3-hydroxy 6 methyl chromone	Yellow	Reddish Brown	Yellowish Brown	--	Blue
2-(9-phenanthryl 3-hydroxy chromone	Yellow	Reddish Brown	Green	Yellow	Violet
2-(1-naphthyl) 3-hydroxy chromone	Brown	Yellow	Yellowish Brown	Yellow	Yellow
2-(2-naphthyl) 3-hydroxy chromone	Brown	Yellow	Yellow	Brown	Yellow
2-(2-thiophene) 3-hydroxy chromone	Yellow	Yellow	Yellowish Brown	Yellow	Yellow
2-(2-pyridyl) 3-hydroxy chromone	Brown	Yellow	Yellow	Pale Yellow	Yellow
2-(3-pyridyl) 3-hydroxy chromone	Brown	Reddish Brown	Yellow	Yellow	Greenish Yellow
2-(2-pyridyl 6-methyl) 3-hydroxy chromone	Brown	Yellow	Yellow	--	Yellowish Green
2-(2-quinoline) 3-hydroxy chromone	Orange	Yellow	Yellowish Brown	Yellow	Orange

TABLE 2

COLOR REACTIONS OF THE SYNTHESIZED CHALCONES

Compound	H_2SO_4 Conc.	$SbCl_4$ in CCl_4
1-(2-hydroxyphenyl) 3-(-anthracyl) propenone	Dark green	Blue*
1-(2-hydroxy-5 methyl-phenyl)3-(9-anthracyl) propenone	Dark green	Violet*
1-(2-hydroxyphenyl)3-(9-phenanthryl) propenone	Red	Red brown*
1-(2-hydroxyphenyl)-3-(1-naphthyl) propenone	Red	Red*
1-(2-hydroxyphenyl)-3-(2-naphthyl) propenone	Red	Red*
1-(2-hydroxyphenyl)-3-(2-thienyl) propenone	Orange	Deep orange*
1-(2-hydroxyphenyl)-3-(2-pyridyl) propenone	Orange	Red*
1-(2-hydroxyphenyl)-3(3-pyridyl) propenone	Orange	Orange
1-(2-hydroxyphenyl)-3-(4-pyridyl) propenone	Orange	Orange*
1-(2-hydroxyphenyl)-3-(2-pyridyl 6-methyl) propenone	Orange	Red*
1-(2-hydroxyphenyl)-3-(2-quinonyl) propenone	Red	Red*

*formation of a precipitate.

Ultra-violet Spectra

Ultra-violet absorption spectra of absolute ethyl alcohol solutions of these synthesized compounds were obtained using a Beckman Spectrophotometer, Model DU. Two drops of 2% alcoholic aluminum chloride solution were then added to each solution and the new absorption spectrum of each was again recorded. The resulting spectral data are found in Table 3 and Figs. 8 to 17.

Flavones and flavonols show a general similarity in the position of maximum absorption in the ultra-violet region. Two regions of high intensity absorption are usually observed; a high-frequency region at about 240-260 mμ and a lower frequency region at about 330-375 mμ. The absorption spectra obtained for these synthesized flavonol-type compounds showed both these regions of high intensity absorption.

Aluminum chloride causes shifts with flavonols. Jurd (31) reports aluminum chloride shifts of 58,58,61.5 and 62.5 mμ for quercetin, kaempferol, 3-hydroxy flavone and 3, 3',4' -trihydroxy flavone. The shifts obtained with the synthesized chromones and aluminum chloride range from 50 to 78 mμ. Eight of the ten compounds studied exhibited shifts in the 57-65 mμ region.

Infra-red Spectra

Infra-red spectra of these synthesized compounds were taken in a chloroform solution on a Perkin-Elmer Infracord Spectrophotometer. It was expected that the absorption

TABLE 3

SPECTRAL DATA FOR THE SYNTHESIZED 3-HYDROXY CHROMONES

Compound	max. mμ	max. $AlCl_3$ mμ.	Shift mμ.
1. 2-(9-anthracyl) 3-hydroxy chromone. .	325	385	60
2. 2-(9-anthracyl) 3-hydroxy 6 methyl chromone	322	385	57
3. 2-(9-phenanthryl) 3-hydroxy chromone	332	390	58
4. 2-(1-naphthyl)-3-hydroxy chromone	333	390	57
5. 2-(2-naphthyl) 3-hydroxy chromone	355	420	65
6. 2-(2-thienyl) 3-hydroxy chromone	333	390	57
7. 2-(2-pyridyl) 3-hydroxy chromone	345	405	60
8. 2-(3-pyridyl) 3-hydroxy chromone	340	400	60
9. 2-(2-pyridyl 6-methyl) 3-hydroxy chromone	350	400	50
10. 2-(2-quinonyl) 3-hydroxy chromone	322	400	78
1*. Quercetin	377	431	58
2*. Kaempferol	367.5	426	58
3*. 3-hydroxy flavone	343.5	405	61.5
4*. 3,3,4'-trihydroxy flavone	369.5	432	62.5

*Data from Jurd and Geissman (J.Org.Chem. Vol. 21, 1400(1956)).

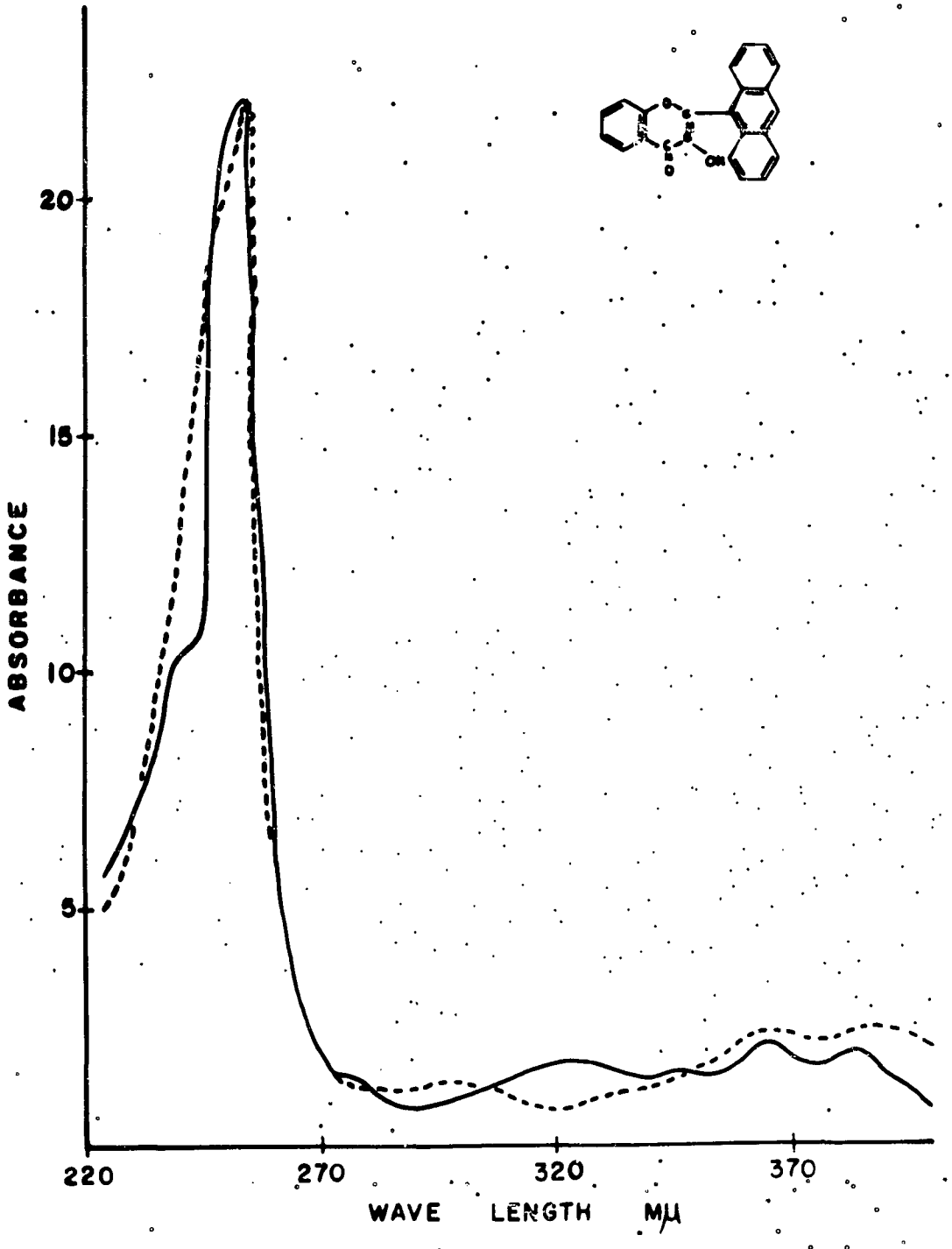


FIGURE 8

Ultra-violet spectrum of 2-(9-anthracyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

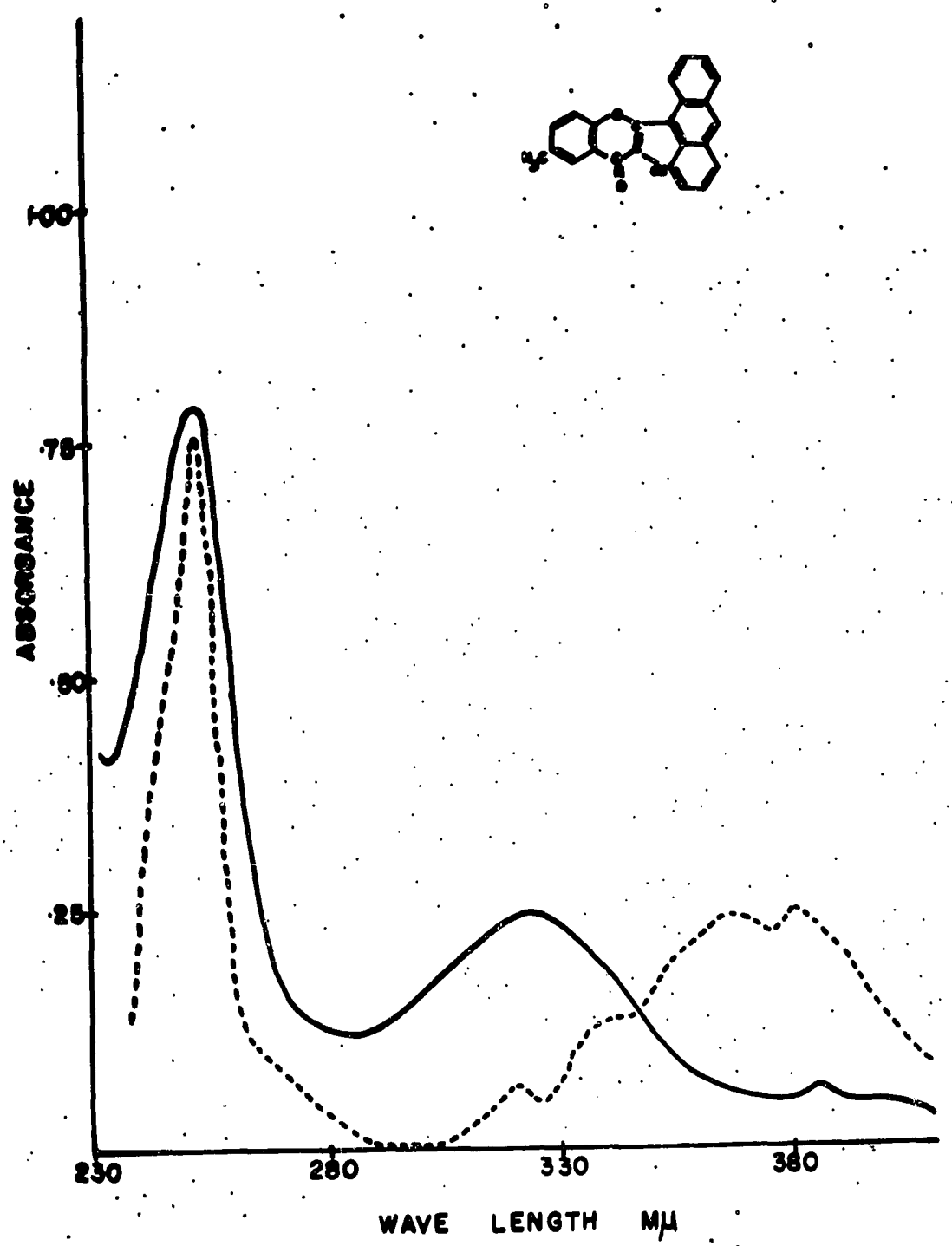


FIGURE 9

Ultra-violet spectrum of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

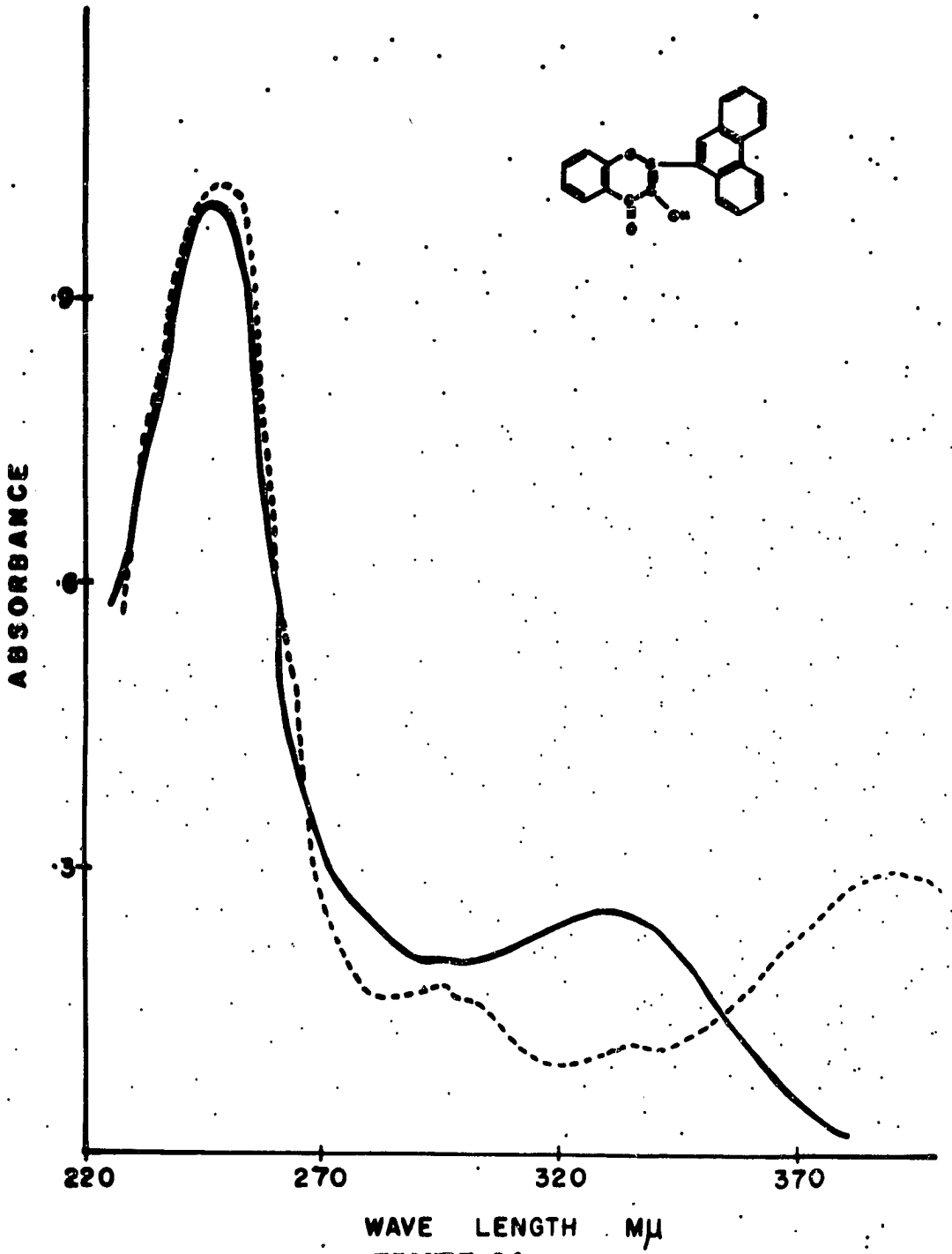


FIGURE 10

Ultra-violet spectrum of 2-(9-phenanthryl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

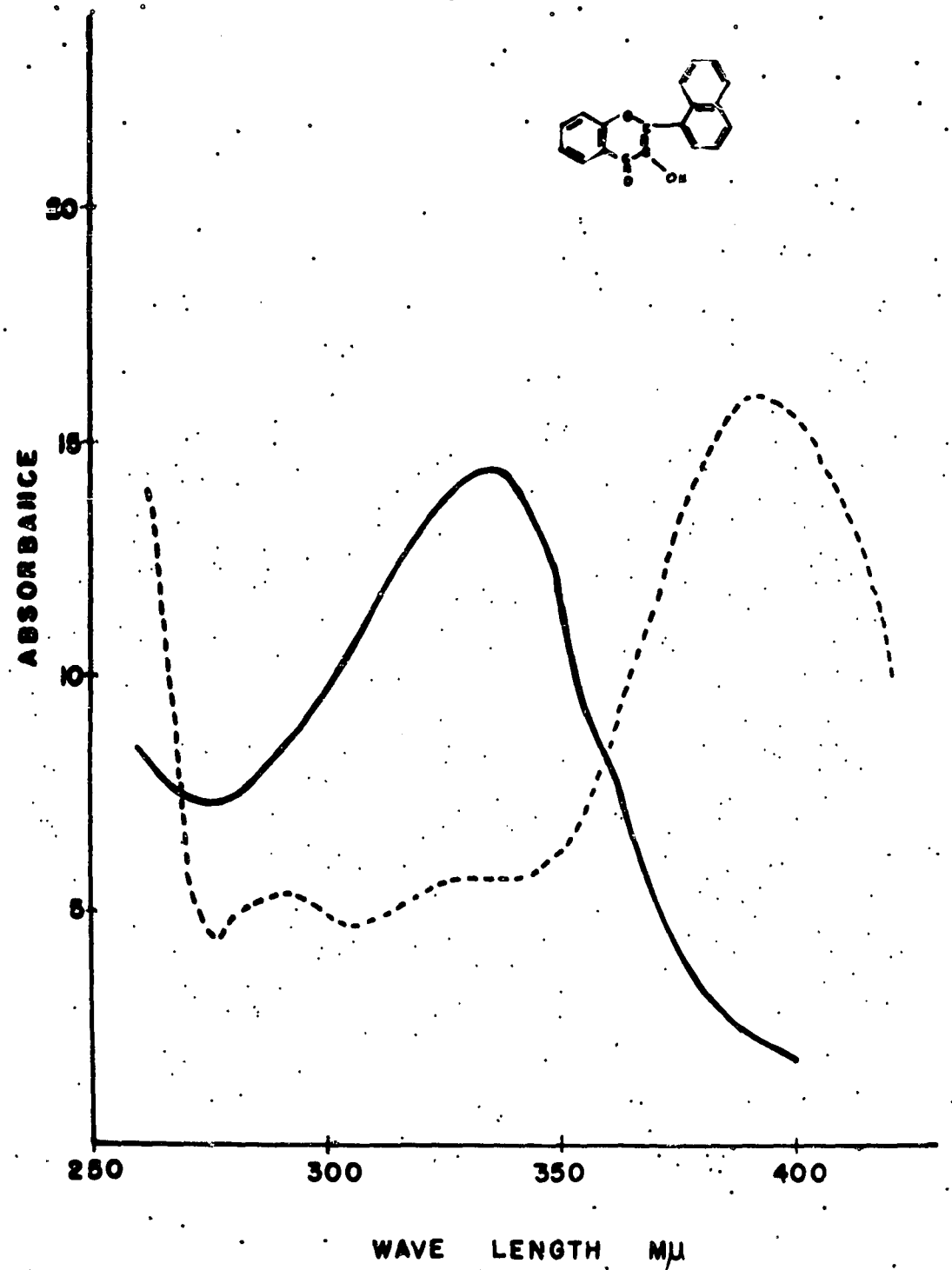


FIGURE 11

Ultra-violet spectrum of 2-(1-naphthyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

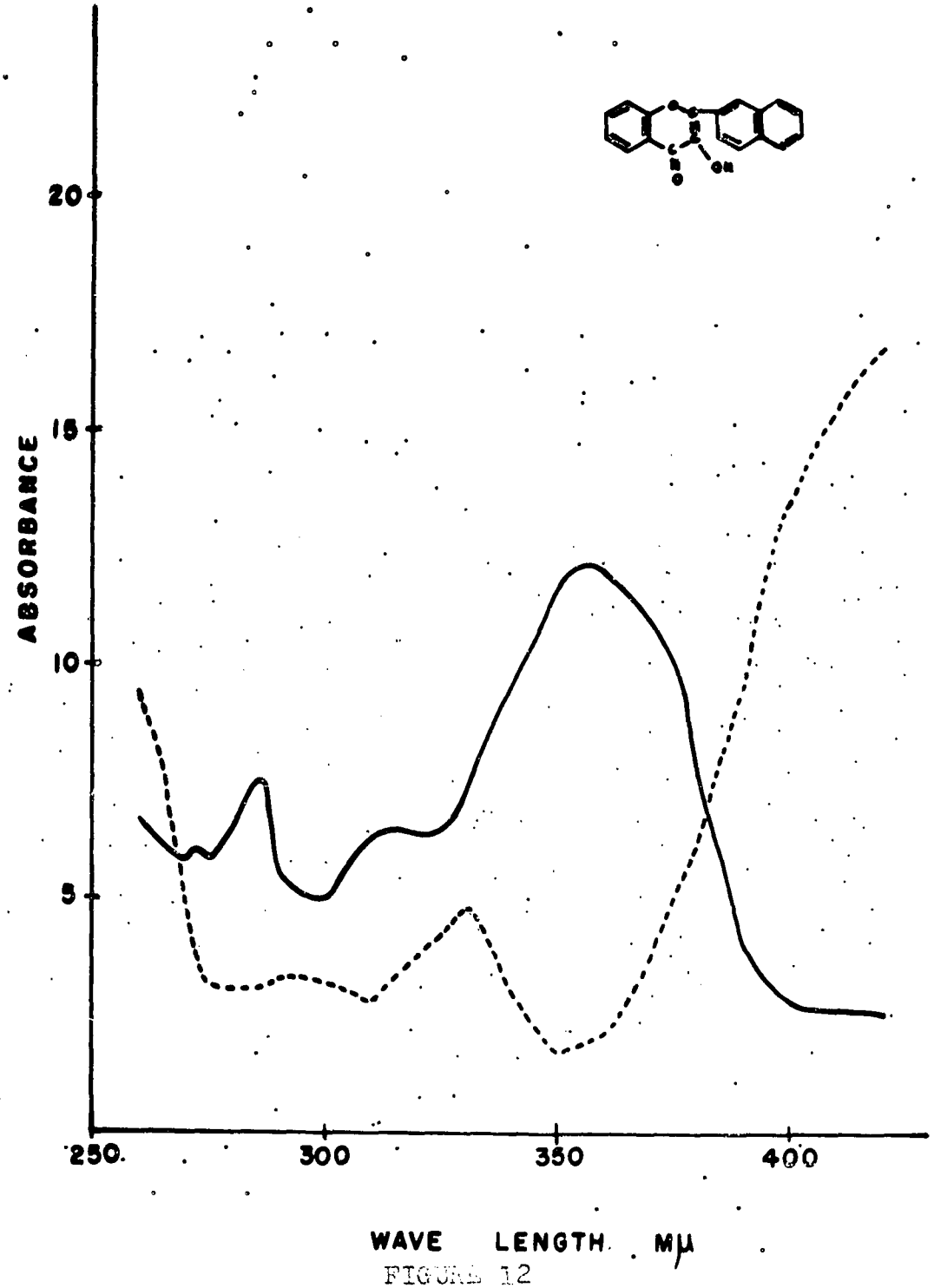


FIGURE 12

Ultra-violet spectrum of 2-(2-naphthyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminium chloride (---)

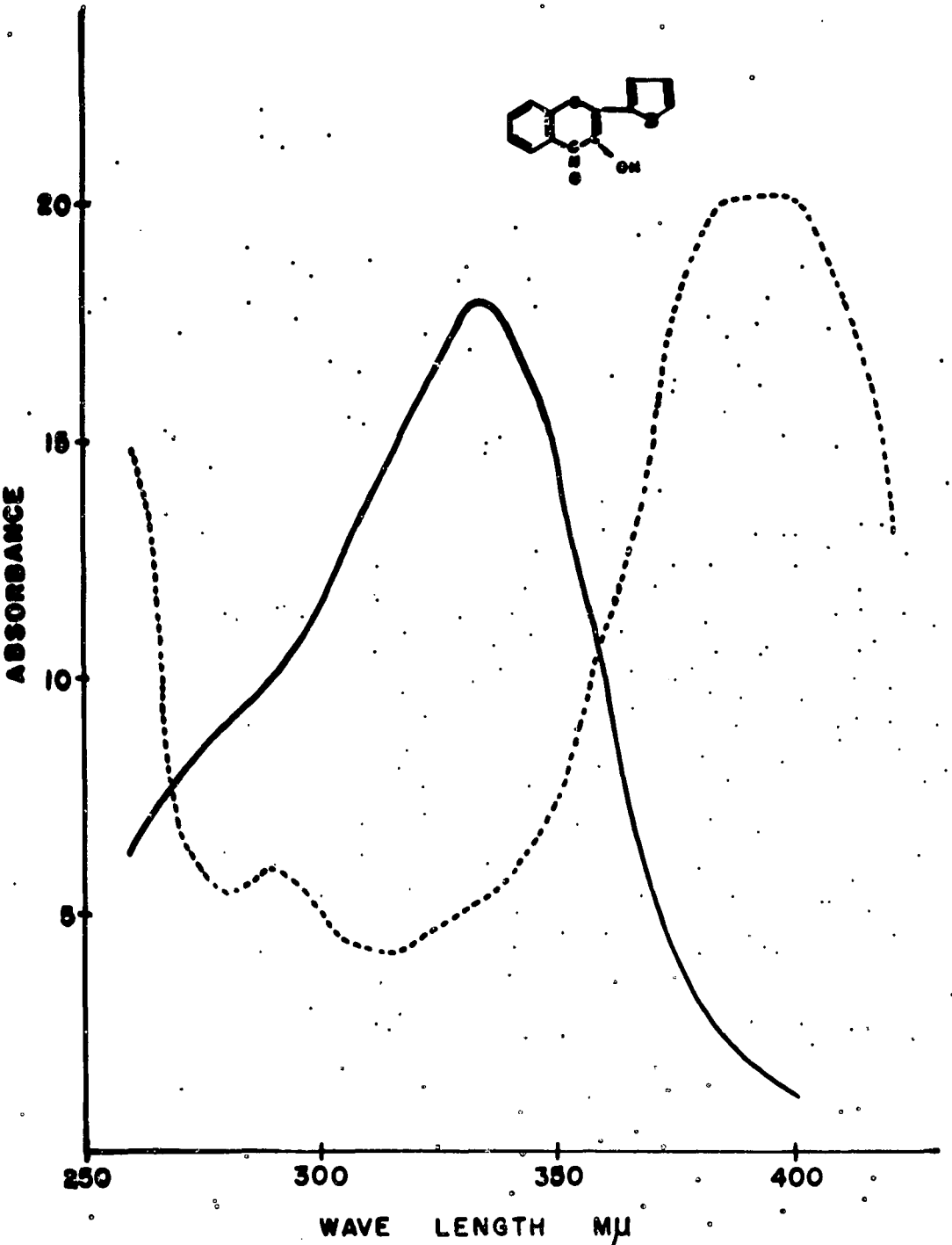


FIGURE 13

Ultra-violet spectrum of 2-(2-thienyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminium chloride (---)

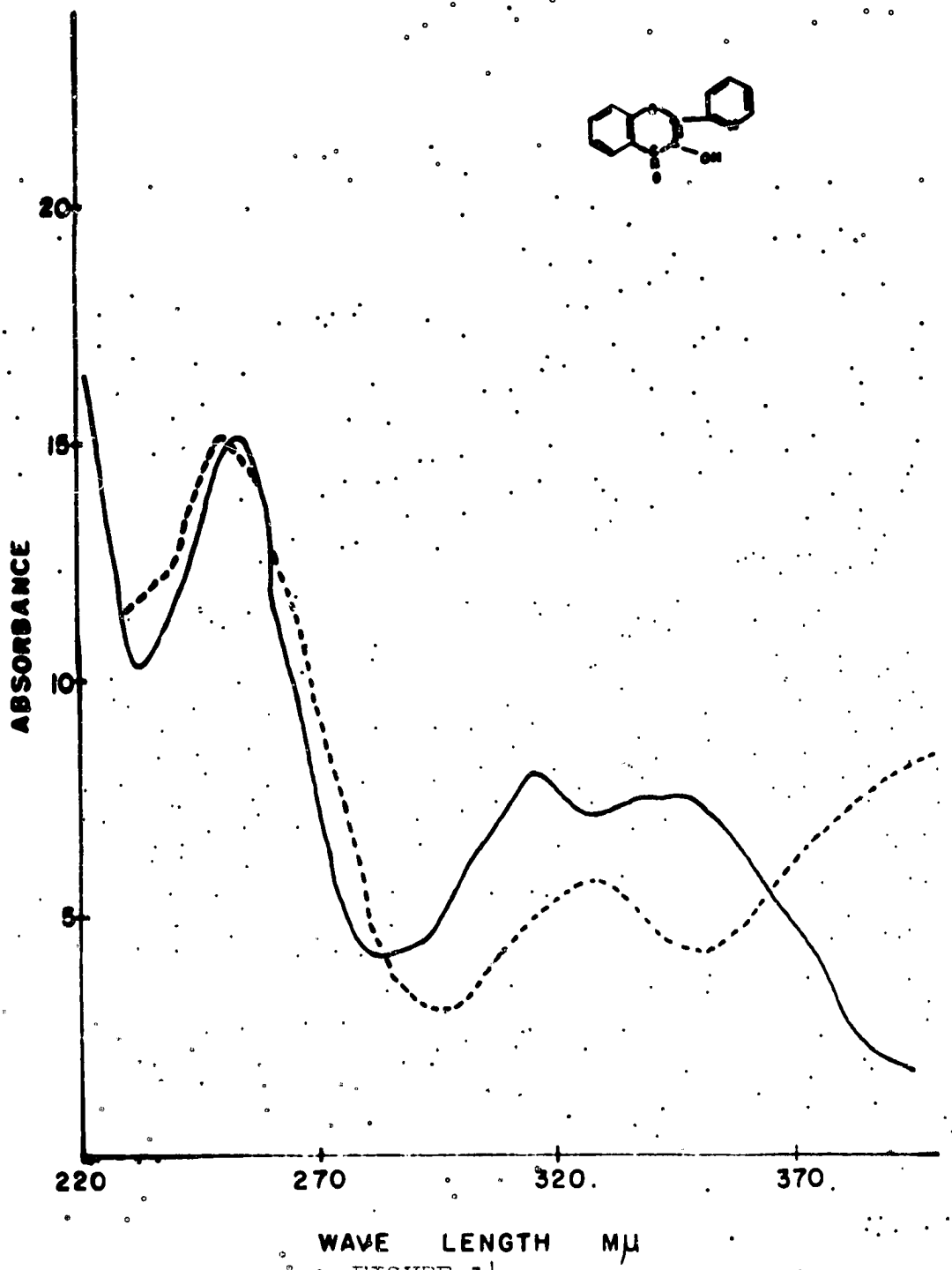


FIGURE 14

Ultra-violet spectrum of 2-(2-pyridyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (-·--)

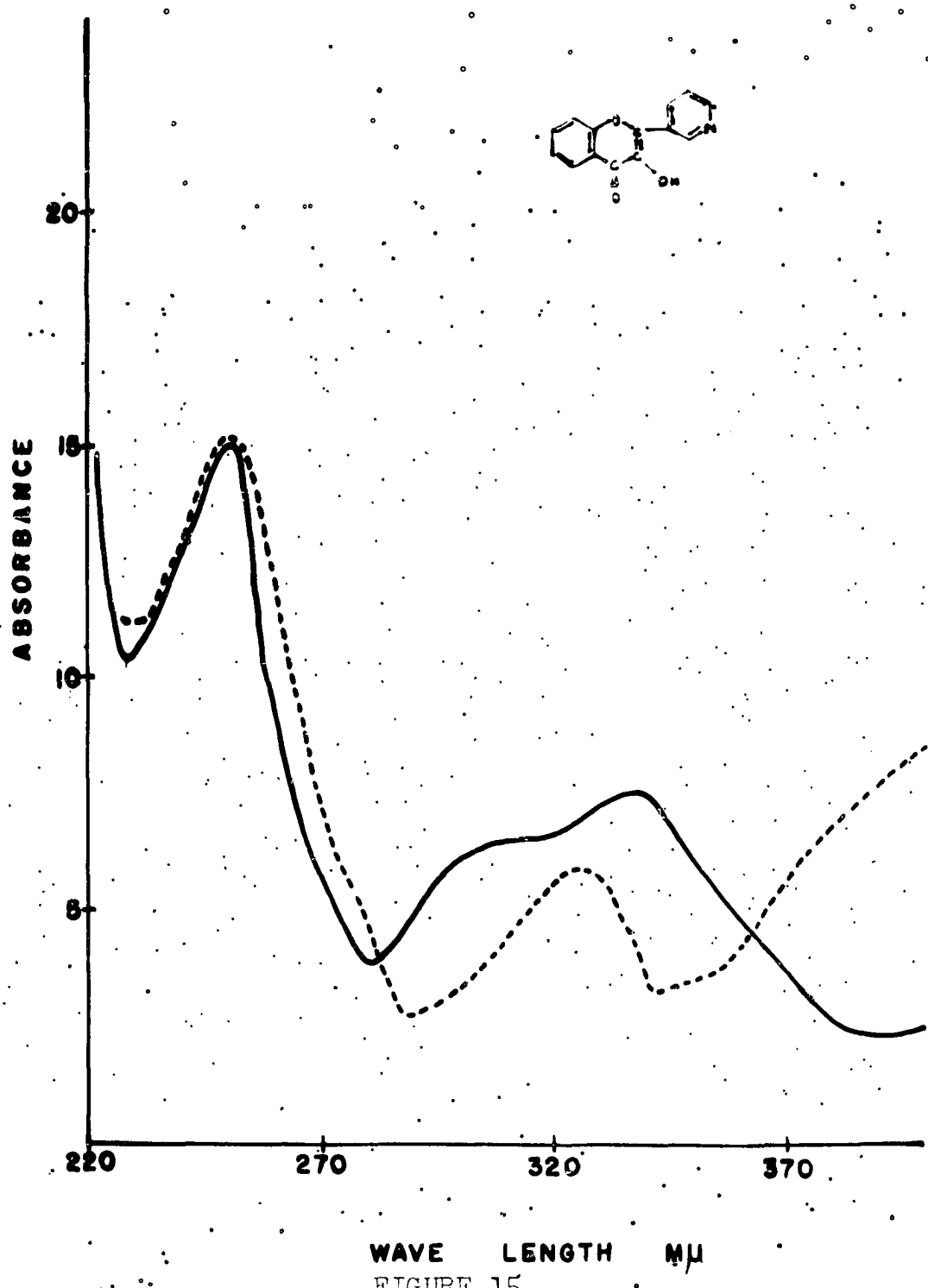


FIGURE 15

Ultra-violet spectrum of 2-(3-pyridyl) 3-Hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

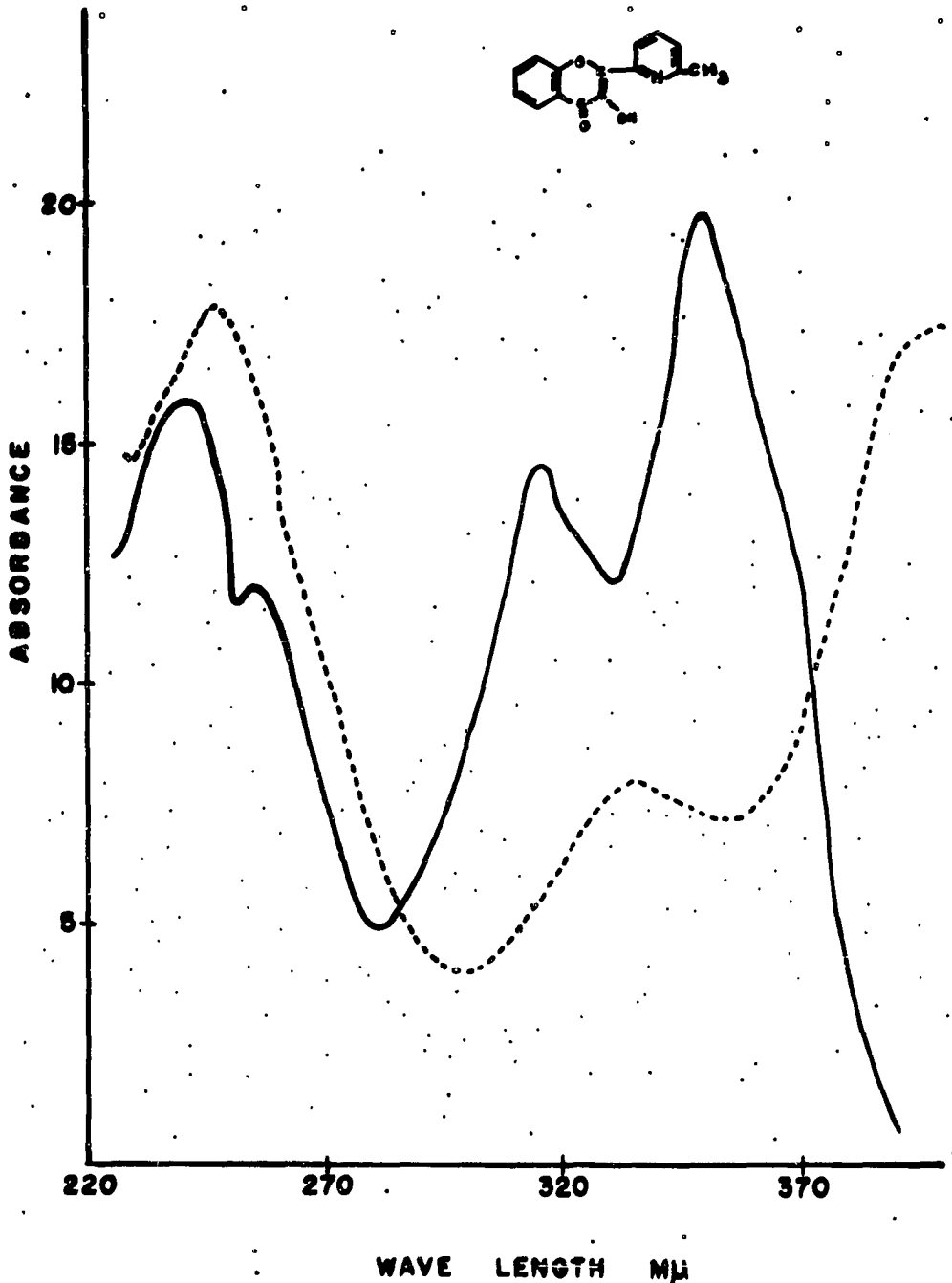


FIGURE 16

Ultra-violet spectrum of 2-(2-pyridyl-6-methyl) 3-hydroxy chromone in absolute ethanol (——), and in absolute ethanol after addition of aluminum chloride (---)

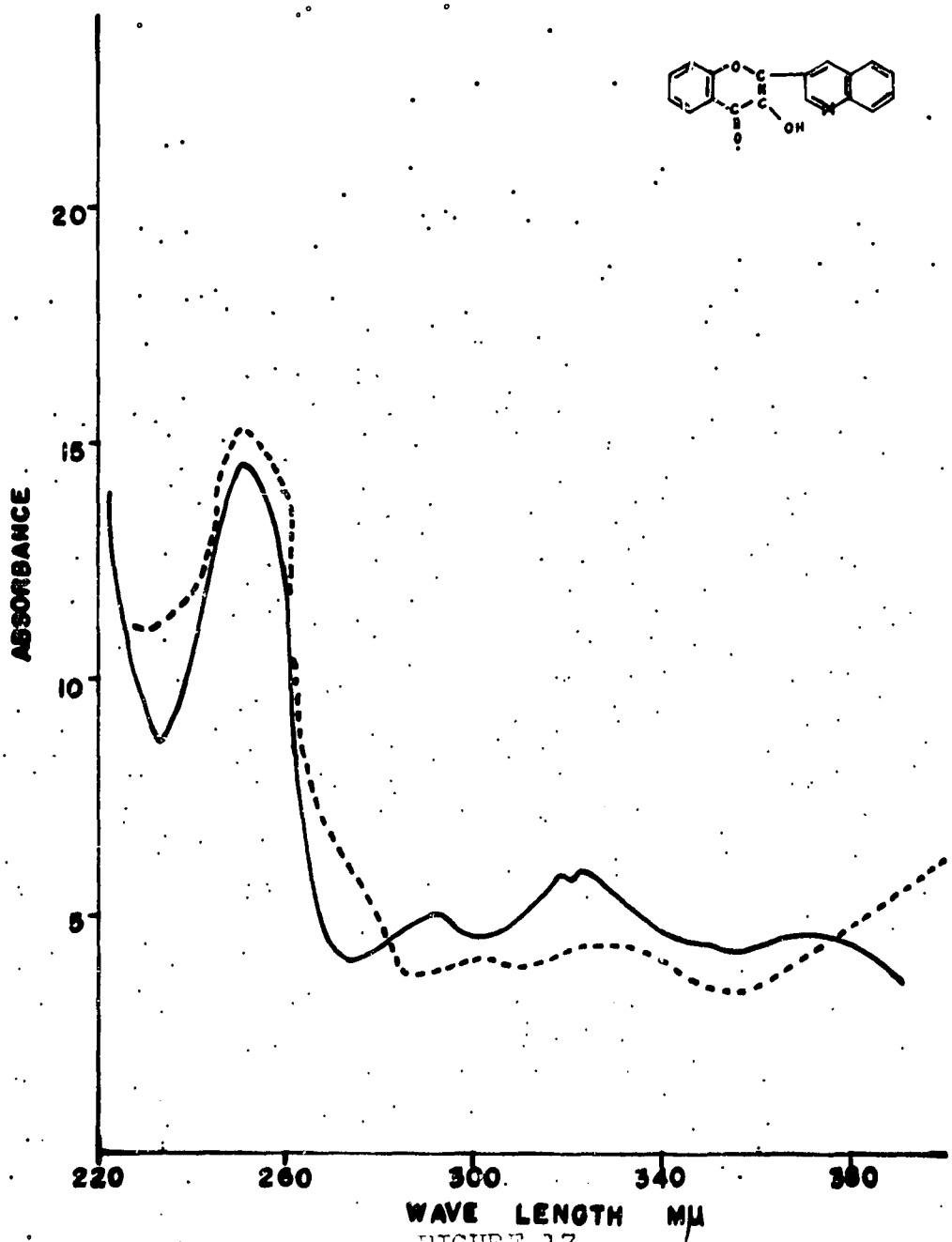


FIGURE 17

Ultra-violet spectrum of 2-(2-quinonyl) 3-hydroxy chromone in absolute ethanol (——) and in absolute ethanol after addition of aluminum chloride (---)

frequencies for the hydroxy and the carbonyl groups would be somewhat similar to those found for several naturally occurring flavonols. The absorption frequencies for the carbonyl group of the synthesized chromones were found to be between 1625cm^{-1} and 1650cm^{-1}. In the case of the several naturally occurring flavonols studied these values lie between 1652 cm^{-1} and 1658 cm^{-1}(32).

The absorption frequencies for the hydroxyl group for several flavonols studied lie between 3140 cm^{-1} and 3340 cm^{-1}.

The absorption peaks for the hydroxyl group of the synthesized chromones were found in this region, but they were not sharp. In some cases they were absent altogether. This may be due to a hydrogen bond linkage between the hydrogen of the hydroxyl group and oxygen of the carbonyl group or nitrogen of the heterocyclic ring in the number two position of the chromone. The compounds which showed the absence of the free hydroxyl group were 2-(2-pyridyl 6-methyl) 3-hydroxy chromone and 2-(2-quinonyl) 3-hydroxy chromone. The carbonyl and hydroxyl absorption frequencies of 3,3',4', 5-7 pentahydroxyflavone were found by Herbert and Kurth (33) to be at 1654.cm^{-1} and 3290 cm^{-1}. They have also stated that the hydroxyl band was broad and not sharply defined. The infra-red spectra are shown in Figs. 18 to 28.

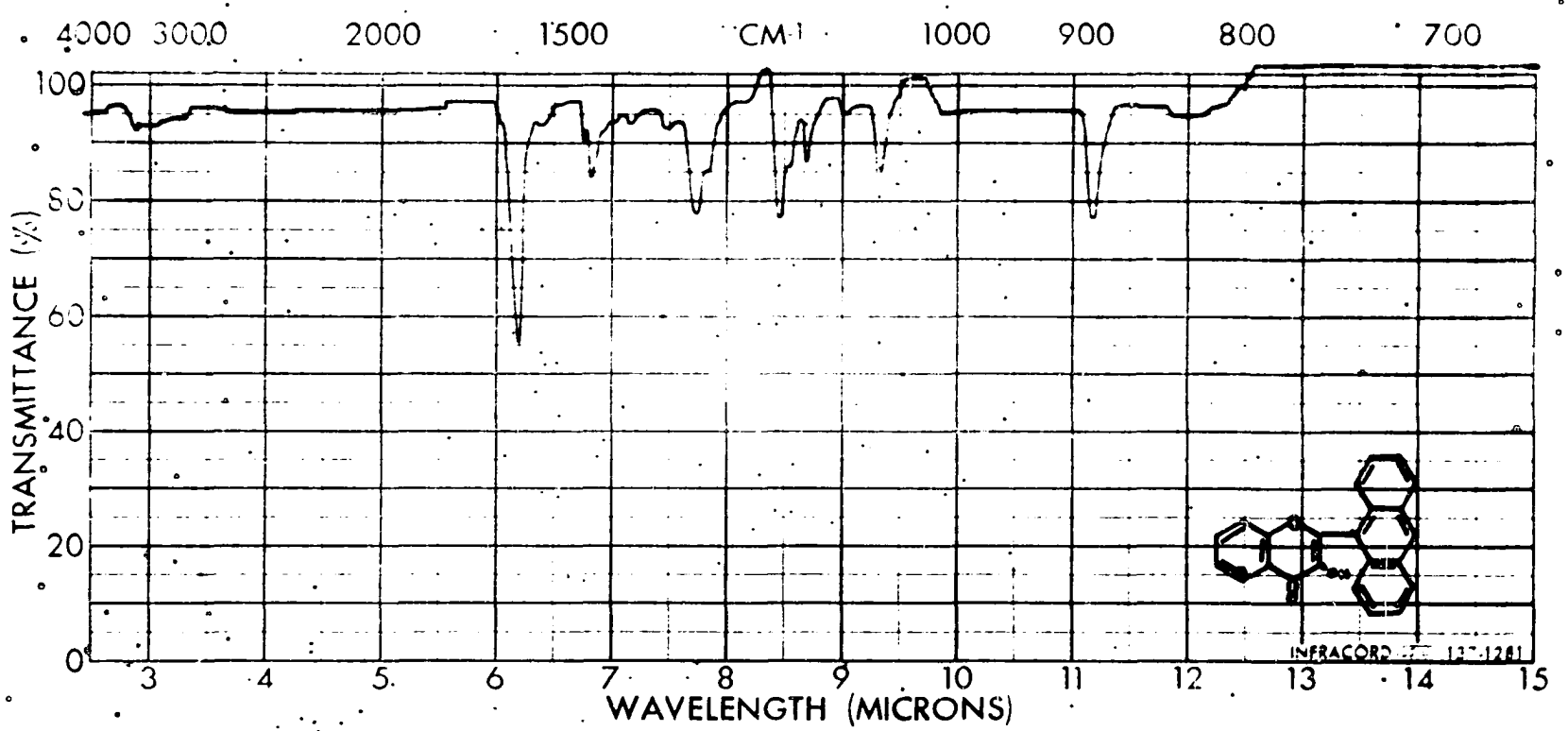


FIGURE 18
Infra-red spectrum of 2-(9-anthracyl) 3-hydroxy chromone

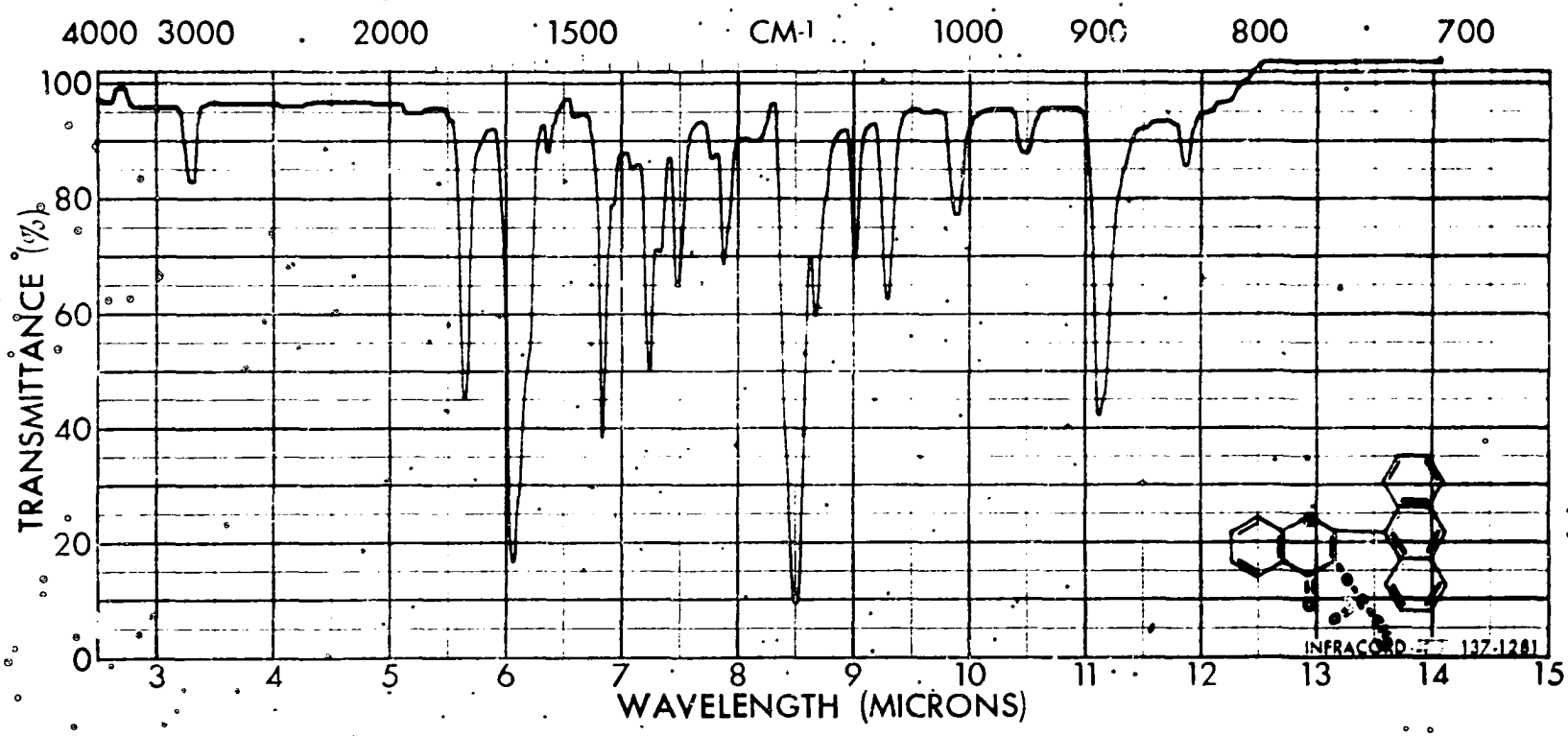


FIGURE 19
Infra-red spectrum of the acetate of 2-(2-anthracyl) 3-hydroxy chromone

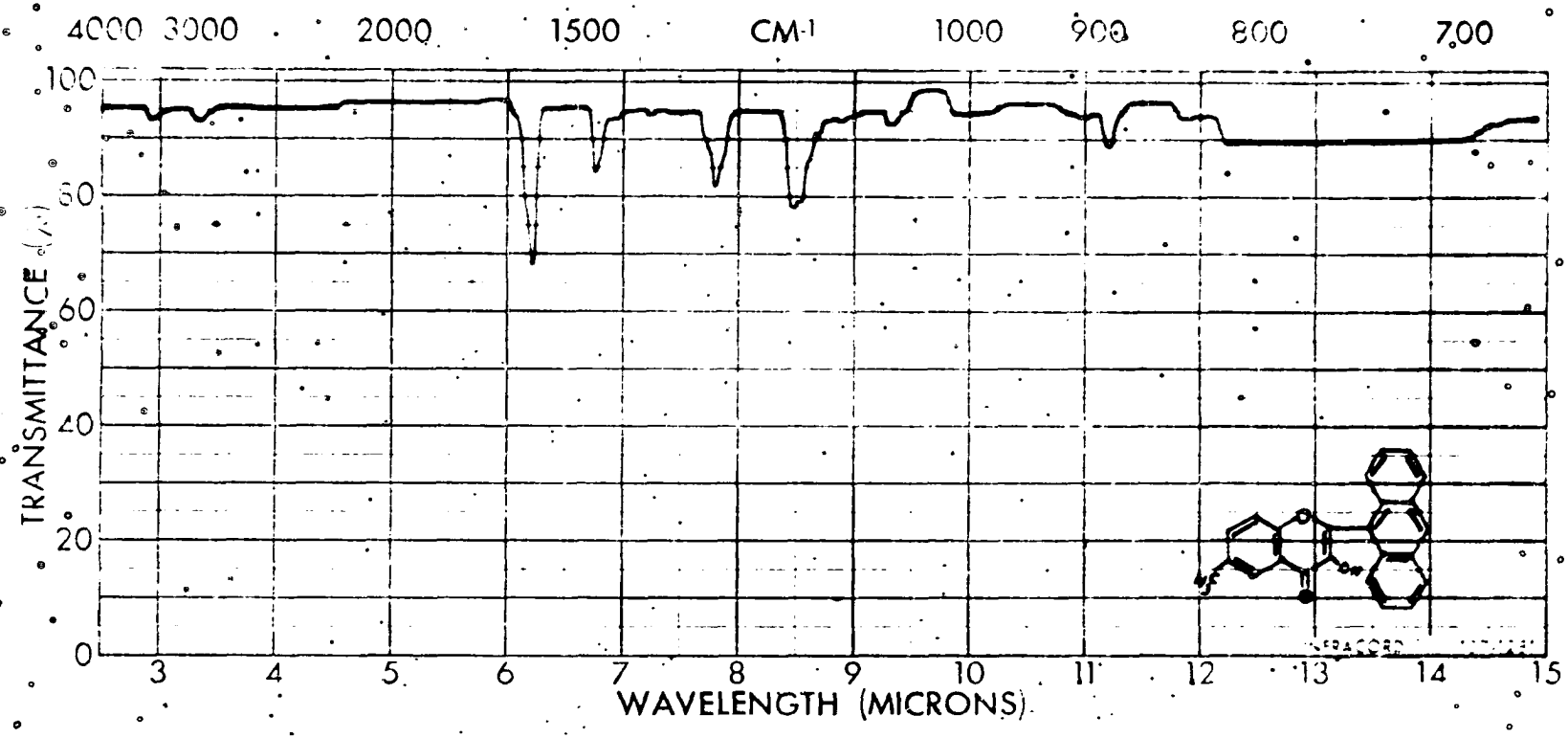


FIGURE 20
Infra-red spectrum of 2-(9-anthracyl) 3-hydroxy 6-methyl chromone

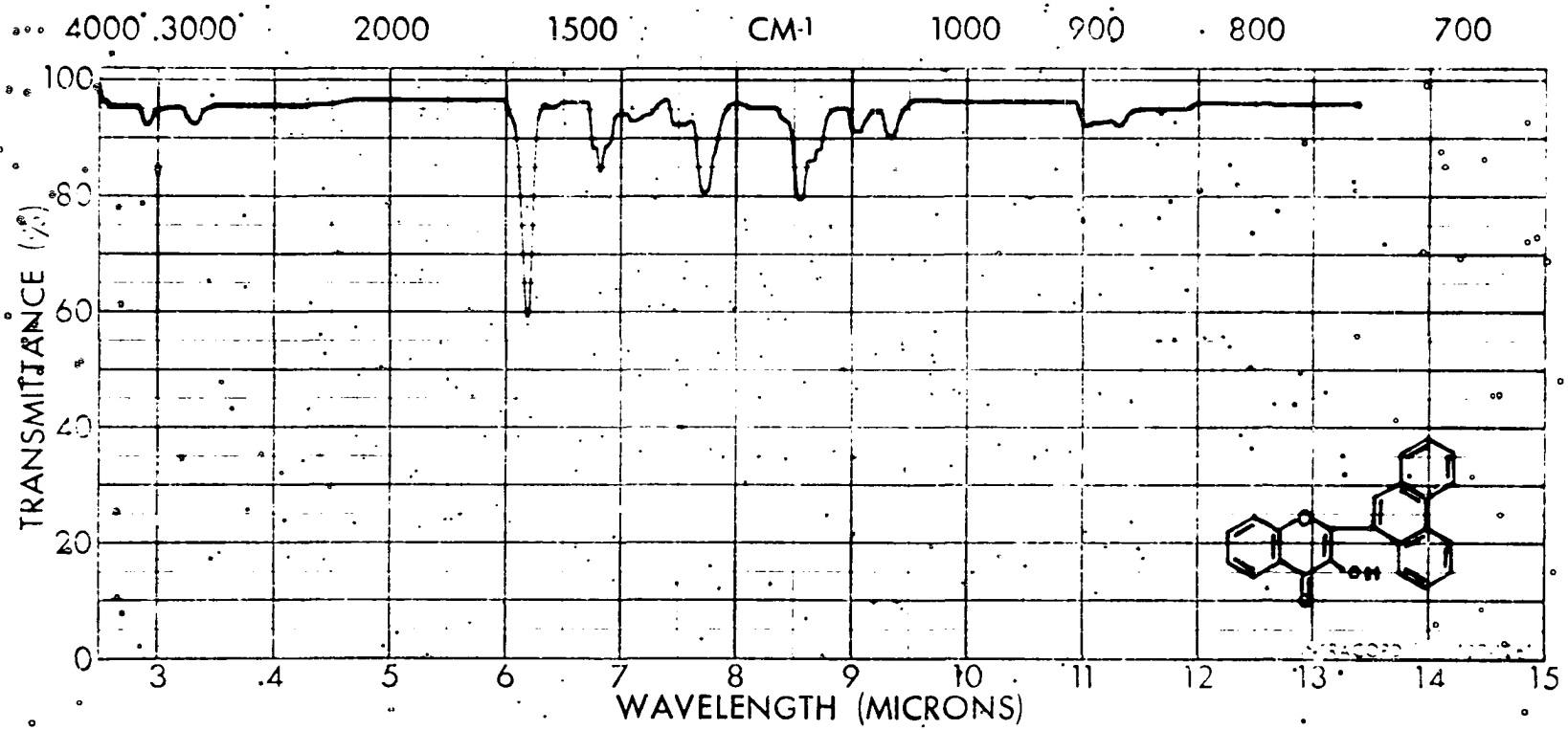


FIGURE 21
Infra-red spectrum of 2-(9-phenanthryl) 3-hydroxy chromone

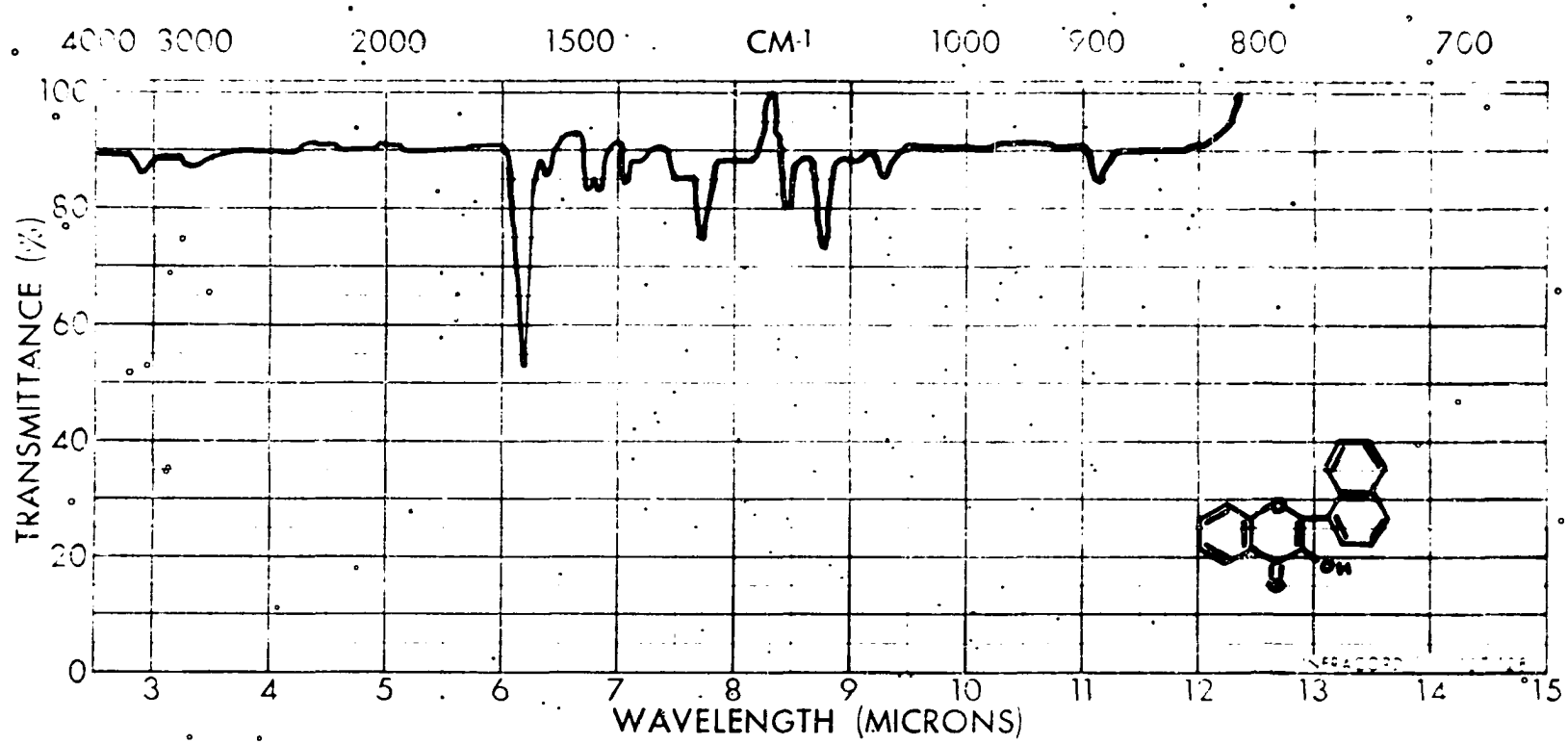


FIGURE 22
Infra-red spectrum of 2-(1-naphthyl) 3-hydroxy chromone

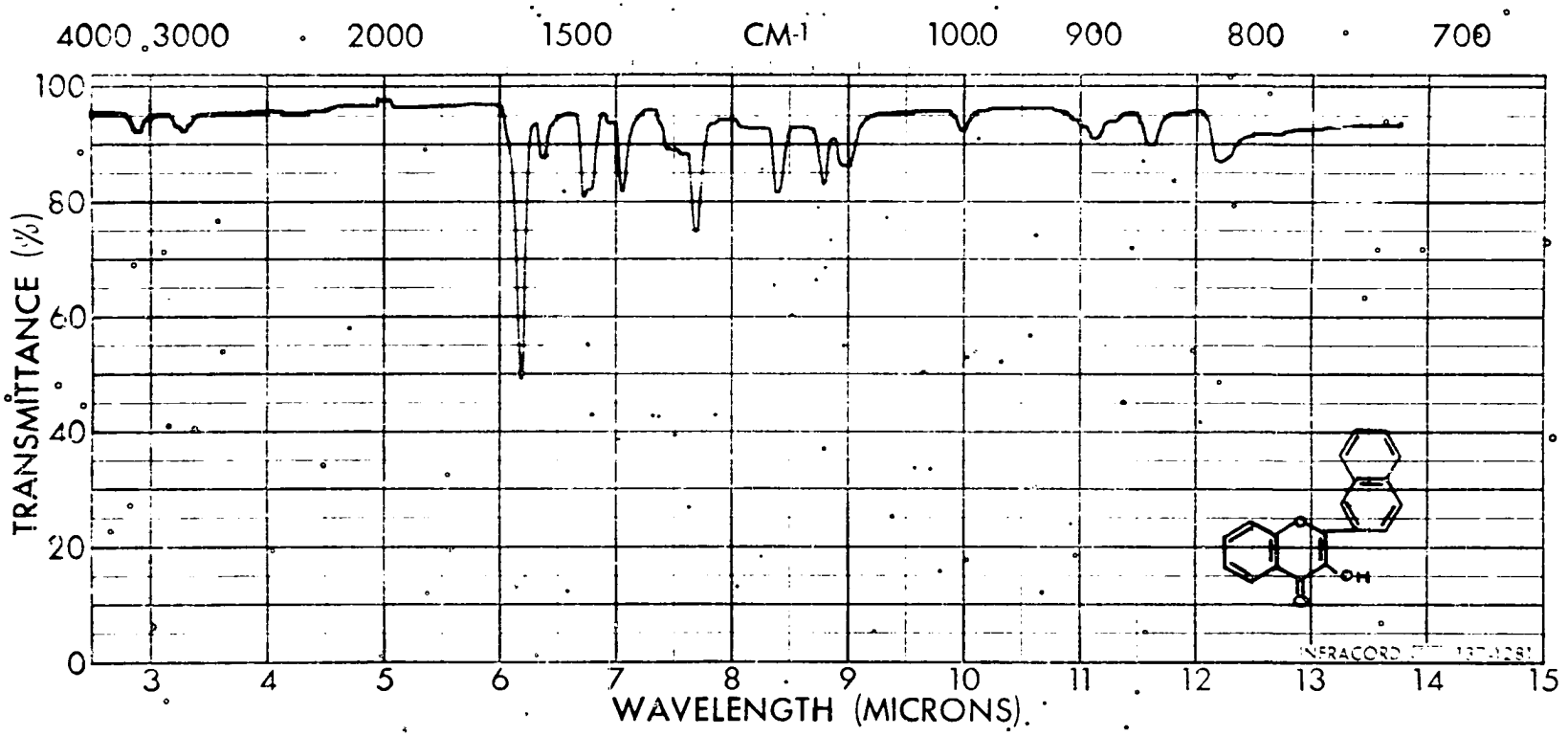


FIGURE 23
Infra-red spectrum of 2-(2-naphthyl) 3-hydroxy chromone.

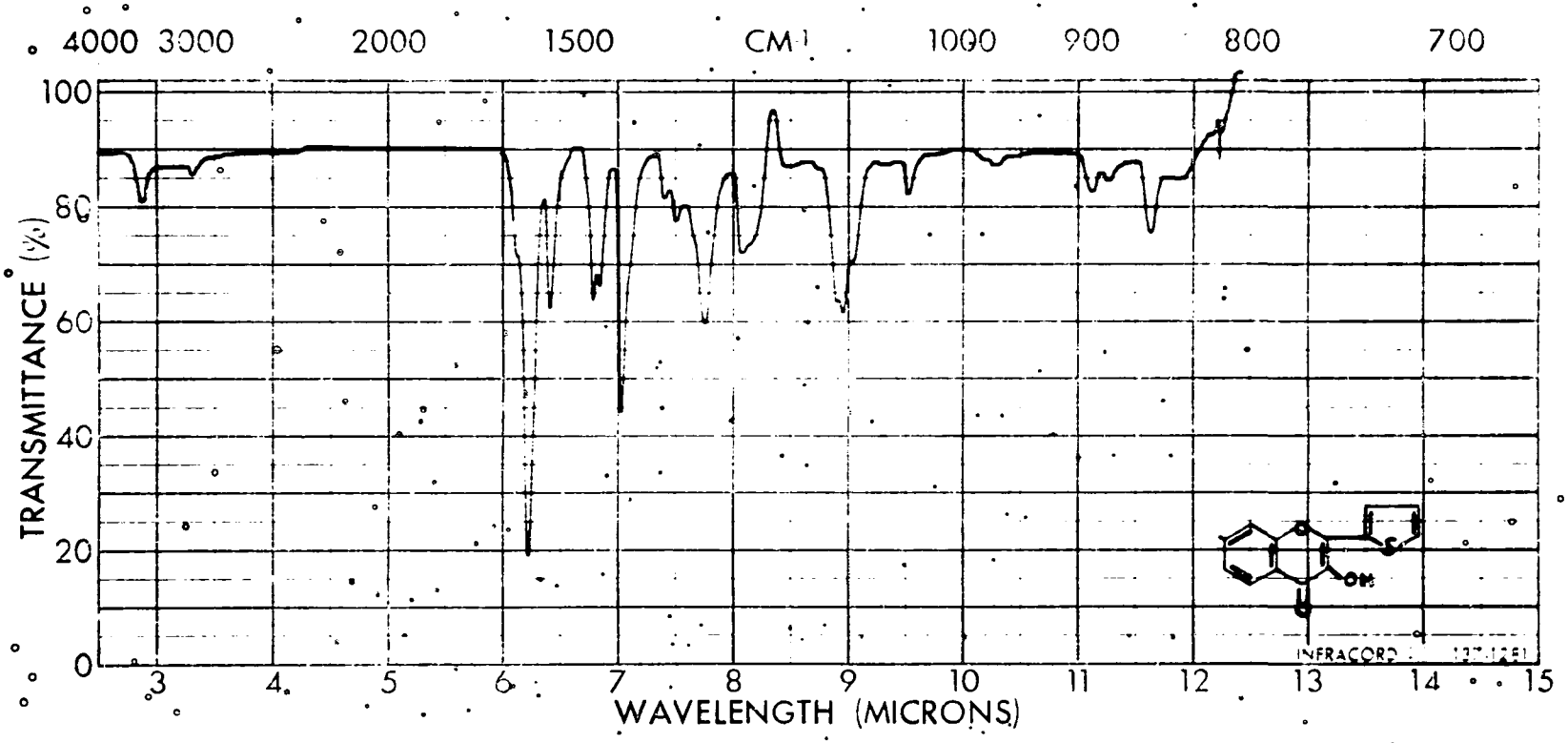


FIGURE 24
Infra-red spectrum of 2-(2-thienyl) 3-hydroxy chromone

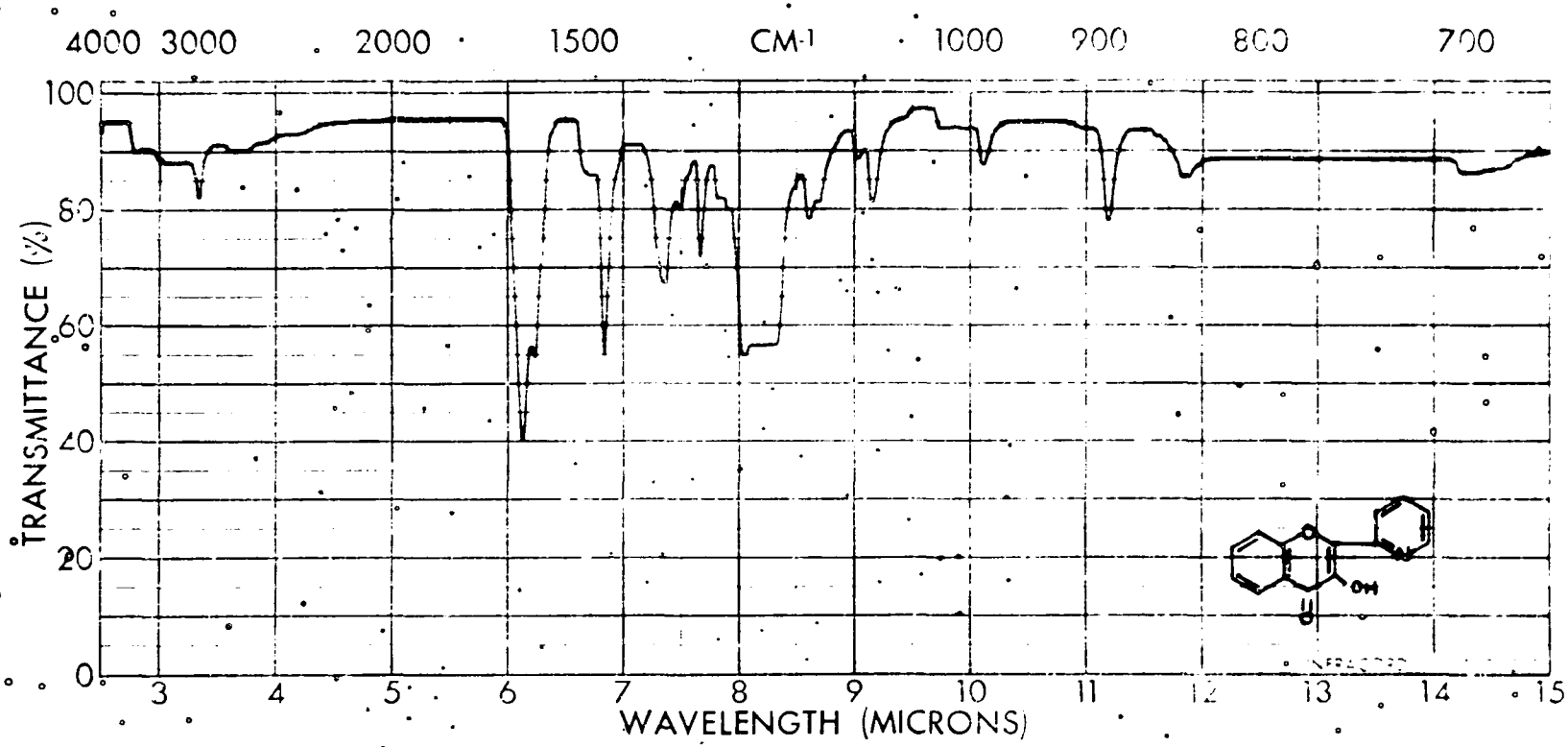


FIGURE 25.
Infra-red spectrum of 2-(2-pyridyl) 3-hydroxy chromone

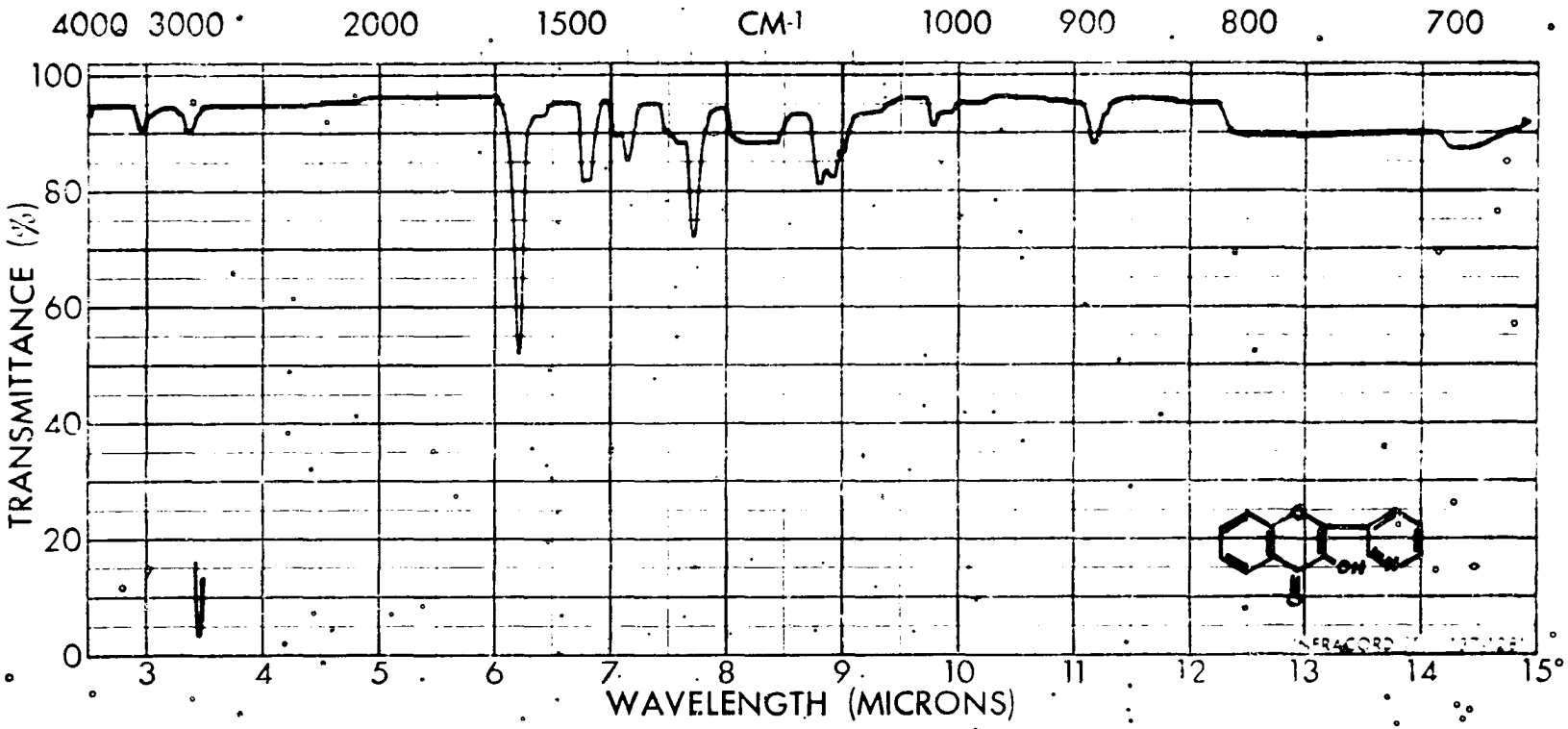


FIGURE 26.
Infra-red spectrum of 2-(3-pyridyl) 3-hydroxy chromone

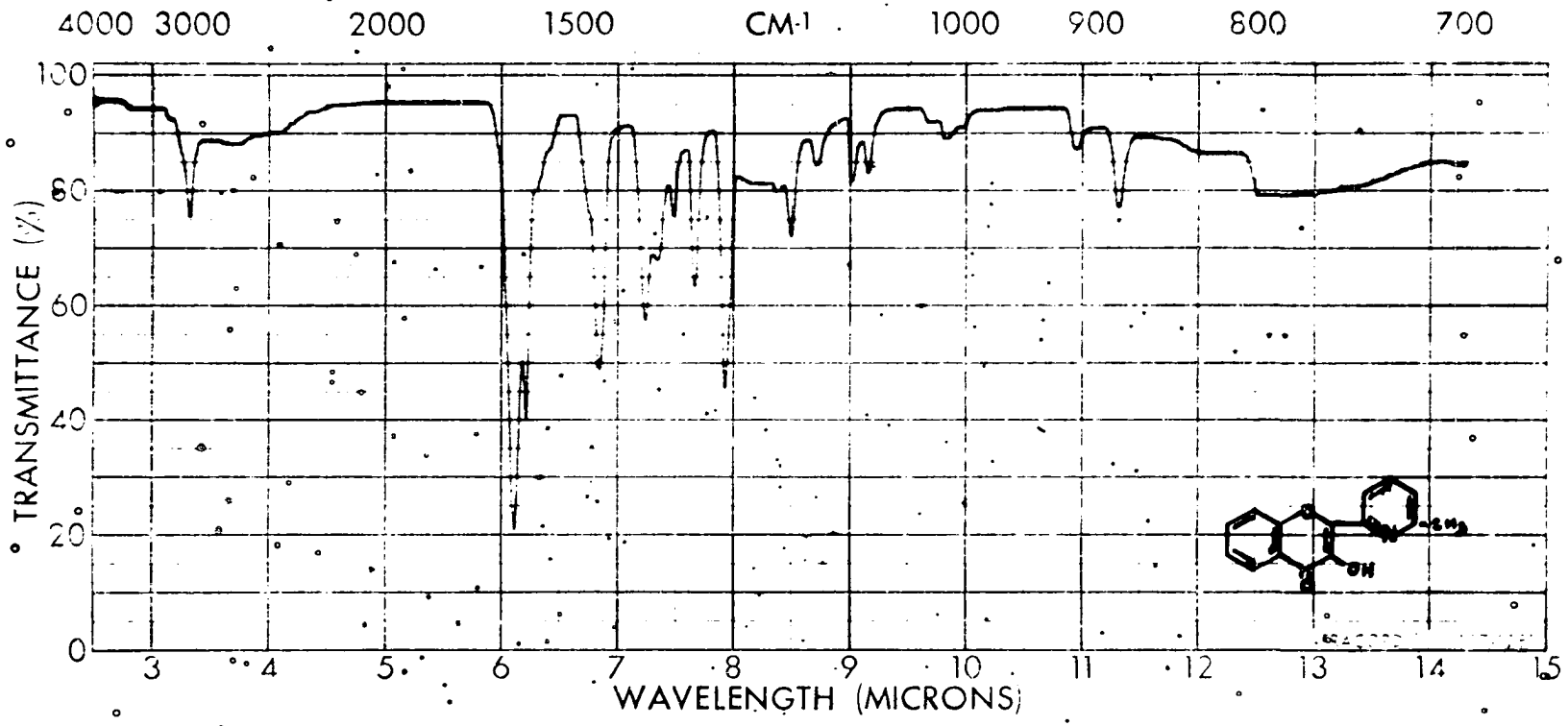


FIGURE 27

Infra-red spectrum of 2-(2-pyridyl-6-methyl)-3-hydroxy chromone

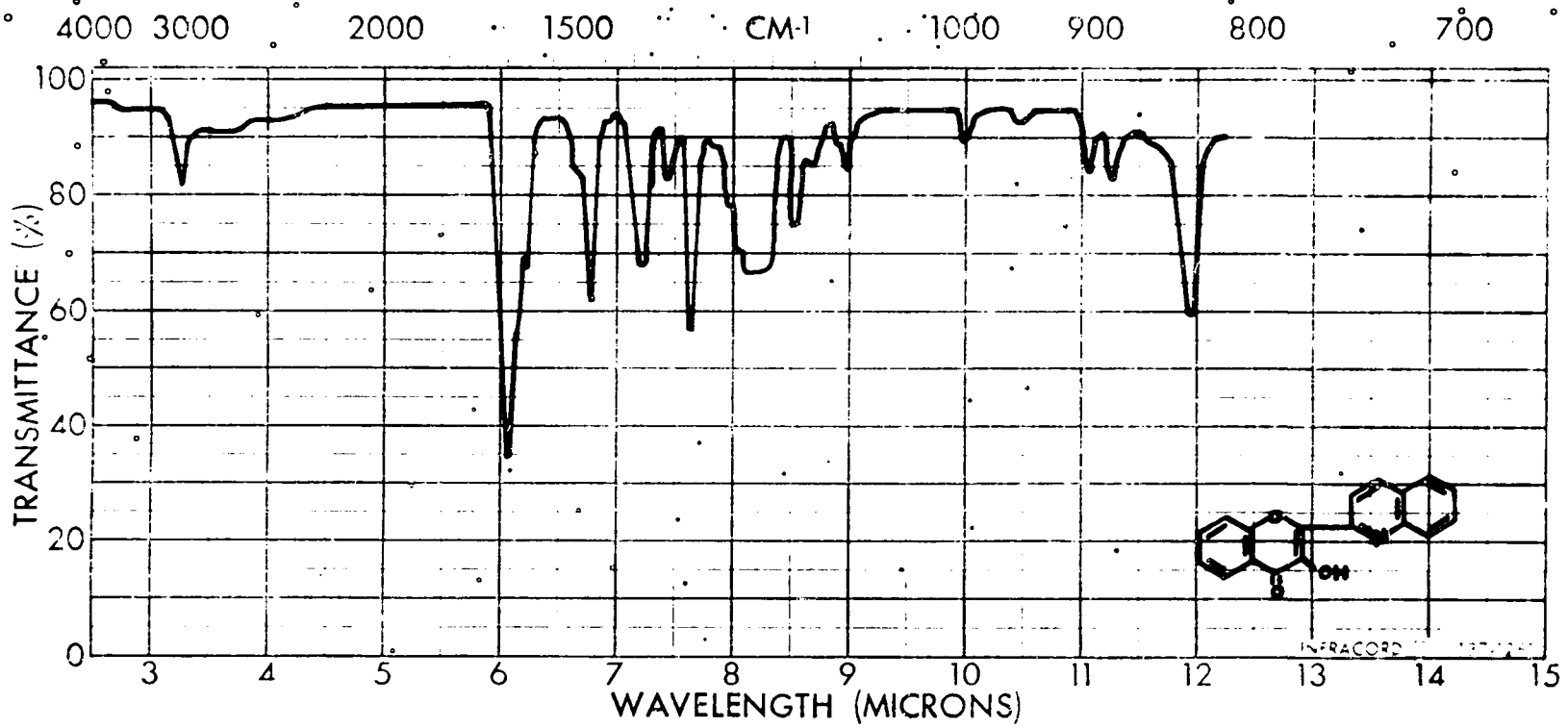


FIGURE 28
Infra-red spectrum of 2-(2-quinonyl) 3-hydroxy chromone

Melting Points of the New Synthesized Compounds

S.No.	Name of the compound.	Melting point in deg.C.
1.	1-(2-hydroxyphenyl)-3-(9-anthracyl) propenone	166 - 167
2.	1-(2-hydroxy-5-methyl-phenyl)-3-(9-anthracyl) propenone	171 - 172
3.	1-(2-hydroxyphenyl)-3-(9-phenanthryl) propenone	158 - 159.
4.	1-(2-hydroxyphenyl)-3-(1-naphthyl) propenone	115 - 116
5.	1-(2-hydroxyphenyl)-3-(2-naphthyl) propenone	155 - 156
6.	1-(2-hydroxyphenyl)-3-(2-thienyl) propenone	101 - 102
7.	1-(2-hydroxyphenyl)-3-(2-pyridyl) propenone	101 - 102
8.	1-(2-hydroxyphenyl)-3-(3-pyridyl) propenone	161 - 162
9.	1-(2-hydroxyphenyl)-3-(4-pyridyl) propenone	119 - 120
10.	1-(2-hydroxyphenyl)-3-(2-pyridyl 6 methyl) propenone	96 - 97
11.	1-(2-hydroxyphenyl)-3-(2-quinonyl) propenone	135 - 136
12.	2-(9-anthracyl) 3-hydroxy chromone	331 - 332
13.	2-(9-anthracyl) 3-hydroxy 6 methyl chromone	306 - 307
14.	2-(9-phenanthryl) 3-hydroxy chromone	246 - 247
15.	2-(1-naphthyl) 3-hydroxy chromone	231 - 232
16.	2-(2-naphthyl) 3-hydroxy chromone	207 - 208
17.	2-(2-thienyl) 3-hydroxy chromone	206 - 208

S.No.	Name of the compound.	Melting point in deg.C.
18.	2-(2-pyridyl) 3-hydroxy chromone	178 - 179
19.	2-(3-pyridyl) -3-hydroxy chromone	206 - 208
20.	2-(2-pyridyl -6 methyl) 3-hydroxy chromone	208 - 209
21.	2-(2-quinonyl) 3-hydroxy chromone	255 - 256
22.	Acetate of 2-(9-anthracyl) 3-hydroxy chromone	194 - 195
23.	Acetate of 2-(9-anthracyl) 3-hydroxy 6 methyl chromone	283 - 285
24.	Acetate of 2-(9-phenanthryl) 3-hydroxy chromone	179 - 181
25.	Acetate of 2-(1-naphthyl) 3-hydroxy chromone	190 - 192
26.	Acetate of 2-(2-naphthyl) 3-hydroxy chromone	145 - 146
27.	Acetate of 2-(2-thienyl) 3-hydroxy chromone	152 - 153
28.	Acetate of 2-(2-pyridyl) 3-hydroxy chromone	138 - 140
29.	Acetate of 2-(3-pyridyl) 3-hydroxy chromone	109 - 110
30.	Acetate of 2-(2-pyridyl 6 methyl) 3-hydroxy chromone	118 - 119
31.	Acetate of 2-(2-quinonyl) 3-hydroxy chromone	181 - 182

CHAPTER IV

SUMMARY

Previous workers have investigated many flavonoid compounds for biological activity in animals. In the present investigation, some new chalcones and 3-hydroxy chromones have been synthesized with a heterocyclic or a polycyclic ring, attached to the number two carbon of the γ-benzo pyrone (Fig. 1). These new compounds would be compared for their biological activity with previously known flavonoid compounds.

The 3-hydroxy chromones were synthesized by preparing the corresponding 2-hydroxy chalcones and oxidizing the chalcones with alkaline hydrogen peroxide by the Algar-Flynn method. In a few cases, 3-hydroxy chromones were prepared in one step by the Ranjorwa reaction. The starting materials were 2-hydroxy acetophenone and the aldehyde of the corresponding polycyclic or heterocyclic compound. In one case, 2-hydroxy-5-methyl acetophenone was used in place of the 2-hydroxy acetophenone. Using these methods the following 3-hydroxy chromones were obtained:

1. 2-(9-anthracyl) 3-hydroxy chromone.
2. 2-(9-anthracyl) 3-hydroxy 6-methyl chromone.
3. 2-(9-phenanthryl) 3-hydroxy chromone.

4. 2-(1-naphthyl) 3-hydroxy chromone.

5. 2-(2-naphthyl) 3-hydroxy chromone.

6. 2-(2-thienyl) 3-hydroxy chromone.

7. 2-(2-pyridyl) 3-hydroxy chromone.

8. 2-(3-pyridyl) 3-hydroxy chromone.

9. 2-(2-pyridyl 6-methyl) 3-hydroxy chromone.

10. 2-(2-quinonyl) 3-hydroxy chromone.

The corresponding hydroxy chalcones and acetates of each 3-hydroxy chromone were also synthesized. Properties of these compounds such as their ultra-violet spectra, infra-red spectra, color reactions and melting points have also been studied.

BIBLIOGRAPHY

(1). Griffith, Krewson, Naghaski; Rutin and related flavonoids; Mack Publishing Company, (1953).

(2). Kostanecki, St., Ber. 41, 783-6 (1908).

(3). Tambor, J., Ber. 41, 787-92 (1908).

(4). Chen, F. C. and Yang, C. H., J. Taiwan Pharm. Assoc. 3, 39-41 (1951); Chem. Abs. 49, 2432 (1955).

(5). Chen, F. C. and Yang, C. H., Ling, Y. S. and Liau, T. K., J. Taiwan Pharm. Assoc. 4, 48-51 (1952); Chem. Abs. 49, 3178 (1955).

(6). Chen, F. C. and Shu, H. S., J. Taiwan Pharm. Assoc. 5, 49-52 (1953); Chem. Abs. 49, 6929 (1955).

(7). Chen, F. C. and Chang, C. T., J. Chinese Chem. Soc. Ser. II 1, 156-8 (1954); Chem. Abs. 49, 13932 (1955).

(8). Raval, A. A. and Shah, N. M., J. Org. Chem. 21, 1408 (1956).

(9). Raval, A. A. and Shah, N. M., J. Org. Chem. 22, 304 (1957).

(10). Virkar, V. V. and Shah, R. C., J. University Bombay, 11, pt. 3, 140-3 (1943); Chem. Abs. 37, 2374 (1943).

(11). Schmutz, J. Hirt, R. Kunzh, F. and Eichenberger, E., Helv. Chim. Acta., 36, 620-6 (1953); Chem. Abs. 48, 11401 (1954).

(12). Dutch Patent, 70, 267 (June 16, 1952), Chem. Abs. 47, 6445 (1953).

(13). Beltols, M., Gazz. Chem. Ital. 71, 653 (1941).

(14). Otsuka, Y., J. Chem. Soc. Japan, 65, 539 (1944); Chem. Abs. 41, 3797 (1947).

(15). Buu-Hoi, N. P. and Hoan, N. G., J. Org. Chem. 16, 874 (1951).

(16). Hai, P. V. Buu-Hoi, N. P. and Yuong, N. D., J. Org. Chem. 23, 39 (1958).

(17). Buu-Hoi, N. P., Yuong, N. D., Bull. Soc. Chem. France, 1956, 1646-1650.

(18). Algar, J. and Flynn, J. P., Proc. Roy. Irish Acad. 42B, 1 (1934); Chem. Abs. 29, 161 (1935).

(19). Oyamada, T., J. Chem Soc. Japan, 55, 1256 (1934); Chem. Abs. 29, 5358 (1935).

(20). Oyamada, T., Bull. Chem. Soc. Japan, 10, 182 (1935); Chem. Abs. 39, 5112 (1935).

(21). Murakami, M. and Irie, T., Proc. Imp. Acad. (Tokyo) 11, 229 (1935); C. A. 29, 6598 (1935).

(22). Reichel, L. and Steudel, J., Ann. 553, 83 (1942).

(23). Kotake, M. and Kubota, T., Ann. 544, 253 (1940).

(24). Row, L. R. and Seshadri, T. R., Proc. Indian Acad. Sci. (A) 21, 190 (1945).

(25). Rajagopalan, S., Row, L. R. and Seshadri, T. R.; Proc. Indian Acad. Sci. (A) 23, 97 (1946).

(26). Auwers, K. and Muller, K., Ber. 41, 4230 (1908).

(27). Allan, J. and Robinson, R., J. Chem. Soc. 125, 2192 (1924).

(28). Limaye, S. D., Rasayanam 2, No. 2, 41-4; Chem. Abs. 47, 4879 (1953).

(29). Limaye, S. D., Rasayanam 2, 1-5 (1950); Chem Abs. 45, 7115 (1951).

(30). Geismann, T. A., Modern methods of plant analysis, Vol. III, p. 467.

(31). Jurd, L., and Geismann, T. A., J. Org. Chem., V 21, 1400 (1956).

(32). Inglett, G. E., J. Org. Chem. 32, 93 (1958).

(33). Hergert, H. L. and Kurth, E. F., J. Am. Chem. Soc. 75; 1622 (1953).